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Radioterapia Oncologica: l'evoluzione al servizio dei pazienti

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Congress Proceedings

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Programme

NUTRITIONAL MANAGEMENT OF CANCER PATIENTS: STATE OF ART AND FUTURE PERSPECTIVES

G. Onfiani, S. Bursi, M. D'Avino, F. Sebastiani

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Cancer is one of the leading cause of death worldwide, with an incidence of 390.700 new cases in Italy last year.[1] At diagnosis, 50% of cancer patients present some nutritional issues and prevalence of malnutrition in cancer has been reported to be greater than 50% in an italian cohort.[2]

Oncologic patients often report cluster of symptoms limiting energy and protein intake, such as depression, pain, fatigue and anorexia. The presence of tumor mass itself could also be associated to mechanical complications and limits food swallowing or nutrients digestion and absorption. In addition, nausea, vomiting, xerostomia, dysgeusia, anosmia and other therapy-related side effects contribute to further worsening of nutritional status by their qualitative and quantitative impact on eating pattern.

Tumor-associated malnutrition differs from common starvation due to its association to metabolic derangements, resulting from tumor-host interaction upregulating immune system, promoting inflammatory response and energy-wasting processes.

According to the latest practical guideline for nutrition management in cancer published by ESPEN in 2021, it has been estimated that up to 10-20% of cancer patients die due to the consequences of malnutrition rather than of the tumor itself.[3] There is a significant association between nutritional status and increased intermediate- and long-term mortality. Malnutrition also impact negatively on quality of life and treatment toxicities: those with poorer nutritional status were less likely to complete planned oncologic treatment.

Thus, ESMO and ESPEN guidelines[3,4] recommend nutritional screening and nutritional assessment at diagnosis and on regular basis subsequently. Numerous validated tools are available to detect malnutrition risk: MUST and NRS-2002 are among the most used. In case of abnormal screening, quantitative measurement of nutritional intake and nutrition impact symptoms, evaluation of muscle mass and physical performance and evaluation of degree of systemic inflammation are recommended.

Nutritional intervention aims to target weight-loss, muscle mass depletion and metabolic derangements by increasing energy and protein intake combined to physical activity. Individualized resistance exercise in addition to aerobic exercise are suggested to maintain muscle mass, muscle strength and physical function. Of note, muscle depletion is associated with poor survival, therapy toxicities, post-operative infection and length of hospital stay[5] (Figure 1).

For patients able to eat but are malnourished or at risk of malnutrition, nutritional intervention is aimed to increase energy and protein intake through enriched diet or additional use of oral nutritional supplements (ONS). Medical nutrition is indicated if, despite nutritional intervention, oral nutrition remains inadequate to cover energy requirements. Enteral tubes represent the preferred route of feeding, with parenteral nutrition as a secondary choice when enteral nutrition (EN) is not sufficient or feasible as in case of ileus, severe mucositis, profuse vomiting/diarrhea, intestinal ischemia and bowel obstruction.

Future strategies reporting anti-catabolic and inflammation-suppressing ingredients are advocated as a part of a multimodal intervention since systemic inflammation may increase the body's metabolic needs, depress appetite, and trigger accelerated muscle protein catabolism.

Considering interventions to specific patients categories, it is recommended that during radiotherapy (RT) an adequate nutritional intake should be ensured primarily by individualized nutritional counseling and/or with use of oral nutritional supplements in order to avoid nutritional deterioration, maintain intake and avoid radiotherapy interruptions. Screening and management of dysphagia on regular basis are also recommended. Enteral feeding using nasogastric or percutaneous gastric tubes is a good option in severe radiation-induced mucositis or in obstructive tumors of head-neck or thorax.[3]

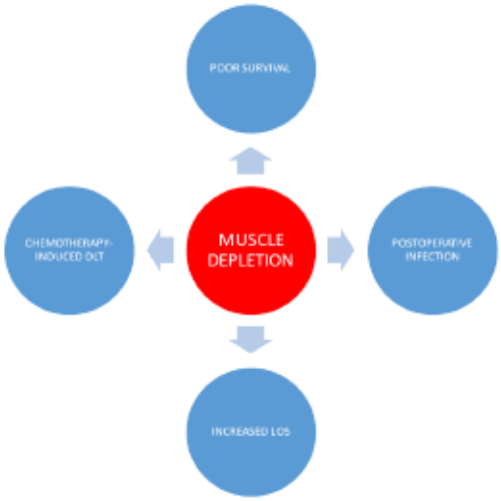

Figure 1. Effects of muscle depletion on clinical outcomes. DLT: dose limiting toxicity; LOS: lenght of stay.

Radiation induced mucositis (RIOM), usually starts at around the 5° to 10° RT fraction and occurs in > 80% of patients during RT. The incidence of ≥ Grade 3 mucositis, with confluent mucositis or severe pain requiring narcotic analgesics, is as high as 56%.[6] Smoking, poor oral hygiene, combined chemotherapy and low nutrition are risk factors associated to RIOM.[7] It has also been pointed out that the protein level in the body during RT affects the severity of oral mucositis, and low protein levels have negative effects on radiation-induced oral mucositis healing.[8]

Early nutritional intervention improves oral mucositis and nutritional status of patients with head and neck malignant tumors who undergo chemo-radiotherapy. In addition, it prevents malnutrition-related complications, avoids the interruption of RT and improves the long-term quality of life of patients.[6] In high-risk situations such as hypopharyngeal primary site, T4 tumor, female sex, combined radio-chemotherapy, prophylactic EN (as opposed to enteral feeding initiated after development of dysphagia) may maintain nutritional status and avoid interruption of treatment.[9]

Finally, there are no sufficient consistent clinical data to recommend glutamine to prevent RIOM, diarrhea, stomatitis, esophagitis or skin toxicity.

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NUTRITIONAL ASSESSMENT IN THE PATIENT UNDERGOING RADIOTHERAPY: CLINICAL CASE

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Aims. The diagnosis of cancer is often correlated with the decay of patients' clinical conditions, with development of cachexia. This may have a significant influence on the patient's tolerance of oncological treatment, such as radiation therapy, with or without chemotherapy

and may result in treatment delay or suspension, thus possibly compromising its efficacy or survival outcomes. Therefore, it is extremely important to evaluate the patient's nutritional status as early as possible and to implement an appropriate nutritional intervention in order to prevent the risk of further weight loss and subsequent cachexia. This clinical case aims to present the clinical-nutritional approach in a patient with locally advanced esophageal cancer (EO).

Methods. A woman, 71 years old, for worsening dysphagia, performed radiological and histological diagnostic exams finding squamous cell carcinoma on cervical esophagus, cT3 cN1cM0, Stage III TNM VIII. After discussion in the multidisciplinary board, the indication was a preoperative concomitant radio-chemotherapy, with subsequent diagnostic restaging before surgery. Throughout the treatment course, the patient underwent dedicated nutritional monitoring and prehabilitation interventions.

Results. At first evaluation, the patient presented a BMI <20 (underweight with respect to the age) and nutritional and functional assessment was performed, resulting in Score Patient – generated Global Assessment (PG-SGA) Stage B (Moderately malnourished) and low appendicular skeletal muscle mass index (ASMI), with high risk of sarcopenia. Approximately 2 months prior to the start of treatments, she undertook a nutritional support course, initially through nutrition education and Oral Nutritional Supplemens (ONS); then she underwent jejunostomy and started enteral nutrition. She completed radiation therapy with a total fractionated dose of 41.4 Gy in 23 fractions, associated with 5 cycles of chemotherapy based on weekly carboplatin and paclitaxel. With the aid of nutritional monitoring, she didn't require any radiation therapy interruption or chemotherapy dose reduction. Regarding toxicity, only mucositis G1 (CTCAE v.5) was reported. At about 1 month after neoadjuvant treatment, she presented a weight gain of about 3 kg and 5 days before surgery started immunonutrition. She underwent to robotic total esophagectomy with pathological response ypT2 ypN1. It was reported a weight loss of 4% at 30 days and 10% at 90 days after surgery, respectively, without other postoperative complications. After 6 months from surgery, she had no evidence of disease.

Conclusions. Early nutritional assessment, monitoring, intervention is of utmost importance to ensure EO patient's preoperative treatment completion, surgery sustainment and postoperative adequate and faster rehabilitation. Considering the organ function hit by such disease, nutritional counseling could be important to improve patients outcome and treatments tolerability in every setting.

GENDER MEDICINE IN RADIOTHERAPY

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Thanks to new biologic drugs, the immune system's role is becoming increasingly prominent. Cancer esearch, nowadays, is targeting personalized medicine. Modern radiotherapy allows for extremely precise treatments. However, since the publication of the QUANTEC[1] study, no distinction based on gender has ever been considered. Gender differences should be given greater consideration. Indeed, very few studies have investigated potential specific gender differences.[2,3] Epidemiological studies providing risk coefficients separately for women and men yield conflicting results regarding gender-specific radiation sensitivity.[4] We know that radiotherapy induces inflammation.[5] Various inflammatory pathways are regulated by different hormonal stimulation, as demonstrated by several studies.[6,7] It is known that females have a higher incidence of autoimmune diseases compared to males.[8]

Therefore, we hypothesize that there may be different radiation sensitivity between men and

women, which could influence tumor response and local control, as well as early and late side effects, including the induction of secondary tumors.[2,4]. It is important to investigate these differences, but further research is needed to fully understand the biological underpinnings to develop tailored gender-guided therapeutic strategies.[9,10] This may help improve cancer outcomes for patients undergoing radiotherapy while reducing the risk of side effects. Thus, it is important to raise awareness among Radiation Oncologists regarding gender differences in cancer care. Finally, we warrant preclinical and clinical studies investigating gender differences regarding treatment response and toxicity.

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COME L'INTELLIGENZA ARTIFICIALE STA CAMBIANDO IL FUTURO DELLA RADIOLOGIA

S. Carriero

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L'Intelligenza Artificiale (IA) sta rivoluzionando molte aree della medicina, e una delle discipline che ne sta beneficiando in modo significativo è la radiologia. Con l'IA, i radiologi hanno a disposizione uno strumento che migliora l'efficienza, l'accuratezza e la velocità nella diagnosi e nell'interpretazione delle immagini radiologiche. In questo articolo, esploreremo come l'IA sta cambiando il futuro della radiologia e quali sono i suoi impatti positivi. L'interpretazione delle immagini è un processo complesso che richiede tempo e attenzione ai dettagli. Con l'IA, è possibile accelerare notevolmente questo processo, gli algoritmi di intelligenza artificiale possono rilevare automaticamente lesioni, anomalie, linee di frattura e altre caratteristiche nelle immagini radiologiche, riducendo al minimo il rischio di errori umani. Ad esempio, in ambito oncologico, l'IA può individuare piccole lesioni tumorali, può eseguire il counting delle lesioni in modo automatico e anche rilevarne le dimensioni velocizzando il lavoro del radiologo. Inoltre, i sistemi di intelligenza artificiale non sono influenzati dall'errore umano e sono riproducibili e standardizzati.

IA sta trasformando anche la radiologia interventistica. Grazie all'IA, i medici interventisti possono accedere a strumenti di assistenza avanzati per guidare procedure diagnostiche e terapeutiche in tempo reale. Questi sistemi di IA forniscono supporto nella navigazione angiografica e percutanea migliorando la precisione e la sicurezza delle procedure.

L'IA è in grado di automatizzare molte attività ripetitive nella radiologia come ad esempio, l'indicizzazione delle immagini, la classificazione delle lesioni e la generazione di report standardizzati. Questo porta a una riduzione dei costi operativi e permette ai radiologi di concentrarsi su compiti più complessi.

L'IA svolge un ruolo cruciale nella ricerca e nell'ambito della medicina personalizzata poiché attraverso l'analisi delle immagini radiologiche può contribuire a identificare nuovi biomarcatori e indici di risposta al trattamento.

Nonostante tutti i benefici, l'uso dell'IA in radiologia solleva alcune sfide e considerazioni etiche. È importante garantire che gli algoritmi siano accurati e attendibili al 100% e che i radiologi rimangano coinvolti nel processo di diagnosi. Inoltre, la privacy dei pazienti e la sicurezza dei dati devono essere rigorosamente preservate.

L'Intelligenza Artificiale sta cambiando il futuro della radiologia migliorando e velocizzando la diagnosi e riducendo l'errore umano. Tuttavia, è fondamentale mantenere un equilibrio tra l'automazione e l'input umano, affinché i pazienti ricevano il massimo beneficio da queste innovazioni.

ARTIFICIAL INTELLIGENCE, HOW IT WILL CHANGE THE FUTURE OF OUR DISCIPLINES: THE NUCLEAR MEDICINE PHYSICIAN'S PERSPECTIVE

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Artificial intelligence (AI) was initially defined during the 1956 Dartmouth conference but the first applications in the field of nuclear medicine date back to the early 2000s. In this scenario, AI faces two main tasks. The first "physical" component concerns image processing and analysis, while the second "clinical" aspect deals with routine workflow and clinical endpoints (*e.g.*, diagnosis, prognosis, and prediction of response to therapy). Specifically, along with improvements in hardware and reconstruction software, several developments have been made in image processing, analysis, and machine learning. First, preprocessing algorithms, which reduce noise and correct partial volume effects that usually characterize nuclear medicine images, have led to improvements in both qualitative and quantitative accuracy. Second, (semi-)automatic algorithms for image segmentation were adapted to identify and delineate lesions of interest with similar accuracy and possibly higher reproducibility than manually made by physicians. Third, the extraction of quantitative metrics from functional images to characterize lesions or organs of interest has grown exponentially and has enabled the exploration of tumor heterogeneity, potentially providing additional biological and prognostic information. Finally, the development of multiparametric models applying machine learning for diagnosis, staging, and outcome prediction has expanded significantly. However, despite the promising application of AI, some important limitations must also be considered. The development of AI normally depends on the availability of a large amount of data which means the need for (standardized) multicenter cooperation and sharing of data, also dealing with data protection regulations.

In this presentation, we focus on the potential applications and challenges that should be sorted out to introduce AI in the field of nuclear medicine and molecular imaging and what we expect in the near future.

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ARTIFICIAL INTELLIGENCE: THE PERSPECTIVES OF RADIATION ONCOLOGY

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Aims. This presentation aims to provide insights into the role of the radiation oncologist in the era of artificial intelligence (AI) and its implications for the future of cancer treatment. It will highlight the key responsibilities, challenges, and opportunities that radiotherapy will face as AI technologies continue to evolve.

Methods. We will discuss the integration of AI into radiation therapy workflows and treatment planning processes. We will also explore how AI-driven tools are enhancing precision and efficiency in radiation therapy delivery. Real-world examples and case studies will be presented to illustrate the practical applications of AI in radiation therapy, as well as the fears of this integration.

Results. The presentation will showcase how AI technologies have already begun to transform the field of radiation oncology. We will share outcomes and experiences from institutions that have implemented AI-driven solutions, including improvements in treatment accuracy, reduced treatment times, and enhanced patient outcomes. The role of radiation oncologists in working alongside AI systems will be highlighted.

Conclusions. In conclusion, this presentation will shed light on the evolving landscape of radiation therapy in the context of AI. It will emphasize the importance of collaboration between radiation oncologists and AI technologies to provide the best possible care for cancer patients. The presentation will leave attendees with a deeper understanding of the future possibilities and challenges that lie ahead in the field of radiation oncology.

LIFE OF A RESIDENT IN THE US & THE SOCIETY FOR WOMEN IN RADIATION ONCOLOGY"

C. Seldon Taswell

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This presentation will describe the current radiation oncology format in the United States of America. The international outreach and collaborative efforts of national radiation oncology societies will be reviewed. Work life integration will be discussed from the viewpoint of an American radiation oncology resident.

NEW EVIDENCE AND CLINICAL PRACTICE IN RADIOTHERAPY FOR PROSTATE CANCER

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Prostate cancer is one of the big killers. The indications for radiotherapy in prostate cancer are numerous and the new data and evidence regard every clinical scenario:

1. Curative treatment (non-metastatic tumor): external beam radiotherapy is a well-established non-invasive alternative to surgical treatment, compared to which it offers equal efficacy in terms of disease control and overall survival. In accordance with the results of numerous randomized studies, today it can be administered with short schedules also called hypofractionated, *i.e*. in approximately 5 weeks (moderate hypofractionation) and even in 5 sessions (ultra-hypofractionation). The latest studies concentrate on patient selection for treatment modality (Valle et al. 2023, Hamdy et al. 2023), RT-induced erectile dysfunction (Le Guevelou et al. 2023) and intensification of treatment (Gomez-Aparicio *et al.* 2023).
2. Post-prostatectomy treatment: radiotherapy is indicated in case of a biochemical recurrence (PSA rise after prostatectomy) as a "salvage treatment". The latest studies concentrate on patient selection for salvage treatment modality (Shore *et al.* 2023, Jiang *et. al.* 2023, Tran *et al.* 2023) and management of nodal disease (Zuur *et al*. 2023)
3. Ablative treatment at the level of the metastases or of the primary tumor in the metastatic phase: stereotactic radiotherapy at the level of the metastasis (oligometastatic phase, *i.e.* with the limited number of metastases) alone or in association with pharmacological therapy allows the control of the diseas. In case of low-volume metastatic disease at diagnosis, radiotherapy to the prostate significantly increases survival. The latest evidence includes combination

with new drugs (Shah *et al.* 2023) and intermittent approach (Tang *et al.* 2023).

4. Palliative treatment that counteracts the symptoms of bone, lung, brain or other metastases. The latest studies concentrate on high precision RT and quality of life issues (Ryu *et al.* 2023, Shah *et al.* 2023).
5. Special situations: The first experiences of ablative stereotactic radiotherapy appear in cases of intraprostatic recurrence after curative radiotherapy. The latest studies concentrate on the patient selection for salvage modality (Shore *et al.* 2023).

In conclusion, innovation is concentrated on all prostate cancer radiotherapy areas. It represents a premise for the continuous improvement of care in the management of prostate cancer.

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NEW EVIDENCE AND CLINICAL PRACTICE IN BREAST CANCER TREATMENT

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This is an overview of the most recent advances in breast cancer treatment, covering both early and advanced disease settings. Profound insights regarding the optimization of treatment choices for early-stage, low-risk breast cancer, including hypofractionation, partial breast irradiation, and genomic profiles, are discussed. Additionally, the latest guidelines and recommendations regarding dosage, radiation volumes, and fractionation techniques are explored. Recent findings regarding the safety of radiation therapy when used in conjunction with new systemic agents are presented. Furthermore, this overview addresses the definitions and classifications of oligometastatic disease, shedding light on the integration of localized and systemic treatments to enhance survival outcomes while maintaining a favourable toxicity profile.

RADIATION ONCOLOGY 2023: NEW EVIDENCE AND CLINICAL PRACTICE FOR LUNG CANCER

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The purpose of this abstract is to report the most relevant studies emerging from the 2023 conferences relating to Lung Cancer, in particular discussing the impact of these works on current and future clinical practice.

During the World Lung Cancer Congress held in Singapore, the I-SABR work[1] was presented. This is a randomized phase II study comparing SBRT (50Gy in 4fx or 70Gy in 10fx) with SBRT associated with immunotherapy in patients with early stage NSCLC or with parenchymal relapse. 156 patients were randomized, of which approximately 60% of patients had a diameter less than or equal to 2 cm. The primary endpoint was event-free survival which in the per protocol analysis resulted in 77% at 4 years in the SBRT and Immunotherapy combination arm *versus* 53% in the SBRT alone arm with a HR = 0.38 (0.19-0.75). The toxicity was acceptable and this results are comparable with those of surgical therapy. A randomized phase III study is required to clarify the benefit.

The other presentation at the WCLC which is significant in perspective, is the INCREASE study.[2] In this phase II study, a therapeutic strategy of immunotherapy-chemotherapy and radiotherapy integration was used for

neoadjuvant purposes in patients with resectable disease. At a time of great interest in preoperative chemoimmunotherapy combinations with the emphasis on the ability of this integration to obtain a high rate of complete pathological responses, the study data of 63% pCR is certainly very interesting when compared with the neoadjuvant chemoradiation or chemo-immune data (INT0139=15%; ESPATUE=33%; CheckMate 816=24%; NADIM2=37%; AEGEAN=17%). Surgical mortality and morbidity were comparable with those of neoadjuvant radiochemotherapy studies and consequently this strategy is an interesting area of investigation.

Two studies regarding the treatment of SCLC were presented in the plenary session at ASTRO 2023. The first study is NRG CC003, a Phase IIR/III Trial of Prophylactic Cranial Irradiation (PCI) with or without Hippocampal Avoidance (HA) for Small Cell Lung Cancer (SCLC).[3] The results of this study on 393 randomized patients, of which approximately 70% in limited stage, document that HA-PCI does not increase the number of recurrences of intracranial disease (14.2% *vs* 14.8%) and at the same time, even if the HVLT-R Delayed recall at 6 months does not show a statistically significant difference, it reduces the first failure in each cognitive domain by 23%. This work fits into the scenario of the other two randomized studies that investigated the same topic and which reached opposite conclusions.

The second work presented in Plenary Session at ASTRO 2023, still relating to SCLC, is entirely dedicated to limited-stage patients. It is a multicenter, open-label randomized phase III trial that compares the use of Volumetric-modulated arc radiotherapy with a dose of 45 Gy in 30 fractions with another treatment arm in which the simultaneous integrated boost (SIB-VMAT) of 54 Gy in 30 fractions to the primary lung tumor and lymph node metastases is also provided.[4] Median overall survival was significantly improved in the 54 Gy group (62.4 months) compared with the 45 Gy group (43.1 months; p=0.001). Median progression-free survival was significantly improved in the 54 Gy group (30.5 months) compared with the 45 Gy group (16.7 months; p=0.044). This study is further confirmation of the role of dose as a determining factor for limited disease as already indicated by the Norwegian study.[5]

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3. Gondi et al. Primary Endpoint Results of NRG CC003, a Phase IIR/III Trial of Prophylactic Cranial Irradiation (PCI) with or without Hippocampal Avoidance (HA) for Small Cell Lung Cancer (SCLC). Plenary Session, ASTRO 2023
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GRANDANGOLO IN RADIOTERAPIA ONCOLOGICA: NUOVE EVIDENZE E PRATICA CLINICA: RETTO-CANALE ANALE

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Aims. Chemoradiation therapy is a key part of rectal and anal cancer treatment. Clinical, molecular, imaging and technological improvements have been made in recent years. The purpose of this lecture is to critically illustrate these developments in rectal and anal cancers.

Methods. Recent results of literature will be reported.

Results. Clinical research in rectal cancer has focused on two main goals: achieving complete response (CR) to avoid major surgery and increasing DFS. This has led to the promotion of preoperative treatment intensification programs, such as radiotherapy boosts, concomitant chemotherapy intensification, and Total Neoadjuvant Therapy. These strategies resulted in a doubled CR, and in a significant improvement in DFS. From the molecular point of view, recent research has revealed that patients MMR deficient (dMMR), the administration of check -point inhibitor immune therapy, obtained 100% cCR avoiding chemotherapy, radiotherapy and surgery. Although astonishing, these results necessitate a confirmation in larger studies, now ongoing. In addition, the beneficial effect is low, being dMMR only 5-7% of rectal cancer patients. The ability to extract quantitative imaging features, radiomics, has ameliorated the prediction of tumor response and is now in use in clinical trials to differentiate radiotherapy dose according to CR prediction. Anal cancer research focuses primarily on dose differentiation and biomarkers prediction of outcomes. The PLATO trial, a platform study aiming to modulate radiotherapy according to tumor presentation: ACT 3 RT avoidance in early-stage anal cancers, ACT 4 RT dose-descalation in intermediate tumors, and ACT 3 dose escalation in locally advanced disease. Preliminary results of the ACT 4 study of 160 patients, showed same response rate with standard versus descalated RT, with better compliance, lower toxicity and better sexual function in the descalated arm. Despite the good results of chemoradiotherapy in anal cancer, there are still differences in response and recurrence. Aside the classic prognosticators, new predictive and prognostic factors are emerging.

P16-HPV infection and tumor-infiltrating lymphocytes (TILs), as well as neutrophil/lymphocyte ratio (NLR) seem to have a strong and independent correlation with anal cancer outcomes and tumor response.

Conclusions. Several innovations in rectal and anal cancer are leading to a paradigm shift in the treatment of these diseases, modulating treatments to achieve the same oncologic outcomes with a less detrimental effect on patients' quality of life. Today, new molecular and imaging biomarkers may support and guide personalized treatments. The development of AI based predictive models will help integrate this information to address the radiation oncologist toward the treatment choice that best fits the disease presentation and patient characteristics.

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UPDATE SUL TUMORE DELLA VAGINA: DALL'INTENSIFICAZIONE DEL TRATTAMENTO ALLE EVIDENZE IN TERMINI DI CONSTRAINTS E DI TERAPIA DI SUPPORTO

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Primary vaginal cancer is rare, accounting for less than 3% of all gynecological malignancies. Given the rarity of these neoplasm, there are no randomized control trials to guide treatment decisions, and clinical care guidelines are based on limited retrospective and comparative studies. The very low prevalence of this tumor, in fact, poses important challenges for advancements in its treatment, and since it resembles cervical cancer in many aspects, treatment strategies are often adopted from evidence in locally advanced cervical cancer. Radical surgery has a limited role in treating vaginal cancer due to the proximity of normal tissues such as the bladder, rectum, and urethra, and is recommended only in small stage I tumors that are limited to the proximal part of the vagina. Radiation therapy, instead, is the treatment of choice in most patients with vaginal cancer, especially in patients with advanced-stage disease. It consists in general of a combination of external beam radiation therapy and cisplatin-based chemotherapy, followed by a brachytherapy boost. The advantage of radiation therapy is the preservation of the vagina as well as other organs.

Technical advancements in radiotherapy during the past three decades have made it possible to deliver high-precision radiotherapy, with consequent reduction of acute and late toxicities. For external beam radiotherapy, these developments include the integration of CT, MRI and PET images for treatment planning and delivery. The introduction of IMRT and VMAT techniques, which allow a better sparing of the surrounding normal tissues, the image-guided radiotherapy as a further daily control to guide treatment beams to precisely target tumor avoiding target missing and unnecessary irradiation of healthy organs at risk. Even for brachytherapy, the introduction of imaged-guided adaptive brachytherapy by CT or MRI has led to a new era of ever more effective treatments. This adaptive strategy accounts for tumor regression during treatment, therefore offering the potential for dose escalation to the residual tumor and dose de-escalation to the surrounding healthy organs at risk. The introduction of IGABT has resulted in improved local control and decreased toxicity. The EMBRACE studies have widely explored the effects of the cumulative dose of ERT and BRT on urinary frequency and continence, sexual function, gastro-intestinal morbidity in patients affected by cervical cancer, which are similar to those of vaginal cancer patients. The dose constraints they have provided can be used in clinical practice to avoid severe toxicities and improve quality of life.

WHAT HAS CHANGED IN THE DEFINITION OF THE TARGET FOR GLIOBLASTOMAS AND WHAT POSSIBLE FUTURE SCENARIO

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The current standard of care for newly diagnosed glioblastoma (GBM) is maximal safe resection followed by adjuvant radiation therapy (RT) with concomitant and maintenance temozolomide (TMZ) chemotherapy. In 2016, European Society for Radiotherapy and Oncology (ESTRO) target delineation guideline recommended a

single clinical target volume (CTV) as defined by an expansion of 2 cm from the residual tumor and resection cavity without the intentional inclusion of peritumoral edema. In the last years, several studies have suggested a reduction of GTV-to-CTV margins, especially when hypofractionated radiation schedules are used. More recently, The ESTRO Guidelines Committee in close interaction with EANO Guidelines Committee analyzed the body of evidence concerning contemporary glioblastoma target delineation, then took part in a two-step modified Delphi process to address open questions. key issues included i) imaging protocols and immobilization, ii) target delineation using standard MRI and novel imaging techniques, and iii) technical aspects of treatment including planning techniques and fractionation. Based on the EORTC recommendation focusing on the resection cavity and residual enhancing regions on T1-sequences with the addition of a reduced 15 mm margin, special situations are presented with corresponding potential adaptations depending on the specific clinical situation. Future research include the use of PET/advanced MRI techniques, further optimization of target delineation according to the new WHO brain tumors classification, and the impact of new target delineation strategies on neurocognitive outcome

HORMONE THERAPY IN PATIENTS WITH PROSTATE CANCER

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Androgen deprivation therapy (ADT) represents one of the cornerstones in prostate cancer (PC) treatment. In the last decades, ADT in PC has dramatically evolved. Upfront ADT agents such as LHRH analogues (leuprolide, triptorelin, goserelin) or antagonists (degarelix) are the most used drugs and have substantially replaced oral peripheral antiandrogens such as bicalutamide or flutamide.[1]

LHRH analogues and antagonists present different mechanisms of action. Agonists bind pituitary LHRH receptors and cause at the beginning an increase in LH and FSH levels and subsequently testosterone. This continuous stimulation of receptors progressively down-regulates LH production and finally a reduction of testosterone levels. LHRH agonists competitively occupy LHRH receptors causing a suppression in production of testosterone, LH and FSH.[2]

More recently, second line hormone therapies such as abiraterone, enzalutamide, apalutamide or darolutamide, have further improved patients' outcomes in different clinical scenarios of PC. These new molecules directly block androgen receptors (enzalutamide, apalutamide, darolutamide) or inhibit androgen production (abiraterone).

ADT can be useful in primary treatment of localized disease in association with radiation therapy, both in short and long course prescriptions. ADT can increase local control due to its synergistic effect together with RT. Moreover, ADT can also prevent micrometastatic dissemination.[3]

In patients with metastatic PC, ADT improves both local and distant failure rates and significantly increases overall survival.[4]

Originally, second-line ADT played a role in the so-called castration resistant PC. This setting defines PCs that showed biochemical or clinical progression during ADT with 1st generation molecules. Recently, several studies demonstrated an increase in biochemical and clinical control of disease with the combination of 1st and 2nd line ADT in earlier stages of PC and even in localized disease.[5]

Although these advantages, several side effects are associated with prolonged ADT and must be taken into account during clinical routine. The most common side effects of ADT are flushes, osteoporosis, and anemia. Furthermore, every new molecule can also cause specifical complications that have to be carefully handled.[1]

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SUPPORTIVE CARE FOR PROSTATE CANCER PATIENTS RECEIVING ANDROGEN DEPRIVATION THERAPY

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Androgen Deprivation Therapy (ADT) is a milestone of treatment for aggressive and advanced prostate cancer (PC), but it has also been associated with adverse effects on bone, metabolic, cardiovascular (CV), sexual, psycho-

logical health as well as body composition.

Adverse effects of ADT include decreases in bone mineral density; metabolic syndrome; CV disease; body changes such as weight gain, decreased muscle mass and strenght; loss of libido, erectile dysfunction, shrinkage of penis and testicles and hair changes; hot flashes; gynecomastia; depression and cognitive dysfunction; and fatigue. Several studies have found value in treatments for some adverse effects including bone loss[1] (calcium/vitamin D, bisphosphonates, denosumab), markers of metabolic syndrome (exercise, diet, metformin), gynecomastia (tamoxifen, prophylactic radiation), muscle loss[2] (resistance and aerobic exercise), and hot flashes (venlafaxine, medroxyprogesterone, cyproterone acetate, gabapentin). Real world data and results from randomized controlled trials (RCTs) suggest a direct class effect for CV risk in patients being administered gonadotropin-releasing hormone (GnRh) agonists and antagonists, with the latter being associated with reduced CV risk.[3]

ADT plays a key role in the treatment of many PC patients, but it has known harms that can impair health and quality of life. Clinicians should be aware of interventions that can help mitigate these adverse effects.

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CHEMOTHERAPY FOR M1 PROSTATE CANCER PATIENTS

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Aims. Taxane chemotherapy has been shown to improve overall survival in metastatic hormone sensitive prostate cancer (mHSPC) patients [Vale 2016], also in association with Androgen Receptor Targeted Agents (ARTAs) administration [Fizazi 2022///Smith 2022] in the so called "triplet therapy" treatment approach. However, benefit of docetaxel addition to up to date androgen deprivation therapy associated with ARTAs is unclear, and could be influenced by factors such as disease volume (high vs low). Moreover, local treatment on primary tumor and metastasis directed therapy significantly improve prognosis of mHSPC patients [Deek 2022///Bossi 2023] and may further reduce benefit of Docetaxel addition to standard systemic therapy, especially in oligometastatic/low volume disease. Thus, different treatment approaches are currently available for de novo mHSPC, and optimal treatment strategy has yet to be determined.

Methods. This work summarizes the current evidence about role of chemotherapy, ARTAs and local treatment of primary tumor and metastasis in mHSPC setting, trying to help clinicians to select the best treatment strategy related to each clinical scenario

Results. High volume *de novo* disease should be treated with standard androgen deprivation therapy (ADT), Docetaxel and concomitant ARTAs accordingo to current evidence. However, a role for radiotherapy on primary tumor in this scenario could be reasonably found for good responders and aiming to delay local symptoms occurrence. Low volume disease is more complex and heterogeneous, and ADT+ARTAs associated with radiotherapy on primary tumour could be considered a standard treatment. Role of metastasis directed therapy in this scenario is not clear but could further increase outcomes for low burden disease.

Conclusions. Exploiting all treatment approaches in mHSPC is crucial in order to improve outcomes in this patients population. Some patients could safely avoid upfront chemotherapy especially if low volume disease is aggressively treated with local radiotherapy. However, role of next generation imaging and metastasis directed therapy should be explored.

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INDICATIONS AND TECHNIQUES OF INTERVENTIONAL RADIOTHERAPY IN THE TREATMENT OF BREAST CANCER

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The purpose of this presentation is to have a global and recent vision of the interventional treatment techniques for breast cancer, in particular partial breast irradiation and/recurrent.

Breast-conserving surgery followed by whole-breast radiotherapy (WBRT) was established by the National Surgical Adjuvant Breast and Bowel Project (NSABP) B06 and Milan trials as the preferred and less radical treatment option compared to mastectomy for women with early-stage breast cancer.[1,2]

The importance of radiation as part of breast-conserving therapy to not only decrease local recurrence but also improve survival was later confirmed by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis.[3]

However, even early on, pathologic data and patterns of failure analysis suggested that the area at risk for recurrence was confined close to lumpectomy cavity and not the whole breast.[4,5,6]

Over the past 20 years, different modalities of PBI have been tested, mostly successfully, in a number of phase 2 and 3 clinical trials. The studied techniques are external beam radiation (photons, protons), single- and multicatheter brachytherapy, electronic brachytherapy, seed brachytherapy, non-invasive brachytherapy, and intraoperative radiation techniques (IORT) either with electrons or with 50-kV photons. Today, results from over 15,000 patients recruited within phase 3 trials testing partial-breast irradiation are available.[7,8]

APBI has been tested in a total of nine phase 3 trials with more than 15,000 patients over the past 10 years These trials show that for strictly selected patients with early breast cancer, PBI by EBRT, multicatheter brachytherapy, or IORT with electrons is non-inferior to the results of whole-breast irradiation in terms of local control, disease-free survival, and overall survival, and is in some aspects superior regarding late side effects and quality of life. In light of current data, EBRT and in particular PBI using multicatheter brachytherapy, or IORT with electrons (interventional radiotheraphy) is a valid alternative treatment option after breast-conserving surgery and can be offered for carefully selected low-risk breast cancer patients in clinical routine using the proposed selection criteria.

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LA FLASH RADIOTHERAPY: RAZIONALE E PROSPETTIVE DI IMPIEGO NELLA PALLIAZIONE

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FLASH radiotherapy (FLASH RT) is a modality of irradiation delivered at ultra-high dose rate, using electrons, X-rays, and protons, which prevents the induction of classical pathogenic patterns observed in normal tissues exposed to radiation delivered at conventional dose rates. The FLASH effect is therefore defined as the combination of decreased normal tissue effects combined

with maintained anti-tumor efficacy. The potential benefits of this approach include improved management of radiation-resistant tumors where dose escalation is necessary, improved quality of life for cancer survivors by reducing or even preventing debilitating side effects, minimized complications associated with organ motion, and a reduction in the workload of cancer treatments.

The transfer of FLASH RT based on X-ray and protons from preclinical into clinical application is still in development, while FLASH RT using electrons is being investigated in the context of intra-operative radiation therapy (IORT) to make the transition from preclinical research to the first clinical applications on superficial tumors and deeper-located tumors.

RADIO-LIGAND THERAPY IN NEUROENDOCRINE TUMORS

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Neuroendocrine neoplasms (NENs) are a heterogeneous group arising from neuroendocrine cells. They mostly have a gastroenteropancreatic origin, but may originate also from several other systems.[1] The classification from the World Health Organization considers primarily the grade of tumor: well-differentiated NENs are called neuroendocrine tumors (NETs), while poorly differentiated ones are called neuroendocrine carcinomas (NEC). NENs are clinically classified as functioning or non-functioning, depending on the ability of the tumor to secrete or not biogenic amines or peptide hormones that determine clinical symptoms onset. A wide range of treatment approaches are now available for NENs, which broadly comprise surgical and ablative treatment, use of somatostatin analogues, targeted agents, chemotherapy, and peptide receptor radionuclide therapy (PRRT)/radioligand therapy (RLT), in addition to watchful waiting in very selected patients.[2] Several societies have issued guidelines for diagnosis and treatment of NENs, including the National Comprehensive Cancer Network, European Society for Medical Oncology, and European Neuroendocrine Tumor Society.[3-5]

NETs are often hypervascular and >80% over-express somatostatin receptor (SSTR) on their surface. This allows the use of SSTR imaging for staging and can help to select patients for specific therapies targeting SSTR. RLT and the radiotheranostic approaches involve the administration of radiolabeled isotopes (^{68}Ga in NET), enabling expression of the therapeutic target to be visualized *in vivo* with a companion imaging method before switching to the radiolabeled therapeutic counterpart. Radiotheranostics can also enable visualization of tumor burden, allowing to 'treat what you see'. Moreover, repeating imaging becomes useful to assess the effects of therapy on target expression. Some radionuclides, in addition to their therapeutic component (as emitters of either auger-, alpha- or beta-radiation), may be visualized in real time (thanks to the emission of either gamma or positron radiation). The therapeutic effects of ^{177}Lu-conjugated are primarily mediated by the emission of beta-radiation, while the gamma-emissions can be used for imaging and to perform dosimetry studies.

The use of ^{177}Lu-Dotatate was evaluated in NETTER-1 trial, the first reported randomized, international, phase 3 trial of RLT in NETs. Patients with advanced, well differentiated, progressive midgut NETs were randomly assigned to receive four cycles of ^{177}Lu-Dotatate plus long-acting octreotide 30 mg every 8 weeks or high-dose long-acting octreotide 60 mg alone every 4 weeks. The trial met the primary objective of significantly improved progression-free survival with ^{177}Lu-Dotatate (hazard ratio 0·18; $p<0.0001$).[6]

Radiotheragnostic applications are increasing prominence in both cancer imaging and therapy, and this is largely related to the advent of diagnostic and therapeutic isotopes that have changed the way we manage cancer. Although both the two main RLT-trial NETTER-1 and VISION[6,7] used standard doses for therapy, the therapeutic index can potentially be improved by optimizing the amount of injected activity, treatment regimens, time intervals and/or number of cycles, and by personalizing treatment basing on dosimetry.

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GENOMIC PROFILING AND RADIATION THERAPY IN BREAST CANCER

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Adjuvant radiation therapy (RT) decreases local recurrence rate (LRR) after breast conserving therapy (BCT), and consequently improves breast cancer mortality (BCM), while postmastectomy RT (PMRT) reduces LRR and improves overall survival (OS) in patients with lymph node (LN) positive breast cancer (BC). Still, for BC patients, benefits versus toxicity must be well balanced and personalized tools in routine practice are needed to guide clinical decisions for such a heterogeneous disease comprised of multiple subtypes with differing response to treatment.

Genomic risk stratification for LR and prediction of RT benefit are investigated in ongoing clinical trials using biological parameters to direct treatment decisions regarding escalation and de-escalation of RT in BC. Prognostic genomic assays may help stratify BC according to their risk of LR, while the development and validation of predictive genomic assays may direct more tailored LR approach to improve oncologic outcomes. Commercially available genomic assays are commonly used in the clinic as prognostic and predictive tools for adjuvant systemic therapy. While ASCO guidelines provide evidence-based recommendations for the use of these tools for guiding adjuvant systemic therapies among early-stage BC, their use in guiding RT remains uncertain. Based on the results of the Danish 82b and 82c trials, The Danish Breast Cancer Cooperative Group developed and validated a seven gene signature in high-risk patients treated with PMRT and identified a low risk group that did not benefit from PMRT.

A high risk 70-gene profile (Mammaprint) showed a positive association with LRR risk within the SweBCGRT cohort of stage I-II: the association was strongest in irradiated patients treated either with BCS + RT or PMRT. A 16-gene signature POLAR (Profile for the Omission of Local Adjuvant Radiation) was found to be a predictive value in terms of efficacy of RT: although promising, the profile was validated in a smaller patient group. The genomic-adjusted radiation dose (GARD) is a non-BC specific, tumour genomic biomarker validated to personalise the RT dose, and was associated with time to first recurrence and OS in a recent pooled-analysis.

Biomarkers in BC may be predictive of radiation dose and outcome, and prospective integral-biomarker RT trial are ongoing. Their results will ultimately allow for precision RT in the management of BC patients.

PROFILAZIONE GENOMICA E RADIOTERAPIA-ENDOMETRIO

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Endometrial carcinoma (EC) is the most common gynecological cancer worlwide. The management of women diagnosed with EC routinely involves several medical specialists dedicated to the gynecological malignancies and Institutional Gynecological-Oncological Tumor Boards. Significant advancements in the diagnosis and risk-assessment stratification of EC patients have been made in recent years, notably in the field of molecular biology. To date, despite inter-observer variation in determining prognostic groups, conventional pathologic analysis is still the gold standard for tumor risk stratification. The molecular classification provides new additional information to the traditional morphologic features and should be included in the pathologic report of the biopsy as well as the final surgical sample. Based on The Cancer Genome Atlas findings, the ProMisE (Proactive Molecular Risk Classifier for Endometrial Cancer) algorithm was developed and it divides EC into 4 groups based on a immunohistochemistry combination of mutation and protein expression analysis (Mismatch repair (MMR), polymerase-epsilon (POLE) exonuclease domain mutations (EDMs) and protein 53 (p53)): MMR-D, POLEmut, p53 wild type (copy number low-CNL- or non-specific molecular profile-NSMP), or p53 null/missense mutations. ESGO-ESTRO and NCCN encourage molecular profiling. Molecular classification should guide clinical management, this allows for an even more individualized approach and permits avoiding unnecessary treatments with potential side effects in patients with a reassuring molecular profile. Validation of the molecular classification in high-grade and/or high-risk endometrial carcinomas shows that the POLE-mut tumors have an excellent prognosis, while the p53-abn neoplasms have a poor prognosis. On the other hand, there is still debate whether molecular classification may play a role in the decision management of daily clinical practices for radiation oncologists. In this presentation it will be discussed the current standards of treatment in the field of EC in the light of the latest scientific evidences regarding molecular classification.

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MICROBIOTA AND RADIOTHERAPY. HEAD AND NECK

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The term microbiota refers to all the microorganisms found in an environment. The relationship between cancer and microbes is complex. The ways in which microbes and the microbiota contribute to carcinogenesis, whether by enhancing or diminishing a host's risk, fall into three broad categories: (1) altering the balance of host cell proliferation and death, (2) guiding immune system function, and (3) influencing metabolism of host-produced factors, ingested foodstuffs, and pharmaceuticals. Given the role of the microbiota in modulating host immunity, it is intuitive that it could significantly influence response and toxicity to various forms of cancer therapy. There are clearly bacterial taxa that are associated with response and toxicity. Gut microbiota is considered the most significant in maintaining our health. Microbiota is also localized in other regions including the oral cavity, lung, vagina, and skin. Oral microbiota is considered the second largest microbial community in human. Radiation induced toxicities like xerostomia and mucositis can be attributed to disruptions not only in the normal cellular environment, but also in the oral microbial colonies, which are essential for basic biological functioning. The interactions between microbiota and cancer therapy are bidirectional. On the one hand, treatment modalities for cancer, including radiation and chemotherapeutic drugs, can promote dysbiosis either directly or by activating an immune response. On the other hand, microbiota composition can influence the effectiveness of cancer treatment Specifically, the composition of microbiota has been found to influence the response to radiation exposure which may occur because of the role of microbiota in the immuno-stimulatory effects of radiotherapy. Moreover, microorganisms have great potential in being used as biomarkers to assess radiation response as well as for the treatment of post-radiation complications. Accordingly, the evaluation of a patient's microbial composition and function and its subsequent targeted modulation represent key elements of future multidisciplinary and precision-medicine approaches.

MICROBIOTA AND RADIOTHERAPY

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Radiotherapy is a mainstay of solid tumor management but often can be associated with side effects impacting patients' quality of life. Tumour radiosensitivity is hugely variable and depends by multiple and complex factors. Also healthy tissues response to radiation varies among patients and can be impacted by multiple variables. Gut microbiota has been found to modulate both the efficacy and toxicity of some types of cancer chemotherapies and immunotherapies. The modulation of radiotherapy by microbiota is a topic less investigated. In the presentation, will be discussed the potential role of gut microbiota on modulating radiotherapy-induced oral and gastrointestinal mucositis and the anti-tumor response to radiotherapy through modulation of immune responses.
Moreover, hypotesis of future targeted microbiota modulation in patients candidates for radiotherapy will be discussed.

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MICROBIOMA AND RADIOTHERAPY IN GYNECOLOGICAL MALIGNANCIES

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The "microbiome" refers to the collective complex ecosystem of bacteria, fungi, viruses, parasites, archaea, and their genomes that inhabit the gut, oral cavity, vagina, respiratory tract, skin and other mucosal surfaces. A

mutualistic relationship exists between commensal microbiota and human cells. A healthy gut microbiome typically consists of 5 major taxa of bacteria that share similar function. A relative increase or decrease in abundance and diversity of bacterial species within an organ, known as "dysbiosis" results in impaired microbiome-host homeostasis. Both the richness and diversity of the species within the gut are critically important because when in balance, the microbiome plays a vital role in human health by regulating metabolism, inflammation, and immunity. In patients with gynecologic cancers, treated with pelvic radiotherapy, with or without chemotherapy, changes in the the diversity and the composition of the gut microbiome over time can be observed; however, prospective data remain scarce, as most studies on the subject have provided only single time-point or retrospective data. Having prospective data is particularly important for studying the temporal changes in the gut microbiome and explore its potential role role in influencing treatment response as a future biomarker.

This mechanism of radiation induced changes in gut microbioma could be related to alteration in the gut epithelium and mucusal layer that are followed by the overgrowth of pathogenic bacteria, which could in turn affect immune cells' maturation and responses to tumor. Cumulative fractions of radiotherapy may induce the outgrowth of radioresistant or pathologic microbial taxa.

Researchers in diverse areas of medicine have studied the treatment-enhancing and toxicity-limiting utility of the gut microbiome. Modifying the gut microbiome to accumulate radiotherapy-tolerant species could potentially be used to reduce treatment toxicity. Personalized treatments could be delivered according to baseline microbioma diversity in order to improve treatment outcomes. Moreover with the same intent, therapeutic interventions as dietary changes or supplementation may be introduced in order to increase beneficial, radioresistant species aimed at increasing immunostimulation.

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VOLUMI DI TRATTAMENTO E FRAZIONAMENTO DELLA DOSE NELLE COMBINAZIONI RADIO-IMMUNOTERAPICHE: EVIDENZE ATTUALI E SFIDE FUTURE – POLMONE

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Aims. Immunotherapy has radically changed the clinical management of patients with lung cancer in recent years. However, response rates to ICIs are around 19-47% among patients with advanced NSCLC. As a result, the development of combined Immune Checkpoint Inhibitors (ICI) and radiotherapy has begun with the aim of strengthening patients' antitumor immunity. Radiotherapy with substantial technological improvements not only achieves local tumor control but also has the potential to mediate immunostimulatory effects that could result in tumor regression beyond irradiated regions. At present, numerous preclinical and clinical research are investigating the efficiency and safety of combining ICI with radiotherapy.

Methods. A review of literature has been conducted in order to define the rationale for combining radiotherapy with immunotherapy and to discuss the opportunities and challenges of combination therapy, including the timing of radiotherapy, optimal dose and fractionations, radiotherapy target and target volume.

Results. Several preclinical studies suggest that radiotherapy is an ideal partner for ICIs. There are also many clinical trials that are assessing the efficacy of this combined therapy. The Immunotherapy-stereotactic radiotherapy combination had more improved distant abscopal response rates than ICI alone, suggesting that non-responders to ICI therapy were turned into responders by radiotherapy. At present, the optimal timing and sequencing of radiotherapy and immunotherapy is unknown. There are currently no significant clinical trials

that demonstrate the optimal dose and fractionation of radiotherapy in combination with immunotherapy. However, we can speculate that radioimmunotherapy might require lower doses of radiation than the maximum tolerated dose.

Conclusions. Based on numerous preclinical and clinical research, combining radiotherapy with ICIs is predicted to be an effective treatment model in the future. At present, a growing body of ongoing clinical trials are investigating a range of treatment options, including diverse immunotherapy regimes, various doses and fractionation schedules, smaller target lesions, and different combination treatment sequences.

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RADIO-IMMUNOTHERAPY FOR HEAD AND NECK CANCER IN 2023: WHERE DO WE STAND?

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The idea of combining the radiotherapy (RT) and immunotherapy (IT) in head and neck cancer (HNC) is not new, with the first preclinical studies on mice having been published in the early 1990s.[1] This has led to an in-depth understanding of both the mechanisms of indirect cell killing (*e.g.* interferon-dependent expression of MHC class I) and of immune escape (*e.g.* upregulation of PD-L1 and infiltration of regulatory T cells). However, the interplay between these aspects of the immunological response to radiation is far from being fully elucidated in the clinic, given the biological variability of HNCs, which is reflected by the presence of multiple subsites, by the possibility of HPV/EBV infection, by different degrees of smoke exposure, and by variations in disease burden, to name a few factors. In addition, the total doses and fractionations used in preclinical models are significantly different from those used to treat patients, which warrants for a more consistent evidence base.[2]

To address this issue, several clinical trials are underway to investigate the efficacy and tolerability of the RT/IT combination, both in the definitive and in the recurrent-metastatic settings.[3] Therefore, the aim of this presentation is to review- and critically discuss- the study designs and available evidence, with a dedicated focus on the Radiation Oncologist's perspective. These topics will be explored: dose-response correlation, the role of regional nodal irradiation, RT/IT timing and sequencing, and the likelihood of achieving an abscopal effect. Moreover, part of the lecture will be devoted to the discussion of RT/IT trials for HPV-positive cases, whose immunological background presents several peculiarities as compared to non-HPV-negative tumors.[4] This will also allow to present the state of the art of candidate biomarkers of response in this clinical setting, for the creation of patient-tailored intensification or de-intensification strategies.

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VOLUMI DI TRATTAMENTO E FRAZIONAMENTO DELLA DOSE NELLE COMBINAZIONI RADIO-IMMUNOTERAPICHE: EVIDENZE ATTUALI E SFIDE FUTURE- GASTROENTERICO

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Multiple evidence supports the concept that radiation enhance immune responses to tumors.[1] However, discordance between preclinical data and clinical trial results have questioned the clinical relevance of the immune-modulatory effects of radiotherapy.[2] In particular, current understanding of the immunological impact of different radiation schedules and volumes is limited. Improvement in the knowledge of the distinct immune modulatory effects of different parameters of RT delivery (site, number of lesions, dose, fractionation, volume, timing from systemic therapy) is capital to translate radiation/immune system synergy into clinical benefit. This is of primary importance in Gastro-Intestinal tumours, an heterogenous group of malignancies characterized by wide differences in intrinsic biology and interaction with their proper

microenvironment.[3] In this presentation, we highlight the need for integration of radiation dose, fractionation and volume considerations in the design of future clinical studies in order to implement more effective radiotherapy regimens.

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EQUITÀ DELLE CURE: ACCESSO AI TRATTAMENTI

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Equity in access to radiotherapy in Italy, as in many other countries, is a critical issue in healthcare. Equity in this context refers to ensuring that all individuals, regardless of their socioeconomic status, geographical location, or other factors, have equal access to high-quality radiotherapy services when they need them. Achieving equity in access to radiotherapy is essential to ensure that cancer patients receive the appropriate and timely treatment they require.

Several factors can impact equity in access to radiotherapy in Italy:

1. Geographic Distribution: Italy has a decentralized healthcare system, with regional governments responsible for healthcare delivery. This can lead to disparities in access to radiotherapy facilities, with some regions having better access than others (i.e. meridional regions). Efforts are made to ensure that radiotherapy services are distributed more evenly, but challenges remain.
2. Healthcare Infrastructure: The availability of radiotherapy facilities and equipment varies from region to region. Some regions may have state-of-the-art facilities, while others may have older or fewer machines. Investments in healthcare infrastructure are crucial to improving equity.
3. Wait Times: Long wait times for radiotherapy can disproportionately affect patients with limited resources or those living in underserved areas. Reducing wait times is essential for equitable access to treatment.
4. Socioeconomic Factors: Socioeconomic status can impact a patient's ability to access radiotherapy. Those with financial constraints may face difficulties in accessing necessary treatments, even if facilities are available.
5. Awareness and Education: Lack of awareness about cancer and available treatments can hinder equitable access. Efforts to educate the public about cancer prevention and early detection can help address this issue.
6. Transportation: For patients living in remote or rural areas, transportation to and from radiotherapy centers can be a significant barrier. Providing transportation services or mobile radiotherapy units can help address this challenge.

To promote equity in access to radiotherapy in Italy, healthcare policymakers, regional authorities, and healthcare providers must collaborate to:

1. Monitor Disparities: Regularly collect data on the distribution of radiotherapy facilities and patient outcomes to identify disparities and target areas in need of improvement.
2. Invest in Infrastructure: Allocate resources to upgrade and expand radiotherapy facilities in underserved regions to ensure that they have the capacity to meet the demand for treatment.
3. Reduce Wait Times: Implement strategies to reduce waiting times for radiotherapy, such as optimizing scheduling (i.e. single or hypofractionated treatment) and increasing the workforce.
4. Provide Financial Support: Develop programs to assist patients with financial constraints, including subsidies or reimbursement for travel and treatment costs.
5. Promote Education and Awareness: Conduct public health campaigns to raise awareness about cancer prevention, early detection, and available treatment options.

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EQUITABLE ACCESS TO CLINICAL TRIALS

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Clinical trials are important to assess if a new intervention is safe and effective compared to a standard treatment, whether early detection strategies may improve patient's outcomes and to establish ways to optimize health-related quality of life[1]. It is crucial that clinical trials include individuals with a variety of lived experiences and living conditions, together with characteristics like race and ethnicity, age, sex, and sexual orientation, so that all communities may benefit from scientific advances. Historically, clinical trials did not always recruit participants who represented the individuals most affected by a particular disease, condition, or behaviour[1]. This shortcoming has created gaps in our understanding of diseases and conditions, preventive factors, and treatment effectiveness across populations. These gaps in knowledge can impede the quality of health care decision making, ability to counsel people on ways to reduce their risk, optimal treatment responses, and even the development of more effective interventions.[1] Filling these gaps is crucial to improve knowledge, science and healthcare, in particular in the field of oncology.[1]

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ORGANIZATIONAL MODELS: THE PERSPECTIVE OF THE RADIATION THERAPY TECHNOLOGIST (RTT)

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In the continually evolving landscape of oncological care, attention to quality and patient-centered care is gaining increasing importance. Over the past two decades, cancer mortality has shown a significant decline, thanks to significant improvements in prevention, diagnosis, and cancer treatment. The increase in survival rates thus leads to a new need for care, aimed at addressing the growing emotional well-being of patients. Technological innovations and scientific advancements provide greater opportunities to personalize radiotherapy to meet the needs of each individual patient. It is, therefore, necessary to reconsider organizational models from a multidisciplinary perspective to better adapt to a more sustainable and inclusive future vision. This reflection has led to the rationalization of new competency frameworks, both in terms of training and organization, to ensure safe and effective performance. The development of new roles to be implemented and consolidated in daily practice opens up new educational scenarios, leading to better management of specific activities and/or care pathways. Radiation Therapy Technologists (RTT) can play a key role in promoting and supporting patient engagement by sharing their knowledge to enhance understanding of the various stages of the treatment journey. It has been shown that patients' experiences are improved thanks to the quality of interactions with radiation therapy technical staff. In this context, a role is identified in which the RTT can serve as a care manager, taking responsibility for the individual care journey of the patient, becoming a reference point for the effective management of ongoing therapy processes, appropriately guiding the patient, and listening to their needs as much as possible.

RTTs can also play an active role in educating patients about procedures, safety measures, and enrollment in research pathways. In the evolving context of radiotherapy, the profile of the RTT can also fit into the areas of quality assurance (QA) and risk management (RM). Continuous improvement, procedure evaluation, incident reporting, certification, and accreditation requirements have made QA and RM a significant area of activity. Finally, a significant contribution can also be considered in the field of Health Technology Assessment (HTA), as RTT can contribute to the implementation and use of new technologies and planning systems to enhance treatment precision and effectiveness.

Implementing one or more of these models can improve overall management of cancer patients and contribute to a better quality of life in collaboration with the rest of the healthcare team. Technology, guided by the knowledge and expertise of healthcare professionals, aims to meet the needs of patients by caring for the sick while also taking care of the person.

However, the RTT will continue to be a important actor in the technological evolution, especially when it comes to the patient relationship. Despite the inevitable and exponential technological and computational advancements in radiotherapy equipment, the 'human' connection with the patient will remain paramount. This is, and will forever be, a role, a duty, and a competence of the RTTs.

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THE MANAGEMENT OF CURE FOR PATIENTS TREATED WITH RADIOTHERAPY: THE ROLE OF THE CASE MANAGER

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Aims. The role of the case manager for patients treated with radiotherapy aim at simplify and optimize the path of the patient through a relational counseling. Case managers are expertised counselors helping in orienting, supporting and developing the potentials of patients temporarily in difficulty.

Methods. Case managers operate through the programming of a work-flow, the use of standardized procedures, and the compilation of a computerized nursing record.

Results. Case managers aim at obtaining a good compliance of the patients, monitoring potential toxicity effects of radiotherapy. A good quality of life become more accessible for patients, according to the guide of the case manager.

Conclusions. The case manager becomes the reference for the patient and his family members, monitoring toxicity and interfacing with the medical team, and creating relationships between the subjects of the path itself.

EVALUATION OF THERAPEUTIC INDEX IN HEAD AND NECK CANCER PATIENTS: MANAGEMENT AND COMMUNICATION

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Head and neck cancer (HNC) accounts about 3% of all cancer diagnoses. The overall incidence of HNC continues to rise, with approximately 25-40% of patients over 70 years old. Smoking, alcohol drinking and HPV infection are major risk factors for HNC. The mainstay of treatment for locoregionally advanced HNC is either surgery followed by adjuvant radiation therapy (RT) or definitive concurrent chemoradiation (CRT) reserving surgery as salvage therapy.

Because of the complex anatomy of the H&N region, several critical structures like brainstem, spinal cord, brachial plexus, salivary glands, mucosa, major blood vessels, and swallowing musculature receive radiation dose that can lead to severe toxicities. Many studies have shown several impairment related to feeding, nutrition, pain and psychological problems with quality of life (QOL) deterioration.

In some cases is very difficult, for physician, to reach curative doses avoiding toxicities. Numerous factors weigh into treatment decision, including age, performance status, social supports and contest, individual preferences to undergo curative treatment and the individual's physical and mental reserve.

We performed a literature research with the aim to examine clinical aspects and radiotherapy treatment details that can influence the therapeutic index. Moreover we investigated the presence of predictive models of toxicity that can lead us to a therapeutic choice with favorable risk/benefit balance.

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QUANDO L'INDICE TERAPEUTICO È AI LIMITI: GESTIONE E COMUNICAZIONE - LINFOMI

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The association between radiation therapy (RT) and late complications is nowadays well known for patients cured from lymphomas. The late effects may rise up several years after the end of the treatment, usually appearing in the second to the third decade post-therapy. Radiation induced heart disease and second tumors have become important arguments of research, leading to intensive debate on the risk-benefit ratio of RT in lymphoma patients. Indeed, many prospective randomized studies have tried to omit altogether RT from first line, with the aim of reducing life threatening long term complications (mainly cardiac events and second cancer), admitting in change a slight reduction of disease control in patients receiving chemotherapy alone. However, the recent prominent improvement of RT techniques has significantly reduced the inadvertent irradiation of organs at risk, with a particular attention in the recent years for the heart. Highly conformal delivery techniques as intensity-modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT), combined with image-guided radiotherapy (IGRT) and, eventually, with technique to manage respiratory-motion have the clear goal to decrease fields and doses of RT to all the organs at risk, including the heart, without compromising long-term disease related outcomes. On top of these hi-tech RT solutions, particle therapy may further decrease the exposure of healthy tissues to RT doses in selected patients. For that reason, RT-related complications are expected to reduce dramatically in the future even though, given the long latency of these events, the magnitude of the residual risk is still uncertain.

Purpose of this lecture is to describe the potential contribution of modern RT techniques in minimizing the risk-benefit ratio of long term survivors treated for lymphomas.

AT THE LIMITS OF THE THERAPEUTIC INDEX: MANAGEMENT AND COMMUNICATION IN PEDIATRIC TUMORS

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Paediatric tumours present a challenge in oncological management, due to their intersection with the nuances of developmental biology, therapeutic safety, and complex communication dynamics involving children and their caregivers. Approximately 16,000 cases of cancer are diagnosed each year in children in the United States.[1] The advances in the multi-disciplinary management of cancer have resulted in increased rates of survivorship;[2] unfortunately, an estimated 20% of children with cancer still die of their disease.[1] Radiotherapy is an important part of the multi-disciplinary strategy treatment and beside the aim of a successful local control, the therapy-associated side effects of irradiation have to be included in a patient oriented therapy plan to consider the risk–benefit ratio.

In the cotext of long term effetcs after irradiation the main challenge is the lack of evidences.[3] A systematic review investigated the long-term issues and supportive care needs of adolescent and young adult childhood brain tumour survivors and their caregivers.[4] They reported survivors experienced poorer social function-ing and sexual functioning and were less likely to be employed or

have children, when compared with other AYA cancer survivors; moreover survivors expressed a need for better educational support and age-specific psychosocial services. Effective communication is associated also with improved quality of life[5] and is essential for promoting and facilitating shared decision-making between HCPs, patients, and families.[6] In fact optimal communication in the context of pediatric oncology should begin at the time of diagnosis[5] and continue throughout the illness trajectory to enhance the therapeutic relationship, explore the hopes and goals of patients and families, and deliver care.

Therefore there is a need of exploration into the criticality of effective communication strategies among multidisciplinary teams and between clinicians and families, ensuring that the intricate balance of aggressive treatment and safeguarding quality of life is maintained.

In our department a project, the RADAR-project aims to monitor the health needs of the patient and family by all staff in order to identify needs early, manage them and make the patient and family feel listened to and welcomed during radiotherapy.

We argue the necessity of not only embracing advancements in precision medicine tailored to pediatric oncology but also advancing empathetic and clear communication models. This equilibrium ensures that medical decisions are thoroughly elucidated, ethical considerations are transparent, and that children and families are active, informed participants throughout the treatment journey.

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CONTRATTO DIRIGENTI MEDICI

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Mentre scrivo questo abstract dovremmo essere alle fasi finali della trattativa tra Aran e sindacati per il rinnovo del contratto (2019-2021) della Dirigenza medica e sanitaria del Ssn. Se si arrivasse alla firma della pre-intesa entro luglio vorrebbe dire avere l'attuazione del contratto entro l'anno in corso. Il rinnovo riguarda circa 130 mila professionisti che in media porteranno a casa un aumento medio lordo di 200 euro al mese cui vanno sommati i circa 8-9 mila euro di arretrati. Molte le novità quali materie decisive per l'organizzazione del lavoro come straordinari, guardie e pronta disponibilità. Altra novità riguarda l'assegnazione degli incarichi che sarà resa più esigibile. L'incarico dovrà essere assegnato ai dirigenti subito dopo il periodo prova e subito dopo la valutazione positiva. Verrà poi regolamentato il lavoro fuori sede per cui verrà riconosciuto un rimborso quando si andrà a lavorare fuori dalla propria sede di origine. Il vero nodo riguarda l'orario di lavoro perché a causa della carenza di personale la flessibilità oraria viene utilizzata dalle aziende sostanzialmente per coprire i servizi scoperti. Un medico 'regala' circa 300 ore l'anno di lavoro extra. Il problema è che per dare un segnale tangibile servono risorse. Negli incontri al ministero della Salute sono stati ribaditi gli ambiti, sia legislativi che contrattuali, per i quali è necessario e urgente un immediato intervento: abolizione del tetto di spesa per l'assunzione di personale; riforma del Dm 70; riforma della legge 502 che proponga nuovi modelli organizzativi del sistema; defiscalizzazione di parte del salario; incentivi per trattenere i medici nel servizio pubblico. Inoltre c'è una questione che riguarda la conciliazione vita-lavoro per le donne medico.

LA CARATTERIZZAZIONE DELLA MALATTIA OLIGOMETASTATICA: NUMERO DI LESIONI O VOLUME DI MALATTIA?

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In the context of managing oligometastatic disease, essential questions arise regarding patient selection for personalized treatment. The most common definition of oligometastatic disease is based on the number of detected metastases, typically set at 3 or 5 oligometastases. However, emerging data are investigating the feasibility of using the volume of metastatic disease to correlate with a patient's outcome. This presentation aims to thoroughly explore and critically evaluate the significance of lesion count versus disease volume in the context of oligometastatic disease. We will delve into the current state of research, discuss clinical implications, and consider potential therapeutic decisions influenced by these two distinct approaches to disease characterization.

LA REIRRADIAZIONE: STANDARD MINIMI RICHIESTI

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Local and regional relapse are common following an initial course of radiotherapy, yet management of these recurrences still represents a challenge, in particular for the radiation oncologist; in this scenario, reirradiation plays a crucial role, right in the forefront. Technological improvements as well as modern irradiation modalities (PT, SBRT or HDR-brachytherapy), due to better OAR sparing, has made reirradiation nowadays increasingly applied in clinics. Aim of this talk is to review and discuss available evidence, focusing on some important points such as patient selection with evaluation of risk/benefit balance (taking into account sequelae resulting from previous RT course), irradiation modalities as well as technical challenges (from target volume definition, to dose and fractionation up to uncertainty of dose summation).

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STEREOTACTIC ABLATIVE RADIATION THERAPY (SABR) FOR CARDIAC ARRHYTHMIA: STATE OF ART AND FUTURE PROSPECTIVE

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Aims. Cardiac arrhythmias are frequent in general population. Catheter ablation aims to eliminate the electrical cells that cause cardiac arrhythmia. To date, ablative techniques use either radiofrequency energy to heat tissues in direct contact or cryoablation, which uses a freezer inside the catheter to destroy tissue. In both cases, there is the necrosis of the target tissue, and consequently the inactivation of the substrate underlying arrhythmia. Recently, Stereotactic ablative radiation therapy (SABR) is used for cardiac arrhythmias. Thus, aim of this analysis is to review preclinical, early clinical evidences and future direction of the latter new treatment approach.

Methods. Radiotherapy utilizes high dose of radiation to ablatethe target. From a radiobiological point of view, the higher dose of radiation (SABR) may theoretically produce greater biological cell kill respect conventional radiotherapy. Its action mechanism is partly unknown. A collection of available data regarding SABR and cardiac arrhythmias was made, including preclinical, clinical and technical data. A review of ongoing trials was conducted on ClinicalTrials.gov.

Results. Preclinical research conducted in animal models showed that a safe and effective noninvasive treatment approach for cardiac arrhythmias could be represented by SABR with a median time of response around 2–3 months. The treatment dose plays a crucial role: the atrioventricular node would seem more radiosensitive than the other cardiac electric zones. Clinical data, such as published case series, case reports and early prospective studies, have already suggested the feasibility, efficacy and safety of SABR (25 Gy in one session) for refractory ventricular tachycardia. Few data are available for Atrial Fibrillation, but the preliminary analysis showed no side effect and a possible advantage in the setting of elderly patients.

Conclusions. Considering the ongoing trials of SABR and new technological improvements in radiotherapy (e.g. hybrid magnetic resonance) and in arrhythmias noninvasive mapping systems, the future analyses will improve the reliability of those preliminary results.

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TUMORI PRIMITIVI DEL SISTEMA NERVOSO CENTRALE

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Currently, treatment for glioblastoma (GBM) includes radical surgery followed by standard radiotherapy course (60 Gy in 30 fraction) alongside concomitant and adjuvant temozolamide (TMZ).[1] Stereotactic radiotherapy is being investigated as the future standard of care for primary treatment in elderly/fragile patients and for recurrent disease. Elderly and/or frail individuals have a worse outcome, with an average OS of 6 months. Roa W. *et al.,*[2] proved that patients age 60 years or older benefit the most from hypo fractionations (40 Gy in 15 fractions) compared to conventional RT. The prospective phase III study[3] demonstrates that fractionated stereotactic radiosurgery (FSRT) (25 Gy in 5 fractions) is non-inferior to the 3-week course RT (40Gy in 15 fractions). The phase I/II study[4] defined the maximal tolerated dose for 5-fraction FSRT and concurrent TMZ 75 mg/mq^2, is 40 Gy. A multi-institutional randomized phase III trial[5] is ongoing. It aims to confirm the non-inferiority of FSRT (25 Gy in 5 fractions) and concomitant TMZ (150 mg/m2/day) over 40 Gy in 15 fractions and concurrent TMZ (75 mg/m^2/day). For recurrent GBM no standard of care exists. The median survival time after progression is 6.2 months.[6] Time to progression since the first RT course and the target volume are prognostic factors for survival. Patients maintaining good PS ECOG and having unifocal recurrence may benefit from local therapy with surgery and/or re-irradiation. Chemotherapy is given alone or after radical treatment based on the patient's clinical condition and the extent of the recurrent disease. Several studies showed patients with small and localized disease (4-10cc) can benefit from a single fraction radiosurgery of 15-18 Gy. If the cumulative EQD2 remains below 120 Gy, the rate of radionecrosis (RN) is <10%. Hypofractionated RT (hypo-RT) has also been investigated. The median OS varies between 7.5 to 12.5 months. Moderately hypo-RT included 10-15 fractions for a total doses up to 30-45 Gy. FSRT is a short RT course delivering least 5 Gy per fraction. The concomitant use of systemic therapies and RT improves outcome in both hypo-RT and FSRT with a median OS of 10 months. The risk of RN remains reasonable if the RT course is chosen according to the final volume of treatment and EQD2 dose calculation.[7] Stereotactic radiotherapy can be considered a reasonable treatment option for selected GBM patients, given its safer toxicity profile and survival advantage.

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RADIOCHIRURGIA ENCEFALICA: QUALE STANDARD NEL 2023? TUMORI SECONDARI DEL SISTEMA NERVOSO CENTRALE

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Aims. To analyze the role of radiosurgery in the treatment of brain metastases

Methods. PubMed searches were performed for reports published regarding radiosurgery in single and multi fraction for brain metastaes.

Results. Brain metastases (BMs) are the most common intracranial tumors in adults. The incidence is increasing due to the longer overall survival related to modern systemic therapies and the greater use of magnetic resonance imaging (MRI) able to detect also small lesions. Despite availability of new systemic therapies, in cases of limited number and/or volume of BMs, local treatment remains the mainstay: radiosurgery (SRS) or hypofractionated radiosurgery (HSRS) exclusive or after

surgery.[1]Recent guidelines recommend radiosurgery for the treatment of patients with limited brain disease (<4) and good performance status (PS), with local control rates >90%. In case of large and/or symptomatic brain lesions, surgical evaluation is necessary. In case of surgical removal of a brain metastasis, single or multifraction radiosurgery on surgical bed is recommended.[2] However, there are several potential drawbacks with postoperative SRS or HSRS, including a possible increase in symptomatic radionecrosis, due to uncertainty in target delineation and use of margins, and risk of leptomeningeal disease, uo to 30%. Therefore, there is a greater interest in use of preoperative SRS and several studies are currently ongoing.[3] If patient has asymptomatic brain metastases and is undergoing specific systemic therapy with an effect on the brain disease, such as ipilimumab plus nivolumab, osimertinib, tucatinib, alectinib, multidisciplinary discussion is mandatory, and local therapy may be delayed until there is evidence of intracranial progression.[4] Yamamoto et al. evaluated 3 groups of patients with 1, 2-4 and 5-10 brain metastases treated with radiosurgery. The OS of groups 2-4 and -10 was comparable.[5] For patients with intact brain metastases, up to 3 cm in diameter, single-fraction SRS is recommended. In case of lesion greater than 3 cm, multifraction radiosurgery is recommended, to reduce risk of radionecrosis.[6]

Conclusions. Radiosurgery is effective and safe treatment for intact brain metastases or after surgery, even in the era of new drugs.

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RADIOSURGERY FOR BRAIN BENIGN LESIONS: WHAT IS THE STANDARD IN 2023?

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Aims. Radiosurgery (SRS) has emerged as a highly effective and minimally invasive treatment modality for various brain benign lesions. This focused, non-invasive approach utilizes precisely targeted radiation beams to deliver therapeutic doses to pathological tissue while sparing surrounding healthy brain structures. Brain benign lesions encompass a wide spectrum of conditions, including meningiomas, vestibular schwannomas, arteriovenous malformations, craniopharyngiomas, and pituitary adenomas, among others. There are many treatment techniques including conservative, surgery and radiosurgery. For benign intracranial lesions, SRS provides a valuable alternative or adjunct to surgery, particularly for lesions situated in surgically challenging or critical brain regions. Moreover, it offers excellent prospects for patients who may not be suitable candidates for open surgery due to comorbidities or advanced age. We aimed to review safety and efficacy of SRS for intracranial benign lesions.

Methods. A comprehensive literature search focused on SRS for meningioma, schwannoma, arteriovenous malformations, craniopharyngiomas, and pituitary adenomas was performed. Analysis of clinical trials and guidelines was carried out.

Results. Primary SRS finds its indication in cases of intracranial meningiomas, schwannomas, and pituitary adenomas that are either asymptomatic or minimally symptomatic. Additionally, it is recommended when these tumors show growth on follow-up neuroimaging, when surgical risk is high, when patients have contraindications for surgery, or when they choose not to undergo surgery. SRS is also a suitable option following subtotal resection of WHO Grade I meningiomas, pituitary adenomas and schwannomas, either as an adjuvant therapy or in cases where follow-up reveals growth of the remaining tumor. For larger volumes or specific cases, hypo-fractionated SRS can often be considered. Furthermore, SRS serves as an effective treatment for certain arteriovenous malformations (AVMs), with an impressive 3-year obliteration rate of 80%. Finally, a combination of microsurgery and radiation therapy offers comparable local control and a 5-year survival rate exceeding 90%, all while demonstrating a superior toxicity profile when compared to total resection for craniopharyngiomas.

Conclusions. SRS provide good results in terms of safety and efficacy for intracranial benign lesions. Ensuring the best possible care is paramount because of the life expectancy and the potential for morbidity resulting from both tumor growth and recurrence, as well as the therapeutic interventions. Achieving optimal outcomes necessitates a multidisciplinary approach for the effective management of these brain lesions.

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RELAPSE PATTERNS AND TREATMENT INTENSIFICATION IN LOCALLY ADVANCED CERVICAL CARCINOMA

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Standard treatment in locally advanced cervical cancer patients is represented by exclusive platinum-based chemotherapy in combination with radiotherapy, which is then followed by brachytherapy. The frequency of cancer recurrence or persistent disease tends to be influenced by several factors. These factors include the initial stage and histology of the cancer, the incorrect dosage of radiotherapy administered, and other underlying risk factors.

For patients experiencing recurrence or persistence of the disease, various treatment options can be considered. These options include surgery, re-irradiation, and chemotherapy. Additionally, alternative strategies, such as thermoablation or cryotherapy, may be recommended to specific patients based on their unique needs and conditions.

Typically, when there is a small, centrally located recurrence or persistent disease, surgical intervention (through either a radical hysterectomy or exenteratio) is the primary treatment choice. However, in certain cases, brachytherapy can be an alternative. For patients with lateropelvic recurrences, the advancements in radiation technologies, including IMRT and heavy particle therapy, have paved the way for re-irradiation – a treatment that was historically considered unfeasible due to the risk associated with previous radiation doses. Since surgery is not recommended if the disease extends towards the pelvic wall, intraoperative radiotherapy (IORT) might be a viable option to effectively treat these sites.

In terms of chemotherapy, a regimen based on platinum and taxol, with or without the addition of bevacizumab, is the first line of treatment. Recent research, however, indicates that the inclusion of immunotherapy to this regimen could potentially enhance treatment outcomes. It is crucial to approach the treatment of locally advanced cervical cancer holistically. An interdisciplinary evaluation that takes into account various parameters - such as the patient's age, cancer histology, time elapsed since the relapse or persistence of the disease, co-existing medical conditions, specific anatomical details, and radiological imaging—is paramount. This comprehensive assessment ensures that patients receive tailored and optimal treatment. We will discuss the advantages and disadvantages of all these therapeutic alternatives, providing a comprehensive guide for radiation oncologists.

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VAGINAL RECURRENCE IN PREVIOUSLY IRRADIATED GYNECOLOGICAL CANCER: ROLE OF INTERVENTIONAL RADIOTHERAPY (3D IMAGE GUIDED BRACHYTHERAPY)

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Background. Local recurrence in gynecologic remains a highly challenging clinical issue, especially when it developes in a previously irradiated field. Most local cancer recurrences occur at the vaginal cuff, which is commonly within an area of prior radiation.[1] The most frequentlyproposed curative-intent treatment is surgery. Performing salvage surgery in previously irradiatedsites is technically challenging, with a high perioperative morbidity rate and substantial impact onlong-term quality of life.[2] Reirradiation may be an alternative option, but only scarce data based on retrospective series are available in this setting and no clear recommendations can guideirradiation technique or dose. Reirradiation, using three-dimensional image-guided brachytherapy(3D-IGBT), might be a suitable alternative. In the last decade, 3D-IGBT has benefited from majortechnological improvements. The use of computed tomography (CT) and magnetic resonanceimaging (MRI) for treatment planning has allowed a precise delineation of the tumor and organs atrisk(OARs), improving target dose coverage and minimizing doses to normal tissue.[3]

Methods. We reviewed recent literature on 3D-IGBT reirradiation as salvage treatment in previously irradiated vaginal recurrent gynecological tumors. We did a systematic literature search on PubMed using the following search terms and boolean operators: “vaginal recurrence” AND (“gynecologic neoplasm” OR “gynecologic malignancies” OR “gynecologic cancer” AND“brachytherapy” AND “reirradiation”.

Results. Considerable heterogeneity was found in many aspects: 3D-IGBT dose schedules, modalities of prior radiotherapy, target volume and OARs dose reporting and type of primary disease. Results in terms of outcome and toxicities were also highly variable among studies. These iusses make the formulation of strict recommendations difficult for 3D-IGBT reirradiation in recurrent pelvic malignancies.

Conclusions. 3D-IGBT reirradiation seems to be a feasible alternative to salvage surgery, with an acceptable outcome and toxicity for vaginal in previously irradiated gynecological cancers. Patients should be referred to highly experienced expert centers. Centralization of data and large-scale multicentric international prospective trials are warranted.

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GYNECOLOGICAL MALIGNANCIES AND RETREATMENT BY MEANS OF SBRT: IS THERE A ROLE?

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Aims. In the context of gynaecological cancers, SABR has three potential indications: (a) central recurrences after a previous course of conventional radiotherapy; (b) isolated nodal metastasis; (c) boost to central disease when brachytherapy is not feasible. There is an increasing interest for SABR for GYN malignancies in the field of recurrent disease (nodal or primary) in patients who have had prior radiation and/or have contraindications to brachytherapy or surgery. Unfortunately, there are some weaknesses such as the small number of single arm prospective clinical trials and several smaller retrospective series. Thus, clinical indications and techniques in these studies are vastly different and a standardized approach has not been adopted for GYN tumours worldwide.

Methods. A systematic literature review by means of PICO criteria was conducted, as follow:

- Population: GYN pts affected by central recurrences after radiotherapy
- Intervention: SABR after a previous course of radiotherapy
- Comparison: BRT on vaginal/cervical recurrence or chemotherapy on nodal recurrences
- Outcomes: LC, PFS, OS, toxicity

Results. Nine articles were identified. A total of 222 patients were analyzed. Primary tumor were mostly cervix and uterus with recurrent disease manly on nodal pelvic. The majority of re-SBRT were performed by means of cyberknife platform. Concerning the reference dose/fraction regimen the following recommendations were included: for lymph node recurrence (EQD2) = 36 Gy (15.6–60 Gy)/3–5 fx for recurrence at the primary site: EQD2 = 40.4 Gy (27–71.2 Gy)/3–5 fx. For the entire population of patients analyzed the median follow up was 29 months. One-year LC ranged from 51-95%. For the

cohorts with longer follow up 5-years LC was 79%. One-year OS ranged from 61-85%. For the cohorts with longer follow up 5-years LC ranged from 33-59%. Concerning the tolerability profile (physicians' reported outcomes) gastrointestinal grade ≥ 3 ranged from 5-14%.

Conclusions. There is limited data on re-treatment with SBRT in gynecologic cancers. Herein, it was provided some recommendations regarding results, appropriate indications and dose/fractionation for SBRT of pelvic recurrences in the previously irradiated pelvis. Prospective data are needed to ensure a standardized treatment paradigm and follow-up so that we can better understand how best to implement this treatment modality.

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THE ELDERLY PATIENT: PERSONALISING TREATMENT IN BREAST CANCER

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Aims. Breast cancer in the elderly patients is the most frequent cancer. As older patients tend to be excluded from clinical trials, randomized evidence for elderly patients receiving loco-regional treatment is limited. In these patients radiation therapy (RT) must take into account not only the biopathological features of the disease, but also the patients' general condition and comorbidities and must not have a detrimental effect on quality of life. Therefore, treatment should be as personalised as possible in order to achieve the best results with minimal side effects.

Methods. A narrative overview of the literature on different radiation treatment strategies for breast cancer in the elderly has been explored, with a focus on new strategies: ultra-hypofractionation for whole-breast irradiation, accelerated partial breast irradiation and omission of radiotherapy.

Results. For patients with early stage breast cancer, whole breast irradiation with moderate hypofractionation after breast conserving surgery represents the standard of care based on randomized data with long-term efficacy and toxicity outcomes. Whole breast radiotherapy with ultra-hypofractionated scheme according to the FAST-Forward protocol has demonstrated non-inferiority to standard fractionation and safety in terms of side effects. Accelerated partial breast irradiation has been found, in several randomized trials, to be effective and appropriate in selected patients with the potential to reduce toxicities as compared to whole breast irradiation. Results of some trials in patients older than 70 years treated with endocrine therapy show a small absolute benefit of RT, coupled with its potential for morbidity, therefore new clinical guidelines have included omission of RT as an option for elderly patients.

Conclusions. Evaluation of RT strategies in elderly patients should be handled with caution, taking into account tumour biology, comorbidities, performance status and patients preferences. The fear of side effects should not be the main criterion for omitting postoperative radiation therapy in elderly patients. Modern adjuvant radiotherapy strategies, such as accelerate partial breast irradiation and whole breast irradiation in five fractions may became an attractive treatment alternative for selected elderly patients.

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IL PAZIENTE ANZIANO: PERSONALIZZAZIONE DEL TRATTAMENTO - PROSTATA

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In 2022, the number of adults in Italy aged 65 or more was 13 million (23.5% of the total population), with 7 million being older than 75.[1] Prostate cancer represents the second most frequent neoplasm occurring in males worldwide and[2] in Italy the annual incidence is 37.000 cases, representing the more frequent cancer type in men older than 70.[1] In elderly patients, it can be extremely dif-

ficult to choose the appropriate therapeutic approach and this issue has led to a progressively diffuse under-treatment of such patients in the clinical practice. Moreover, this group is usually scarcely represented in clinical trials, and it is, therefore, ambitious to drive some conclusions about codified clinical management or get some data that are specific to this group from published randomized studies.[3] New developments in imaging, molecular biology, and genetics are going to help physicians in the clinical decision-making process through the integration of information coming from new biomarkers.

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THE ELDERLY PATIENT: PERSONALIZATION OF TREATMENT

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Non small cell lung cancer (NSCLC) is a neoplasm of the lung frequently diagnosed as locally advanced disease. The standard of care for unresectable tumors is chemo-radiation followed by consolidation immunotherapy, even among elderly patients.[1,2] This abstract aims to explore the optimal management approaches for this specific patient population, often characterized by relevant frailty, intended as a condition of increased vulnerability to stressors, regardless of age.[3] In this context it is necessary an accurate assessment of the patient performance status, in order to consequently define the best therapeutic approach. G8 scale and abbreviated comprehensive geriatric assessment (aCGA) are commonly used to determine the grade of frailty, thus allowing therapeutic schedules tailored on individual patient characteristics.[4] This approach may not necessarily improve overall survival (OS), but it can effectively impact on patients quality of life by reducing treatment-related toxicities.[5] RT remains a crucial component of the treatment for LA-NSCLC (locally advanced-NSCLC); in fact recent trials have proven its favorable toxicity profile, also in association with concomitant chemotherapy; also, the use of new radiation techniques enable the delivery of up to 60-66 Gy without causing severe side effects, providing the patient's functional pulmonary assessment (FEV1, DLCO).[6] CT-RT has demonstrated improved OS in all patients, making platinum-based doublets the preferred choice. Carboplatin-paclitaxel is favored over cisplatin-etoposide due to its better tolerability. In cases when doublets drugs administration is not feasible due to patient frailty, a low-dose carboplatin regimen can be considered.[7] Given the complexity of treating these patients, a multidisciplinary approach is essential to ensure effective treatment management and minimize treatment related-toxicities.[8] In recent years, immunotherapy has shown promising results in LA-NSCLC treatment. The PACIFIC trial has proven that platinum-based CT-RT, followed by consolidation durvalumab, improved OS[2] even in elderly patients. Subgroup analyses suggest that age does not significantly impact on the efficacy of immunotherapy, with senescent immune phenotypes potentially influencing treatment responses.[9] Regarding those patients who are not suitable for chemotherapy, the results of the DUART trial (radical RT followed by durvalumab) are strongly awaited.

In conclusion, when managing LA-NSCLC in elderly or frail populations, it is imperative to grade frailty with useful tools like CGA, allowing tailored treatments. In this context, immunotherapy and radiation therapy appear to be promising, because their effectiveness and toxicity is apparently influenced by patient health status and not necessarily by age.

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ELDERLY PATIENT WITH RECTAL CANCER: PERSONALIZED APPROACH

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Abstract. The number of older patients with rectal cancer is expected to rise significantly, paralleling the aging population.[1] Thus, the management of cancer in the older patients represents a priority for health care in the immediate future. Despite this fast-growing population, prospective data to guide the management of elderly patients are historically limited by their exclusion or underrepresentation in clinical trials, then the optimal treatment approach in this population remains unclear.

Although several studies reported that older patients with locally advanced rectal cancer (LARC, stage II/III) were less likely to receive standard therapy, some retrospective series showed that patients ≥70 years old had similar survival outcomes as younger patients treated with neoadjuvant chemoradiotherapy (CRT) and surgery.[2,3] Some evidence supports the benefits of short-course radiotherapy for elderly patients instead of standard long-course CRT in limiting toxicity,[4] with better compliance and improved outcomes among patients ≥75 years old.[5] Moreover, in node negative LARC organ preservation with local excision and a "watch and wait" approach was deemed to be feasible in the ACOSOG Z6041 trial, which included patients up to age 83.[6]

Total neoadjuvant treatment has recently been adopted for LARC. The PRODIGE-23 trial had an age cut-off of 75 years old, whereas older patients were not excluded from the OPRA or RAPIDO trials. Subgroup analysis by age of these studies is not yet available and their application in older or vulnerable patients is not clear. Then, a risk-adapted treatment remains a challenge and a personalized and tailored approach should be considered.

Comprehensive geriatric assessments (GA) are useful in predicting treatment-related toxicities and outcomes in older patients[7] using a multidisciplinary valuation of a patient's functional status, comorbidities, nutritional status, sensory deficits, social support, psychiatric well-being, and cognitive function, which are factors that may directly impact outcomes of older patients with cancer. A GA-guided treatment can assist in directing these treatment options and it is currently recommended for adapting the surgical, radiation, and chemotherapy approaches based on a patient's vulnerability.[8-9]

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IMAGE GUIDANCE ED INTELLIGENZA ARTIFICIALE IN RADIOTERAPIA INTERVENTISTICA

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Artificial intelligence (AI) plays a central role in building decision supporting systems (DSS), and its application in healthcare is rapidly increasing in interventional radiotherapy (brachytherapy - IRT).

Together with AI also image guidance allows modern treatments to be delivered in an adaptive way.

AI in IRT could have a significant impact in providing clinical decision support, data mining and advanced imaging analysis, automating repetitive tasks, optimizing time, and modelling patients and physicians' behaviours in heterogeneous contexts. Implementing AI and automation in IRT can successfully facilitate all the steps of treatment workflow, such as patient consultation, target volume delineation, treatment planning, and treatment delivery. AI could contribute to improve clinical outcomes through the application of predictive models and DSS optimization. This approach could lead to reducing time-consuming repetitive tasks, healthcare costs, and improving treatment quality assurance and patient's assistance in IRT. Large databases are very useful tools for generating

evidence, especially in the field of AI-based software which needs to be further implemented and integrated into clinical practice.

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RE-IRRADIATION: FROM IMRT TO PARTICLE THERAPY

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During the last decade a growing number of Re-RTs was performed, mainly due to the advancement of RT technology, such as SRT, IGRT and particle therapy. Actually, re-irradiation can be delivered for almost all recurrent tumors, and depending from different prognosis, with a curative or palliative intent. Anyway, due to the heterogenous group of patients, techniques, dose and fraction, the outcomes of reirradiation can be difficult to interpret.

The major challenge is to assess the adequate risk before Re-RT of potential complications in normal tissue. To date, there is a lack of sufficient data on recovery from radiation injury, so modern radiotherapy techniques allow to improve the organ at risks sparing, widening the therapeutic window.

Stereotactic radiosurgery and SBRT have helped create new indications for re-irradiation due to the delivery of an ablative dose to small tumours with a favourable side-effect profile.

Re-irradiation with particle therapy, thanks to the radiation dosimetry, is associated with comparable or potentially improved local control and less toxicity rates or compared to historical studies using photons. Prospective multi-institutional studies reporting oncologic outcomes, toxicity, and dosimetric treatment planning data are ongoing, probably will validate these findings and will improve the understanding of the clinical benefits of charged particle radiotherapy in the reRT setting. Currently, access to charged particle therapy varies widely, and criteria for its use is an area of research.

For all modalities, appropriate patient selection is of utmost importance and clinical trials are needed.

THE EVOLVING SCENARIO OF RADIOMETABOLIC THERAPY

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In the last decades the therapeutic options for patients with cancer increased dramatically with even more personalized, targeted directed cures and reduction of treatment related toxicity. The identification of tumor specific molecular targets, the availability of innovative technologies and the growing interest in quality of life of patients drove the developments in all the fields of oncology. Radionuclides (RN) therapy conjugates the properties of a systemic treatment with the mechanism of action of radiotherapy (RT) and experienced continuous innovation in the last decades. RN therapy history started in the 50s with the use of ^{32}P, ^{131}I and ^{89}Sr. Those RNs demonstrated efficacy in oncologic and non-oncologic diseased. The action of RNs principally consists in mimicking normal metabolic pathways. What makes metabolic RT unique is theranostics (TN), an invaluable tool in personalized medicine that allows to integrate diagnosis and therapy by targeting the same biological target with the same or a similar RNs. This is true for ^{131}I that works as tracer to define iodine-sensitive disease and as a therapeutic agent for iodine avid lesions.

What's new? Radio-ligand therapy (RLT) innovates this field enriching the concept of TN with a personalized and targeted approach. RLT acts through radiolabeled molecules (RMs) directed to specific cellular receptors to determine the expression of these biomarkers, like an in vivo immunohistochemistry, and to use these receptors as therapeutic targets. Nowadays, somatostatin and PSMA receptors have been identified for RLT approach in midgut neuroendocrine tumors (GEP-NET) and prostate cancer (PC), respectively. In 2017 phase III NETTER-1 study demonstrated that ^{177}-Lu-DOTATATE, increased progression free survival and response rate in comparison to octreotide LAR therapy in GEP-NET. More recently, the phase III VISION trial concluded that the addition of ^{177}-Lu-PSMA to standard of care can prolong progression

free survival and overall survival when compared to the standard of care alone in patients with metastatic castration resistant PC. The toxicity profile of RLT is acceptable since the activity of these RMs is limited to tumor cells that express the receptor.

RLT represent the evolving scenario from a metabolic to a molecular RT and is a powerful strategy of personalized cancer therapy that need to find an optimal timing in the clinical history of patients and a precise integration with other treatments.

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ADAPTIVE ONLINE RADIOTHERAPY: EVIDENCE AND FUTURE PERSPECTIVE

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The traditional approach to radiotherapy involves a static treatment plan that is determined prior to the start of treatment. However, recent advancements in imaging technology, computational power, and treatment delivery systems have enabled the development of adaptive online radiotherapy (AORT), a dynamic and personalized approach that adapts treatment plans in real-time based on the patient's anatomy and response.

AORT utilizes advanced imaging techniques, such as cone-beam computed tomography (CBCT) and magnetic resonance imaging (MRI), to capture the current anatomical information of the patient at each treatment fraction. By incorporating these imaging data into the treatment planning process, AORT enables the modification of the treatment plan to account for changes in tumor size, shape, and position, as well as organ motion. This dynamic adaptation improves treatment accuracy, increases tumor control probability, and minimizes radiation-related toxicity to surrounding healthy tissues.

Several studies have demonstrated the efficacy of AORT in various cancer types, including lung, prostate, and head and neck cancers. For instance, in lung cancer, AORT has been shown to reduce target volume margins, resulting in better sparing of nearby critical structures. Furthermore, the use of AORT in prostate cancer allows for a reduction in the volume of irradiated normal tissues, potentially reducing the risk of long-term side effects. These findings suggest that AORT has the potential to improve treatment outcomes and enhance patients' quality of life.

The implementation of AORT requires a robust integration of imaging, treatment planning, and delivery systems. Techniques such as deformable image registration, automated segmentation algorithms, and online plan optimization algorithms are crucial components of AORT. Additionally, real-time imaging modalities, such as MRI-guided radiotherapy, have shown promise in providing accurate and timely anatomical information for adaptive replanning. While AORT presents numerous advantages, there are challenges to overcome for its widespread adoption. Technical considerations, such as the computational demands of real-time replanning and the limitations of current imaging technologies, need to be addressed. Furthermore, the development of standardized protocols and guidelines for AORT implementation is necessary to ensure consistency across different treatment centers.

Looking ahead, the future of AORT holds great promise. Emerging technologies, such as machine learning and artificial intelligence, have the potential to further enhance the capabilities of AORT. These technologies can assist in real-time treatment plan adaptation, predict treatment response, and optimize individualized treatment strategies. Moreover, the integration of AORT with other treatment modalities, such as immunotherapy and targeted therapies, may lead to synergistic effects and improved patient outcomes.

Selected Oral Communications

B01

THE RADIOTHERAPY OMISSION WITHIN THE SINODAR ONE PROTOCOL: SURVIVAL AND RELAPSE OUTCOMES

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Aims. We conducted a re-analysis of the data from the SINODAR-ONE phase III randomized trial, focusing on the omission of radiotherapy. The primary objectives of the study were overall survival (OS) and locoregional relapse (LRR).

Methods. Patients with T1-2 breast cancer and 1-2 macrometastatic sentinel lymph nodes were randomly assigned in a 1:1 ratio to either undergo removal of ≥10 axillary level I/II non-sentinel lymph nodes followed by adjuvant radiotherapy (standard arm) or receive no further axillary treatment (experimental arm).

Results. From 2015 to 2020, a total of 889 patients were enrolled and randomized. The median follow-up period was 34.0 months. Radiotherapy data were available for 510 patients, with 238 in the control arm (ARM 1) and 272 in the experimental arm (ARM 2). The radiotherapy techniques used were as follows: 206 patients received 3D conformal radiotherapy, 80 received VMAT, 46 received IMRT, 2 received Tomo, 1 received IORT, and for 175 patients, the technique used was not known. In ARM 1, 30 patients (12.6%) were found to have N2-3 disease after nodal dissection, and 46 patients underwent locoregional irradiation (15 with stage I-II disease, 33 with stage III-IV disease, and 1 with IMC) according to institutional guidelines. In ARM 2, no axillary dissection was performed, and no locoregional radiotherapy was administered. In ARM 1 and ARM 2, we observed 1 and 2 deaths, and the rates of locoregional relapse were 5 (2.1%) and 7 (2.5%), respectively. Statistical analysis did not reveal any significant differences between the two arms.

Conclusions. In T1-2 breast cancer patients with 1-2 macrometastatic sentinel lymph nodes treated with sentinel lymph node biopsy alone, the 3-year survival and relapse rates were not inferior to those of patients treated with axillary lymph node dissection plus or minus locoregional radiotherapy.

B02

CARDIOLOGICAL SAFETY OF 5-FRACTION WHOLE BREAST IRRADIATION: SAFE-FORWARD TRIAL

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Aims. Our study aims to assess heart toxic effect using a reliable cardiac assessment with standard and 3-dimensional (3D) echocardiography and left ventricular (LV) global longitudinal strain (GLS) in breast cancer (BC) patients receiving postoperative whole breast irradiation (WBI) with Fast Forward schedule (total dose 26Gy in 5 fractions).

Methods. SAFE-FORWARD is an observational prospective cohort study (NCT04842409). Inclusion criteria were invasive BC with indication to receive ultra-hypofractionated WBI (26 Gy in 5 fractions) after breast conserving surgery (BCS) without cardiovascular comorbidity and previous thoracic irradiation. All enrolled patients have been prospectively monitored for 12 months, receiving a complex cardiological assessment before RT start (baseline), and at 2-, 6-, and 12-month after the end of treatment. Both acute and early late toxicity have been evaluated according to Common Terminology Criteria for Adverse Events (CTCAE) v.5.0 scales. The primary endpoint was the detection of any subclinical impairment in myocardial function and deformation (decrease ≥10%) measured with standard and 3D echocardiography and LV GLS.

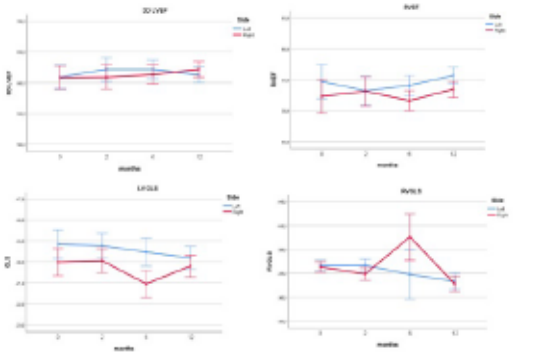

Figure 1.

Results. Overall, 40 women (median age 66 years; range 48-84) were enrolled in the study. We analyzed patients who had completed the cardiological assessment at 12 months. All patients received ultra-hypofractionated WBI, 25 patients also received adjuvant endocrine therapy. GLS worsened 4% or less, both for left- and right-sided treated breast, and remained in normal range for all the time points. The only exception was for right ventricular (RV) GLS at 6 months for right-sided treatment where a borderline value was reached (-17.4±4.9 SE). 3D LV Ejection Fraction (EF) remains stable during observation, both for the left- and right-side treated breast.

Conclusions. The 5-fraction WBI schedule after BCS is well tolerated and the intensive 1-year cardiological monitoring showed no significant differences overtime in cardiac functioning.

B03

PRE-OPERATIVE SINGLE-FRACTION STEREOTACTIC RADIOSURGERY (SRS) FOR EARLY-STAGE BREAST CANCER: PATHOLOGICAL AND RADIOLOGICAL RESULTS

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Aims. We present pathological and radiological data of the Phase II clinical trial investigates toxicity related to pre-operative SRS in early stage breast cancer.

Methods. The phase II clinical trial enrolled women older than 50, with proven breast invasive non special type carcinoma, hormonal receptors positive/HER2NEU negative, any grade, tumor size < 3cm, unifocal, with no nodal involvement candidates to conservative surgery. A qualified radiologist injected with ultrasound-guidance, a fiducial marker to identify the Gross Tumor Volume exactly. The Planning Target Volume is created by adding a 3mm margin to GTV. The total dose prescribed to the 95% of PTV was 30-36Gy. Patients had a breast MRI scan 6-12 weeks after treatment to evaluate the rate of radiological response. Patients had outpatient surgery 9 to 16 weeks post SRS.

Results. From January 2022 to December 2022, we treated 32 patients with a single-fraction SRS upfront breast conserving surgery. According to the study protocol, for the initial 15 patients, the total dose prescribed was 30 Gy and surgery was performed at 10 weeks. We prescribed 33 Gy to the next 15 patients and delayed their surgery to 15 weeks. We treated the last 2 patients with 36 Gy and performed surgery at 19 weeks. Twenty-six patients (81%) had a breast MRI scan before surgery. Fifty-four percent of the participants achieved a radiological complete response. The pathological response was

defined as complete response (pCR) if no residual tumor cells were found, pathological partial response (pPR), or no response. The pPR group was subdivided into 3 categories based on the rate of residual disease: < 10%, 10-50%, and > 50%. Two patients (6%) achieved pCR, 3 patients (9%) had no response. Twenty-seven patients (84%) had pPR, of which 7 patients had residual disease < 10%, 10 patients between 10-50% and 10 patients over 50%. All patients had sentinel lymph node biopsy at the time of surgery. Positive micrometastatic nodal involvement was found in 3 patients (11%), of which 2 patients (7%) had macrometastases (pN1a) and got subsequent axillary lymph node dissection. One patient had close margins for the in situ tumor and underwent additional surgery. Four patients (12%) got surgical complications: 1 breast seroma, 2 axillary seromas and 1 mastitis.

Conclusions. Most of the patients after SRS achieved partial or complete pathological response. Currently, data are not sufficient to compare radiological and pathological analyses.

B04

SUBJECTIVE AND OBJECTIVE DEGLUTITION OUTCOMES AFTER SWALLOWING (SWOARS)-SPARING IMRT IN HEAD AND NECK CANCERS: DEFINITIVE RESULTS FROM A PROSPECTIVE MULTICENTER STUDY ENDORSED BY THE HEAD AND NECK STUDY GROUP (HNSG) OF THE ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY (AIRO)

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Aims. To prospectively investigate changes in objective deglutition scores and to correlate them with MDADI scores in patients (pts) affected by naso and oropharynx cancer after definitive radiochemotherapy using SWOARs-sparing IMRT (Clinical Trial ID NCT03448341).

Methods. Pts underwent objective evaluation by means of Fiberoptic Endoscopic Evaluation of Swallowing (FEES) and Videofluoroscopy (VFS) together with subjective evaluation by means of MDADI questionnaire at baseline and at 6 and 12 months after treatment. Pts were categorized in two groups based on baseline MDADI-C value: MDADI-C≥80 and MDADI-C<80. The amount of pharyngeal residue (PR) and the occurrence of penetration and/or aspiration (P/A) were considered as surrogate of dysphagia. Specifically, PR was categorized as 0: absence; 1: mild; 2: moderate; 3: severe and dichotomized as 0-1 *vs* 2-3.

Results. Between August 2015 and November 2021 we enrolled 75 pts of whom 40 (53%) were MDADI-C >80 and 35 (47%) were MDADI-C<80 at baseline. Among MDADI-C≥ 80 pts group the mean baseline PR-score at FEES was 0,42 rising to 1,36 at 6 months (p=0,001) and stabilizing to 1,15 at 12 months (p= 0,21); indeed, the mean baseline PR-score at VFS was 0,55 rising to 1 at 6 months (p=0,069) and slightly dropping to 0,7 at 12 months (p=0,069). Among MDADI-C <80 pts group the mean baseline PR-score at FEES was 0,56 rising to 1,07 at 6 months (p=0,012) and stabilizing to 1,07 at 12 months (p=0,99); indeed the mean baseline PR-score at VFS was 0,67 rising to 1,19 at 6 months (p=0,04) and dropping to 0,78 at 12 months (p=0,04). No correlation was found between baseline dichotomized MDADI-C group and PR-score both at FEES and VFS at the 3 different time intervals. Indeed, a statistical significant correlation was found between PR-score and P/A at VFS at 12 months after treatment (p<0,001).

Conclusions. Our results suggest objective deglutition benefit of dose optimization to SWOARs by means of mean low objective scores after treatment both in MDADI-C ≥ 80 and MDADI-C<80 pts group. This means that subjective referred dysphagia is likely not to be associated to a major functional deglutition impairment in our daily clinical practice.

B05

HIGHLY TAILORED ANAL CANCER MRI GUIDED INTERVENTIONAL RADIOTHERAPY: HIT-ART STUDY UPDATE

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Aims. The aim of this study is to investigate the outcomes in terms of treatment compliance, in terms of overall treatment time (OTT), toxicity, treatment response (cCR), loco-regional failure (LRF), colostomy failure

(CFS) and overall survival (OS) in a cohort of patients treated with personalized chemoradiation (CRT) followed by image (MRI) guided Interventional Radiotherapy (IRT, also called brachytherapy, BT).

Method. We analyzed patients with histologically proven squamous anal carcinoma, prospectively treated using intensity modulated radiation therapy (IMRT) and IRT boost. External beam radiation was delivered using personalized IMRT technique with a SIB to deliver 45 to 55 Gy in 25 fractions according to clinical stage. Two to three weeks after the end of the CRT patients underwent clinical and imaging re-evaluation, and according to initial stage of disease and tumor response, a radiotherapy boost was administered via Image Guided Interventional Radiotherapy (IG-IRT), performing MRI with IRT applicator on site (trans-anal position) and defining GTV on MRI imaging.

Results. 62 patients treated between January 2012 and October 2021 were included in the analysis. 69% were female, with a median age of 64.8 years (range 39.1-90). 55 were staged T2-T4 (T2 43.5%, T3 19.4%, T4 25.8%) and 42 (67.7%) had positive nodes. OTT median was 79 days (range 44-225). Acute toxicity ≥G3 was recorded in 11 patients (17.7%). No acute severe toxicity was recorded after boost IRT. Late urinary tract toxicity levels were negligible (G1 in 4 pts). No severe G4 late toxicity was recorded. The LC at 3 and 5 years was 84%. CFS was 90.1% at 3y (CI 82.1-98.8%) and 74.1% at 5y (CI 59.8-91.8%). OS at 3 and 5 years were, respectively, 87.6% (CI 77.8-98.6%) and 79.1% (CI 65.8-95.2%). At univariate analysis we verified that OS was higher in patients who had an OTT lower than 93 days. There was no correlation between outcomes and initial T and N stage.

Conclusions. Image Guided Interventional Radiotherapy boost is a feasible treatment option with low toxicity burden and significant impact on outcomes. IRT boost can offer the opportunity to pursue a real treatment personalization due to the possibility to decrease the dose to organs at risk while increasing the dose to the tumor according to risk factors (mainly stage at diagnosis) and response to IMRT treatment. Our experience prompts the definition of a multicentric study to validate such approach.

B06

STEREOTACTIC BODY RADIOTHERAPY AND ARTIFICIAL INTELLIGENCE IN OLIGOMETASTATIC GYNAECOLOGIC CANCER: A LARGE, REAL-WORLD STUDY ON RESPONSE PREDICTION, EFFICACY, AND OUTCOMES

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Aims. No accurate prediction models for clinical outcomes of gynaecologic oligometastatic cancer treated with SBRT exist, nor is it clear if attaining a complete response (CR) following SBRT influences oncologic outcomes.

Methods. A pooled real-world analysis of gynecological oligometastases in terms of efficacy and clinical outcomes as well an exploratory machine learning model to predict the CR to SBRT were carried out. The clinical CR rate of disease following SBRT was the study main endpoint. The secondary endpoint included the 2-year actuarial local control (LC) rate, defined on a "per-lesion" basis as the disease progression within the SBRT field of irradiation. The machine learning analysis included the selection of reliable prognostic variables and the model training, validation, and testing.

Results. 501 patients from 21 radiation oncology institutions with 846 gynecological metastases were selected for analysis. The majority of lesions were ovarian (449, 53.1%) and uterine metastases (272, 32.1%) in origin, followed by 125 (14.8%) lesions from cervical cancer. Multiple fraction radiotherapy was used to treat 762 metastases (90.1%). The most frequent schedule was 24 Gy in 3 fractions (13.4%). Complete response (CR) was observed in 538 (63.7%) lesions. According to the machine learning model, in uterine cancer, if BED10>78.3Gy, the CR probability was 75.4%; moreover, if volume was less than 13.7cc, the CR probability became 85.1%. In ovarian cancer, if the lesion was a lymph node, the CR probability was 71.4%; if volume was less than 17.0cc, the CR probability rose to 78.4%. The overall 2-year actuarial local control rate was 79.2%, however, it was 91.5% for CR and 52.5% for not CR lesions (p<0.001). The overall 2-year actuarial PFS and OS rates were 27.3% and 71.0%, respectively, with significant differences between CR and not CR.

Conclusions. CR to SBRT was substantially associated to patient outcomes in a large series of oligometastatic lesions from gynecological cancer. The ability to predict a CR through artificial intelligence can also drive treatment choices in the context of personalized oncology.

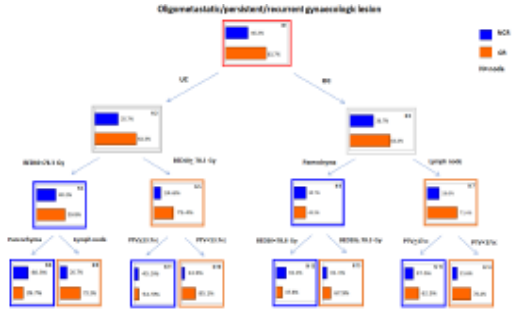

Figure 1. Classification and Regression Tree analysis (CART) for the most informative variables.

B07

EARLY SALVAGE RADIOTHERAPY IN PATIENTS WITH INTERMEDIATE-RISK PROSTATE CANCER: IS IT FEASIBLE? PRELIMINARY RESULTS OF A PROSPECTIVE STUDY ON 721 PATIENTS (EASY-1: EARLY SALVAGE RADIOTHERAPY-1)

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Aims. Postoperative treatment in patients with prostate cancer (PCa) treated with radical prostatectomy (RP) and adverse pathology is still matter of debate since adjuvant (aRT) and early salvage radiotherapy (esRT) showed comparable biochemical recurrence free survival (BCR-FS). The aim of this analysis is to evaluate feasibility and early oncological outcome of intense surveillance and esRT in the postoperative management of PCa patients with intermediate risk of recurrence after surgery.

Methods. We enrolled 721 PCa patients who underwent RP in a prospective trial (EASY-1: EArly Salvage radiotherapY-1). Inclusion criteria were: PCa treated with RP, pT2 with positive surgical margins (R1) or pT3a regardless of surgical margins status or pT3b with negative surgical margins (R0), and PSA undetectable 40 days after surgery (<0.01). Patients with nodal metastases were excluded. The surveillance protocol included PSA assessment every 2 months after surgery during the 1st year, every 3 months during the 2nd and 3rd year, followed by PSA every 4 months until the 5th year, then every 6 months until the 10th year after surgery. EsRT was delivered in case of biochemical relapse (BCR, two consecutive values of PSA ≥0.2 ng/ml). A multivariate Cox regression model was used to assess independent predictors of BCR.

Results. Overall, 262 (38%), 251 (36.4%), 121 (17.6%) and 53 (7.7%) patients had pT2R1, pT3aR0, pT3aR1 and pT3bR0 PCa, respectively. Considering R1 patients, a positive surgical margin ≥3 mm has been found in 59% of men. Gleason Grade at margin was 3, 4, 5 in 178 (46.1%), 139 (36%) and 5 (0.3%), respectively. Overall, 64 (9.3%) patients experienced BCR (median follow-up: 39 months). The median time to BCR was 15 months (IQR 8-21), and the median PSA at BCR was 0.21 ng/mL (IQR 0.18-0.32). Out of 64 patients with BCR, 60 (90%) were treated with esRT. The 5-year BCR-

FS rate was 85.5%. Patients with pT2R1/ISUP 4-5 and those with pT3/ISUP 4-5 regardless margin status had significantly lower BCR-FS compared to men with pT2R1/ISUP 1-3 and pT3/ISUP 1-3 ($p \leq 0.01$). At multivariate analysis, pathologic ISUP 4-5 (HR 2.2) and pT3R1 (HR 2.56) were independent predictors of BCR (all $p \leq 0.003$).

Conclusions. Intense surveillance with PSA monitoring after RP and early detection of BCR followed by esRT may allow for high BCR-FS rates in patients with intermediate-high risk PCa; pISUP 4-5 and pT3aR1 status are independent predictors of BCR.

B08

PROFILING PCA PATIENTS WITH BCR IN THE ERA OF EARLY IMAGING DETECTION: AN AIRO-URO GROUP STUDY

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Aims. Although radical prostatectomy (RP) represents a curative treatment, 44% of pts experience BCR at least 6 months after surgery. While in low-risk pts the interval between surgery and BCR does not influence mortality, in pts with unfavorable disease characteristics early disease recurrence increases mortality risk. Aim of this study is to create a predictive model to identify the category of pts most at risk of local or distant metastasis to undergo early imaging investigations.

Methods. Data have been acquired from Italian centers joining the AIRO-URO initiative. Pts who underwent RP and salvage RT after experiencing BCR have been considered. Descriptive and frequency analysis has been performed and mean time to event has been calculated. Disease progression after salvage RT (sRT) has been considered as event in time-to-event analysis. Univariate Cox regression was used and significative covariates ($p<.05$) were included in multivariate Cox regression.

Results. A total of 1650 pts (median age 64.3 y) with a median follow-up of 4.4 y (range 0.1-15.9) were included in the analysis, 647 of them (39.2%) underwent imaging pre-sRT. IMRT/VMAT accounted for 96.2% of treatments. A Total of 555 of 1450 evaluable cases (38.2%) of biochemical disease progression events have been considered eligible for the analysis, of which 492 (33.9%) were also considered as clinical progression. Site of progression (available for 482 pts) was pelvic and distant progression in 42% and 57% of the pts. The covariates found significantly in the univariate analysis with BCR after sRT as outcome were: post-operative ISUP grade ($p<.05$), pT ($p<.05$), pN ($p<.05$), HT during sRT ($p<.05$), boost at prostatic fossa ($p<.05$), boost at positive LN ($p<.05$), time <12 months at sRT ($p<.05$). At multivariate analysis, HT during sRT ($p<.05$), post-operative ISUP grade ($p<.05$), boost at prostatic fossa ($p<.05$) were considered significant.

Conclusions. Given the results of the present preliminary analysis which reports a high recurrence rate, it remains of relevant importance to continue to offer potentially curative salvage treatment. In the PSMA-PET and WB-MRI era, and the ability to detect potentially distant metastatic disease so early, it becomes crucial to select pts for such examination based on criteria and clinical stratification. The present and future analyses based on a retrospective experience will lay the foundation for better understanding how to target care in this patient setting.

B09

PHASE 2 TRIAL EVALUATING ABLATIVE STEREOTACTIC BODY RADIOTHERAPY (SBRT) AFTER INDUCTION CHEMOTHERAPY (CHT) FOR PATIENTS WITH UNRESECTABLE LOCALLY ADVANCED PANCREATIC CANCER (LAPC): FINAL RESULTS OF LAPC02 STUDY (NCT03158779)

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Aims. Stereotactic Body Radiotherapy (SBRT) represents a safe and effective therapeutic option for patients with unresectable locally advanced pancreatic cancer (LAPC), but disappointing overall survival (OS) rates of these patients remains a relevant open issue. The aim of this study is to assess the efficacy of sequentially integrated treatment of CHT and ablative pancreatic SBRT.

Methods. Unresectable LAPC patients were enrolled

in a prospective monocentre phase II trial (NCT03158779) of sequentially integrated CHT and ablative SBRT. All patients received induction CHT with FOLFIRINOX or Gemcitabine-NabPaclitaxel scheme. For all patients radiation dose was 54 Gy in 6 fractions. Primary end point was overall survival (OS). Secondary end points were toxicity, freedom from local progression (FFLP) and progression free-survival (PFS). In selected patients, markers were implanted into the tumor, to evaluate the ability to guide the application of SBRT.

Results. From 2017 to 2019, we enrolled 45 patients, with a median follow up of 23.2 months. Median age was 67 years. Median tumor diameter and median Ca 19.9 value at the time of diagnosis were 40 mm and 2030 U/mL, respectively. Chemotherapy schemes were FOLFIRINOX in 17 (38%) patients and Gemcitabine-NabPaclitaxel in 28 (62%) patients, with a median number of administered CHT cycles of six. Median OS was 23,2 months, with an OS rates at 1, 2 and 3 years of 91,1%, 46,7%, and 15,6%, respectively. Median FFLP was not reached and FFLP at 1, 2 and 3 years were 93,1%, 75,7%, and 70,7%, respectively. Median PFS was 13,4 months, with a PFS rates at 1, 2 and 3 years of 55,6%, 15,6% and 6,7%, respectively. At multivariate analysis, CHT response was related to a better OS (p= 0.015). In 12 (27%) patients, at least 2 gold markers were implanted into the tumor before the SBRT. In 7 patients, fiducial placement was made difficult due to increased hardness of lesion nearest vessels and poor control in the first marker release. One patient showed a minimal migration of one fiducial (<3 mm). No patients experienced acute and/or late G3 toxicity or higher.

Conclusions. Multimodality treatment of induction CHT and ablative SBRT showed promising results in terms of OS and local control for patients with unresectable LAPC. Tumor response after induction CHT proved to be a significant prognostic factor for survival.

B10

THERAGNOSTIC UTILITIES FOR NEOPLASTIC DISEASES OF THE RECTUM BY MRI GUIDED RADIOTHERAPY (THUNDER 2) PHASE II TRIAL: INTERIM SAFETY ANALYSIS

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Aims. Thunder 2 is a prospective clinical trial that focuses on exploring the potential therapeutic and diagnostic benefits of MRI-guided radiotherapy (MRIgRT) for locally advanced rectal cancer (LARC). Its primary aim is to assess the impact of escalating radiotherapy (RT) doses in LARC patients who have been identified as poor responders based on the Early Tumour Regression Index (ERI) on likelihood of achieving both pathological and clinical complete response. This interim analysis aims to evaluate the safety and feasibility of implementing the dose escalation MRIgRT strategy within the clinical trial.

Methods. The trial enrolled LARC patients at stage cT2-3, N0-2, or cT4 with anal sphincter involvement, N0-2a, M0, but without high-risk features. All patients underwent MRIgRT treatment, which involved an initial RT dose of 55 Gy to the Gross Tumor Volume (GTV) along with the corresponding mesorectum, and 45 Gy to the mesorectum and drainage nodes delivered in 25 fractions. Continuous administration of fluoropyrimidine-based chemotherapy was combined. A 0.35 Tesla MRI was obtained at the simulation phase and daily throughout the MRIgRT treatment. At the 10th fraction, the ERI was calculated. If the ERI value was found to be <13.1, the patient continued with the original treatment plan. However, if the ERI was>13.1, the patient was considered "non-responder" and underwent a re-optimization of the treatment plan, intensifying the RT dose to the GTV from the 11th fraction onwards to reach a total dose of 60.1 Gy. Acute toxicity was assessed using the CTCAE v.5 scale. Data were retrospectively collected and analysed.

Table 1.

32 pts tot	Toxicity (CTCAE v 5.0) N (%)			
	G1 21 (65.6)	G2 7 (21.9)	G3 1 (3.2)	
15 boost	11 (34.4)	4 (12.5)		
17 no boost	10 (31.2)	3 (9.4)	1 (3.2)	
Proctitis	7 (21.9)	1 (3.2)	1 (3.2)	9 (28.1)
Diarrhoea	12 (37.5)	2 (6.3)	1 (3.2)	15 (46.9)
Tenesmus	13 (40.7)	1 (3.2)		14 (43.9)
Mucorrhoea	15 (46.9)	3 (9.4)		18 (56.3)
Cystitis	8 (25)		1 (3.2)	9 (28.1)
Asthenia	8 (25)	1 (3.2)		9 (28.1)

Results. Between March 2021 and November 2022, a total of 33 out of 63 patients (52.4%) were enrolled in the study. Of these, one patient withdrew from the study due to the development of cardiac disorders unrelated to the proposed treatment. 15 out of 32 patients (46.9%) underwent replanning with the boost. The treatment was generally well tolerated, with only one patient (3.1%) developing acute Grade 3 diarrhea, proctitis, and cystitis observed in the group receiving standard treatment. No significant differences in toxicity were found between the two groups, as indicated in Table 1.

Conclusions. Our findings indicate that MRIgRT treatment, incorporating dose escalation up to 60.1 Gy based on predicted response using the ERI index for

LARC patients, is well-tolerated. Analyses of primary and secondary outcomes are pending completion of patient enrolment.

B11

SURVIVAL OUTCOMES AND PREDICTORS OF RESPONSE IN OLIGOMETASTATIC COLORECTAL CANCER PATIENTS TREATED WITH STEREOTACTIC BODY RADIATION THERAPY (SBRT): IMPORTANCE OF TUMOUR VOLUME

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Aims. Understanding and identifying predictive factors is strongly necessary for a successful treatment strategy of oligometastatic colorectal cancer (CRC) patients. The aim of our study is to describe clinical outcomes and predictive factors of a large cohort of oligometastatic patients affected by CRC treated with Stereotactic body radiation therapy (SBRT).

Methods. In this single-centre analysis, we included all the oligometastatic CRC patients treated with SBRT on up to 5 metastases in maximum 3 organs. Concomitant systemic therapy was allowed. All the patients were treated with Volumetric Modulated Arc Therapy (VMAT) technique. End-pints were local control (LC), progression-free survival (PFS), and overall survival (OS). Univariate and multivariate analysis was performed by Stata14 to correlate outcomes to prognostic factors.

Results. From 2008 to 2022, 347 patients were treated for a total of 516 oligometastases. Median follow-up was 32.4 months (6-157.6). Patients and treatment characteristics are reported in Table 1. Median OS was 51.6 months, with rates of 94.9% (91.9-96.8), 63.8% (58.0-69.1), and 45.1% (38.9-51.2) at 1, 3, and 5 years respectively. Factors associated with a worse OS were performance status [95%CI 1.09-2.56 p=0.018], in-field progression [95%CI 1.10-2.06, p=0.010], and tumor volume > 14.1 cc [95%CI 1.07-1.97 p=0.014]. Median LC was not reached, with 1, 3 and 5-years rates of 79.4%, 67.8%, and 67.8%, respectively. The number of treated metastases [95%CI 1.11-3.03 p=0.017] and the BED [95%CI 0.98-0.99 p=0.000] were significantly associated with local recurrence. The median PFS was 8.9 months. After one year, 38.9% of our patients reached a stable disease status [33.7-44.2], which was maintained by 16.2% and 15.2% after 3 and 5 years respectively [12.2-20.7 and 11.3-19.7]. Worse PFS was observed for multiple metastases [95%CI 1.03-2.10 p=0.030], and incomplete ablation [95%CI 1.38-2.34 p=0.000].

Conclusions. SBRT is an effective treatment, achieving promising outcomes in oligometastatic CRC. Our study highlights the importance of both the number of treated metastases and the total tumour volume for the prediction of patient's outcomes. Further prospective trials are required to better identify which class of patients could benefit more from SBRT.

Table 1. Patients and treatment characteristics.

CHARACTERISTICS	FREQUENCY (%)
N° patients	347
N° treatments	516
GENDER	
Female	125 (36%)
Male	222 (64%)
PS	
0	231 (66.6%)
1	80 (23.0%)
2	36 (10.4%)
PRIMARY SITE	
Colon	236 (68%)
Rectum	89 (25.6%)
Sigma	22 (6.4%)
TREATED METASTASES	
1	207 (59.65%)
2	85 (24.50%)
3	44 (12.68%)
4	5 (1.44%)
5	6 (1.73%)
TREATED ORGANS	
1	307 (88.4%)
2	36 (10.37%)
3	4 (1.15%)
UNTREATED LESIONS	
No	199 (57.51%)
Yes	147 (42.49%)
SYSTEMIC THERAPY BEFORE SBRT	
No	86 (24.78%)
Yes	261 (75.22%)
N TREATMENTS PER PATIENT	
1	396
2	85
3	25
4	7
5	2
6	1
Time to metastases	21.2 months (0 - 167.9)
Tumor volume, median in cc	14.1 cc (0.4 cc - 596.9 cc)
Total delivered dose	48 Gy (25 Gy – 75 Gy)
Number fractions	4 fractions (1 – 10)
BED minimum	105.6 Gy (35.7 Gy - 262.5 Gy)

B12

PERMANENT ALOPECIA AFTER CRANIOSPINAL IRRADIATION IN SURVIVORS OF PEDIATRIC BRAIN TUMORS: A MULTIFACTORIAL ANALYSIS

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Aims. To define the threshold doses to scalp for permanent alopecia onset combining endocrine, chemotherapy, and clinical data with radiotherapy data.

Methods. We retrospectively analyzed patients treated for childhood brain tumors (Medulloblastoma, Ependymoma, Germinoma) with craniospinal irradiation (CSI) at our center between 2006 and 2021. We created an Atlas-based self-segmentation using RayStation version 12A-SP1 to provide a more efficient and accurate method for identifying specific areas of the scalp. To validate the atlas, we calculated the average contouring time, standard similarity metrics of 3D DICE similarity coefficient and mean agreement distance (MDA). We then conducted a preliminary analysis of the data on a smaller cohort of patients (the atlas control cohort) to identify threshold doses that may justify the onset of permanent damage. We collected clinical data to stratify the threshold dose based on clinical, chemotherapy, radiotherapy, and endocrine factors. All patients were followed up with regular oncological follow-up. Alopecia was assessed according to CTCAE version 5.0 scale (G1 mild alopecia, G2 severe alopecia, G0 no alopecia).

Results. We evaluated 56 patients treated with CSI. 15 (27%) patients experienced G1 and 14 (25%) patients experienced G2 whole scalp alopecia. Table 1 shows the distribution of toxicity in the variables under study. The use of the atlas demonstrated an 80% time saving for the operator, with the following results. DICE 0.76±0.05; Sensibility 0.77±0.05; Specificity 0.78±0.09; MDA 0.50±0.02. Preliminary analyses of the first patient sample identified that the median Dose hair skin was statistically significant (OR: 1.216; 95%CI: 1.030-1.435; p=0.021), with a cut-off value of 28.7 Gy. If the median dose of each Gy unit of D median is exceeded, the probability of alopecia increases by 21.6% (3.0-43.5%), with a specificity of 90.9%.

Conclusions. The scalp self-segmentation atlas provides valuable support for rapid scalp contouring. Permanent hair loss is confirmed to be dose-dependent. The data identifying the threshold dose to the scalp stratified based on the risk factors included in the study will be presented at the congress.

Table 1.

	Totale	Grado di alopecia n (%)		
	n: 56	G1 15 (26.8)	G2 14 (25)	G0 27 (48)
Age at diagnosis (years)	media 8.04 (2.6-17)			
	(%)			
HD-CT (n =)	29 (51.8)	7 (46.7)	13 (93)	9 (33)
Thotepa	20 (35.7)	5 (33)	11 (78.6)	4 (14.8)
Others	9 (16)	3 (20)	2 (14)	5 (18.5)
Timing HD-CT				
Pre-RT	10 (14)	5 (33)	0 (0)	3 (11)
Post-RT	8 (14.3)	1 (6.7)	11 (78.6)	1 (3.7)
Unknown	8 (14.3)	2 (13)	1 (7)	5 (18.5)
RT-Technique CSI				
3D-CRT	37 (66)	11 (73)	9 (64)	17 (63)
IMRT-Hel	19 (34)	4 (26.7)	5 (35.7)	10 (37)
Total Dose CSI				
39.00 Gy (HD)	10 (17.85)	1 (6.7)	8 (57)	1 (3.7)
36.00 Gy (HD)	8 (14.3)	5 (33)	0 (0)	3 (11)
25.20–31.20 Gy (AD)	10 (17.85)	1 (6.7)	4 (28.6)	5 (18.5)
23.40 Gy (SD)	24 (42.85)	7 (46.7)	1 (7)	16 (59)
Daily dose CSI				
1.60 Gy	4 (7)	1 (6,7)	1 (7)	2 (7.4)
1.80 Gy	30 (53.6)	9 (60)	2 (14)	19 (70)
2.00 Gy	5 (9)	4 (26.7)	0 (0)	1 (3.7)
2.60 Gy	17 (30)	1 (6.7)	11 (78.6)	5 (18.5)
PCF boost Tumor-bed	15 (32)	4 (26.7)	5 (35.7)	9 (33)
W-PCF	21 (37.5)	7 (46.7)	4 (28.6)	10 (37)
PCF boost+ W-PCF	8 (14)	1 (6.7)	4 (28.6)	3 (11)
RT-Technique boost				
3D-CRT	26 (46)	11 (73)	4 (28.6)	11 (40.7)
IMRT-Helicoidal	29 (51.8)	4 (26.7)	10 (71)	16 (59)
Daily Dose PCF				
1.50 Gy	1 (1.8)	0	1 (7)	0
1.80 Gy	26 (46)	7 (46.7)	2 (14)	17 (63)
2.00 Gy	6 (10.7)	5 (33)	0	1 (3.7)
3.00 Gy	16 (28.6)	1 (6.7)	10 (71)	5 (18.5)
Total dose tumor bed				
≤ 54.00 Gy	5 (9)	0 (0)	1 (7)	4 (14.8)
54.00 Gy	13 (23)	3 (20)	1 (7)	9 (33)

> 54.00 Gy	38 (67.85)	12 (60)	12 (86)	14 (51.8)
Hypothyroidism Primary	18 (32)	3 (20)	5 (35.7)	6 (22)
Secondary	8 (14)	0 (0)	2 (14)	2 (7.4)
Mixed	4 (7)	2 (13)	1 (7)	1 (3.7)
No	34 (60.7)	10 (66.7)	6 (43)	18 (66.7)
Hypogonadism	16 (28.6)	3 (20)	6 (43)	7 (26)
No	40 (71)	12 (80)	8 (57)	20 (74)
Hypovitaminosis D				
Yes	26 (46.4)	9 (60)	5 (35.7)	12 (44)
No	30 (53.6)	6 (40)	9 (64)	15 (55.5)
Deficit GH				
Yes	25 (44.6)	10 (66.7)	7 (50)	14 (51.8)
No	31 (55)	5 (33)	7 (50)	13 (48)
Adrenal insufficiency				
Yes	16 (28.6)	4 (26.7)	6 (43)	6 (22)
No	40 (71)	11 (73)	8 (57)	21 (77.7)
Total number of endocrine abnormalities				
5	3 (5)	1 (6.7)	1 (7)	1 (3.7)
4	6 (10.7)	1 (6.7)	2 (14)	3 (11)
3	9 (16)	3 (20)	2 (14)	4 (14.8)
2	11 (19.6)	2 (13)	3 (21)	6 (22)
1	17 (30)	7 (46.7)	5 (35.7)	5 (18.5)
No	10 (17.85)	1 (6.7)	1 (7)	8 (29.6)

CTCAE scale v5.0 G1 mild alopecia, G2 severe alopecia, G0 no alopecia
HD high dose, AD adapted dose, SD standard dose, HD-CT high dose chemotherapy, RT radiotherapy, CSI craniospinal irradiation, PCF posterior cranial fossa, GH growth hormone

AIRO GIOVANI
Oral Communications

C01

CLASSICAL PROGNOSTIC FACTORS PREDICT PROGNOSIS BETTER THAN PRE-TREATMENT PROGNOSTIC NUTRITIONAL INDEX AND INFLAMMATORY INDICES IN LOCALLY ADVANCED CERVICAL CANCER. RESULTS OF A COMPREHENSIVE OBSERVATIONAL STUDY INCLUDING TUMOR-, PATIENT-, AND TREATMENT-RELATED DATA

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Aims. Systemic inflammatory indices were found to be significantly correlated with therapeutic outcome in several cancers. The aim of this study was to analyze the predictive role of the prognostic nutritional index (PNI) and of a broad range of systemic inflammatory markers (pre-treatment values) in a large population of patients with locally advanced cervical cancer (LACC) including patient-, tumor-, and treatment-related potential prognostic factors.

Methods. Cervical cancer patients treated in our institution from 2007 to 2021 were retrospectively analyzed. All patients underwent definitive chemoradiation plus brachytherapy boost and pre-treatment values of PNI and of several inflammatory indices (neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, monocyte/lymphocyte ratio, systemic immune inflammation index, leukocyte/lymphocyte ratio, combination of platelet count and neutrophil/lymphocyte ratio, aspartate aminotransferase/platelet ratio index, aspartate aminotransferase/lymphocyte ratio index, systemic inflammatory response index, aspartate transaminase/neutrophil ratio index) were calculated. Their correlation with local control (LC), distant metastasis-free (DMFS), disease-free (DFS), and overall survival (OS) was analyzed using univariate and multivariate Cox's regression. The analysis included several clinical (age, hemoglobin level, BMI), and tumor- (FIGO, diameter) and treatment-related data (dose, fractionation, technique, overall treatment time).

Results. One hundred and seventy-three patients were included. At multivariable analysis the following significant ($p<0.05$) correlations were recorded: older age (worse DMFS and OS), advanced FIGO stage (worse

DMFS, DFS and OS), lower hemoglobin levels (worse LC, DFS and OS), larger tumor size (worse LC), higher body mass index values (worse DFS and OS). Among PNI and all analyzed inflammation indices, the multivariate analysis showed only the significant correlation between higher systemic immune inflammation index values and lower DMFS rates ($p<0.01$) (Table 1).

Conclusions. Our analysis of PNI and pre-treatment inflammatory indices in LACC, including several potentially confounding factors, showed no significant correlation between PNI and inflammatory indices with DSF or OS. Further studies are needed to clarify the role of nutritional and inflammatory indices as candidates for inclusion in predictive models in this clinical setting.

Table 1. Univariate and multivariable Cox's analysis.

	LC			DMFS			DFS			OS		
	Univariate		Multivariable*	Univariate		Multivariable*	Univariate		Multivariable*	Univariate		Multivariable*
	HR (95%CI)	p	HR (95%CI) p	HR (95%CI)	p	HR (95%CI) p	HR (95%CI)	p	HR (95%CI) p	HR (95%CI)	p	HR (95%CI) p
Age	0.98 (0.95-1)	0.23		1 (1-1)	**0.03**	1.03 (1.00-1.06) **0.02**	1 (0.98-1)	0.76		1 (1-1)	**0.02**	1.04 (1.01-1.07) **<0.01**
BMI	1 (0.88-1.1)	0.22		1.1 (1-1.1)	0.05		1.1 (1-1.1)	**<0.01**	1.05 (1.01-1.10)	1.1 (1-1.1)	**0.02**	1.07 (1.01-1.13) **0.02**
PNI	1 (0.97-1)	0.81		0.99 (0.97-1)	0.68		1 (0.98-1)	0.98		0.99 (0.96-1)	0.43	
FIGO (I-II)	*Ref.*			*Ref.*			*Ref.*			*Ref.*		
FIGO (III)	2.55 (1.04-6.27)	**0.04**		2.51 (1.25 – 5.06)	**<0.01**	2.88 (1.41-5.82) **<0.01**	2.14 (1.19 -3.85)	**0.01**	1.98 (1.07-3.67)	2.66 (1.33 – 5.34)	**0.03**	**<0.01** 3.27 (1.58-6.79) **<0.01**
FIGO (IV)	4.91 (1.77-13.58)	**<0.01**		2.47 (0.96 – 6.31)	0.06		3.24 (1.56 -6.74)	**<0.01**		2.03 (0.75 – 5.54)	0.165	
T diamet. (cont.)	1 (1-1)	**<0.001**	1.02 (1.01-1.03) **<0.01**	1 (0.99-1)	0.22		1 (1-1)	**<0.001**		1 (1-1)	**<0.01**	
RBC	0.46 (0.27-0.76)	**< 0.01**		1.1 (0.64-2)	0.68		0.78 (0.5-1.2)	0.28		0.63 (0.39-1)	0.06	
Hb (<10)	*Ref.*			*Ref.*			*Ref.*			*Ref.*		
Hb (10-12)	0.41 (0.17-1.01)	0.05		0.41 (0.13 – 1.25)	0.11		0.44 (0.19 – 1.01)	0.05	0.41 (0.17-0.98)	0.58 (0.22 – 1.52)	**0.04**	0.27
Hb (>12)	0.11 (0.04 – 0.28)	**<0.001**	0.14 (0.05-0.36) **<0.001**	0.52 (0.2 -1.35)	0.18		0.32 (0.15 – 0.67)	**<0.01**	0.37 (0.17-0.79)	0.34 (0.14 – 0.85)	**0.01**	**0.02** 0.23 (0.08-0.61) **<0.01**
NLR	1 (0.98-1.1)	0.26		1 (0.97-1.1)	0.37		1 (0.99-1.1)	0.18		1 (0.94-1.1)	0.89	
PLR	1 (1-1)	0.28		1 (1-1)	**0.02**		1 (1-1)	**0.02**		1 (1-1)	0.46	
MLR	1.3 (0.49-3.5)	0.60		1.4 (0.52-3.5)	0.53		1.2 (0.53-2.7)	0.67		0.62 (0.14-2.7)	0.52	
SII	1 (1-1)	0.15		1 (1-1)	**<0.01**	1.00 (1.00-1.00) **<0.01**	1 (1-1)	**<0.01**		1 (1-1)	0.27	
LMR	1 (0.88-1.1)	0.19		1 (0.88-1.1)	0.81		1 (0.92-1.1)	0.99		1 (0.84-1.1)	0.82	
COP-NLR (II)	*Ref.*			*Ref.*			*Ref.*			*Ref.*		
COP-NLR (1)	1.11 (0.44 – 2.77)	0.81		0.79 (0.40 – 1.58)	0.51		0.69 (0.38 – 1.23)	0.21		0.570 (0.28-1.16)	0.12	
COP-NLR (2)	2.72 (1.09 – 6.79)	0.03		0.97 (0.43-2.21)	0.95		1.07 (0.55-2.07)	0.83		1.110 (0.51-2.39)	0.78	
APRI	0.23 (0.01-7.70)	0.42		0.75 (0.19-3.1)	0.69		0.81 (0.38-1.7)	0.59		0.85 (0.3-2.4)	0.76	
ALRI	0.99 (0.95-1.01)	0.77		1 (0.99-1)	0.46		1 (0.98-1)	0.67		0.99 (0.95-1)	0.50	
SIRI	0.99 (0.96-1)	0.37		0.99 (0.96-1)	0.52		0.99 (0.98-1)	0.36		0.99 (0.96-1)	0.31	
ANRI	0.79 (0.64-0.98)	**0.02**		1 (0.82-1.1)	0.73		0.96 (0.9-1.1)	0.81		0.97 (0.85-1.1)	0.68	

legend: ALRI: aspartate aminotransferase to lymphocyte ratio index; ANRI: aspartate transaminase to neutrophil ratio index; APRI: aspartate aminotransferase/platelet count ratio index; BMI: body mass index; COP-NLR: combination of platelet count and neutrophil to lymphocyte ratio ; DFS: disease free survival; DMFS: distant metastasis free survival; FIGO: International Federation of Gynecology and Obstetrics; Hb: hemoglobin; HR: hazard-ratio; LC: local control; LMR: leukocyte-to-lymphocyte ratio; MLR: monocyte to lymphocyte ratio; NLR: neutrophil to lymphocyte ratio; OS: overall survival; PLR: platelet to lymphocyte ratio; PNI: prognostic nutritional index; RBC: red blood cells; SII: systemic immune inflammation index; SIRI: systemic inflammatory response index; T: tumor.

C02

EARLY AND SYSTEMATIC NUTRITIONAL COUNSELLING AND INTERVENTION IN HEAD AND NECK CANCER PATIENTS UNDERGOING CHEMO-RADIATION: IMPACT ON QUALITY OF LIFE AND OUTCOME

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Aims. Chemoradiotherapy is often an effective treatment in head and neck (HN) cancer patients (pts) but potentially deteriorates nutritional status. The aim of this prospective, mono-institutional, osservational study is to quantify the impact of systematic nutritional counseling on the quality of life and oncological treatments' adherence and tolerance.

Methods. From May 2021 to March 2023, 60 consecutive HN cancer pts undergoing chemo-radiotherapy with curative intent were considered. Twenty-eight pts were treated with radical intent and a Simultaneous Integrated Boost (SIB) technique based on 18 FDG PET/CT-based planning (54 Gy in 30 fractions to the clinically negative neck region and 66 Gy in 30 fractions to tumor and positive nodal regions). Thirty-two patients were treated in post-operative setting: 54 Gy in 30 fractions to the low risk regions with SIB to high risk regions (61.5/64 Gy in 30 fractions). All pts were treated with helical IMRT (Tomotherapy®, Accuray, Wisconsin) and daily IGRT (MVCT) and received high-dose cisplatin chemotherapy (CT, at least 200 mg/m^2). Pts' characteristics are reported in Table 1. Several biochemical and anthropometrical parameters, handgrip strength, questionnaires associated with malnutrition & quality of life (MNA, FACT H&N and EORTC QLQH& N35) and body composition (obtained by Bioelectrical Impedance Vector Analysis) were performed before, during and after CT-RT. A linear mixed-effects model was used to detect temporal trends. Data were replaced by their ranks prior to performing the mixed model.

Table 1.

Variables	Categories	Statistics	Values
Age (years)	-	N	60
		Median (min-max)	59.3 (27.2 - 78.9)
Gender	Female	N (%)	17 (28.3)
	Male	N (%)	43 (71.7)
BMI (kg/m²)	-	N	60
		Median (min-max)	25.3 (16.1-38.3)
Smoke	No	N (%)	9 (15.0)
	Ex-smoker	N (%)	37 (61.7)
	Smoker	N (%)	14 (23.3)
Tumor site	Oropharynx	N (%)	24 (40.0)
	Mouth	N (%)	10 (16.7)
	Nasopharynx	N (%)	9 (15.0)
	Hypopharynx	N (%)	4 (6.7)
	Larynx	N (%)	3 (5.0)
	Other	N (%)	10 (16.7)
Stage	I	N (%)	2 (3.3)
	III	N (%)	8 (13.3)
	IV	N (%)	50 (83.3)
Potus	No	N (%)	25 (41.7)
	Yes	N (%)	35 (58.3)
Previous surgery	No	N (%)	28 (46.7)
	Yes	N (%)	32 (53.3)

Results. All pts completed the designed RT treatment without interruption dueing to severe malnutrition and 96.4% of them completed CT without disabling toxicities. No statistically significant results are available in terms of variation of body composition from the beginning to the end of the treatment. A significant improvement of quality of life and nutritional status was observed with EORTC QLQ-HN35 and MNA ($p<0.001$) provided 1, 3 and 6 months (T4, T5 and T6) after therapies.

Conclusions. These results seems to suggest that early and systematic nutritional counseling pre-during-

post CT-RT has an impact on improving quality of life (rated with QoL questionnaires), nutritional status (measured by body composition variations) and treatments' adherence. In our opinion, the introduction of an expert nutritional counselor could be crucial in order to improve not only our pts QoL but also their oncological outcomes.

C03

THE EFFECT OF NUTRITIONAL COUNSELLING ON PATIENT MANAGEMENT AND CLINICAL OUTCOME IN PATIENTS WITH PROSTATIC OR URO-GYNECOLOGICAL CANCER WHO UNDERGO PELVIC RADIOTHERAPY: AN OBSERVATIONAL PILOT STUDY

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Aims. A nutritional counselling service for patients undergoing pelvic radiotherapy(RT)was established and its impact on patient compliance with RT treatment as well as acute and late intestinal toxicity was evaluated within the framework of a prospective study.

Methods. In this Ethics Committee-approved [CE1408/2020] monocentric observational pilot study, patients with age>18years, capacity to sign informed consent, women with gynecological cancer candidates for adjuvant RT or men with prostate cancer planned to undergo adjuvant or salvage RT to the prostate bed, PS ECOG 0-1, absence of conditions that contraindicate RT to the pelvis were included. Nutritional counselling consisted in a preliminary visit within 5 days from the enrollment with nutritional indications (based on the food diary compiled by the patients, reporting their prior nutritional habits).Treatment planning CT scan was scheduled at least ten days after the nutritionist intervention. Nutritional appointments were planned halfway through and at the end of RT. During the treatment, in case of inappropriate intestinal preparation, the radiation oncologist could schedule an additional nutritional consultation. Primary endpoint was the evaluation of the effect of tailored nutritional counselling on intestinal preparation and the consequent impact on patient management during RT.Compliance to nutritional counselling, number of repeated treatment planning CTs and set up evaluations with MVCT/CBCT were the primarily analyzed parameters. Acute and late toxicity>grade 2, scored with CTCAE v5.0, was evaluated as secondary endpoint.

Results. From April 2021, 19 patients were enrolled in this ongoing study. One patient was excluded from analysis because of the detection of metastatic disease before the initiation of RT. Eight patients were male and 10 were female (Table 1). Fourteen patients completed the RT treatment and 4 were undergoing treatment at time of writing this abstract. No acute >G2 toxicities were observed. Only 1 patient had to repeat the treatment planning CT scan (5,6%). The average number of CBCTs/MVCTs that exceeded the number of treatment fractions was only 2(range 0-9).

Conclusions. Personalized nutritional counselling may improve patient compliance to RT and intestinal preparation and thus reduce the number of IGRT-procedures during the course of RT. Consequently, it might also reduce acute and late toxicities, with definitive results being available after full enrollment.

Table 1. Characteristics of the study population.

Characteristics	Category	Prevalence number (%)
Sex	Male	8 (44,4)
	Female	10 (55,6)
Treatment course	Ended	14 (77,8)
	Ongoing	4 (22,2)
Aim of radiotherapy	Adjuvant	14 (77,8)
	Radical	0 (0)
	Salvage	4 (22,2)
Radiotherapy technique	VMAT	9 (50)
	Tomotherapy	9 (50)
No. of repeat planning CTs	No	17 (94,4)
	Yes	1 (5,6)
Side effects registered	Diarrhea	5 (28)
	G1	4 (22,2)
	G2	1 (5,5)
	>G3	0 (0)
	Abdominal Pain	1 (10)
	G1	1 (5,5)
	G2	0 (0)
	>G3	0 (0)
	Rectal Bleeding	2 (11)
	G1	2 (11,1)
	G2	0 (0)
	>G3	0 (0)

C04

WEIGHT LOSS AND BMI CHANGES IN HEAD AND NECK CANCER PATIENTS SUPPORTED WITH IMMUNONUTRITION: PRELIMINARY DATA FROM A MONO-INSTITUTIONAL RANDOMIZED TRIAL

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Aims. To evaluate the impact of immunonutrients inside a specifically designed path of nutritional support for patients (pts) undergoing concomitant radical Radio-Chemotherapy (RCT) for Head and Neck (H&N) cancer. Does immunonutrition play a role in reducing weight loss in such a challenging population?

Methods. Sixty-two pts undergoing RCT for H&N cancer (Karnofsky index >50) were enrolled in this prospective study, randomized to a control arm (A) receiving standard of care (SOC) nutritional evaluation and support and to a intervention arm (B) receiving immunonutrition in addition to SOC from the beginning of radical RCT. Both arms received equal total caloric integration based on their metabolism. Nutritional evaluation (collecting weight, BMI, daily calories intake, bioimpedentiometry, body circumferences as well as other parameters) was performed at baseline, after RCT and then repeated at 1st and 3rd month of follow up.

Results. Preliminary data is now available for 47 pts, completing a 3 month follow up period: 24 pts in arm A, 23 in arm B. No significant differences in characteristics in the two groups except for alcohol intake, higher in the arm B. Results show how both arms are affected by BMI loss at the end of RCT and at first month of follow up (p=0,00). After the first month curves concerning the BMI start to diverge: pts in arm A keep loosing weight also in 2nd-3rd month of follow up while arm B shows a stabilization (p=0,003 and p=0,001 respectively from baseline, Figure 1A-B). Analyzing only the changes between the end or RCT and 3rd month of follow up no statistical significance has been reached for now.

Conclusions. These studies are particularly challenging in terms of poor baseline conditions of H&N cancer pts (poor diet, smoking and drinking habits, poor dental status, impaired swallowing) and low short/long term compliance. Weight loss continues after the end of RCT especially when pts do not receive a proper and tailored nutritional support. An increasing number of publications underline the importance of a proper nutritional support for this population. This study outstands other reported clinical experiences due to the availability of data concerning a control arm. Further investigation is ongoing thanks to the increasing set of data from the follow up period, more information regarding BMI changes on the long term, acute/chronic toxicities patterns, hospitalization and long term effects on anthropometry measures will follow.

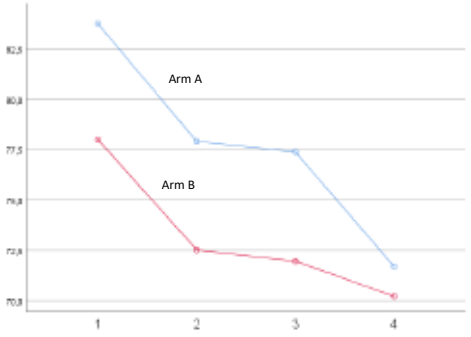

Figura 1.A - Mean weight values to: 1.Baseline 2.RCT End 3.Thirty days 4.Three months

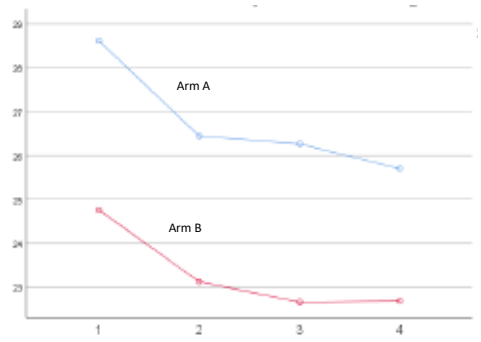

Figura 1.B - Mean BMI values to: 1.Baseline 2.RCT End 3.Thirty days 4.Three months

Figure 1.

C05

IMPACT OF NUTRITIONAL COUNSELING FOR HEAD AND NECK CANCER PATIENTS UNDERGOING RADIOTHERAPY OR RADIOCHEMOTHERAPY: A PILOT PROSPECTIVE STUDY

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Purpose. Radiation therapy, alone or in combination with chemotherapy, plays a pivotal role in head and neck cancer (HNC) both in primary and adjuvant setting. However, treatments are often burdened with severe toxicity, resulting in 55% of patients losing additional weight, thereby increasing treatment time and worsening oncological outcomes. Thus, we aimed to determine the

impact of dietary counselling in a prospective cohort of patients with HNC undergoing radio-chemotherapy.

Methods. This single-centre prospective study's conducted between November 2020 and March 2021. Seventeen patients treated for HNC with radio-chemotherapy or radiotherapy alone were included. Nutritional assessment was performed at baseline (T0), mid-treatment (T1), at the end of treatment (T2) and one month after (T3). Nutrition risk was assessed at baseline using the Malnutrition Universal Screening Tool (MUST). Nutritional outcome and morbidity were recorded during treatment and 1 month after the end. Delays to radiotherapy were recorded as >7 days.

Results. Mean age was 66,6 years (range 56-81 years)[Table 1].

Table 1. Patient's baseline characteristics.

	N°	%
Patients	17	100
Age		
mean	66,6	
range	56-81	
Sex		
Male	13	77,5
Female	4	23,5
Performance Status (ECOG)		
0	15	88
1	2	12
2	0	
Tumor Site		
Oral Cavity	3	17,65
Salivary Gland	2	11,76
Larynx	3	17,65
Oropharynx	7	41,17
Rhynopharynx	1	5,88
Unknown Primary	1	5,88
Smoker Status		
Non smokers	4	23,5
Smokers	13	76,5
Inactive	7	
Active	6	
HPV Status		
Positive (all oropharynx)	7	39
Negative or not tested	10	61
Chemotherapy		
No	6	35
Yes	11	65
CDDP/qT	5	
CDDP/q21	5	
Cetuximab	1	
Treatment setting		
Adjuvant	4	18
Radical	13	82
Surgical intervention	4	18
No surgical intervention	13	82
Treatment		
Radiotherapy	6	35
Chemo-Radiotherapy	11	65

Four patients (18%) underwent surgical intervention and subsequent adjuvant treatment, 13 patients (82%) were treated with radiotherapy or radio-chemotherapy with a curative intent. All patients completed the planned fractions of RT treatment and chemotherapy. Nutrition risk assessed by compiling the Malnutrition Universal Screening Tool (MUST) was equal in each category: low (MUST = 0) in 41% of cases (7 patients), average nutritional risk (MUST = 1) in 29.5% of cases (5 patients) and high nutritional risk (MUST ≥ 2) in 29.5% of cases (5 patients). Most relevant issues at baseline were inadequate oral intake and involuntary weight loss, with inadequate energy intake as the most frequent cause (38%)[Table 2]. At mid-treatment (T1), mean body weight showed a reduction from baseline (75.2 *vs* 73.0 kg), with a slight increase at the end of therapies (74.4 kg). Overall, body weight stability was observed throughout the treatment, with a recovery from the minimum weight (mean 74.3 *vs* 74.4 kg, min 59 *vs* 57.3 kg). One-month data (T3) were available for only 9 patients and showed a decrease in mean weight to 70.4 kg.

Conclusions. Our data, albeit with limitations due to a small cohort and short observation time, suggest that adequate nutritional counselling should be considered in HNC cancer patients to ensure adequate dietary intake, improve treatment adherence and oncological outcomes.

Table 2. Principal nutritional parameters evaluated during observation.

Parameters	Baseline (T0) (n=17)	T 1 (n=17)	T2 (n=14)	T3 (n=9)
Weight (kg)				
Mean	75,2	73	74,4	70,4
Min	55,5	54,5	57,3	56
Max	94,5	95	93,5	92,3
BMI (kg/m2)				
Mean	25,7	25	25,3	23,23
Intake E (Kcal)	1734	1711	1753	1955
Intake P (g)	72	74	77	88
ONS (% pz)	29	65	78	22

BMI: Body Mass Index; ONS: oral nutritional supplements

C06

^{18F}-FDG-PET-BASED FUNCTIONAL RESPONSE AFTER CHEMORADIATION OF CERVICAL CANCER: OUTCOME PREDICTION AND EARLY DETECTION OF OLIGO-METASTATIC DISEASE.

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Aims. Concurrent chemoradiation (CRT) followed by brachytherapy (BRT) boost is the standard treatment option in locally advanced cervical cancer (LACC). However, a non-negligible rate of patients experience pelvic recurrence or distant metastases after CRT-BRT. Attempts to improve outcomes with adjuvant systemic treatments have been unsuccessful in most trials, probably because these therapies were applied to all patients without selection based on risk of failure. At the same

time, the availability of stereotactic body radiotherapy (SBRT) could allow, in patients with early oligometastases, to offer a second curative treatment option. The aims of this analysis were to evaluate whether post-CRT-BRT ^{18F}-FDG-PET/CT could: i) provide prognostic indications, ii) allow early detection of patients with oligometastatic disease as potential candidates for SBRT.

Methods. LACC patients treated in our institution from 2007 to 2021 were retrospectively analyzed. All patients underwent definitive CRT plus BRT boost and ^{18F}-FDG-PET/CT 2-3 months after treatment completion. Survival curves were calculated with the Kaplan-Meier method and compared with the log-rank test.

Results. One hundred and sixty-eight patients were included. The results of this analysis are shown in Table 1. Five-year overall survival was 89.5%, 0.0%, and 16.3% in patients with CR, PR, and NC/PD at the first ^{18F}-FDG-PET/CT after CRT-BRT, respectively (p<0.001). Of patients with disease progression but no local progressive/residual LACC on first ^{18F}-FDG-PET/CT after CRT-BRT, 37.5% had only oligometastatic disease. Furthermore, of patients with CR at the first ^{18F}-FDG-PET/CT after CRT-BRT, 18 had treatment failure at subsequent follow-up evaluations. Of these, 61% had only isolated nodal recurrences or distant oligometastases.

Conclusions. Our study confirms the utility of PET evaluation after CRT/BRT in LACC patients. In fact, this examination allows: i) a reliable prediction of the prognosis; ii) the early identification of a non-negligible rate of patients eligible for SBRT (37.5%); iii) the identification of a population of patients (CR at ^{18F}-FDG-PET/CT) in which eventual treatment failures can undergo SBRT in a high rate of cases (61.1%).

Table 1.

Table 1: Impact of functional response on DFS-OS and pattern of failures (numbers and percentages in bold indicate patients potentially eligible for SBRT)

Functional response	No. of patients	5-year DFS (%)	5-year OS (%)	p:
All patients	168	66.0	72.1	
CR	129	84.8	89.5	
PR	8	0.0	0.0	<0.001
NC-PD	31	6.7	16.3	
Distant metastases at first ^{18F}-FDG-PET/CT (only patients with local CR)	**No. of patients**		**%**	
All	8		100.0	
Oligo-metastases (< 5)	**3**		**37.5**	
Multiple-metastases (> 5)	5		62.5	
Treatment failures during the follow-up (only patients with CR at first ^{18F}-FDG-PET/CT)	**No. of patients**		**%**	
All	18		100.0	
Local recurrences +/- metastasis	2		11.1	
Isolated nodal recurrence	**5**		**27.8**	
Oligo-metastases (≤ 5)	**6**		**33.3**	
Multiple-metastases (> 5)	5		27.8	

Legend: CR: complete response; DFS: disease-free survival; NC: no change; OS: overall survival; PD: progressive disease; PR: partial response.

C07

STEREOTACTIC BODY RADIATION THERAPY (SBRT) WITH MRI-DEFINED FOCAL SIMULTANEOUS INTEGRATED BOOST FOR PATIENTS WITH LOCALIZED PROSTATE CANCER: ACUTE TOXICITY AND DOSIMETRY RESULTS FROM A PROSPECTIVE OBSERVATIONAL STUDY

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Aims. Dose escalation to the multiparametric magnetic resonance imaging (mpMRI) dominant intraprostatic lesions (DILs) is a novel method to increase the therapeutic ratio in localised prostate cancer (PCa). Aim of the study was to report the early acute toxicity and dosimetry results of prostate Stereotactic Body Radiotherapy with a Simultaneous Integrated Boost to the DIL (SBRT-SIB-DIL).

Methods. PCa patients with cT1-T2c adenocarcinoma, Gleason score <9, prostate-specific antigen (PSA) <20 ng/mL, and prostate volume <90 cc were included in a prospective observational study. DILs were defined using mpMRI T2-weighted, diffusion and perfusion images. Intra-prostatic fiducial markers and recto-prostatic hydrogel spacer were placed under transrectal ultrasound guide. The prescribed dose wes 36.25 Gy to the prostate with an isotoxic SIBDIL of 40 Gy (dose range 100%-120%) (Figure 1). Genitourinary (GU) and gastrointestinal (GI) toxicity was reported using the CTCAE scoring criteria. Toxicity and dosimetry results were compared with PCa patients treated with SBRT without boost in the same period

Results. From January 2022 to March 2023, a total of 46 men underwent prostate SBRT at our Institution. Among these, 21 patients (45.6%) with mpMRI-defined DIL received SBRT-SIBDIL. Median patient age was 78 years (IQR 74-80). 18 patients (85.7%) had cT2 disease, median iPSA was 8.9 ng/ml (IQR 6.5-17.6), and baseline IPSS score was mild and moderate in 57.1 % and 42.9%, respectively. The majority of DILs were in the peripheral zone (85.7%). Most patients had either 3+4 (38%) or 4+3 Gleason (33.3%). Androgen Deprivation Therapy was administered in 8 (38.1%) patients. All the SBRT-SIBDIL plans met the predetermined target coverage and OARs dose constraints objectives. At a median follow up of 6 months (range 3-14), no G≥3 toxicity was observed, with a cumulative acute G1-2 GU and GI toxicity rates of 47.6% and 19.1%, respectively. All patients experienced biochemical response. In comparison with the non-boost SBRT group (25 patients), rectal V40, 36 and 24Gy, and bladder V40, 37 and V18.1Gy did not significantly differ (all p>0.05). Also, no differences were found between

groups in terms of acute G2 GU (14.2% boost *vs* 20.0% no-boost; p=0.71) and GI toxicity (4.7% boost *vs* 8.0% no-boost; p=0.98)

Conclusions. Our preliminary results show that approaching PCa with five-fractions mpMRI-defined SBRT-SIBDIL is safe and effective, with excellent adherence to the planning protocol

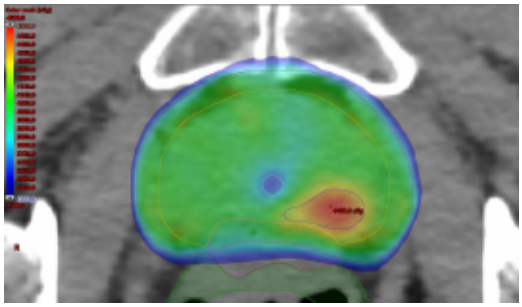

Figure 1. Typical dose distribution (color wash) for prostate SBRT plan with Simultaneous Integrated Boost (SIB) to the DIL. The prescribed dose is 36.25 Gy in 5 fractions to the whole gland (PTVprostate, *red*) with a 40 Gy focal boost to the dominant lesion (PTVboost, *blue*, D_{max} 45 Gy). Hot spots to the urethra (*pink*) are avoided (D_{max} ≤36.25 Gy). The recto-prostatic hydrogel spacer (*magenta*) allows for dose reduction to the anterior rectal wall (*green*).

C08

PSMA GUIDED APPROACH FOR BIOCHEMICAL RELAPSE AFTER PROSTATECTOMY- (PSICHE) TRIAL (NCT05022914). DETECTION RATE AND TREATMENT DECISION AFTER 68GA-PSMA PET/CT WITHIN A PROSPECTIVE STUDY

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Aims. Biochemical relapse (BR) after radical prostatectomy (RP) is currently managed with salvage radiotherapy (SRT). Prostate-specific membrane antigen positron emission tomography–computed tomography (PSMA PET/CT) radically changed this scenario. Guidelines recommend to perform PSMA PET/CT in patients with PSA > 0.2 if results will influence treatment decisions, but little is known about the clinical impact on treatment options. In order to evaluate the role of PSMA PET/CT imaging within a metastasis directed therapy framework, we designed a prospective trial.

Methods. PSICHE (NCT05022914) is a prospective multicenter study that included patients experiencing biochemical relapse (BR) after RP. BR was defined as PSA > 0.2 ng/ml, ≤1 ng/ml. Patients underwent centralized staging with 68Ga-PSMA PET/CT and were managed according to a pre-defined treatment algorithm based on the following approaches: prostate bed SRT for patients with negative 68Ga-PSMA PET/CT or positive findings within prostate bed, SBRT for patients with pelvic nodal recurrences or oligometastatic disease, ADT or other systemic therapies available at physician discretion for patients with non oligometastatic disease.

Results. PSMA results were negative or positive in the prostate bed in 72 patients (72%), while pelvic nodal or extrapelvic metastatic disease were detected in 23 (23%) and 5 (5%) patients, respectively. After re-staging, 21 patients (21%) underwent observation because of prior postoperative RT (16) or refusal of treatment (5). Fifty (50%) patients were treated with prostate bed SRT, 23 (23%) underwent SBRT to the pelvic nodal disease, 5 patients (5%) were treated with SBRT to extrapelvic oligometastatic disease. Non oligometastatic disease was detected in 1 patient who underwent ADT for low burden metastatic disease.

Conclusions. The results of PSMA PET/CT imaging provides an important and reliable means to tailor treatment in a significant percentage of the patient cohort studied. PSICHE trial could constitute a useful prospective platform to collect data within a current clinical scenario where modern imaging and metastasis directed therapy are available.

C09

IMPACT OF PRE-TREATMENT CLINICAL DATA AND OF DYNAMIC EVALUATION OF 18-F-FDG-PET SUVMAX, INFLAMMATORY INDICES AND PROGNOSTIC NUTRITIONAL INDEX IN 173 CERVICAL CANCER PATIENTS TREATED WITH CONCURRENT CHEMORADIATION

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Aims. Aim of this study was to analyze the predictive role of 18-F-FDG-PET Δ-SUVmax (tumor SUV pre-minus post-treatment) and several inflammatory markers (post- minus pre-treatment) in a large population of patients with locally advanced cervical cancer (LACC) treated with concurrent chemoradiation (CRT) plus brachytherapy boost.

Methods. Patients with LACC treated in our institution with definitive CRT from 2007 to 2021 were retrospectively analyzed. Pre- and post-treatment values of 18-F-FDG-PET tumor SUVmax, of prognostic nutritional index, and of several inflammatory indices (neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, monocyte/lymphocyte ratio, systemic immune inflammation index, leukocyte/lymphocyte ratio, combination of platelet count and NLR, aspartate aminotransferase/ platelet ratio index, aspartate aminotransferase/lymphocyte ratio index, systemic inflammatory response index, aspartate transaminase/neutrophil ratio index) were recorded and Δ-values were calculated. Their correlation with local control (LC), distant metastasis-free (DMFS), disease-free (DFS), and overall survival (OS) was analyzed using univariate and multivariate Cox's regression. The analysis included several clinical (age, hemoglobin level, BMI), and tumor- (FIGO, diameter) and treatment-related data (dose, fractionation, technique, overall treatment time).

Results. One hundred and seventy-three patients were included. At univariate analysis no Δ of inflammatory indices was correlated with outcomes, while higher Δ-SUVmax was significantly correlated with higher LC (p=0.001), DFS (p=0.030), and OS (p=0.010) rates. At multivariable analysis none of the analyzed parameters was significantly correlated with LC and DMFS. However, both higher Hb level (continuous variable) and 18-F-FDG-PET Δ-SUVmax ≥12.35 were significantly correlated with DFS. Moreover, higher Hb level, 18-F-FDG-PET Δ-SUVmax ≥12.35, less advanced tumors not requiring extended nodal irradiation, and Δ-aspartate aminotransferase to neutrophil ratio index (ANRI) ≥3.56 were significantly correlated with improved OS. (Table 1)

Conclusions. Our analysis suggests that the prognosis in LACC patients can be accurately predicted by evaluating, in addition to the traditional patient- and treatment-related prognostic factors, also the SUV and of ANRI pre-post-treatment variations.

Table 1. Multivariable analysis (only parameters significantly correlated with outcomes are shown).

Parameter	Values	DFS			OS		
		HR	95%CI	p	HR	95%CI	p
Δ aspartate aminotransferase to neutrophil ratio index (ANRI)	< 3.56	Rif.			Rif.		
	≥ 3.56	0.595	0.352 – 1.008	.053	0.383	0.191 – 0.767	**.007**
Irradiated lymph nodes	Pelvic only	Rif.			Rif.		
	Pelvic plus para-aortic or inguinal	2.034	0.908 – 4.557	.085	2.720	1.029 – 7.191	**.044**
Hb	Continuous variable	0.753	0.599 – 0.945	**.014**	0.649	0.498 – 0.846	**.001**
Δ SUV T	< 12.35	Rif.			Rif.		
	≥ 12.35	0.590	0.349 – 0.998	**.049**	0.486	0.256 – 0.919	**.027**

Legend: ANRI: aspartate aminotransferase to neutrophil ratio index; CI: confidence interval; DFS: disease free survival; Hb: hemoglobin; OS: overall survival; HR: hazard ratio; SUV: standardized uptake value; T: tumor.

C10

MPMRI SENSITIVITY IN DETECTING MACROSCOPIC LOCAL RECURRENCES IN PROSTATE CANCER PATIENTS WITH PLANNED SALVAGE RADIOTHERAPY: UPDATED RESULTS OF AN OBSERVATIONAL STUDY

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Aims. Biochemical recurrences of prostate cancer (PCa) after radical prostatectomy are recorded in approximately 15-30% of cases. Treatment options are represented by salvage radiotherapy (sRT), androgen deprivation therapy, or observation with PSA level monitoring. In patients eligible for sRT, current guidelines recommend PSMA-PET in order to detect any distant metastases. An observational study was carried out in our center to evaluate a possible role of multiparametric magnetic resonance imaging (mpMRI) before sRT. Aim of this report was to describe the preliminary results.

Methods. Over a 5-year period, all PCa patients eligible to sRT without contraindications to mpMRI underwent clinical and instrumental examination including pelvic mpMRI with endorectal coil, possibly associated with choline or PSMA-PET. The following data were prospectively collected: PSA at biochemical relapse, ISUP score, sRT treatment plan, and site and size of any

macroscopic recurrence.

Results. Ninety-one patients were evaluated in this study. Median age was 67 years (range: 41-78), median PSA level at biochemical recurrence was 0.4 ng/ml (range: 0.01-6.24, I.Q.: 0.22-1.04), and most patients (75.8%) had ISUP 3-5. Pre-sRT mpMRI was positive for locally recurrent PCa in 54/91 patients (59.3%), for pelvic nodal metastases in 1/91 (1.0%), and for pelvic bone metastases in 1/91 (1.0%). The site of local recurrence was as follows: bladder neck 37/54 (68.5%), vesico-urethral anastomosis 11/54 (20.4%), recto-vesical space 5/54 (9.2%), and prostatic fossa 1/54 (1.9%). Forty-two patients (75.0%) with positive MRI underwent also choline or PSMA-PET. Of these, only 16 patients (38.1%) showed pathological uptake at the same sites of positive mpMRI. Conversely, in 26 patients (61.9%) MRI results did not match the PET result.

Conclusions. An unexpectedly high rate of macroscopic local failures was recorded in a cohort of patients with biochemical recurrence after radical prostatectomy and prospectively assessed with mpMRI. These results challenge current recommendations on the most appropriate imaging exams in this clinical setting.

Oral Communications

CO01

UPDATE ANALYSIS OF STEREOTACTIC ABLATIVE RADIOTHERAPY IN NEWLY DIAGNOSED AND RECURRENT LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER PATIENTS UNFIT FOR CONCURRENT RADIO-CHEMOTHERAPY: THE START-NEW-ERA NON-RANDOMISED PHASE II TRIAL

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Aims. This is an update of single arm phase 2 trial (Clinical trials.gov NCT05291780) to assess local control (LC) and safety of stereotactic ablative radiotherapy (SAbR) in unresectable locally advanced non-small cell lung cancer (LA-NSCLC) patients unfit for concurrent chemo-radiotherapy (ChT-RT). Early results on first 50 enrolled patients were recently published.[1]

Methods and Materials. Neoadjuvant ChT was prescribed in fit patients. The tumor volume included primary tumor (T) and any regionally positive node/s (N). The co-primary study endpoints were LC and safety.

Results. Between December 31, 2015 and Janauary 31, 2023 77 LA-NSCLC patients were enrolled. Histology was squamous cell carcinoma (SCC) and adenocarcinoma (ADC) in 38% and 62%, respectively. 66 (86%) patients had ultra-central tumor. Forty-three (56%) received neoadjuvant ChT and 16 (21%) adjuvant Durvalumab. Median prescribed dose was 45 Gy (range, 35-55) and 40 Gy (35-50) in 5 daily fractions to T and N, respectively. After a median follow-up of 27 months (range, 4-92), 24 (31%) patients had experienced local recurrence (LR) at a median time of 13 months (range, 4-34). The median LR-free survival (FS) was not reached (95% CI, 28 to not reached). The 1-, 2- and 4- year LR-FS rates were 84±5%, 67±6% and 58±7%, respectively. At last follow-up, 50 (65%) patients were alive. Median overall survival (OS) was 55 months (95% CI, 43-55 months). The 1, 2, and 4-year OS rates were 92±3%, 72±6% and 58±7%, respectively. Twenty-four (31%) patients developed distant progression (dP). The median dP-FS was not reached (95% CI, 24 to not reached). The 1, 2, and 4-year dP-FS rates were 85±4%, 64±6% and 60±7%, respectively. Two patients developed grade (G) 3 esophageal and lung toxicity.

Conclusions. LA-NSCLC patients treated with SAbR had optimal LC and promising OS with low rate of G3 toxicity. Our updated clinical outcomes confirm the feasibility of using this approach in LA-NSCLC patients unfit for concurrent ChT-RT.

Reference

1. Int J Radiat Oncol Biol Phys 2022;S0360-3016(22)03459-9. doi: 10.1016/j.ijrobp.2022.10.025

CO02

RADIOTHERAPY FOR HEPATOCELLULAR CARCINOMA (HCC) WITH PORTAL VEIN TUMOR THROMBOSIS (PVTT) AND/OR VENA CAVA INVOLVEMENT (VCI): CLINICAL OUTCOMES ON 41 PATIENTS

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Aims. Hepatocellular carcinoma (HCC) patients with portal vein tumor thrombosis (PVTT) have a worse prognosis. Ablative radiotherapy (RT) showed an improved local control (LC) in selected patients with inoperable HCC. This study investigated the efficacy of RT in unfavorably selected HCC patients with PVTT and/or vena cava involvement (VCI).

Methods. A retrospective study was conducted consisting of HCC patients with PVTT and/or VCI, treated at Humanitas Research Hospital from 2011 up to 2022. Prescription radiation dose ranged from 60 to 30 Gy in 5, 6 or 10 fractions, with a median biological equivalent dose (BED)10 of 56 Gy (range 37-120 Gy). Local control (LC), extra-field liver progression free survival (EL-PFS), systemic progression free survival (S-PFS), overall survival (OS) and toxicity were analyzed.

Results. The study population includes a total of 41 patients with a mean age at the time of RT was 78 years. Median follow up was 14.3 months. With an overall response of 75.6%, 19 (46.3%) patients had partial response and 2 (4.9%) had complete response. There was no correlation between median BED and local progression of disease (p=0.233). Median OS was 14.9 months and 1 and 2 years rates were 60.9% (95%CI 43.7-74.3) and 8.3% (95%CI 1.7-21.5). At univariate analysis, no factors were significantly associated with OS. Median EL-PFS was 13.2 months, and 1 and 2 years rates were 54.2% (95%CI 36.1-69.3) and 26.0% (95%CI 10.1-45.4). At univariate analysis, BED10 (HR 0.98, 95%CI 0.96-0.99; p=0.031) and in-field progression (HR 5.91, 95%CI 2.13 – 16.3; p=0.001) were associated with EL-PFS. At multivariate analysis, only in-field progression remained statistically significant (HR 4.43, 95%CI 1.52-12.84; p=0.006). Median S-PFS was not reached. One and two years rates of S-PFS were 60.3% (95%CI 40.3-75.4) and 56.3% (95%CI 36.3-72.2). At univariate analysis, BED10 ≥ 56 Gy was associated with improved SPFS (HR 0.96, 95%CI 0.94- 0.99; p=0.042). A total of 3 patients experienced G3 late liver toxicity after RT.

Conclusions. In our experience, radiotherapy represents a promising therapeutic option for HCC patients with PTTV and/or VCI. Considering the multimodality treatment of these unfavorably selected patients, RT was associated with an encouraging response of tumor thrombosis and intra-hepatic disease control. Radiation dose with higher BED10 ≥ 56 Gy was associated with an increased time to systemic progression.

Table 1. Univariate analysis for OS.

	Overall survival			Extrafield liver progression free survival			Systemic progression free survival		
	Univariate analysis								
	HR	95%CI	P value	HR	95%CI	P value	HR	95%CI	P value
Age	0.99	0.95 – 1.03	0.691	1.00	0.96 – 1.04	0.810	0.98	0.93 – 1.04	0.660
Child score	1.01	0.48 – 2.11	0.968	0.42	0.16 – 1.07	0.070	0.53	0.15 – 1.87	0.327
HCV	1.16	0.58 – 2.32	0.667	1.68	0.72 – 3.93	0.228	0.94	0.13 – 2.81	0.920
HBV	1.26	0.51 – 3.10	0.600	2.40	0.88 – 6.58	0.087	2.01	0.55 – 7.36	0.288
BED10	0.99	0.98 – 1.00	0.244	**0.98**	**0.96 – 0.99**	**0.031**	**0.96**	**0.94 – 0.99**	**0.042**
Local progression	2.08	0.90 – 4.79	0.082	**5.91**	**2.13 – 16.3**	**0.001**	2.26	0.68 – 7.43	0.179
Extra-field liver progression	1.24	0.61 – 2.52	0.537	-	-	-	1.67	0.50 – 5.35	0.407
Systemic progression	1.53	0.73 – 3.20	0.249	1.52	0.63 – 3.68	0.345	-	-	-
	Multivariate analysis								
	HR	95%CI	P value	HR	95%CI	P value	HR	95%CI	P value
BED10	-	-	-	0.98	0.96 – 1.00	0.143	**0.96**	**0.94 – 0.99**	**0.042**
Local progression	-	-	-	**4.43**	**1.52 – 12.84**	**0.006**	-	-	-

CO03

A GEOMETRIC SCORE TO IDENTIFY THE RISK OF LOCAL FAILURE AFTER SBRT IN PATIENTS WITH LOCAL ADVANCED OR BORDERLINE RESECTABLE PANCREATIC CANCER

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Aims. Local failures (LFs) after SBRT in borderline or local advanced pancreatic cancer (PC) patients (pts) are often within the RT field. This suggests a specific efficacy of a complete covering of the macroscopic (GTV) aggressive disease with high doses (i.e. simultaneous boost [SIB] doses).This is often not feasible due to the proximity of organs at risk, which forces the use of "Simultaneous Integrated Protection" (SIP), limiting the dose to safe values in a portion of the GTV. This analysis aimed to quantitatively assess the role of GTV size and incomplete GTV covering from SIB in increasing the risk of LF.

Methods. We included 51 PC pts treated with SBRT

(Nov 2016 - Nov 2019): 30 Gy in 5 fractions to the tumor PTV, 50 Gy SIB to the region of vessel, 25 Gy SIP to the overlap between tumor PTV and the Planning OAR volumes. We used univariate/multivariable survival analysis (UVA/MVA, Cox regression, Kaplan-Meier Curves, Log-Rank test) to assess the association of LF with the GTV size and the amount of the GTV which the SIB did not cover. We defined a set of incomplete GTV-covering levels: GTV75 (=yes if less than 75% of the GTV was included in the 50 Gy SIB isodose), GTV70, GTV50 and GTV30. Variables with p≤0.2 at UVA were included for MVA assessment.

Results. With a median follow-up of 17 months (range 1.4-47) 12/51 pts (23.5%) experienced LF. The GTV size (p=0.007, risk factor for LF, Hazard Ratio [HR] 1.04 for 1 cc increase in GTV size) and GTV70 (p=0.2, risk factor, HR= 3.73 for GTV70=yes) were selected at UVA and included in MVA. We dichotomized the GTV size as below/above 25 cc: HR=9.3 if GTV>25 cc. We used dichotomized GTV size and GTV70 to build a 3-level Geometric Score for the prediction of the risk of LF: [Low Risk (LR)] if "GTV<25cc AND GTV70=no"; [Intermediate Risk (IR)] if "GTV>25cc OR GTV70=yes"; [High Risk (HiR)] if "GTV>25cc AND GTV70=yes". Pts classified at HiR had a significantly higher probability of LF: HR=6.9 (95%CI 1.5-32.9) compared to LR, and HR=13.2 (95%CI 3.6-48.4) when compared to IR. 10/12 LFs are in the HiR group.

Conclusions. A large GTV size coupled with an incomplete (<70%) covering of GTV from the SIB highly increases the risk of LF: 62% actuarial probability in the HiR group *vs* 7% in the LR/IR groups. Our Geometric Score could be used to select pts for the online tumor tracking (e.g. possible with an MRI Linac),allowing a reduction of the SIP and a consequent decrease in the amount of GTV left uncovered by the SIB.

CO04

ADJUVANT STEREOTACTIC PANCREATIC RADIOTHERAPY (SPARTA TRIAL): PRELIMINARY TOXICITY RESULTS OF AN ONGOING PHASE II SINGLE CENTER PROSPECTIVE STUDY (NCT05043857)

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Aims. This preliminary analysis aims to assess toxicity profile of an ongoing phase II prospective trial evaluating the impact of adjuvant stereotactic body radiation therapy (SBRT) after surgery of pancreatic cancer with high risk features (SPARTA trial), with the purpose of deliver a dose-intensive treatment in a shorter time allowing better integration of chemotherapy (ChT) and surgery.

Table 1. Treatment-related toxicities.

	Grade 1 N° of patients (%)	Grade 2 N° of patients (%)
During radiotherapy		
Asthenia	5 (11.9%)	
Nausea	6 (14.2%)	4 (9.5%)
Vomiting	2 (4.7%)	
Dyspepsia	2 (4.7%)	
Abdominal pain	5 (11.9%)	1 (2.4%)
Bloating	1 (2.4%)	
Diarrhea	5 (11.9%)	1 (2.4%)
Three months after radiotherapy		
Asthenia		1 (2.4%)
Nausea		
Vomiting		
Dyspepsia		
Abdominal pain	3 (7.1%)	
Bloating	1 (2.4%)	
Diarrhea	2 (4.7%)	
Six months after radiotherapy		
Asthenia		
Nausea		
Vomiting		
Dyspepsia		
Abdominal pain	3 (7.1%)	1 (2.4%)
Bloating		
Diarrhea	3 (7.1%)	
Malabsorption		1 (2.4%)
One year after radiotherapy		
Asthenia		
Nausea		
Vomiting		
Dyspepsia		
Abdominal pain		2 (4.7%)
Bloating		
Diarrhea	1 (2.4%)	
Malabsorption		1 (2.4%)

Methods. The study started in May 2021. Enrolment will last 36 months, followed by 12 months of follow-up for a duration of 4 years and 50 patients to enroll. The inclusion criteria are: surgically treated T1-T4 adenocarcinoma with or without prior ChT and close (<2.5mm)/positive resection margin and/or N1 at lymphadenectomy, ECOG PS <2, estimated life expectancy > 6 months. The exclusion criteria are: metastatic disease, biliary tract or neuroendocrine tumors, history of malignancies except for non-melanoma cutaneous tumors. The primary endpoint is local relapse rate. The secondary endpoints are disease-free survival, overall survival, patterns of failure, acute and late toxicity and clinical-pathological factors related to disease recurrence. SBRT is administered within 4-6 weeks from surgery and adjuvant ChT. We performed 2 volumes in 5 fractions: CTV1 (40 Gy) which covers clips+isotropic 5mm expansion edited on anatomic barriers and CTV2 (30 Gy) which covers

CTV1+ anisotropic 10-15 mm expansion edited on anatomic barriers. Toxicities were recorded according to CTCAE v.5.0.

Results. This preliminary toxicity analysis was focused on 42 patients. Neoadjuvant ChT was performed in 19 patients (45.2%) and 18 (42.8%) underwent adjuvant ChT. Surgery consisted of pancreatoduodenectomy (24 patients, 57%), distal (11,26%) and total pancreatectomy (7,16.6%). All toxicities are shown in Table 1. No patients experienced G3 toxicity. The most frequent toxicities during SBRT were: asthenia (G1, 11.9%), nausea (G1, 14.2%; G2, 9.5%), abdominal pain (G1, 11.9%; G2, 2.4%) and diarrhea (G1, 11.9%; G2, 2.4%). After 3 and 6 months, abdominal pain (16.6%) and diarrhea (11.9%) remained the most observed G1-G2 toxicities. After 1 year, we recorded G2 abdominal pain (4.7%) and G1 diarrhea (2.4%). After 6 and 12 months we observed due cases of G2 malabsorption returned after therapy with pancrealipase.

Conclusions. In this preliminary analysis, adjuvant SBRT in pancreatic cancer proved to be a safe and well tolerated approach without ≥G3 toxicity. We will await the final results to confirm these data.

CO05

COMBINATION OF PARP INHIBITORS AND SBRT FOR THE TREATMENT OF OLIGOMETASTATIC OVARIAN CANCER

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Background. Poly-ADP-Ribose-polymerase inhibitors (PARPi) represent a major line of treatment in high-grade epithelial ovarian cancer. For patients with limited recurrent disease on regular PARPi, local treatments such as surgery or stereotactic body radiation therapy (SBRT) could play a relevant role in deferring the change of systemic therapy. This retrospective, multicenter study aims to evaluate the outcomes and toxicity of SBRT in combination with PARPi in patients with oligometastatic recurrent ovarian cancer.

Materials and Methods. The study included patients who received SBRT for oligorecurrent/oligoprogressive disease in ovarian cancer during PARPi systemic therapy. Data on primary and recurrent diseases, follow-up reports, oncological outcomes and toxicities of SBRT were collected and retrospectively analyzed. Descriptive statistics, including frequencies, medians, and interquartile ranges (IQRs), were used to summarize the data. Statistical significance in the Kaplan-Meier analysis was determined using the log-rank test.

Results. A total of 80 lesions treated in a cohort of 45 patients received SBRT in combination with PARPi were identified in 3 centers between august 2014 and December 2022. The cohort had a median follow-up duration of 6.30 years (IQR: 2.00-17.88 years), with 12 recorded deaths at the last follow-up. The median age at the time of initial diagnosis was 53 years (IQR, 36 - 75 years). Among the participants, 18 patients were identified as BRCA1+ (40.0%), 4 as BRCA2+ (8.89%), 18 as wild type (40.0%), and 5 cases had missing information (11.11%) regarding BRCA status. Actuarial 2-year LC was 86.4% and 5-years OS was 91,9%. Pattern of failure was predominantly outfield (80%). Median dose for SBRT treatment was 25 Gy (range 15-50 Gy) in 5 fractions (range 3-10 fractions). Complete radiologic response, partial response, stabilization and progressive disease were observed in 34(42,5 %), 19 (23,75 %),14 (17,5%) and 6 (7,5%) lesions, respectively, out of 80 evaluable lesions. No > G2 acute or late toxicities were observed.

Conclusions. This study reports the feasibility and potential benefit of this combined strategy in patients with oligometastatic progression under PARPi. Further studies with wider populations are needed to better address the potential role of concurrent PARPi in SBRT treatments.

CO06

STEREOTACTIC RADIOSURGERY FOR THE TREATMENT OF TRIGEMINAL NEURALGIA: QUALITY OF LIFE ANALYSIS

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Aims. Trigeminal neuralgia (TN) is a craniofacial pain syndrome that affects the trigeminal nerve and corresponding branches. Among non-invasive treatment options, stereotactic radiosurgery (SRS) has proven to be a valuable method with satisfying rates of pain relief. In the aim to investigate efficacy of SRS, we performed a retrospective study on 103 patients treated at our institution from 2009 to 2022 with this technique. Primary endpoints were facial pain relief, pain recurrence and occur-

rence of sensory disturbance. Second endpoint was patients' reported quality of life (QoL).

Methods. The delineation of trigeminal nerve and organs at risk (OARs) was obtained by co-registered Computed Tomography (CT) and magnetic resonance (MR) imaging. The target segment of the trigeminal nerve was delineated starting from 2-3 mm away from the root entry zone with a length of about 6 mm, while keeping a certain distance to the brainstem and temporal lobe. Average prescription dose was 58,82 Gy ± 1,49 to the isodose of 80%. All patients were treated using CyberKnife® Robotic Arm Stereotactic Radiosurgery, an image-guided robotic system using non-isocentric irradiation delivery with 6D skull tracking. After the end of the treatment, follow-up information was obtained by outpatient clinical evaluation or telephone interviews, 3-6 months after SRS and then once per year. Pain control and sensory disturbance were estimated using Barrow Neurological Institute Scale (BNI). Median follow-up is 93.2 months.

Results. In terms of pain relief, the best result was obtained after 6 months (97 patients, 94.1%) with a slow decrease after 12 and 24 months (90 and 85 patients, 87.3% and 82.5% respectively). About adverse events, after 24 months, only a small percentage reported the presence of facial numbness (10 patients, 9.4%) or mild sensory disturbances (12 patients, 11.6%). No further complications, such as temporal lobe radionecrosis, weakness of the mandible, diplopia or hearing loss, were reported. The majority of patient reported significant increase of QoL (90%), along with a decrease of depression rates.

Conclusions. Basing on the results of our study, it can be concluded that CK SRS is safe and effective minimally invasive therapeutic option to interrupt the trigeminal nociceptive pathways and improve pain relief and QoL in patients with TN.

CO07

LINAC-BASED STEREOTACTIC ARRYTHMIA RADIOABLATION (STAR) FOR PAROXYSMAL ATRIAL FIBRILLATION IN ELDERLY: RESULTS OF THE FIRST WORLDWIDE PROSPECTIVE PHASE II TRIAL

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Aims. To investigate the feasibility of stereotactic arrhythmia radioablation (STAR) for the treatment of paroxysmal atrial fibrillation (AF) in elderly patients (NCT04575662).

Methods. The inclusion criteria are age > 70 years, symptomatic AF, antiarrhythmic drugs intolerance or non-response. A sample size of 20 patients is planned to complete trial. All patients undergo to 4D CT simulation. The clinical target volume (CTV) is identified in the area around PVs. Internal target volume (ITV) and Organs at Risks (OaRs) planning risk volume (PRV) are created to compensate heart and respiratory movement. The planning target volume (PTV) is defined adding 0-3 mm to the ITV in all directions. STAR is performed with a total dose of 25Gy (single fraction).

Results. From May 2021 and June 2022, the enrollment goal was achieved (20 enrolled patients). Eighteen patients underwent STAR. One patient withdrew informed consent before treatment and one patient was excluded after the enrollment due to the unfavorable anatomy. With a median follow-up of 16 months (range 12-23), no acute toxicity more than G3 was reported, demonstrating the safety of STAR in this setting of patients. Five patients had a G1 esophagitis 24 hours after STAR; the symptoms resolved after 1 week using proton pump inhibitors and sucralfate. Eight patients had an asymptomatic grade 1 pericardial effusion (max 2 mm) documented after 3-6 months from STAR treatment. Only, one patient had a clinically significant acute event after STAR. In particular, after 1 hour from STAR, patient 13 had a torsade de pointes treated effectively by electrical cardioversion and subsequent cardiac ICD implantation. It is not possible to determine if this event was due to STAR or to a chance. Frequent atrial ectopies and atrial tachycardias episodes were documented in all patients during the first 2 months after STAR. Most patients had a significant reduction in AF episodes. Five patients performed electrophysiological study after STAR. Patient 1 and 3 performed the study after 6 months while patients 9,10 and 13 after 12 months from STAR. In all patients the electric ablation of PVs was highlighted. Finally, a significant improvement of quality of life was documented (48±15 at enrollment *vs* 75±15 at 12 months FU; $p<0.001$).

Conclusions. The present phase II trial demonstrated the safety of STAR in AF elderly patients, reporting also promising results in terms of outcome and quality of life. Surely, robust data are needed.

CO08

PATTERNS OF PRACTICE FOR BREAST CANCER POST-OPERATIVE RADIOTHERAPY IN ITALY ACCORDING TO THE ESTRO-ACROP CONSENSUS AND AIRO POSITION PAPER: A NATIONAL SURVEY ON THE BEHALF OF AIRO BREAST CANCER GROUP

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Aims. Purpose of this survey is to report heterogeneities in current Italian clinical practice after the publication of both ESTRO-ACROP consensus and AIRO Breast Cancer (BC) Group position statement, with regard to radiotherapy (RT) fractionation in the setting of whole breast irradiation (WBI), chest wall irradiation (CWI), regional nodes irradiation (RNI) and partial breast irradiation (PBI).

Methods. A nationwide 35-point questionnaire was distributed online via SurveyMonkey to the Italian RT Centers (general topic:9 items; WBI:10 items; CWI:10 items; RNI:8 items; PBI:5 items). For each issue, use of hypofractionation, clinical decision making, RT techniques and dose prescription were analyzed. The survey was approved by the scientific committee of AIRO (N 32/2022). Results were reported with SurveyMonkey advanced tool by percentage and weighted average.

Results. One hundred and twenty Italian RT Centers answered the survey. In most cases (70%), responders treated more than 200 BC patients/year with both pre- and post-operative multidisciplinary discussion for all the patients (>75%). Moderate hypofractionation (15 fractions) was used for WBI, CWI and RNI by 99%, 60% and 63% of the responders. Ultra-hypofractionation (5 fractions) was less common with 65%, 13% and 5% adopting this scheme for WBI, CWI and RNI, respectively. The two main reasons for not using ultra-hypofractionation were lack of adequate recommendations and major expected severe toxicity. For WBI, 3D conformal RT was the most widely used technique while volumetric-modulated arc therapy was more frequent for both CWI and RNI, regardless of fractionation. PBI was used by 57% of responders. The Florence scheme (30 Gy/5 fractions) and VMAT were the most used scheme (55%) and technique (47%), respectively. Practice changing after ESTRO-ACROP consensus and AIRO-BC Group position statement publication are shown in Table 1. Interest in multicentric studies about ultra-hypofractionation was high with 34.59% of the responders with the intention to collaborate in the future.

Conclusions. Moderate hypofractionation appears to be consolidated for WBI, while its use for PMRT and RNI is less frequent, but not lower (>60%). Five fractions are currently used more frequently for WBI compared to PMRT and RNI. The AIRO BC Group will try to harmonize the current indications and understand strategies to standardize heterogeneity of Italian Centers, overcoming the critical issues highlighted by the survey.

Table 1. Italian Radiotherapy Centers practice changing after ESTRO-ACROP consensus and AIRO-BREAST position statement.

	Moderate hypofractionation for all the patients	Moderate hypofractionation for an increasing number of patients	Start using ultra-hypofractionation	No change
Whole Breast Irradiation	15.32%	22.52%	13.51%	48.64%
Chest Wall Irradiation	16.04%	24.53%	8.49 %	50.94%
Regional Nodes Irradiation	18.10%	22.86%	2.86%	56.19%

CO09

PRE-OPERATIVE SINGLE FRACTION STEREOTACTIC RADIOSURGERY (SRS) FOR EARLY STAGE BREAST CANCER. PHASE II CLINICAL TRIAL, PRELIMINARY REPORTS

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Aims. We present preliminary data of the phase II clinical trial after completing the first stage of recruitment.

Methods. The single arm, phase II clinical trial is designed by using the 2-stage Simon's Method. Patients over 50 years of age, with unifocal, invasive ductal carcinoma (no special type), clinical stage: tumor < 3cm, nodes negative, estrogen receptor (ER) positive, human epidermal grow factor receptor-2 (HER2) negative, of any grades, who were eligible for conservative surgery, were included. Patients who agreed to take part in the clinical trial had a breast MRI scan for disease extent assessment. A fiducial marker positioned by an expert radiologist with ultrasound guidance identifies the Gross Tumor Volume (GTV). Planning Tumor Volume (PTV) is created by adding 3 mm margins to the GTV. The total

dose prescribed is 30-36Gy to 95% of the PTV. Surgery was performed 4 months after SRS. In the first phase of the study, we have enrolled 40 patients, aiming to show the rate of Grade 2 (G2) of local toxicity is less than 7%. We scored toxicity on the Common Toxicity Criteria (v4.0) scale. We document local side effects like skin redness, breast oedema, fibrosis, telangiectasia, atrophy and breast pain.

Results. From January 2022 until April 2023, we completed the first phase of the study. We screened 52 patients, excluded 11 (21%) and treated 40 patients according to the study protocol. The median follow-up after SRS was 11 months (range 2-15 months). We observed no G2 acute toxicity events. One month after SRS, 9 patients (22%) reported grade 1 (G1) acute toxicity reactions such as pain (4), localized skin erythema (6), skin pruritus (1), asthenia (1). Three months after surgery, 3 patients (7%) had G2 late toxicity as 2 induration and 1 erythema. Nineteen patients (47%) declared G1 toxicity: 11 fibrosis, 5 breast pain, 6 limited skin redness, 1 overall breast oedema, 1 skin irritation, 1 atrophy. Six months after surgery, no G2 outcomes were detected. Ten patients (25%) showed late G1 toxicity occurrences: 7 fibrosis, 2 breast discomfort, 1 atrophy.

Conclusions. We have completed the first stage of the Phase II clinical trial by treating 40 patients. Following the study protocol, due to the low toxicity rate, we will move forward with the second stage of the study that will treat 148 patients.

CO10

AXILLARY MANAGEMENT IN BREAST CANCER PATIENTS UNDERGOING UPFRONT SURGERY: RESULTS FROM A NATIONWIDE SURVEY ON BEHALF OF THE CLINICAL ONCOLOGY BREAST CANCER GROUP (COBCG) AND THE BREAST CANCER STUDY GROUP OF THE ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY

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Aims. We assessed the current practice concerning the axillary management of breast cancer (BC) patients undergoing upfront surgery, amongst radiation oncologists (ROs) practicing in Italy.

Methods. An online survey via SurveyMonkey (including 21 questions) was distributed amongst ROs in Italy through personal contacts and the Italian Association for Radiotherapy and Clinical Oncology (AIRO) network, from August to September 2022. We particularly focused on the emerging omission of axillary lymph node dissection (ALND) in presence of 1-2 sentinel node-positive, and the consequent change in the role of regional nodal irradiation (RNI). The survey was conducted according to the CHERRIES statement and was revised and approved by the scientific committee of AIRO (Nr. 15/2023). The statistical analyses included descriptive statistics and chi-squared testing to assess any meaningful statistical difference in the axillary management amongst certain subgroups of participating ROs.

Results. A total of 101/195 (51% response rate) Italian Radiotherapy Cancer Care Centres answered the survey. With respect to patients with 1-2 sentinel node–positive, the relative proportion of respondents that offer patients ALND a) always, b) only in selected cases and c) never, was 37.6%, 60.4% and 2.0%, respectively, with no significant geographical (North *vs* Centre-South Italy; p=0.92), nor institutional (Academic *vs* non-Academic; p=0.49) differences. Radiation therapy indications varied widely in patients who did not undergo ALND. About a third of the responders (17/56, 30.4%) stated that regional nodal irradiation (RNI) was constantly performed. Half of the responders offered RNI in selected cases, stating that unfavourable biologic tumour profile and extracapsular nodal extension were considered drivers of their decision.

Conclusions. Results of the present survey show the variability of axillary management offered in clinical practice for BC patients undergoing conserving surgery upfront in Italy. Analysis of these attitudes may give trigger to modify some clinical approaches through multidisciplinary collaboration and create the background for future clinical investigation.

CO11

STEREOTACTIC RADIATION THERAPY FOR BREAST CANCER PATIENTS NON SUITABLE FOR SURGERY

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Aims. To identify the maximum tolerated dose (MTD) of stereotactic body radiotherapy (SBRT) for unresected breast cancer (BC).

Method. This is a two-center, prospective, open-label, phase I study of dose escalation SBRT in two settings of patients with histologically confirmed diagnosis of BC unfit for surgery at time of enrollment: at one side elderly pts candidate to receive endocrine therapy alone for age-related comorbidity, on the other metastatic pts. not progressing after 6 months of I line systemic therapy with persistent breast disease. Treatment dose levels I, II and III were respectively 40Gy, 42.5Gy and 45Gy, delivered in 5 fractions on every- other-day scheme. The time-to-event Keyboard (TITE-Keyboard) design will be used for conducting the trials and to assign the dose to the next cohort of pts. Primary end-point was the MTD, defined as the dose level associated with a ≤ 20% rate pre-specified treatment-related dose -limiting toxicity (DLT). DLT was defined as any grade 3 or worse toxicity (per CTCAE v.5.0) occurring within 6 months from the start of treatment. Co-secondary endpoints were patients reported quality of life (QoL), evaluated using the combined EORTC QLC-C30 and QLQ-BR23 questionnaires, breast cosmesis and primary tumor better response in terms of locoregional control (LRC) and clinical response (CR).

Results. From January 2019 to May 2023 we have enrolled and treated 21 pts. at I dose level of 40Gy/5fx and 4 pts at intermediate dose level of 42.5Gy/fx with excellent tolerance to treatment (Tox o%≥G3; 16% G2; 28% G1; 56% G0). Median follow-up was 12.4 months. 16 pts. have reached at least 6 months of observation after treatment and MTD was not reached. 13 pts achieved a clinical complete response (cCR) and 13 pts. a radiological one (rCR). Median time to cCR is 6.9 months and 8.4 months for rCR. In this small number of patients no differences were observed in the EORTC QLC-C30 score and the breast cancer-specific score (QLQ-BR23) from the baseline at 6 months follow-up, while all patients showed an excellent or good cosmesis.

Conclusions. These are preliminary data of an ongoing phase I study, that will be updated at AIRO congress. According to these early data, SBRT could rapresent a short, highly effective and well tolerated treatment in pts not candidated to surgery approach, with the possibility of continuing systemic treatment without interruption.

CO12

SINGLE FRACTION ABLATIVE PREOPERATIVE RT FOR EARLY-STAGE BC, THE CRYSTAL TRIAL: PRELIMINARY RESULTS

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Purpose/Objective. Breast-conserving surgery (BCS) and WBRT are the standard of care for early-stage BC. Based on the observation that most local recurrences occurred near the tumor bed, APBI, consisting of a higher dose per fraction to the tumor bed over a reduced treatment time, has been gaining ground as an attractive alternative in selected patients with low-risk BC. The aim of this study is to report preliminary results of the Phase I of the CRYSTAL trial, in which preoperative RT is delivered in a single fraction using CyberKnife for selected BC patients.

Methods. CRYSTAL trial (NCT04679454) is a monocentric phase I/II, single-arm and open-label study planning to enroll 79 patients over 5 years. Patients will receive an ablative dose (18-24 Gy) to the tumor before surgery using CyberKnife. The primary endpoint for the phase I study is the identification of the maximum tolerated dose (MTD) which meets a specific target toxicity level (no grade 3-4 toxicity). For the phase II study, the primary aim is the evaluation of treatment efficacy measured in terms of pathological complete response rate.

Results. A total of 9 patients with a median age at enrollment of 63 years have been enrolled and treated within the phase I of the study (3 patients for each dose step: 18-21-24 Gy). Stage at diagnosis was T1N0 for 6 patients and T2N0 for 3 patients (luminal A for 7 patients, luminal B for 1 patient and luminal B-HER2+ for 1 patient). Median PTV volume was 18.9 cm3 (range 5.9-47.8 cm^3). At pre-surgery MRI 7 patients experienced stability disease and 2 patients partial response. Median time to surgery was 33 days (range 28-36 days) with three

patients who underwent mastectomy and 6 QUAD+BLS. One post-surgical complications (liponecrosis) has been reported. All patients experienced a reduction in Ki67 proliferation index (median change between biopsy and histologic exam 6%). Six among the nine treated patients have received post-operative RT according to study protocol, with one patient receiving also chemotherapy. No G>2 acute toxicities have been reported and only one G1 chronic toxicity (breast pain) has been reported at last follow-up. At a medium follow up of 7.8 months (range 4.9 – 16.23 months) one patient developed a nodal relapse and one a secondary tumor. All the other patients are alive with no evidence of disease.

Conclusions. The present analysis reports preliminary results of the Phase I study. Since no G > 2 toxicities have been reported in this phase the 24 Gy dose step will be used for the treatment in Phase II. Data about late toxicities will be collected when updated follow-up data will become available. The findings of this study, updated with additional patients and longer follow-up, along with the data that will become available from similar ongoing investigations, may serve as a hypothesis-generating step towards a change of the current treatment paradigm in early stage BC.

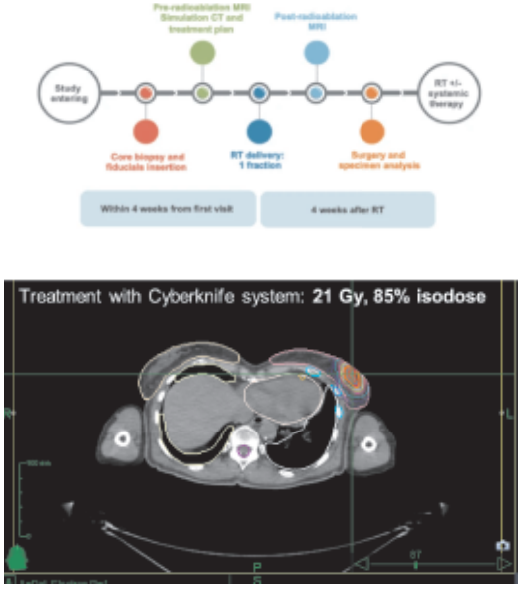

Figure 1. (a) Overview of the study protocol and (b) example of a preoperative RT treatment plan (21 Gy, 85% isodose).

CO13

SINGLE-FRACTION PARTIAL BREAST IRRADIATION (PBI) TO THE TUMOR BED: TOXICITY OUTCOME OF A PHASE II CLINICAL TRIAL

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Aims. To report toxicity findings of a phase II clinical trial. During the initial stage of the study, 40 patients were recruited and treated, aiming to demonstrate local Grade 2 (G2) toxicity below 7%.

Methods. The phase II clinical trial currently ongoing investigates toxicity of a single-fraction PBI for early stage breast cancer patients after lumpectomy. We delineate 2 groups of patients eligible for local therapy. Group 1 includes patients over 50, with ductal cancer, single lesion ≤ 3 cm and nodes negative (pN0), of any grades and any molecular subtypes. In the Group 2, for patients aged 70 years or more, the lobular histology, presence of multifocal tumor or nodes positive (pN1a) were not criteria of exclusion. The Clinical Target Volume (CTV) was created in line with NSABP B-39/RTOG 0413 guidelines. The Planning Total Volume (PTV) was obtained by adding 3 mm isotropic margins to the CTV. Treatment was delivered as a single dose of 17.5Gy prescribed to the 95% of the PTV with GammaPod Technology. Toxicity was evaluated using the Common Toxicity Criteria (v4.0), such as pain, erythema, hyperpigmentation and fibrosis. Toxicity was assessed by a radiation oncologist every 1, 3, 6 and 12 months.

Results. From December 2021 to September 2022, 52 patients were eligible to be enrolled in the research protocol. Twelve (23%) were excluded and 40 patients were treated. The median follow-up time was 11 months (range 8-15). No local G2, acute and late toxicity events were registered. One patient reported late G2 fatigue. One month after PBI, 14 patients (35%) presented Grade 1 (G1) toxicity: 8 breast erythema, 5 breast pain and 1 induration. At 3 months, 14 patients (35%) referred G1 events: 6 pain, 5 erythema, 3 induration and 3 atrophy. Late toxicity occurrence (at 6 months) was described by 19 patients as 2 dermatitis, 3 induration, 8 breast pain, 4 local hyper-pigmentation and 7 atrophy. Sixteen patients had mammography 1 year after PBI: in 3 (18%) cases, radionecrosis was documented, none were symptomatic.

Conclusions. After a median follow-up period of 11 months, no Grade 2 acute and late local events were observed. The study will continue until the enrollment of 148 patients.

CO14

ADJUVANT HYPOFRACTIONATED RADIOTHERAPY (HYPO-RT) IN 10 FRACTIONS IN NODE POSITIVE LOCALLY ADVANCED BREAST CANCER: 5 YEAR-RESULTS OF A PHASE II STUDY

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Aims. Post-operative loco-regional hypofractionated radiotherapy (Hypo-RT) is an attractive approach in locally advanced breast cancer (LABC). In this phase II study we report results at 5-years of Hypo-RT in 10 fractions (fxs) targeting the primary tumor and the involved regional lymph nodes in patients (pts) with resected LABC.

Methods. A schedule of 34 Gy/10 fxs/2 weeks to the whole breast/chest wall and to the draining lymph nodes was used; an optional boost of 8 Gy in single fraction was administered to the tumor bed in pts underwent lumpectomy. All pts but those who underwent mastectomy with or without reconstruction were also asked to rate their cosmetic outcome according to the Harvard scale. Acute toxicity was weekly assessed according to CTCAE 4.0 scale during RT and at 1 month after the end of RT. Late toxicity was recorded according to LENT/SOMA scoring system at 3 and 6 months after the end RT and then yearly during follow-up (fup) examination. Cancer related endpoints in terms of local control (LC), distant metastases-free survival (DM-FS), specific disease-free survival (SD-FS) and overall survival (OS) were evaluated from the start of RT to the diagnosis of local relapse, distant metastases or to the last fup, respectively. Kaplan-Meier method was used for analysis.

Results. From February 2015 to March 2019, 59 women (median age 60 years, IQR: 48.3-68.8) with a stage II-IIIA breast cancer were accrued. All pts underwent axillary dissection and lumpectomy (83%) or mastectomy (17%). One patient withdrew consent to protocol. Evaluable pts underwent neo-adjuvant or adjuvant chemotherapy (27.5% and 57% respectively) or exclusive hormone therapy (15.5%). During RT, no grade ≥2 acute toxicity was recorded. After a median fup of 63 months (range: 25-92), the cumulative incidence of any grade of late toxicity was 43.4% (95% CI), 30.0% and 46.1% for patients undergone mastectomy and lumpectomy, respectively. Peak 2 events were found for fibrosis (1.7%), telangiectasia (1.7%) and lymphoedema (1.7%). One patient (1.7%) experienced grade 3 breast retraction. Cosmetic outcome was reported as excellent (51.7%), good (22.4%), fair (10.3%) and poor (3.4%). Regarding clinical outcomes at 5-years, LC was 98%, DM-FS 89.2%, SD-FS 80.8% and OS 93.7%.

Conclusions. Our experience supports the efficacy and safety with an acceptable toxicity profile of 10-fxs Hypo-RT schedule targeting the primary site as well as the draining lymph node stations in pts with resected LABC.

CO15

TREATMENT EFFECTS AND DISEASE PROGRESSION DISTINCTION IN TREATED BRAIN TUMORS IS A CHALLENGE. PROMISING RESULTS USING DELAYED CONTRAST MRI

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Aims. Published studies report up to 30% of radiant treatment effects in patients with glioblastoma and up to 24% in brain metastatic ones after radiosurgery, defined as pseudoprogression (within 3 months from treatment) or radionecrosis (RN – later than 3 months). Unfortunately, the presence of contrast enhancing lesions leads to difficult data interpretation and treatment decisions. We prospectively evaluated patients with doubtful framework between treatment effects and disease progression aiming to assess the ability of contrast clearance analysis (CCA) and treatment response assessment maps (TRAMs) in differentiating this two conditions.

Methods. From February 2021 to November 2022, 62 patients for 96 delayed-contrast MRI performed with doubtful framework between treatment effect and disease progression were evaluated. Twenty-five had primary brain tumors receiving surgery and radiation therapy with or without concomitant and adjuvant chemotherapy; among them 13 underwent re-irradiation for recurrent gliomas; 37 patients had brain metastasis, and radiosurgery in single or multifractions were administered. In the latter delayed contrast MRI has been performed at a median time of 32 months from radiosurgery. TRAMs were calculated by subtracting T1 contrast enhanced MRI images acquired 5 minutes after contrast injection from the images at least 60-105 minutes after. Diagnosis of persistent tumors or disease progression was based on the presence of blue areas on TRAMs, and that of treatment effects was made in cases of red regions. All images were uploaded, coregistered and elaborate into the image workstation ([Brainlab AG, Olof-Palme-Straße 9, 81829 Munich]).

Results. During their follow-up, 24 patients (38%) showed a clinic and radiologic suspicion of persistent tumoral lesion or progressive disease, and 40 (62%) a suspicion of RN. For 14 patients a brain MET-PET has been performed. TRAMs analysis have shown a fair

agreement with clinicoradiologic diagnosis, perfusion-weighted MRI, and PET imaging. Moreover, 7 patients underwent surgical resection, with histopathological confirm of persistent disease in 4 and RN in 3.

Conclusions. These preliminary results show the ability of TRAMs evaluation in distinguish between RN and progressive disease. The recruitment of new patients continues, and further evaluations are ongoing to evaluate sensitivity and positive predictive value of TRAMs analysis.

CO16

THE MICROVASCULAR HEALTH STATUS PREDICTS RADIO-INDUCED ACUTE TOXICITIES IN BREAST, PROSTATE AND HEAD & NECK CANCER PATIENTS

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Aims. To investigate the role of healthy/unhealthy microcirculation in predicting acute toxicity for breast (BC), prostate (PC) and Head & Neck (HNC) RT.

Methods. We enrolled BC patients (pts) treated with adjuvant hypofractionated-RT (42.4 Gy + 10 Gy boost), PC pts receiving radical-RT (65 Gy / 26 fractions) and HNC pts treated with conventional RT (54-70 Gy @ 2Gy/fr) or moderately hypofractionation (46.6-69.9 Gy @ 2.1-2.2 Gy/fr). We assessed baseline sublingual-microvasculature (MV) health status before RT using a sidestream dark-field camera coupled to the GlycoCheck™ software. The system records videos of the circulation in the microvessels and computes functional parameters:

- Perfused boundary region (PBR), estimating the dynamic lateral movement of red blood cell into the permeable part of the endothelial glycocalyx. Higher PBR values result from damaged glycocalyx and impaired microcirculation.
- Total density of capillaries (1/mm^3)
- Blood Flow in the analyzed area (103 µm^3/s/mm^2)
- MV_HealthScore (MVHS™), higher values indicate healthier MV. MVHS is computed by weighting information from capillary density, PBR, blood flow and recruitment capacity.

Endpoints were: (i) grade≥2 erythema (G2+E) for BC, (ii) any grade≥3 toxicity (G3Tox) for HNC and (iii) persistent grade≥1 gastrointestinal + genitourinary toxicity (G1+GIGU) for PC. We used logistic regression to assess MV functional parameters' association with toxicity.

Results. We evaluated 63 BC, 38 PC and 39 HNC pts. 77 (55%) had an evaluation for MVHS. 23/63 BC pts presented with G2+E, 12/38 PC pts with G1+GIGU, 12/39 HNC pts with G3Tox. The MVHS was associated with toxicity: healthy MV protects from toxicity (continuous, OR=0.66 for 1 point increase, p=0.01, AUC=0.69). Categorizing pts as low MVHS (<2.5), average MVHS (2.5-6.5) and high MVHA (>6.5), the observed toxicity rates in the 3 classes were 50%, 26%, 0% (p=0.02). A multivariate model including the separated functional parameters predicted toxicity (AUC=0.67): higher PBR and blood flow are a risk (OR=7.6;Logarithm, OR=14.2), higher capillary density protects (Logarithm, OR=0.002).

Conclusions. MVHS predicts acute toxicity in BC/PC/HN pts: impaired MV is associated with increased radio-susceptibility. This kind of systemic functional information derived by a sublingual microscope could be exploited in different cancer districts, boosting the personalization of predictive models and tailoring them to the single-patient functional status.

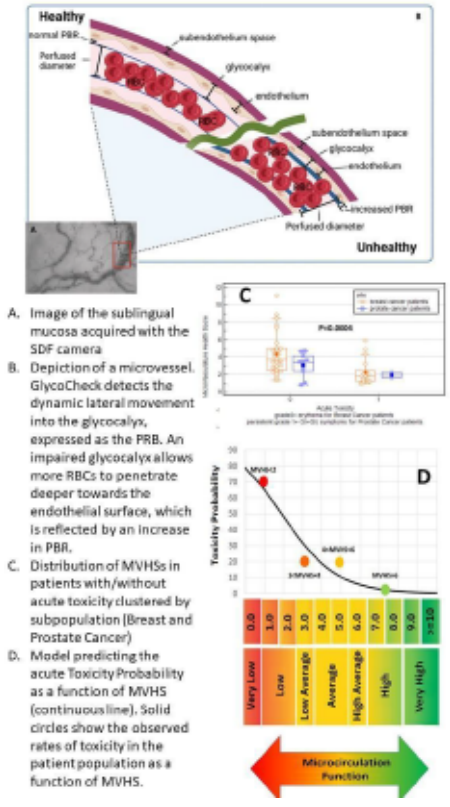

Figure 1.

CO17

INTER-CONTOURING VARIABILITY OF LEFT DESCENDING ARTERY (LAD) IN POST-MASTECTOMY RADIOTHERAPY FOR LEFT BREAST CANCER PATIENTS

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Aims. The left anterior descending artery (LAD) is one vulnerable part of the heart that should be spared during radiation therapy. However, its contouring is very critical due to the poor visibility of this organ on planning CT scans (CTp) without contrast enhancement. In this study, the contouring of the LAD, with and without the aid of contrast enhanced CT (CTce), was compared over 6 experienced radiation oncologists (ROs).

Methods. Ten left breast cancer patients were enrolled for this study. All patients underwent mastectomy and immediate reconstruction after neoadjuvant chemotherapy (NACT). For each patient, a CTp and a CTce were available. First, each RO blindly and independently contoured the LAD on CTp. Then a rigid match, based on the heart, was performed between CTp and CTmdc and, LAD contours were segmented on CTp with the aid of CTce. For LAD contouring, CT window set at 150 width and 50 level, a brush of 3mm-diameter were chosen and interpolation was performed in the slices were the LAD was not visible. For each modality (CTp *vs* CTce), contouring variability between ROs was measured using the Dice similarity coefficient (DSC) (threshold≥0.7 for good agreement) and 95% Hausdorff distance (95HUD). For each patient, median DSC and 95HUD of LAD contours were assessed, then mean DSC and 95HUD was computed overall patients. Inter-modality differences were assessed by means of a two-tailed T-test.

Results. Poor agreement was found for Lads contoured on CTp, with Mean DSC and 95HUD of (0.45±0.09) and (6.62±2.85)mm, respectively. All contours on CTce, conversely, revealed a better concordance with Mean DSC and 95HUD of (0.62±0.06) and (4.34±1.79)mm. A statistically significant difference was found between the two modalities (CTp *vs* CTce, p-value<0.05).

Conclusions. The use of a contrast enhaced CT in the radiotherapy planning of left breast cancer patients is recommended in order to better identify the LAD. However, uncertainties on LAD contouring for this modality are still high (DSC<0.7). We, therefore, estimated that an isotropic margin of 4-5 mm around the LAD could geometrically compensate for the inter-observer variability only. Further studies on the dosimetric validation of the LAD margin are still in progress.

CO18

BIOMARKERS OF RADIATION-INDUCED HEART INJURIES IN CONTEMPORARY ADJUVANT RADIOTHERAPY FOR EARLY STAGE BREAST CANCER: AN EXPERIMENTAL PROSPECTIVE TRIAL

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Aims. To explore the potential role of radiation-induced heart injuries biomarkers using intensity modulated radiotherapy (IMRT) for early stage breast cancer (BC).

Methods. The present study is no-profit, monocentric, prospective trial approved by Ethical committee in 2019 (n. Prot. XXXX 2019-27). Inclusion criteria were: age > 18 years old, absence of cardiologis diseases neither diabetes or hypertension, early stage breast cancer (*i.e.* stage pT1-2 pN0-mic), Luminal A or Luminal B not amenable for adjuvant, negative surgical margins, absence of distant metastases, Karnofsky performance status > 70, informed consent signed by patient. Patients were submitted to echocardiography and venous blood sampling at the first day of RT, at the end of RT, after 6- and 12 months post-RT. For each patient enrolled in the protocol, the following parameters were analyzed: troponin I high sensitivity, N-terminal pro-BNP, LVEF-left ventricular ejection fraction and GLS-global longitudinal strand. These parameters were related to heart d-mean, V5, V10, V20 and left anterior descending (LAD) coronary artery d-mean. All patients were treated with IMRT using conventional fractionation.

Results. According to inclusion criteria, 34 patients affected by left side BC and 31 patients affected by right side BC were analyzed. Median age was 54 years old (range, 35-77). Patients were stratified at the 75th percentile for dosimetric variables. At statistical analysis, there was an increase of troponin I high sensitivity values at the end of RT with a subsequent recovery at 6 and 12 months post-RT for patients with heart d-mean > 2Gy (p<0.5). Of contrast, there was a stastically significant increase of N-terminal Pro-BNP lately, at 12 months, post-RT (p<0.5) for dmean LAD > 4Gy. Regarding the eocardiographic parameters here analyzed, there was a

1% LVEF reduction at the end of RT for heart d-mean > 2Gy, similarly to troponin I behaviour (p-value < 0.4). No statistically significance regarding GLS-variable variation over time.

Conclusions. The current prospective study have documented new biochemical and instrumental markers of radiation-induced heart injuries using IMRT with conventional fractionation for early stage breast cancer. Long-term results are awaited to understand the clinical risk of cardiac events. Starting form this background, a new trial will be designed using hypofraction regimens

CO19

RELATIONSHIP BETWEEN DOSIMETRIC PARAMETERS AND INCIDENCE OF PELVIC FRACTURES IN PATIENTS TREATED WITH ADVANCED RADIOTHERAPY TECHNIQUES WITH CURATIVE INTENT FOR GYNAECOLOGICAL MALIGNANCIES

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Aims. To evaluate the relationship between dosimetric parameters and pelvic insufficiency fractures (PIF) in patients treated with advanced radiotherapy techniques with curative intent for gynaecological malignancies.

Methods. Between 01/01/2018 and 31/12/2021, at a single radiotherapy center 130 patients (pts) with gynaecological malignancies were treated with radiotherapy to pelvis or pelvis and para-aortic lymph nodes. Most pts (96.2%) underwent IG-IMRT, 33.1% received neoadjuvant chemotherapy and 27.7% received concomitant chemotherapy. Median follow-up was 14.4 months (range 3-44).

Results. PIF were identified in 18/130 pts (13.8%) of which 7 (38.9%) were not explicitly diagnosed during follow-up but later confirmed by an expert radiologist. A total of 34 lesions were identified in all pelvic bones. The site most frequently involved was the sacrum with 13 fractures (41%), the sacroiliac joints with 10 fractures (32%) ischio-pubic branches (18%) and iliac wings (9%). Median time to fracture diagnosis was 9.57 months (range 1.8-28.07). The analysed dosimetric parameters were D50%, V15Gy, V30Gy and V45Gy for each bone segment. In the group with PIF, all of these parameters had a higher mean value than in the non-PIF group. We found a statistically significant difference for right and left ischiopubic region for V30Gy (p=0.039 and p=0.020, respectively) as well as for left ischiopubic region V45Gy (p=0.043). We identified a significantly increased risk of PIF when left ischiopubic branch V30Gy exceeded 65% (OR 4.167, 95% CI 1.321-13.139), for body weight <55 Kg (OR 4,856, 95% CI 1,380-17,081, p=0.007) and for concomitant chemotherapy (OR 4,135, 95% CI 1,478-11,558, p=0.004).

Conclusions. Our analysis demonstrated a consistently higher risk of PIF with higher bone doses for all examined bone segments. These relationships reached statistical significance for some segments already in this monocentric analysis. Bone exposure should therefore be minimized as much as possible during treatment planning. The importance of clinical-anamnestic factors such as low body weight and concomitant chemotherapy, already described in other series, was confirmed. The expansion of the database across a second center will likely improve the robustness of the observation.

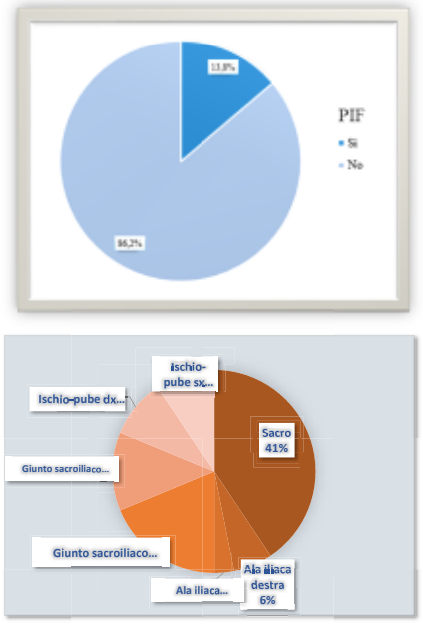

Figure 1.

CO20

MULTIPLE OLIGOMETASTASES TREATED WITH SINGLE COURSE STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR): OUTCOME AND PREDICTIVE FACTORS

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Aims. Delivering stereotactic ablative radiotherapy (SABR) in patients with multiple oligometastases represents a challenge for clinical and technical reasons. The purpose of this study was to evaluate survival and toxicity of a large sample of patients affected by multiple oligometastases treated with single course SABR and to investigate the impact of tumor volume on patients' outcome.

Methods. Data of patients with 3 to 5 extracranial oligometastases from any solid tumors treated with single course SABR were retrospectively analysed. All patients were treated with volumetric modulated arc therapy (VMAT) technique with ablative intent. Endpoints of the analysis were overall survival (OS), progression free survival (PFS), local control (LC) and pattern of toxicity. Univariate analysis and multivariate Cox regression (backward conditional) model were carried out to evaluate the association between clinical factors and survival.

Results. From 2012 to 2020 136 patients were treated on 451 oligometastases. Most common primary tumor was colorectal cancer (44.1%) followed by lung cancer (11.8%) and prostate cancer (5.9%). A total of 3, 4 and 5 lesions were simultaneously treated in 102 (75.0%), 26 (19.1%), and 8 (5.9%) patients, respectively. Median total tumor volume (TTV) was 19.1 cc (range 0.6-245.1). With a median follow-up of 25.0 months, OS at 1 and 3 years was 88.4% and 50.2%, respectively. On univariate analysis higher age, higher Eastern Cooperative Oncology Group (ECOG) performance status (PS), lower EQD2 and higher TTV were associated with worse OS. At multivariate analysis, however, only increased TTV was an independent predictive factor of worse OS (HR 2.37, 95%CI 1.18- 4.78, p=0.014) and PFS (HR 1.63, 95%CI 1.05-2.54; p=0.028). Median OS was 80.6 months if tumor volume was ≤ 10 cc (1- and 3-years OS rate 93.6% and 77.5%, respectively), and 31.1 months if TTV was higher than 10 cc (1- and 3-years OS rate 86.7% and 42.3%, respectively). Rates of LC at 1 and 3 years were 89.3% and 76.5%. In terms of toxicity, no grade 3 or higher toxicity was reported both in the acute and late settings.

Conclusions. Our study demonstrated that total tumor volume is a better predictor of survival than the number of lesions in patients affected by 3 to 5 oligometastases treated with single course SABR. In the absence of valid biomarkers, disease volume should be considered as a relevant factor for the therapeutic choice to assess which patients can benefit from SABR.

Table 1. Patients and disease characteristics.

N. patients	136
N. oligometastases	450
Age, median (range)	67.8 (28.0 – 87.1)
Gender	
Male	80 (58.8)
Female	56 (41.2)
Performance status	
0	91 (66.9)
1	36 (26.5)
2	9 (6.6)
Primary tumor	
Colorectal	60 (44.1)
Lung	16 (11.8)
Prostate	8 (5.9)
Breast	7 (5.1)
Others	45 (33.1)
Histology	
Adenocarcinoma	110 (80.8)
Non-adenocarcinoma	26 (19.2)
Disease free interval, median (range)	14.1 months (0 – 222.1)
Timing of metastases	
Synchronous	39 (28.7)
Metachronous	97 (71.3)
ESTRO-EORTC classification	
1 De novo sincrono	6 (4.4)
2 De novo metacrono oligorecurrence	20 (14.7)
3 De novo metacrono oligoprogression	2 (1.5)
4 Repeat oligorecurrence	25 (18.4)
7 Induced oligorecurrence	59 (43.4)
8 Induced oligopersistence	16 (11.8)
9 Induced oligoprogression	8 (5.9)
Previous local treatment	
No	82 (60.3)
Yes	54 (39.7)
Previous systemic therapy	
No	36 (26.5)
1 line	43 (31.6)
2 lines	35 (25.7)
3 or more lines	22 (16.2)
Treated metastases	
3	102 (75.0)
4	26 (19.1)
5	8 (5.9)
Total tumor volume in cc, median (range)	19.1 (0.6 – 245.1)
Treated site	
Lung	47 (34.6)

CO21

CLONOGENIC ASSAYS IN THE B16 MELANOMA: RESPONSE TO FLASH-RT *VS* CONV-RT

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Aims. Radiotherapy has been proven to be insuffi-

cient in melanoma management due to the intrinsic radioresistance of melanoma cells, correlate not only with efficient DNA damage repair, but also with a high fraction of hypoxic cells, long volume doubling time, slow growth, high cell loss, and low vascular density. The aim of this study is to compare the effect of FLASH and CONV radiotherapy (RT) modalities on Melanoma (B16) cells at increasing doses of radiation.

Methods. We irradiated 8 plates with 6 multiwells: 4 plates were irradiated with CONV-RT and the rest with FLASH-RT at the dose of 4, 8, 16 and 32 Gy for each RT modality. Every plate had 3 wells with 300 cells, 1 well with 150 cells. The Average Dose-rate for the FLASH-RT was 250 Gy/s instead for the CONV-RT it was 5Gy/s. We used clonogenic assay to quantify the effect of FLASH and CONV RT. Moreover, we evaluated the morphological change of B16 cells, expression of senescence process. We performed the one-way Anova test to determine whether there was a significant statistical difference between the two RT modalities.

Results. After performing the clonogenic assays we manually counted the colonies for each treatment condition and represented the data as a survival curve. Clonogenic assays showed a higher colony formation in FLASH-RT than in CONV-RT after 4 Gy with a significant difference (P=0.0319). No significant difference in colony formation between the RT modalities was detected with higher irradiations doses (P<0,001). No colonies were found in the plates irradiated at doses of 16 and 32 Gy in both RT modalities. Morphological changes were observed in B16 cells after RT (CONV and FLASH). This changes corresponds to a cellular senescence process highlighted with the Beta gal assay. Senescent B16 cells are SA-β-gal positive evidenced by perinuclear blue staining. With respect to senescence, no statistically significant differences were observed between FLASH and CONV.

Conclutions: *In vitro* studies are necessary as they are useful as a bridge to translate the results into the clinic, our results showed that CONV-RT has a superior citotoxic activity on B16 cells compared with FLASH-RT at 4 Gy. B16 cells following RT underwent a morphological change. This change corresponds to a cellular senescence process. In the future FLASH-RT would allow to treat radioresistant tumor increasing total dose without the associated surrounding tissue toxicity of CONV-RT.

CO22

T1 PAPILLARY CARCINOMA OF THE THYROID: SINGLE CENTRE RETROSPECTIVE ANALYSIS

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Aims. To evaluate the clinicopathologic features and the pattern of failure of patients diagnosed with T1 papillary carcinoma (PTC).

Methods. This is a retrospective analysis of patients treated at our Institution between 2000 and 2020. All patients were restaged with TNM 8th edition. Descriptive statistics was performed to evaluate patients and disease characteristics, type of treatment, incidence of recurrence and vital status at the last follow up. Time to recurrence was calculated from the date of surgery to the date of recurrence diagnosis. Median follow up was calculated from the date of surgery to the date of the last follow up.

Results. In the period of observation, 1318 patients were affected by PTC out of 1554 patients with thyroid malignancies followed at our Institution. At diagnosis, 770 out of 1318 were found with T1 N0 PTC (according to the TNM 8th edition). Median age was 51 years and 611 were females. Diagnosis was incidental in 402 (52%) of patients. Surgery was the primary treatment in all cases and 666 (86%), 48 (6%), 17 (3%) and 39 (5%) patients received total thyroidectomy, total thyroidectomy+central compartment dissection, total thyroidectomy+central compartment dissection and uni/bilateral neck dissection and hemithyroidectomy, respectively. At the surgical specimen, median diameter of tumor was 10mm and an unfavorable variant was found in 45 (6%) cases. According to previous TNM editions, 8, 116 and 1 patients were classified as T2, T3 and T4, respectively. After surgery 476 (62%) received adjuvant radioiodine therapy with a median activity of 100mCi. In 30 (4%) out of 770 patients, recurrent disease was diagnosed after a median time of 22.5 months (range 2-239 months). Nodal recurrence in the neck, distant metastases (lung) and biochemical only recurrence was found in 25, 3 and 2 patients, respectively. After a median follow up of 48 months (range 6-456 months), 735, 13 and 22 are alive, dead and lost at follow up, respectively. Only 1 patient was dead due to the disease progression.

Conclutions: Stage T1 PTC is a favorable disease characterized by good prognosis, low rates of recurrence and very low rate of mortality. Additionally, 1 out of 2 patients is diagnosed incidentally. In our cohort 4% of patients experienced recurrence and only 1 patient died due to progressive disease. These findings should be taken in account in the diagnostic and therapeutic decision process as well as in the follow up strategies.

CO23

CEMIPLIMAB COMBINED WITH RADIOTHERAPY IN ADVANCED CUTANEOUS SQUAMOUS CELL CARCINOMA: A SINGLE INSTITUTION EXPERIENCE

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Aims. Cemiplimab is a new immunotherapy treatment based on the use of a monoclonal antibody that targets PD-1. There are several phase II trials that have shown its efficacy in the treatment of advanced cutaneous squamous cell carcinoma in patients who are not eligible for a curative approach either with surgery or with radiotherapy. Moreover, the use of radiotherapy in addition to cemiplimab has demonstrated a synergistic antitumoral response; however, only a very few real-life studies have confirmed this effect in the setting of advanced cutaneous squamous cell carcinoma.

Methods. We performed a retrospective analysis of patients treated by cemiplimab combined with radiotherapy from 2020 to 2022 at our institution for advanced cutaneous squamous cell carcinoma. The total dose and the fractionation schedule of radiotherapy treatments were tailored according to the radiation target and clinical patient's conditions (total dose range from 20 Gy to 55 Gy with an average PTV volume of 80 cc). Cemiplimab was always started before radiotherapy. The infusions were always continued in short course schedules of radiotherapy; whereas in the case of long course radiotherapy one infusion was postponed in order not to be concomitant. All patients were evaluated after radiotherapy treatment in multidisciplinary follow-up visits, including always both radiation oncologists and dermatologists, in order to investigate the clinical benefits and side effects.

Results. We identified 13 patients, with a majority of males (males 85%, females 15%), and an average age of 82 years (range 70-90). In 92% of the patients the clinical target volume (either primary tumour or lymph nodes metastasis) was located at the head and neck region. The average number of infusions before radiotherapy was 4 cycles. All clinical responses were evaluated by restaging the patients by imaging (CT or MRI) using the iRECIST and the overall response rate was 77%, with a complete response rate of 46%. No G3 or higher skin acute side effects were observed.

Conclusions. Our preliminary results confirm the feasibility of radiotherapy delivered in combination to cemiplimab in the management of advanced cutaneous squamous cell carcinoma. Combination therapy was proven to be both effective and with no G3 or higher skin acute side effects in our cohort of patients.

CO24

INDEPENDENT EXTERNAL VALIDATION OF FOUR NTCP MODELS FOR HEAD AND NECK CANCER PATIENTS

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Aims. External validation of Normal Tissue Complication Probability (NTCP) models for radiation-related toxicity in head and neck cancer (HNC) patients (pts) treated with curative (chemo) radiotherapy [(CH) RT].

Methods. Retrospective analysis of pts treated from 2010 to 2022. Four NTCP models were evaluated: 1) physician-rated swallowing dysfunction Grade (G) ≥ 2, 6 months (m) after completion of RT (Christianen *et al.*); 2) tube feeding dependence at 6 m (TUBEM6) (Wopken et al.); 3) Incidence of G ≥ 2 laryngeal edema within 15 m from RT (Rancati *et al.*); 4) acute oral and oropharyngeal mucositis (OM) G ≥ 3 at any time during RT and OM mean G during RT treatment weeks ≥ 1.5 (Orlandi *et al.*). Validation analyses included: 1) Model performance using the Brier score; 2) discrimination ability using the area under the receiver operating characteristic curve (AUC); 3) calibration using calibration intercept and slope; 4) Hosmer–Lemeshow goodness-of-fit test to evaluate the calibration of the model. The model's predictions fit the data at an acceptable level if the Hosmer–Lemeshow goodness-of-fit test statistic is > 0.05.

Results. The study population included 150 pts eligible (Table 1): 97 for dysphagia at 6 m (5% events); 88 for TUBEM6 (3% events); 102 for G ≥ 2 laryngeal edema (21% events); 113 for OM G ≥ 3 (42% events) and 114

for OM mean G ≥ 1.5 (63% events). Considering all validation tests, all models, except for swallowing dysfunction, shown adequate fit. Best AUC was reached by TUBEM6 (0.73) (Figure 1); however, the limited number of events influenced the precision of the estimates, as can be seen by the wide confidence interval (CI 95%: 0.67-0.98).

Table 1. Patients and tumor characteristics.

		Patients (total 158)	
		n	%
Sex	Male	113	75
	Female	37	25
Age (years)	Median [range]	62 [25-84]	
Smoke	Yes	42	28
	No	47	31
	Former*	50	34
	Not available	11	7
Alcohol abuse	Yes	8	5
	No	112	75
	Ex	1	1
	Not available	29	19
HPV status	Yes	82	55
	No	19	13
	Not available	49	32
Tumor Primary site			
	Oropharynx	88	59
	Larynx	12	8
	Nasopharynx	19	12
	Unknown primary	12	8
	Hypopharynx	11	7
	Oral cavity	6	4
	Other	2	2
Histology (WHO tumor classification)	CIS (glottic larynx)	1	1
	SCC	137	91
	Differentiated Nonkeratinizing carcinoma	2	1
	Undifferentiated Nonkeratinizing carcinoma	10	7
	0 (CIS)	1	1
	I	40	26
	II	32	21
	III	34	23
TNM (AJCC 8th Ed.)	IV A	30	20
	IV B	13	9

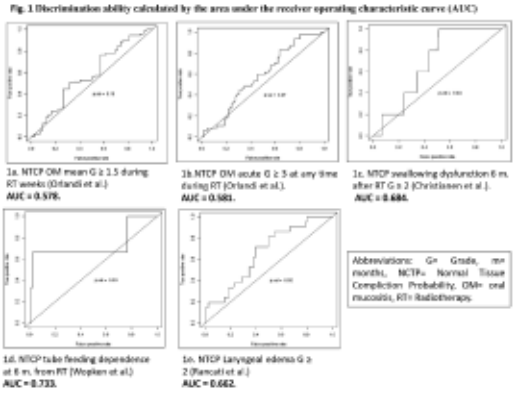

Figure 1.

No model shown good calibration. Only for laryngeal edema model non-parametric tests shown a significant difference between pts with events and the others (p=0.02). The low number of events for dysphagia and TUBEM6 endpoint prevented statistically robust results. The different population setting (nasopharynx in the training cohort *vs* mixed cohort in the present study) could justify the low performance of OM models.

Conclusions. NTCP model for laryngeal edema showed the best performance in the present cohort. This finding could be probably due to either the sufficient number of events found in our cohort or the similarities between the original training and validation cohort. Further investigations are required to validate other NTCP models.

CO25

ROLE OF ADJUVANT RADIOTHERAPY IN PATIENTS WITH LARYNGEAL CANCER TREATED WITH PARTIAL LARYNGECTOMY: A PROPENSITY SCORE MATCHING ANALYSIS

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Aims. To assess the effect of adjuvant treatment (PORT) on the survival of a multicenter cohort of patients with laryngeal cancer who have undergone partial laryngectomy in a real-world setting.

Methods. We retrospectively recruited 312 consecutive laryngeal cancer patients who were treated in three centers from 2005 to 2022. Inclusion criteria were: (i) supraglottic or glottic cancer, (ii) partial laryngeal surgery, and (iii) availability of subsequent clinical and radiological follow up. We divided patients into two groups, those who received PORT and those who not received it and used a propensity score analysis to compare them. PORT was indicated according to international guidelines. Primary endpoints were overall survival (OS) and disease-free survival (DFS).

Results. Table 1 shows the clinical characteristics of the patients and the baseline imbalance between the two groups. Median follow up was 44.4 months (estimated by reverse Kaplan Meier estimation). In terms of DFS, PORT results in a significantly greater benefit (HR = 0.44; 95%CI from 0.25 to 0.77). The 95% confidence interval of the median disease-free time improvement of PORT ranged from 0.4 to 11 years. We estimated a non-

significant improvement in OS (HR=0.75; 95%CI from 0.40 to 1.37) between those who received PORT and those who did not. 12/312 (3.8%) patients developed a locoregional recurrence (10 in no PORT group and 2 in PORT group) and 19 (6%) distant metastases (7 in no PORT group and 12 in PORT group). We did not find a significant association between the type of partial laryngectomy (TLM *vs* OPHL) and OS or PFS.

Conclusions. From our analysis, PORT after partial laryngectomy reduces the risk of recurrence, progression, or death by 66%. Moreover, in this specific context, subjects with worse prognosis are expected to have poorer OS, but the addition of PORT allows them to achieve similar OS performance to subjects with better prognosis: this could already indicate a therapeutic improvement.

Table 1.

	level	Adjuvant treatment No	Adjuvant treatment Yes	p	SMD
n		175	137		
Age (years) (mean (SD))		68.21 (10.75)	62.69 (8.52)	0.035	-0.58
Sex (%)	M	152 (86.9)	119 (86.9)	1.000	-0.00
	F	23 (13.1)	18 (13.1)		
Tumor site (%)	Glottic	111 (63.4)	71 (51.8)	0.051	0.24
	Supraglottic	64 (36.6)	66 (48.2)		
Minor surgery (%)	Single	13 (7.4)	6 (4.4)	0.143	-0.13
	Multiple	9 (5.1)	14 (10.2)		0.19
	None	153 (87.4)	117 (85.4)		-0.06
Year of major surgery (%)	2005 to 2014	73 (42.9)	51 (37.2)	0.190	-0.12
	2015 to 2018	71 (40.6)	52 (38.0)		-0.05
	2019 to 2022	29 (16.6)	34 (24.8)		0.20
Type of major surgery (%)	OPHL	90 (51.4)	108 (78.8)	<0.001	0.60
	TLM	85 (48.6)	29 (21.2)		
Neck Dissection (%)	Monolateral	69 (39.0)	37 (27.0)	<0.001	-0.02
	Bilateral	48 (27.4)	71 (51.8)		0.52
	None	78 (44.6)	29 (21.2)		-0.51
Residual tumor (R) (%)	R0	121 (69.1)	78 (56.9)	0.039	-0.25
	Relose	25 (14.3)	18 (13.1)		-0.03
	R1	29 (16.6)	41 (29.9)		0.32
Grading (G) (%)	G1-2	132 (75.4)	70 (51.1)	<0.001	0.52
	G3	43 (24.6)	67 (48.9)		
Tumor size and extent (T) (%)	pT0-2	74 (42.3)	40 (29.2)	0.024	0.28
	pT3-4	101 (57.7)	97 (70.8)		
Lymph nodes status (N) (%)	pN1-3	21 (12.0)	72 (52.6)	<0.001	0.86
	c/pN0	154 (88.0)	65 (47.4)		
Cancer stage (%)	I	154 (88.0)	65 (47.4)	<0.001	
	II	14 (8.0)	24 (17.5)		0.29
	III	3 (1.7)	22 (16.1)		0.52
	IV	4 (2.3)	26 (19.0)		0.56
Perineural invasion (%)	No	137 (78.3)	56 (40.9)	<0.001	0.82
	Yes	38 (21.7)	81 (59.1)		
Lymphovascular invasion (%)	No	134 (76.6)	48 (35.0)	<0.001	0.92

[1]Rubin, D.B. (2004). "Using Propensity Scores to Help Design Observational Studies: Application to the Tobacco Litigation". Health Services & Outcomes Research Methodology 2, 169–188.

CO26

RESPIRATORY MANAGEMENT FOR LEFT-SIDED BREAST CANCER RADIOTHERAPY: PRELIMINARY DATA FROM AN ARTIFICIAL INTELLIGENCE ORIENTED DECISION PROCESS

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Aims. To build an automated decision-making model to select the most suitable treatment between Deep Inspiration Breath-Hold (DIBH) and Free Breathing (FB) techniques in the setting of adjuvant radiotherapy for left sided breast cancer (LSBC) with Volumetric Modulated Arc Therapy (VMAT).

Methods. Dosimetric data from VMAT DIBH and FB rival plans were retrospectively retrieved for patients (pts) treated with adjuvant radiotherapy for LSBC. Risk of acute and late treatment-related clinically relevant toxicities was assessed by employing NTCP (Normal Tissue Complication Probability) models. Clinical data regarding cardiovascular risk factors (CRF - blood pressure, blood cholesterol levels, smoking and diabetes history) were also retrieved and combined in a global Atherosclerotic Cardiovascular Disease (ASCVD) score. Models features consisted of results of NTCP models and ASCVD scores. A decision tree (DT) model and an artificial neural network (ANN) model were then constructed to choose between DIBH and FB plans.

Results. Dosimetric and clinical data were retrieved for 50 LSBC pts. The analysis was applied to 48/50 patients due to lack of necessary data. Delivered dose consisted of 40.05-42.4 Gy/15-16 fractions in 47/50 patients while 3/50 pts received 26 Gy/5 fractions as per Fast Forward schedule. For the selected plans, physicians' choice was DIBH in 40/50 and FB in 8/50 cases respectively, based on clinical experience. Median ASCVD score was 2.4 (0.2-26.9). In 9/50 pts CRF were not retrievable. Endpoint of NTCP models were lung pneumonitis and fibrosis, acute coronary events and secondary lung and breast cancer. After training the models, accuracy in predicting the choice between DIBH e FB plans was tested, resulting in 81% versus 84% for the DT model and the ANN model, respectively.

Conclusions. Both models require a negligible computation time compared to that required for planning and comparing DIBH and FB plans. Preliminary results for this artificial intelligence approach to support clinical decisions look promising. Nevertheless, clinical validation in a bigger dataset and further model training are warranted to confirm these results.

CO27

FIRST EXPERIENCE OF COMBINED RADIOTHERAPY AND TRASTUZUMAB DERUXTECAN IN METASTATIC HER2+ BREAST CANCER PATIENTS

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Introduction. Trastuzumab Deruxtecan (T-DXd) is one of the most effective systemic therapy in patients with HER2+metastatic breast cancer. There is little evidence regarding the safety and efficacy of the combination of T-DXd plus radiotherapy (RT). The aim of study is to evaluate the early toxicity of concurrent use of RT with T-Dxd in metastatic breast cancer (BC) patients.

Materials and Methods. Patients with histologically proven metastatic HER2 positive breast cancer treated with RT and T-DXd delivered within 1 week or concurrently with RT course were selected. Toxicity was assessed according to the NCI-CTCAE V5.0).

Results. Among 45 patients treated with T-DXd in our institution, 15 patients received T-DXd within 1 week or concurrently with RT to a total of 26 RT treatments. Median age was 57 years (range 32-80). Median follow-up time was 6 months (range 1-17 months). The sites of treatments were mainly bone metastases (n=15, 57.7%); other sites were: lung metastases (n=2, 7.6%), liver metastasis (n=1, 3.8%) brain metastases (n=5, 19.2%) and lymphnodes metastases (n=3; 11.5%). Fourteen treatments had a palliative intent (53.9%, median total dose= 30 Gy, range= 20-45 Gy), 12 (46.1%) treatments had a radical intent (SBRT to oligometastatic/ oligorecurrent/ oligopersistent sites of disease; dose per fraction range 6-12 Gy, median number of fraction 3, range 3-5). No patients suspended RT. One patient treated to a femur metastasis developed grade 2 neutropenia. All patients treated for bone metastases achieved pain relief (mean value NRS pre-RT 1.8 mean value NRS post RT 0.4 p=<0.014). To date among patients treated to brain metastases (n=2, treated lesions= 5), no one developed symptomatic or asymptomatic radionecrosis on follow-up MRI (median follow up: 8 months, range 3-14 months). No one of the two patients treated to lung metastases developed radiation pneumonitis either symptomatic or radiological (median follow-up: 5 months; range 4-6 months)

Conclusions. In our case series RT delivered during T-DXd showed mild toxicity. Longer follow-up and larger number of patients and treatments are needed to better understand the safety profile of RT during T-DXd.

CO28

WHAT IS THE VIEW OF PALLIATIVE RADIOTHERAPY FROM RADIATION AND PEDIATRIC ONCOLOGISTS? AN AIRO-AIEOP MULTI-SOCIETY SURVEY

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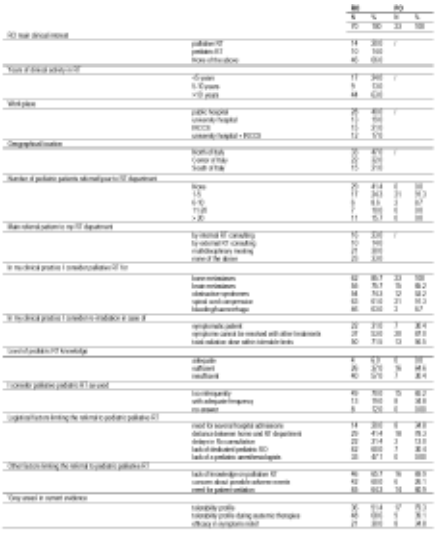
Aims. Palliative radiotherapy (PRT) is a standard treatment option for symptom relief in adult patients with advanced cancer, while it is less used in pediatric patients. The Italian Association of Radiotherapy and Clinical Oncology (AIRO) and the Italian Association of Pediatric Hematology and Oncology (AIEOP) promoted a national survey on the use of PRT in pediatric cancer patients to analyze the degree of knowledge on this topic by radiation oncologists (ROs) and pediatric oncologists (POs) and to identify potential barriers to patient referral.

Methods. A 13-item questionnaire and an 8-item questionnaire were sent to all Italian departments of Radiotherapy and Pediatric Oncology, respectively, on knowledge, use, potential barriers and gray areas of evidence regarding PRT. Seventy ROs and 23 POs returned their responses.

Table 1.



Results. The main statistically significant differences were as follows. The rate of specialists considering PRT in cases of bleeding/haemorrhage was 70% and 8.7% for ROs and POs, respectively (p<0.05). The level of knowledge of pediatric PRT was judged sufficient or inadequate by 37% and 57% of ROs, while it was judged sufficient or inadequate by 65% and 30% of POs, respectively. Furthermore, analyzing this data in ROs not dedicated to

pediatric oncology, knowledge of pediatric PRT was found to be insufficient in 70% of cases ($p<0.05$). The most relevant logistic barrier to PRT for POs was the distance from the RT department, whereas for ROs it was the lack of dedicated ROs and pediatric anesthesiologists ($p<0.05$; $p=0.03$). Concern about possible side effects was higher for ROs than for POs, who instead considered the lack of knowledge on the topic as an obstacle to RT ($p=0.01$). Finally, among the 'grey areas' of evidence, the tolerability profile of PRT both in general and in combination with systemic therapies was the most reported ($p=0.04$) (Table 1).

Conclusions. The results of this survey suggest the lack of knowledge on pediatric PRT even by specialists and that this therapy is underutilized due to several barriers. However, the latter are identified differently from ROs and POs. Increased dissemination and sharing of knowledge, as well as the development of interdisciplinary guidelines, are needed to improve access-to and quality-of PRT. This requires a common effort of ROs and POs and the improvement of education in PRT both in graduate schools and during professional life through continuing medical education.

CO29

QUALITY OF LIFE AND SIDE EFFECTS IN A POST-PROSTATECTOMY ABLATIVE RADIATION THERAPY (POPART) MULTICENTRIC TRIAL

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Aims. The use of hypofractionated radiotherapy (HFRT) for prostate cancer (PCa) has been widely investigated in nonsurgical patients, being nowadays a standard of care. Conversely, the role of HFRT in the postoperative setting is unclear, pending on late toxicity data. This prospective, observational, multicentric trial (POPART study-NCT04831970) is designed to assess the feasibility of SBRT for the treatment of biochemical and/or clinical recurrence in men who underwent radical prostatectomy (RP).

Methods. Patients (pts) with PSA levels of ≥0.1–2.0 ng/mL after RP and/or local relapse at PSMA PET/CT or multiparametric MRI were enrolled at four Italian Institutions. Median age at the time of SBRT was 69 (52-83) years. Androgen deprivation therapy (ADT) was prescribed to 9 pts. Linac-based SBRT was delivered to the prostate bed up to a total dose of 32.5 Gy in five fractions every other day (EQD21.5 = 74.2 Gy). Treatment related toxicity (primary endpoint) was measured by the CTCAE v5.0. In addition, quality of life (sexual, rectal, urinary domains) and biochemical control have been evaluated as secondary endpoints with EPIC-CP, ICIQ-SF, IIEF-5 questionnaires and PSA serum levels, respectively. Scores were assessed at baseline and during the follow-up.

Results. From April 2021 to May 2023 a total of 73 pts were treated. Median follow-up was 8.4 (1-23) months. No ≥G3 acute and late genitourinary (GU) and gastrointestinal (GI) toxicity was observed; one patient experienced a G2 acute GI toxicity. The incidence of G1 acute and late GU side effects was 10% and 15%, respectively. No changes in bowel and sexual domains of EPIC-CP were observed, while a slight worsening was registered in the urinary domains (incontinence and irritative/obstructive items). These variations were confirmed in the results of ICIQ-SF and IIEF-5 questionnaires. Median pre-SBRT PSA of 0.29 (0.1-2.0) ng/mL decreased to 0.04 (0.0-0.84) ng/mL at the last follow up.

Conclusions. Our preliminary findings show that SBRT can be safely extended to the postoperative setting, without an increase in short-term toxicity or a significant decline in QoL. Long-term results are awaited to confirm this strategy.

CO30

A NOMOGRAM FOR PREDICTING LOCAL RECURRENCE RISK IN BREAST CANCER PATIENTS TREATED WITH INTRAOPERATIVE RADIOTHERAPY WITH ELECTRONS

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Aims. This study aimed to identify a useful tool for predicting local recurrence (LR) in breast cancer (BC) patients treated with intraoperative radiotherapy with electrons (IOERT) as the sole treatment.

Materials and Methods. We included patients diagnosed with primary breast cancer (BC) who underwent IOERT at a single institution in the period 2000-2016.

The primary outcome was LR rate, including events either in the same quadrant as the primary BC or in other quadrants of the ipsilateral breast, with or without synchronous nodal involvement or distant metastasis. Statistically significant predictors were identified at univariate and multivariate (MV) analyses. A predictive nomogram based on logistic model was developed. The nomogram was internally validated for discrimination and calibration using Hosmer& Lemeshow Goddness of fit method.

Results. A total of 3397 patients were analyzed. AT MV analysis, predictors for LR included younger age, tumor grade 2-3, histologic subtype, ER and PR negative status, tumor size ≥ 1.5 cm, nodal involvement, molecular subtype other the Luminal A and HER 2positive receiving anti-HER2 therapy. At 6.1 years median FU (range 4.3-8.0) there were 265 local events (7.8%) resulting in a LR cumulative incidence (CIF) of 4.4% (95% CI 3.7-5.2) at 5 years and 13.5% (95% CI, 11.7-15.5) at 10 years. Internal validation was performed on the IOERT arm of the ELIOT phase III randomized trial (585 women). Calibration plots showed that the observed proportion of LR in the ELIOT arm well fit with the expected proportion as predicted by the logistic models at 5 years (26 CIF observed *vs* 23.9 CIF predicted, Chi square= 8.38 with 9D, p= 0.50 , while for 10 years the estimated probability was not so close to the probability observed in the data, even if the difference was not significant (49 CIF observed *vs* 69.8 CIF predicted, Chi square= 9.91 with 9 D , p=0.36).

Conclusions. The nomogram-predicted results were well fitted to the actual outcomes in an internal validation using the ELIOT trial population, with a better risk prediction at 5 years and it can be an useful tool for guiding treatment decision making for patients candidates to IOERT.

CO31

ARTO (NCT03449719), RANDOMIZED PHASE II TRIAL TESTING STEREOTACTIC BODY RADIOTHERAPHY AND ABIRATERONE ACETATE IN OLIGOMETASTATIC CASTRATE-RESISTANT PROSTATE CANCER PATIENTS

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Aims. Stereotactic Body Radiation Therapy (SBRT) offers a non-invasive treatment approach for oligometastatic disease. However, there is currently no prospective evidence available on the combined utilization of SBRT with androgen receptor targeted agents in patients with metastatic castrate-resistant prostate cancer (mCRPC). To address this gap, the multicenter phase II randomized clinical trial ARTO (NCT03449719) has been initiated to assess the potential benefits of adding SBRT to abiraterone acetate (AA) in patients with oligometastatic CRPC.

Methods. The study enrolled patients diagnosed with oligometastatic castrate-resistant prostate cancer (CRPC), defined as ≤3 non-visceral metastatic lesions. Patients were randomly assigned in a 1:1 ratio to receive either abiraterone acetate (AA) alone (control arm) or AA in combination with simultaneous Stereotactic Body Radiation Therapy (SBRT) targeting all sites of disease (experimental arm). The primary endpoint of the study was the rate of biochemical response (BR), defined as a decrease in PSA levels of at least 50% from baseline, measured at 6 months from the initiation of treatment. Secondary endpoints included the assessment of complete biochemical response (CBR), defined as a PSA < 0.2 ng/ml at 6 months from treatment, and progression-free survival (PFS).

Results. Between January 2019 and September 2022, a total of 157 patients were enrolled in the study. BR was observed in 79.6% of the patients, with a higher percentage in the experimental arm (90.6%) compared to the control arm (68.2%). The odds ratio (OR) favoring the experimental arm was 4.50 (95% CI 1.70-11.95; p= .003). CBR was detected in 38.8% of patients, with a higher rate in the experimental arm (56%) compared to the control arm (23.2%) with an OR of 3.64 (95% CI 1.80-7.38; p<.001). The use of SBRT led to a significant improvement in PFS, with a hazard ratio for progression of 0.35 (95% CI 0.21-0.57; p<.001) in the experimental arm compared to the control arm.

Conclusions. The trial successfully achieved its primary endpoint of biochemical control and PFS, indicating a clinical benefit of adding SBRT to first-line AA treatment in patients with mCRPC. These findings support the need for phase III trials on larger patient cohorts to further evaluate survival endpoints.

CO32

RADIOABLATION WITH OR WITHOUT HORMONOTHERAPY FOR OLIGORECURRENT PROSTATE CANCER: PRELIMINARY RESULTS OF THE RADIOSA TRIAL

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Aims. In oligometastatic prostate cancer (PCa), metastasis directed therapy (MDT) have demonstrated benefits in terms of disease control and toxicity. The aim of the RADIOSA trial (AIRC IG-22159, NCT03940235) is to compare time to clinical progression (CR) between the two study arms: SBRT only or SBRT + ADT, with the final purpose of identifying the patient who can benefit from local treatment with MDT alone versus those who require treatment intensification.

Methods. Oligorecurrent PCa pts with 3 or less bone or lymph nodal localizations where randomized 1:1 to receive SBRT alone (arm A) or SBRT + 6 months of ADT (arm B). The primary objective was to compare the progression-free survival (PFS) defined as the absence of new metastatic lesions (local, regional or distant) between the two arms. SBRT treatment consisted in a fractionation schedule of BED > 100 Gy ($\alpha/\beta = 1.5$ Gy).

Results. Eighty-eight pts were included in the present analysis. Median time from last active treatment to enrollment was 37 months (IQR 18 – 65). Patients characteristics and FU data are shown in Figure 1a. After a median FU of 12 months (IQR 9 – 22) 42 pts (47%) experienced a biochemical relapse (BR) with a median time to BR of 10.5 months and a median PSA at relapse of 3.36 ng/ml (range 0.26 – 23.90). Of them 36 pts developed a CR (20 oligo and 16 poli relapses) with a median overall time to CR of 11.9 months. At CR 17, 15, and 4 pts received ADT, RT and RT+ADT respectively. Two pts died from non-PCa related causes. When stratified by treatment arm, median time to CR was 13 months for arm A and 37 months for arm B. Kaplan-Meier estimates of clinical PFS showed a statistically significant advantage for the combined treatment arm (arm B MDT + ADT) (HR 0.28, 95%CI 0.14-0.57, p=.0001 – Figure 1b). Similarly, a clinical PFS advantage was observed for pts with a PSA < 1.91 ng/ml at the oligorecurrence (Figure 1c).

Conclusion. Clinical PFS was significantly improved with the combination of MDT and 6 months ADT. Longer FU data and analysis of quality of life questionnaire will provide clearer indication about the safety and effectiveness of such approach in this clinical setting. Molecular analyses of biological samples collected within the trial are actually ongoing, and will hopefully help to identify a genomic signature to be integrated with next-generation imaging allowing for a more refined oligometastatic pts stratification and treatment personalization.

Pts characteristics (n = 88)	
Enrollment	Median (IQR)
Age (years)	69 (64 – 75)
Testosterone baseline (µg/L)	3.7 (3.2 – 4.9)
PSA baseline (ng/ml)	1.95 (0.84 – 3.55)
	ARM A (SBRT) / **ARM B (SBRT + ADT)**
Lesions	
Bone (n = 28)	17 / 11
Lymph node (n = 56)	27 / 29
Bone + lymph node (n = 4)	1 / 3
Follow-up data	**ARM A** / **ARM B**
Clinical relapse	25 / 13
Oligo (n = 20)	**n = 13** / **n = 7**
Intraprostatic relapse	2 / 2
Intraprostatic relapse + lymph node lesions	1 / 1
Bone lesions	5 (1 in field) / 1
Lymph node lesions	5 / 2
Bone and lymph node lesions	- / 1
Poli (n = 16)	**n = 12** / **n = 4**
Visceral lesions	1 / -
Intraprostatic relapse + lymph node + bone lesions	1 / -
Bone lesions	5 / -
Lymph node lesions	2 / 2
Bone and lymph node lesions	1 / 2
Visceral + bone + lymph node lesions	1 / -
Visceral + bone	1 / -

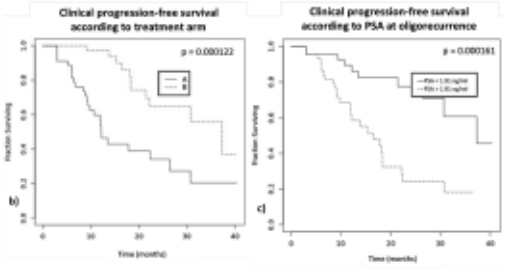

Figure 1. (a) Summary of patient baseline characteristics and follow-up data and (b) Kaplan-Meier estimates of the clinical progression-free survival according to treatment arm and (c) according to PSA at oligorecurrence.

CO33

REAL WORLD RESULTS OF TARGETED INTRAOPERATIVE RADIOTHERAPY (TARGIT-IORT) AS PARTIAL BREAST IRRADIATION MODALITY

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Aims. Partial breast irradiation (PBI) with targeted intraoperative radiotherapy (TARGIT-IORT) for early stage breast cancer was investigated in TARGIT A trial. However the majority of national guidelines do not consider TARGIT-IORT as a standard PBI modality and additional clinical evidence is necessary. In this study we

present "real world" outcome measures of TARGIT-IORT as PBI modality.

Methods. Patients were treated with TARGIT-IORT as PBI modality between 2004 and 2021 in a single institute. Inclusion criteria were consistent with TARGIT-A protocol. Primary outcome was 5-years survival without in breast tumour recurrence (IBTR), secondary analyses were regional and distant recurrence risks, disease-free survival, overall survival and tumour-related survival. Primary and secondary outcomes were estimated with Kaplan Meyer method and the analysis was conducted in all study population and in a subgroup of patients that received exclusive TARGIT-IORT (without the addition of whole breast EBRT). High grade toxicity events were described and scored according to Common Terminology Criteria of Adverse Events scale 4.0.

Table 1. Five-years Kaplan Meyer estimates of outcomes measures for all population and for exclusive IORT cohort.

Outcomes	All study populatio	Exclusive IORT coho
	Kaplan-Meyer esti (95%CI)	Kaplan-Meyer esti (95%CI)
5 years regional recurrence	0.9% (0.4-1.2)	0.8% (0.3-2.3)
5 years distant recurrence	1.7%(1-3.2)	1.7% (0.8-3.7)
5 years mastectomy risk	1.2% (0.6-2.5)	2% (1-4.1)
5 years overall survival	96.6% (94.8-97.8)	96.1% (93-97.6)
5 years tumour related surv	98.9% (97.6-99.5)	98.8% (96.9-99.6)
5 year not tumour related s	97.7% (96.2-98.6)	97.2% (95-98.4)

Results. The study included 825 patients, with a median follow up of 64 months (range:3-203). The majority of patients (60%) received only TARGIT-IORT ("exclusive IORT" group), while 40% of patients were considered unsuitable for PBI after definitive histopathological report and received additional whole breast radiation therapy. A total of 10 IBTR and 27 deaths (24 not-tumor related, 3 due to breast cancer) occurred within the first 5 years, with an estimated risk of local recurrence of 1.6% (95%CI=0.9%-3%) and a 5-year survival without IBRT of 95.2% (95%CI=93.1%-96.6%). In "exclusive IORT" group (494 patients) the 5-year IBRT risk was 2.5% (95%CI=1.3%-4.7%) and the 5 year survival without IBRT was 93.7% (95%CI=90.6%-95.7%). Survival analysis results for secondary endpoints were reported in Table 1. High grade toxicity (CTCAE Grade 3-4) events were rare (incidence=0.6%) and consisted in 1 case of skin necrosis, 3 cases of severe fibrosis and 1 radiation induced angiosarcoma.

Conclusions. In this large population the IBRT risk after TARGIT IORT for early stage breast cancer is very limited. Real word results of TARGIT IORT as a risk adapted strategy for PBI are consistent with TARGIT A trial publication.

CO34

RADIATION THERAPY IN NON-MELANOMA SKIN CANCER (NMSC): AN ITALIAN SURVEY ON BEHALF OF PALLIATIVE CARE AND INTERVENTIONAL RADIOTHERAPY STUDY GROUPS OF ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY (AIRO)

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Aims. This survey's aim was to obtain a "snapshot" of the real-word practice of Non-Melanoma skin cancer (NMSC) treatments in Italy.

Methods. The survey was elaborated on SurveyMonkey's online interface and was sent via e-mail to all Radiation Oncologists of AIRO. The questionnaire was prepared by the AIRO "Palliative care" and "Interventional Radiotherapy" Study Groups and it consisted of 29 questions: 23 multiple-choice questions and 6 open questions.

Results. 58 Italian Radiation Oncologists (ROs), representing 54 centers in 20 Italian regions, answered the survey. 75% of ROS had more than 10 years of experience. More than 1000 patients are seen annually at 46% of the centers. 13% of the ROs declared they would treat fewer than 10 NMSC lesions annually, 36% would treat between 11 and 20, and 51% would treat more than 20 lesions annually. 86% of the ROs administered integrated treatment in fewer than 10% of cases. For the 42.5% of ROs, palliative care amounted to less than 10 per year, 11-20 per year for the 42.5% of ROs, and >20 per year for the 15% of ROs. 89% of the ROs registered fewer than 10 re-RT instances annually. BT was reportedly offered, with customized applicators being the most popular ones, for

25% of the ROs, and every case was reportedly discussed by a multidisciplinary team (71% of the ROs). Electrons (74%), VMAT (57%), 3DCRT (43%) and BT (26%) were the main treatment options for the NMSC lesions. With EBRT, there were 46 and 53 different RT schedules that could be used for curative and palliative care, respectively; with BT, the options varied from 21 for curative care to 7 for palliative care. For EBRT curative settings, the most popular alternatives were 50-70.95/22-35 fractions (fz) and 50-70 Gy/16-20 fz and for EBRT palliative settings, 30Gy/10fz, and 20-35Gy/5fz. In the curative context for BT, the most popular alternatives were 32-50Gy/8-10fz and 30-54Gy/3-5fz, whereas 30Gy/6fz was the option of choice in the palliative environment. Regarding re-RT, there were less than 10 cases annually in 42.5% of the ROs, 11-20 cases annually in 42.5% of the ROs, and >20 cases annually in 15% of the ROs. Electrons (61%), VMAT (49%), and BRT (25%) were the most widely employed approaches: 20-40Gy in 10fz and 20-25Gy in 5 fz were the recommended fractionations.

Conclusions. The survey shows a variegated reality for the treatment of NMSC lesions in Italy. A national registry with more detailed data could probably help in undercover its causes.

CO35

INTERSTITIAL INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY) OF LOCALLY ADVANCED CERVICAL CANCER: SAFETY AND ACCURACY OF THE HYBRID TECHNIQUE IN SINGLE-INSTITUTIONAL CLINICAL PRACTICE

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Aims. The use of brachytherapy (BT) is part of the standard of care for patients with locally advanced cervical cancer (LACC). Depending on the residual disease (size and homogeneity of the CTV) at the time of BT, interstitial technique is often required, using needles with intracavitary device. Here we want to evaluate feasibility and dosimetric outcomes in LACC patients with a residual disease at the time of BT who received intracavitary BT (ICBT) at first fraction and interstitial BT (ISBT) for the remaining fractions.

Methods. From 2021 to 2023 23 patients with LACC were treated at our center with ICBT at first fraction and ISBT for all the following fractions. For each fraction, imaging was acquired and targets were delineated. Interstitial needles, together with the intracavitary tandem, were selected for patients with large and inhomogeneous cervical lesions (mean GTV volume of 6.82cc at the time of ISBT for those patients who underwent MR). First fraction, comprehensive of gynecological examination and imaging, helped determine where to insert needles to guide the delivered dose. All the target definitions and treatment plans were evaluated following GEC-ESTRO guidelines. Considered Organs At Risk (OARs) were bladder, rectum and sigma. Hard constraints were fulfilled, excepting the cases when the evaluated organ was infiltrated by the initial disease. EQD2 was calculated for targets and OARs taking into account external beam doses and BT doses.

Results. A total of 205 needles were implanted with an average of 2.05 needles per patient per fraction. At the first fraction CTV was covered with a mean D98 of 7.35 Gy and D90 of 9.62 Gy. At the end of the whole treatment 66.7% of the patients had CTV D98>75 Gy while 70.4% achieved CTV D90>85 Gy.

OARs D2cc doses (EQD2) were:

- at bladder <80 Gy in 55.6% of cases and <90 Gy in 100% of cases;
- at rectum <65 Gy in 44.4 % of cases and <75 Gy in 96.3% of cases;
- at sigmoid <70 Gy in 66.7 % of cases and <75 Gy in 92.6% of cases.

Conclusions. It has become clinical practice in our center to treat LACC patients with ICBT at the first fraction and then evaluate the need for ISBT. This approach allows a better and safer programming of the following fractions thanks to the precise assessment of the relationship between device, disease and OARs. Despite the potential dosimetric disadvantage due to not using needles in the first fraction, the latter guarantees to achieve satisfactory dosimetric objectives for CTV and OARs.

Discussed Poster

DP01

THE IMPORTANCE OF PATIENT-REPORTED OUTCOMES IN THE CLINICAL EVALUATION OF ACUTE AND LATE TOXICITY OF RADIOTHERAPY FOR PROSTATE CANCER: AN EXPLORATIVE ANALYSIS OF A COHORT OF PATIENTS TREATED WITH LOW-DOSE RATE (LDR) BRACHYTHERAPY

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Aims. to compare patient-reported outcomes (PROs) via self-administered questionnaires and clinical evaluation of genitourinary (GU) toxicity in patients with localized prostate cancer treated with exclusive, low-dose-rate brachytherapy (LDR-BCT). This study is part of Clinical Outcome of Radiotherapy Treatment in Azienda Toscana Nord-Ovest (CORTATNO) research project funded by Tuscany Region.

Methods. data from 35 patients treated with I-125 permanent intra-prostatic seeds implantation (145 Gy) for low- and favorable intermediate-risk prostate cancer between January 2015 and June 2021 were retrospectively reviewed. Pre-planning ultrasound (US) and 1-month post-implant CT dosimetry, 1-year GU toxicity outcomes (CT-CAE v5.0), baseline and 1-year post-procedure International Prostate Symptoms Score (IPSS) and International Index of Erectile Function (IIEF) tools were recorded and compared.

Table 1. Population in study: dosimetry and PROs comparison.

Patient ID	Age	Date of LDR-BCT	IPSS	1y-IPSS	1y-GU toxicity (CT-CAE v5.0)	IIEF	1y-IIEF	Urethra D_{90}	Urethra D_{50}	Urethra D_{10}	Bladder V_{145Gy}	Penile bulb D_{90}	Penile bulb D_{50}	Penile bulb volume
1	69	2015	0	1	0	25	25	154	193	187	1.02	29	23	3.6
2	68	2015	7	7	0	23	23	136	199	193	0.00	23	21	2.5
3	69	2015	9	23	0	17	20	0	176	172	0.16	14	9	5.6
4	68	2015	8	12	0	17	6	0	176	163	0.87	22	12	7.9
5	57	2015	6	3	0	12	8	0	185	176	0.00	40	22	7.3
6	69	2016	7	7	0	8	8	0	210	202	0.21	0	19	1.8
7	67	2016	0	0	0	19	19	0	216	106	0.07	0	43	1.1
8	76	2016	13	13	0	13	13	0	212	201	0.05	0	15	1.5
9	72	2016	13	15	1	18	12	0	186	182	0.13	20	15	4.5
10	71	2016	18	14	0	16	15	0	203	197	0.02	39	19	8.5
11	66	2016	8	8	1	23	23	89	208	201	0.16	14	11	3.4
12	77	2016	1	0	0	10	5	121	182	176	0.58	18	12	3.4
13	63	2016	8	8	1	13	13	0	187	182	0.00	33	23	3.5
14	73	2016	14	14	0	7	7	0	202	104	1.06	15	9	6.4
15	55	2016	1	1	0	25	25	0	174	169	0.41	19	19	2.1
16	75	2016	5	2	1	18	5	0	205	199	0.6	45	42	2.5
17	75	2017	4	7	0	13	13	0	203	196	0.1	14	8	4.3
18	72	2017	21	22	2	23	21	0	197	190	0.24	20	11	6.2
19	53	2017	4	9	1	23	24	0	191	185	0.00	46	18	8.0
20	76	2017	5	5	0	18	21	0	185	179	0.00	29	22	3.3
21	70	2017	0	0	0	19	19	0	196	185	1.27	25	17	4.3
22	68	2017	0	0	0	24	24	0	197	190	1.10	18	18	2.1
23	76	2017	15	15	0	19	19	0	188	184	0.14	33	17	7.5
24	68	2017	3	3	0	18	18	0	208	197	0.00	27	29	2.1
25	71	2018	8	10	0	16	21	0	201	192	0.00	0	23	1.4
26	76	2018	5	5	0	7	7	0	182	177	0.08	12	11	2.7
27	64	2018	7	7	1	21	21	0	198	194	0.05	41	30	3.9
28	67	2019	0	0	0	24	24	0	189	180	0.00	53	24	7.7
29	74	2019	6	6	0	7	7	0	203	197	1.00	18	14	3.3
30	70	2019	6	6	0	16	16	0	216	196	1.36	70	41	4.7
31	63	2020	7	7	0	7	7	0	195	189	0.00	31	15	6.0
32	59	2020	0	0	0	25	25	0	197	193	0.00	38	23	5.8
33	63	2020	7	5	0	15	17	0	192	185	0.08	14	9	6.8
34	69	2020	7	7	0	20	20	0	182	179	0.00	22	16	5.8
35	74	2021	1	1	0	24	24	0	188	182	0.05	61	38	2.5

IPSS score: 1-7(mild), 8-19(moderate), ≥20(severe); **IIEF score**: 22-25(no dysfunction), 17-21(mild), 12-16(mild to moderate), 8-11(moderate), 5-7(severe); **LDR-BCT**: low dose rate brachytherapy.

Results. Table 1 summarizes dosimetry and PROs. We found ≥G1 urinary toxicity in 7 (20%) patients, no erectile dysfunction complained, worsening of post-LDR-BCT IPSS and IIEF score in 2 (6%) and 6 (17%) cases, respectively. Unchanged or improved 1-year IPSS score despite G1-2 urinary toxicity report was found in 6 (17%) patients, and only 1 (3%) case of worse IPSS score than clinical findings (p=0.20). There was an association between post-implant IPSS worsening, and post-planning bladder V145Gy (p=0.02) and pre-planning urethral D2cc (p=0.045). Both baseline and post-implant IIEF scores correlated with post-planning penile bulb (PB) D2cc

(p=0.006 and p=0.003, respectively), while a slight correlation between post-procedure IIEF score and post-planning PB D90% (p=0.06) was recorded. Patients complaining sexual impairment showed a slightly higher volume of PB than those without (median 5.4 cc (range 2.5-7.9) versus 3.6 cc (range 1.1-8.5), p=0.81), but no differences between radiation dose to the organs at risk (pre-planning prostatic urethra, post-planning bladder and PB). Evaluation of the radiation dose to neurovascular bundles is ongoing.

Conclusions. LDR-BCT confirms as a safe therapeutic option for localized carcinoma of the prostate. Despite the low toxicity rates, in our explorative cohort patient-completed tools were more sensitive and subject to less bias than physician grading about sexual impairment. Prospective evaluation of our promising findings on wider series is desirable to fully assess the cost-effectiveness of curative prostate cancer treatments.

DP02

FAILURE MODE AND EFFECTS ANALYSIS (FMEA) EVALUATION OF THE RADIOTHERAPY TREATMENT DELIVERY PROCESS

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Aims. To ensure the correct delivery of increasingly complex radiotherapy (RT) treatments avoiding undue exposures to patients, it is essential to use proactive methods of risk management. This study describes the application of the Failure Mode and Effect Analysis (FMEA) in order to enhance the safety and quality of the RT treatment delivery process.

Methods. Following the FMEA multidisciplinary approach, a mono-institutional group of 4 RTTs, 1 RTT student, 1 radiation oncologist and 2 medical physicists was set up and met on a weekly basis from May to October 2022. FMEA was applied to the treatment delivery proceeding as follows: 1) identification of the single steps (phases and activities); 2) for each activity, identification of the potential failure modes (FM), together with their causes and effects; 3) for each FM, severity (S), occurrence (O) and detectability (D) were discussed and rated using the AAPM TG-100 radiotherapy specific scales; 4) Risk priority number (RPN) was calculated as the product of S, O, and D (range 1-1000). Additional safety measures, improvements, or mitigations were proposed and considered for FM with a RPN higher than 180.

Results. A total of 56 FM was recognized with RPN ranging from 27 to 576, 23 of them (41%) characterized by an RPN score higher than 180. The highest RPN (576) was associated to wrong IGRT parameters definition. The solutions proposed to mitigate the O of this FM were the adoption of strict IGRT protocols and an accurate training of the involved users. Other critical RPNs were related to wrong or missing bolus application (450), incorrect assessment of patient's clinical conditions (400), wrong evaluation of EPID images (360) and undetected patient's movements (320). Effective strategies identified for risk mitigation included: organizational changes, improved communication modes, and new technologies, such as SGRT systems and EPID in vivo dosimetry.

Conclusions. The FMEA method proved to be a reliable and effective approach of risk management for the RT treatment delivery process. The presented results were generated by consensus of a multidisciplinary group of professionals following RT specific ranking scales, guaranteeing a critical and shared scoring. A continuous review and update of activities, FM and ratings is mandatory to ensure safety and quality to a process in such rapid and constant evolution. The results could be a useful tool to suggest and support the introduction of novel technologies.

DP03

RADIOCHEMOTHERAPY IN VULVAR SQUAMOUS CELL CARCINOMA: OUTCOME AND TOXICITY FROM AN OBSERVATIONAL MULTICENTER ITALIAN STUDY ON VULVAR CANCER (OLDLADY 1.1)

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Aims. Vulvar carcinoma is a rather uncommon gynecological malignancy affecting elderly women and the treatment of loco-regional advanced carcinoma of the vulva (LAVC) is a challenge for both gynecologic and radiation oncologists. Definitive chemoradiation (CRT) is the treatment of choice, but with disappointing results. In this multicenter study (OLDLADY-1.1), several Institutions have combined their retrospective data on LAVC patients to produce a real-world dataset aimed at collecting data on efficacy and safety of CRT.

Methods. The primary study end-point was 2-year-local control (LC), secondary end-points were 2-year-metastasis free-survival (MFS), 2-year-overall survival (OS) and the rate and severity of acute and late toxicities. Participating centres were required to fill data sets including age, stage, histology, grading as well as technical/dosimetric details of CRT. Data about response, local and regional recurrence, acute and late toxicities, follow-up and outcome measures were also collected. The toxicity was a posteriori documented through the Common Terminology Criteria for Adverse Events (CTCAE) version 5 scale.

Results. Retrospective analysis was performed on 65 patients with primary or recurrent LAVC treated at five different radiation oncology institutions covering 11-year time interval (February 2010- November 2021). Median age at diagnosis was 72 years (range: 32–89). With a median follow-up of 19 months (range 1–114 months), 2-year actuarial LC, MFS and OS rate were 43.2%, 84.9% and 59.7%, respectively. In 29 patients (44%), CRT was temporarily stopped (median 5 days, range 1-53 days) due to toxicity. The treatment interruption was statistically significant at univariate analysis of factors predicting LC (p:0.05) and OS rate (p: 0.011), and it was confirmed at the multivariate analysis for LC rate (p: 0.032). In terms of toxicity profile, no G4 event was recorded. Most adverse events were reported as grade 1 or 2. Only 14 acute G3 toxicities, all cutaneous, and 7 late G3 events (3 genitourinary, 3 cutaneous, and 1 vaginal stenosis) were recorded.

Conclusions. In the context of CRT for LAVC the present study reports encouraging results even if there is clearly room for further improvements, in terms of both treatment outcomes, toxicity and treatment interruption management.

DP04

VARIATION AND DOSIMETRIC CHANGES IN FLETCHER APPLICATOR PLACEMENT FROM IMPLANT TO ACTUAL TREATMENT DELIVERY FOR CERVICAL HIGH-DOSE-RATE BRACHYTHERAPY

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Aims. High-dose-rate (HDR) brachytherapy for cervical cancer treatment includes significant uncertainties. The aim of this study was to quantify the dosimetric variation in high-risk clinical target volume (HRCTV) from the prescribed dose and the corresponding effect on organ-at-risk (OAR) dose based. Cone beam CT (CBCT) scans were performed before each treatment session to evaluate the displacements that occur from applicator insertion to the actual delivery of brachytherapy treatment.

Methods. From August 2022 to April 2023 12 patients with cervical carcinoma was treated with HDR intracavity brachytherapy using Fletcher applicator, median dose was 6 Gy per fraction (5-7 Gy/3-4 Fx). CBCT scans were acquired prior to each treatment session to assess applicator position and evaluate potential displacements. Appropriate interventions, including small adjustments and the placement of anal probes, were applied during CBCT scans to mitigate any displacements caused by rectal air or applicator movement. The OARs of interest were the rectum, bladder, sigmoid, and bowel. The OARs and the HRCTV were adapted to the CBCT images by an automatic tool based on the deformable fusion, in order to make this procedure operator independent. Subsequently, treatment plan previously optimized on the CT images, is recalculated on the CBCT series. Finally, the DVH comparison was made to evaluate the CTV coverage and OARs constraints.

Results. Analysis of CBCT images revealed minor displacements of the Fletcher applicator between insertion and treatment delivery. The simulated plan on CBCT demonstrated good agreement with the actual delivered plan, indicating satisfactory dose conformity of the HRCTV in all cases (average change of 1.15%, range between -4.17% and 5%). The mean dose change at OARs was: bladder -2.32% (range -8.83% to 0.14%), rectum -1.32% (range -6.05% to 3.53%), sigmoid colon 2.7% (range between -1.03% and 8%) and bowel -2.21% (range between -11.29% and 7.5%).

Conclusions. Our findings suggest that Fletcher applicator-based brachytherapy, supported by interventions to minimize displacements caused by rectal air or slight applicator movements, remains the best treatment option for cervical carcinoma. The utilization of CBCT scans and appropriate corrective techniques contribute to accurate applicator placement and precise dose delivery. Further studies involving larger patient cohorts need to validate these results and optimize treatment strategies.

DP05

LONG-TERM RECURRENCE AND SURVIVAL OUTCOMES AFTER ELECTRON INTRAOPERATIVE RADIOTHERAPY (IOERT) IN PATIENTS WITH EARLY BREAST CANCER: A SINGLE-CENTER RETROSPECTIVE ANALYSIS

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Aims. To analyze long-term outcomes in breast cancer patients treated with conservative surgery and IOERT as accelerated partial breast irradiation.

Materials and Methods. A retrospective analysis was conducted on patients treated with a single dose of 21 Gy IOERT at our institution from July 2006 to December 2015. All patients included in the study met the criteria for breast-conserving therapy and partial breast irradiation according to ASTRO and ESTRO guidelines. Local recurrence and overall survival were calculated using Kaplan-Meier analysis. These outcomes were also tested in function of patient's age at IOERT (>70 *vs* ≤ 70) and grading of the tumor (G1 *vs* G2).

Results. With a median follow-up of 11.75 years, 15 out of 295 women (5.08%) experienced a true local recurrence (TLC) (reappearance of the tumor in the same quadrant). 12 recurrences developed in pts younger than 70. The cumulative incidence of TLC at 5 and 10 years was 0.34% and 2.37%, respectively. 5 and 10-year overall survival and local recurrence-free survival were 95.3% and 86.9% and 99.7% and 95.7% respectively. No significant differences were found regarding the local recurrence of the two subgroups analyzed (G1*vs* G2 p=0.6 and age ≥70 *vs* age <70 p=0.3). Overall survival was significantly different in pts older than 70 (p<0.0001) (Figure 1A). No deaths for disease occurred in any pts without age difference.

Conclusions. Our retrospective data suggest that a single-dose IOERT can be safely delivered in highly selected early-stage breast cancers with excellent results and very low long-term recurrence rates.

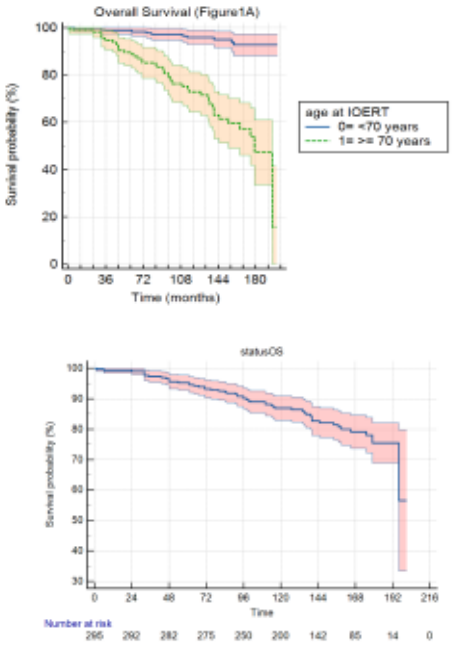

Figure 1.

DP06

SKIN SURFACE DAILY HDR-BRACHYTHERAPY FOR THE TREATMENT OF BASAL CELL CARCINOMA IN ELDERLY PATIENTS

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Aims. About 80% of non-melanoma skin cancers are basal cell carcinoma and surgery remains the primary treatment method. Skin surface High-Dose-Rate Brachytherapy (HDR-BCT) represents a valid alternative for non-surgical candidates or in adjuvant setting, especially in case of positive surgical margins or incomplete resections. The aim of our analysis was to retrospectively review outcome and toxicity in elderly patients treated with daily HDR-BCT.

Methods. From January 2015 to May 2023, twenty-eight elderly patients with basal cell carcinoma were treated with HDR-BCT. Median age was 82 years (range between 73 and 94) and all lesions were localized in the mask areas of the face and scalp and histologically proven as basal cell carcinoma. Thirty-two per cent of patients (32.1%) underwent surgery with positive margins while the remaining patients were non-surgical candidates due to

comorbidities or for tumours involving facial aesthetic units. Median size of the lesions was 28 mm and different Valencia applicators were used depending on tumour size. Treatment was delivered with a median dose of 40 Gy and a median daily dose of 4 Gy; all patients were daily treated (5 days/week). Toxicity was evaluated according to the Radiation Therapy Oncology Group (RTOG) scale. Late toxicity was assessed using the Late Effects Normal Tissue Task Force Subjective, Objective, Management, and Analytic scale (LENT-SOMA).

Results. With a median follow-up of forty-six months, local relapse was observed in two patients (7.1%) and two patients died due to a cardiovascular disease. The median time of local relapse was 15 months. All patients, except one who interrupted treatment for personal reason, completed the planned course of BCT. No patient had >G2 acute skin toxicity, 15.8% of patients had G2 acute toxicity, 31.6% had G1 acute toxicity while the remaining patients had G0 acute toxicity. No patient had >G2 late skin toxicity, 5.2% of patients had G2 late toxicity, 21% had G1 late toxicity while the remaining patients had G0 late toxicity.

Conclusions. HDR-BCT remains an excellent treatment modality for basal cell carcinoma of elderly patients, both in the primary and in the adjuvant setting. Our analysis showed a very low rate of local relapse with an acceptable acute and late toxicity also with daily treatment. Daily fractionation is feasible and it allows elderly patients to complete the planned course of treatment with a minimal discomfort.

DP07

IN VITRO SPARING EFFECT OF ULTRA HIGH DOSE RATE RADIOTHERAPY ON HPV-NEGATIVE HEAD AND NECK SQUAMOUS CARCINOMA

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Aims. Ultra high dose rate (FLASH) radiotherapy (RT) has experimentally highlighted the possibility of increasing the therapeutic window in in vivo models. Concerning head and neck cancers, due to the complex anatomy of the region, several critical structures in and around the area receive radiation treatment. Reducing the incidence and severity of damage to surrounding healthy organs could enable the intensification of RT with enhanced probability of tumor control. However, the results from *in vitro* studies are inconclusive and the biological mechanisms underlying FLASH-RT remain unclear. The purpose of this study is to compare the effect of both FLASH-RT and CONV-RT on normal Human Dermal Fibroblast (nHDF) and Human Oral Squamous Carcinoma (SCC-25) cells viability at increasing doses of radiation.

Methods. nHDF and SCC-25 were irradiated with doses ranging from 4 to 16 Gy using FLASH (average dose rate >200 Gy/s) or CONV dose rates (7 Gy/min), with a 10 MeV electron beam from Sordina Low energy Electron LINAC. Irradiation was delivered under normoxic conditions at room temperature with the plates lying flat on 1 cm of solid water and irradiated from beneath (beam angle 180 degrees). nHDF cells were cultured in Dulbecco's Modified Eagle Medium (DMEM), while SCC-25 cells in a mixture of DMEM and Ham's F12 medium (1:1). Both medium were supplemented with 10% fetal bovine serum (FBS), 4 mM L-glutamine, 1 mM sodium pyruvate, 100 U/mL penicillin, and 100 mg/mL streptomycin. For SCC-25 medium, 400 ng/mL of hydrocortisone was also added. The cells were maintained at 37°C in a humidified incubator with 5% CO2 atmosphere. After irradiation, the cells were returned in the incubator. WST-8 assay was performed after 24 h, 72 h, 6 and 8 days to measure cell viability.

Results. Cell viability was significantly mantained in nHDF FLASH-RT group 8 days after irradiation with lower doses. Both CONV and FLASH treatment showed a late cytotoxic effect on SCC-25 cells, resulting in a significant decrease in viability of ~50% within 6 days.

Conclusions. Overall, these preliminary results highlight a protective effect of FLASH-RT on nHDF cells with iso-effecacy on cancer cells.

DP08

EVALUATION OF RADIOSENSITIZERS EFFECTS OF GOLD ULTRASMALL NANOPARTICLES IN ALTERNATIVE IN VIVO MODEL OF HPV-NEGATIVE HEAD AND NECK SQUAMOUS CELL CARCINOMA

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Aims. Locally advanced head and neck squamous cell carcinoma (LA-HNSCC) is characterized by a high rate of recurrence, leading to poor survival outcomes. Standard treatments are associated with significant toxicities that adversely affect the patient's quality of life. Therefore, there is an urgent need for new effective therapies to improve patient outcomes. Noble metal nanoparticles (NPs) have emerged as promising agents in oncology, serving as drug carriers and radiosensitizers. However, the use of noble metal NPs in combination treatments is still in the preclinical stage due to their persistent presence in the body. This study aimed to evaluate and compare the performance of drug-free non-persistent nanoarchitectures (NAs) with the gold standard (i.e., cisplatin) in combination with radiotherapy using a standardized chorioallantoic membrane (CAM) tumor model of HPV-negative head and neck squamous cell carcinoma (HNSCC).

Methods. CAM models of head and neck carcinoma were established using our standard protocols. Fertilized chicken eggs were punctured on embryonic development day 3 (EDD3), and HPV-negative HNSCC cells (2x106 SCC 25 cells) were inoculated on the CAM at EDD6. The eggs were incubated, and on EDD10, tumor-bearing embryos were randomized and divided into different treatment groups: i) serum-free cell culture medium/RT; ii) cisplatin/RT; iii) NAs/RT. Radiotherapy (RT) was administered on EDD11 using a Varian DHX linear accelerator (LINAC) delivering a total radiation dose of 1 Gy with 6 MV photons. Following RT, the eggs were monitored and photographed daily until EDD14, when the tumors were harvested. Tumor volume was calculated using the formula ½ × (length × width2).

Results. Significant and interesting radiosensitizing effects of the standard NAs were observed, resulting in tumor reduction comparable to the platinum-based strategy. This finding is particularly important as the use of NAs in combination with radiotherapy may overcome the clinical limitations associated with metal NP-based approaches and platinum-based drugs, which are respectively hindered by clearance issues and severe toxicities.

Conclusions. The tested approaches showed comparable effects, suggesting NAs as potential platinum-free agents in concurrent chemoradiotherapy for HNSCCs. To further enhance the potential translation of these nanoarchitectures into clinical practice, these findings will be validated in vivo using HPV-negative orthotopic models of head and neck cancer.

DP09

CONCORDANCE OF QUALITY SCORING FOR MAGNETIC RESONANCE IMAGING RADIOMICS STUDIES IN NASOPHARYNGEAL CARCINOMA: AN AIRO-ENDORSED INTERDISCIPLINARY EVALUATION AMONG MULTIPLE READERS

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Aims. The increasing availability of radiomic studies has led to the creation of several scoring systems, to assess the quality of evidence through a systematic approach. However, the reproducibility of these scores has never been tested. Hence, this work aims to assess the inter-observer agreement among Radiation Oncologists (ROs) and non-clinical professionals in scoring available literature on radiomic applications in magnetic resonance imaging (MRI)-based studies for nasopharyngeal cancer (NPC). Two popular scores were considered, namely the Luo score and the Radiomic Quality Score (RQS).

Methods. In January 2023, a PRISMA-compliant systematic review identified 31 eligible records, to be rated by four ROs, one statistician and one biotechnologist with dedicated experience in radiomics and/or NPC. Inter-observer agreement among all the readers and between ROs and non-clinical researchers was assessed by the interclass correlation coefficient (ICC) with 95% confidence intervals (CIs). The Bland-Altman approach was implemented to provide the average difference between clinical and non-clinical scores with 95% limits of agreement; these were then compared by using the Wilcoxon signed rank test. P-values< 0.05 were considered statistically significant. Analyses were performed with the SAS software v.9.4.

Results. The agreement between readers was higher for the RQS (ICC; 95%CI: 0.79; 0.69-0.88) than the Luo score (0.46; 0.31-0.63) as well as the agreement within the four clinical readers: RQS ICC (95%CI): 0.77 (0.65-0.87); Luo score: 0.64 (0.45-0.79). Agreement within the two non-clinical readers was similar to the one provided by ROs for RQS (ICC; 95%CI: 0.78; 0.66-0.88), while it was higher for the Luo score (0.72; 0.58-0.84). Overall, ROs assigned higher scores than non-clinicians ($p<0.0001$ for both scores), with very low ICC for Luo

score (ICC; 95%CI: 0.15; 0.06-0.30) and fair ICC for RQS (0.57; 0.40-0.74). Bland-Altman plots show that ROs assigned on average 13 points more than non-clinical readers, with 95%LA: 5 to 21 for the Luo score, and they assigned on average 5 points more than non-clinicians, with 95% LA: -1 to 10 for RQS (Figure 1).

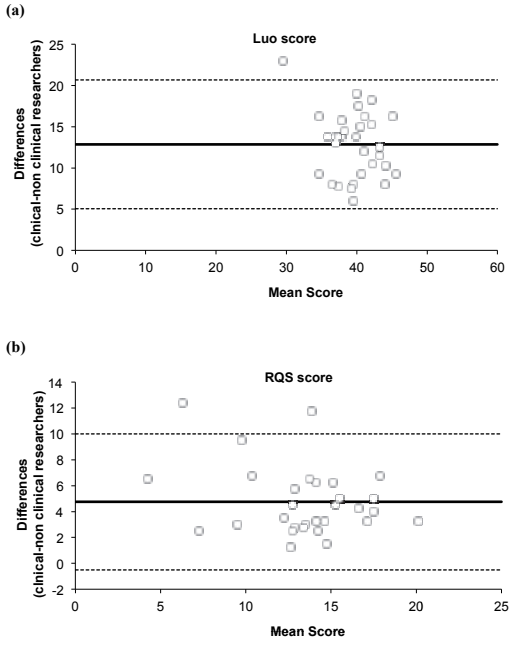

Figure 1. Bland and Altman plots of differences between average scores taken by clinical and non-clinical researchers against the mean of the two scores: (a) Luo score and (b) Radiomic Quality Score (RQS). The graphs show the mean of the differences and the corresponding 95% limits of agreement.

Conclusions. The RQS yielded the highest level of agreement among professionals, with a fair agreement among ROs. Scores assigned by ROs were significantly higher than those provided by non-clinicians. Albeit simpler, the RQS seems to be more user-friendly and reproducible than the Luo score in this setting

DP10

A PREDICTIVE MODEL OF DOSIMETRIC VARIATIONS IN HEAD AND NECK CANCER TREATMENTS: UPDATE OF A MONOCENTRIC EXPERIENCE

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Aims. Adaptive RadioTherapy (ART) requires new indicators to quantify the impact of inter-fraction variations on dose distribution, thus allowing identification of the optimal time to switch towards (online or offline) ART approaches. The aim of our study is the validation of a predictive model able to identify inter treatment fractions with unacceptable dose variations present in head and neck squamous cell carcinoma (HNSCC) patients (pts).

Methods. A total of 14 pts were treated using an Artificial Intelligence (AI)-based linac, acquiring a daily positioning cone beam computed tomography (CBCT) image without online adaptation. Dose regimens ranged between 70 and 60 Gy in 35 and 30 fractions respectively. All CBCT images acquired for patient were rigidly matched to the planning CT (pCT). The variation of V95% of Planning Target Volume High Risk (PTV_HR) and max dose of spinal cord, cervical esophagus and constrictors from the original values reported on pCT were collected along with the treatment. Fractions where PTV V95% decreased by 3% and spinal cord Dmax increase of 3% were considered as needed of ART. Radiological parameters were collected on each daily CBCT aligned with pCT to quantify the inter-fraction variability in each RT fraction once compensated for couch shifts. We measured the absolute body variation along antero-posterior(AP) and latero-lateral(LL) directions in the proximity of the plans passing through different vertebrae (C2, C3) and the corresponding discs (C2-C3, C3-C4). We analysed the correlation between such parameters and the fractions needed for adaptation.

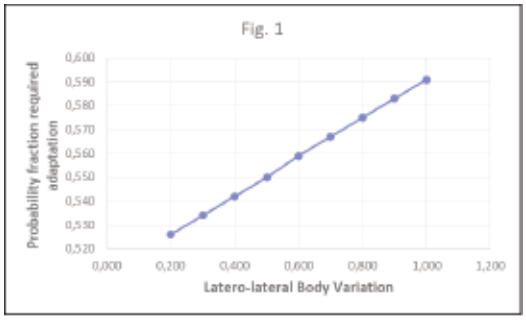

Figure 1.

Results. 212/400 fractions analysed required online adaptation. At the univariate analysis, the most significant parameter was the body variation along the LL direction measured through the C2-C3 disc, able to predict variation of PTV, spinal cord ($p=1.7x10^{-3}$), cervical esophagus

($p=3.44 \times 10^{-13}$) and constrictors (4.78×10^{-4}). Figure 1 reports the probability of obtaining a fraction requiring online adaptation on the basis of the body variation in LL direction, obtained thanks to the predictive model developed.

Conclusions. A new metric to define the need for replanning was proposed based on body variation measured along the LL direction through the C2-C3 disc: if such value results > 5 mm the treatment fraction has to be considered needed of replanning or ART (85% of probability of not meeting the tolerance criteria). More research is needed to address the ART's role in HNSCC.

DP11

GARD MODEL FOR DEINTENSIFICATION OF RADIOTHERAPY IN HPV-RELATED TUMORS: PRELIMINARY RESULTS

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Introduction. Human Papilloma Virus (HPV) is a well-known oncogenic virus. Oropharyngeal cancers (OPC), cervical cancers (CC) and anal cancers (AC) could be HPV-related squamous cell carcinomas. Despite several similarities and high sensitivity to radiation therapy (RT), these cancers are nowadays managed according to organ-specific guidelines. In order to assess the validity of a genome-based model for adjusting radiotherapy dose (GARD model) in HPV-related tumors, we performed a pilot retrospective study on 40 tumor FFPE samples from patients affected by HPV-related tumors and treated with curative RT.

Methods. HPV-related tumors processed in this study were 12 AC, 15 CC, and 13 OPC. To calculate the RSI and GARD values, we extracted RNA from curls of FFPE tumor tissues, checked the RNA quality, and assessed gene expression using in-silico generated and purchased. RNA was hybridized with probes and loaded on nCounter system. Expression results were normalized and used for the linear regression. Then, RSI and GARD were calculated (Figure 1A).We grouped cases of OPC, CC and AC as responders and non responders and checked whether RSI is predictive of RT response in these tumors

Results. Considering RT response, a total of 34 cases had complete response (named responders), and 6 had partial response or progressive disease (named non-responders). The graph (Figure 1B) shows that while OPC responders cases present significant lower RSI values with respect to non-responders, CC shows only a trend. Moreover, AC responder cases do not show any difference in RSI if compared to non-responders. Looking at GARD values, it seems that OPC responder patients would benefit to lower doses of radiations, since they show high GARD values (Figure 1B). On the other hand, CC and AC responder patients, show low GARD values, suggesting that the radiation dose used was the correct one (Figure 1C). These preliminary data suggest that GARD could be a valid model for OPC and CC.

Conclusions. RSI was able to predict RT response in OPC patients, however the pilot study was conducted only on few patients. All non-responder data were put together to check the difference with responder cases. This was due to the low number of non-responders for each anatomical site. Moreover, RSI calculated in CC cases, only showed a trend in predicting RT response. Finally, RSI was not predictive of RT response in AC patients. Further analysis are currently ongoing to increase the number of enrolled patients.

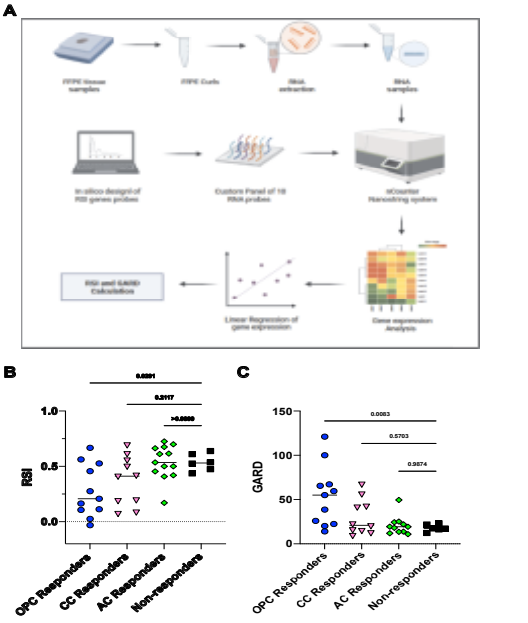

Figure 1. A) Schematic representation of RSI and GARD calculation workflow using Nanostring nCounter. B) Calculated RSI of cases grouped on the basis of site of origin and response. One-way anova with Dunnett correction was performed. C) Calculated GARD of cases grouped on the basis of site of origin and response.

DP12

IMPACT OF ACUPUNCTURE ON ACUTE DYSPHAGIA IN PATIENTS TREATED WITH RADIO-CHEMOTHERAPY FOR HEAD AND NECK SQUAMOUS CELL CARCINOMA: PRELIMINARY RESULTS FROM A RANDOMIZED PHASE 2 STUDY (NCT 05143268)

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Aims. In HNSCC patients undergoing curatively-intended radio-chemotherapy (RCT), dysphagia, both disease- and treatment-related, is frequently reported and it can lead to malnutrition and clinical deterioration. Acupuncture (ACP) has been investigated for xerostomia and pain management, but its impact on dysphagia remains unclear. An Italian, multicentric, randomized phase 2 study is currently ongoing with the primary aim to compare the effect of ACP and standard treatment on swallowing function assessed with MDADI scale (MD Anderson Dysphagia Inventory) 2 weeks after the end of RT. Here, we report a preliminary analysis on ACP compliance in the experimental arm.

Materials and Methods. Patients with histological diagnosis of HNSCC amenable to radical non-surgical treatment (RT alone, platinum based CTRT, RT+ cetuximab) from 6 Italian centers are deemed eligible. Inclusion criteria are age ≥18, ECOG PS 0-2, stage I-III for oropharyngeal cancer (OPC) HPV+, stage II-IVB for non-OPC HPV- carcinoma and accessibility to ACP service with oncological experience. Patients are randomized in a 1:1 ratio to experimental arm (weekly ACP from 2 weeks before the beginning of RT up to 2 weeks after the end of treatment for a total of 11 sessions) or to standard arm. Patients are asked to fill in EORTC QLQ-C30, QLQ-HN43 and MDADI questionnaires at baseline and 2, 12 and 24 weeks after treatment. The use of ACP is hypotesized to yield a 10 point improvement in mean MDADI composite score compared with historical data (from 58 to 68; α=0.05, beta=0.80, sample size=90).

Results. From June 2021 to May 2023, 78 patients were enrolled (ACP, n=39; standard arm, n=39). All were treated with IMRT and 59 with concomitant systemic therapy, whereas 68 underwent bilateral neck irradiation. Baseline characteristics of patients treated at the coordinating center (=37) are reported (Table 1). Among those udergoing ACP, compliance was excellent (100%), very good (99-75%), good (74-50%), poor (49-25%) and very poor (<25%) in 17, 4, 4, 1 and 3 cases, respectively. Most frequent reason for APC early discontinuation was worsening of clinical conditions requiring hospitalization (n=2) or supportive care (n= 2). None had side effects from ACP.

Conclusions. Our preliminary results showed that weekly ACP is feasible and well tolerated in patients undergoing radiation-based treatment for locally advanced HNSCC. Its impact on acute dysphagia is still under investigation.

Table 1. Patient characteristics (coordinating center cohort).

CHARACTERISTICS	N (%)
Total patients	37
Males	27 (73)
Females	10 (27)
Age (years)	
Mean	65.07
Range	50-80
Charlson Comorbidity Index (CCI)	
Mean	4.8
Range	2-8
Weight (kg)	
Mean	73.32
Range	47.7-117
Tobacco exposure	
Never smoker	13 (35)
<10 p/y	2 (5)
10-20 p/y	7 (19)
> 20 p/y	15 (41)
Alcohol exposure	
No/light drinking	31 (84)
Moderate drinking	4 (11)
Heavy drinking	2 (5)
Caregiver	
Absent	12 (32)
Present	25 (68)
Tumor primary	
Larynx	9 (24)
Nasopharynx	4 (11)
Oropharynx	24 (65)
Hypopharynx (H)	0 (0)

DP13

MANAGEMENT AND ONCOLOGIC OUTCOMES OF LOCAL PERSISTENT AND RECURRENT DISEASE OF ANAL SQUAMOUS CELL CARCINOMA AFTER RADIOCHEMOTHERAPY TREATMENT: A SUB-GROUP ANALYSIS OF A MULTICENTER STUDY ON BEHALF OF AIRO GASTROINTESTINAL STUDY GROUP

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Aims. Up to 30% of patients with squamous cell cancer of the anus (SCCA) will require treatment for persistent or recurrent disease. The aim of this study was drawing a picture of management and outcomes in this setting at a population level.

Table 1. Distribution of variables in persistent disease (PD) and local recurrence (LR) patients.

Variables	Persistent Disease	Local Recurrence
	N=94	*N=45*
Gender		
Male	32 (34%)	11 (24.4%)
Female	**62 (66%)**	**34 (75.6%)**
Baseline ECOG performance status		
0	**63 (67%)**	**33 (73.3%)**
1-2	31 (33%)	12 (26.7%)
Biopsy		
Yes	**50 (53.2%)**	**36 (80%)**
No	35 (37.2%)	6 (13.3%)
Missing	9 (9.6%)	3 (6.7%)
Site of disease (Anatomical)		
Anal canal	**51 (54%)**	**32 (71.3%)**
Anal margin	11 (11.7%)	2 (4.3%)
Pelvis	11 (11.7%)	4 (8.9%)
Inguinal nodes	5 (5.3%)	2 (4.3%)
Iliac nodes	2 (2.1%)	1 (2.3%)
Multiple	3 (3.2%)	0
Missing	10 (10.7%)	4 (8.9%)
Site of disease (Treatment Volumes)		
Tumor GTV	**70 (74.5%)**	**38 (84.4%)**
Nodal GTV	10 (10.7%)	3 (6.7%)
Elective Nodal CTV	3 (3.2%)	2 (4.3%)
Multiple	3 (3.2%)	1 (2.3%)
Missing	8 (8.5%)	1 (2.3%)
Salvage Surgery	***N=64 (68%)***	***N=41 (91%)***
Abdominal Perineal Resection	**47 (73.3%)**	**23 (56.1%)**
Trans Anal Resection	3 (4.7%)	2 (4.8%)
Multivisceral resection	4 (6.4%)	5 (12.2%)
Missing	10 (15.6%)	11 (26.8%)
Perioperative complications *(Clavien-Dindo Grading)*		
0	**19 (29.7%)**	**20 (48.8%)**
1	7 (10.9%)	2 (4.8%)
2	7 (10.9%)	1 (2.4%)
3a	1 (15.6%)	1 (2.4%)
3b	1 (15.6%)	1 (2.4%)
4a	2 (3.7%)	0
5	3 (4.7%)	0
Missing	24 (37.6%)	16 (39.2%)
Re-Irradiation	***N=10 (10.7%)***	***N=9 (20%)***
In-field	2 (20%)	**5 (55.6%)**
Out-field	**8 (80%)**	4 (44.4%)
Treatment purpose		
Curative	5 (50%)	**7 (77.7%)**
Palliative	5 (50%)	2 (22.3%)
Acute Re-Irradiation toxicity (CTCAE v5)		
G0	4 (40%)	0
G1 pain	2 (20%)	0
G1 diarrhea	1 (10%)	0
G1-2 dysuria	1 (10%)	1 (11.1%)
G2-3 proctitis	2 (20%)	1 (11.1%)
Median Follow-up	21 months (range: 3-146)	50 months (range:14-148)

Methods. In 2020 a multi-institutional retrospective study was conducted to evaluate clinical outcomes of SCCA treated with IMRT (RAINSTORM study). A subgroup analysis was did considering patients with persistent disease (PD) after 6 months from primary chemoradiation, or local recurrences (LR), defined as proven disease after an initial period of clinical response. Primary outcome was overall survival (OS). Secondary outcomes included perioperative complications according to Clavien-Dindo and Re-irradiation (Re-I) toxicity by CTCAE v5.

Results. Overall, 139 patients (94 PD and 45 LC) with SCCA were analysed. Distribution of variables in PD and LR groups are detailed in Table 1. Anal canal and tumor GTV (gross tumor volume) have been reported as

the main sites of persistent (54% and 74.5%) and recurrence disease (71.3% and 84.4%), respectively. Chemotherapy with pre-operative or exclusive intent was administered in 28 PD (29.8%) and 7 LR (15.5%) patients. Surgery was performed in 64 PD (68%) and 41 LR (91%) patients. The overall probability of surviving at 24 and 60 months for PD patients were 64.1% ±0.54 and 39.9% ±0.65. In PD patients underwent salvage surgery the 24- and 60-months OS reached 75.9% ±0.59 and 55.3% ±0.76. The 24- and 60-months OS for LR patients were 89.9% ±0.48 and 80.1% ±0.68. Overall, severe perioperative complications were low reported in both groups. Re-I was done in 10 PD (1.7%) and in 9 LR (20%) patients with good tolerability. Lymphoedema in one patient was reported as a single late toxicity in PD group.

Conclusions. In our analysis, salvage surgery was confirmed the main treatment for both persistent and recurrent disease and was related with optimal OS. Moreover, although the data on perioperative complications were missing in about 40% of patients, surgery resulted safe in both groups. No severe acute and late toxicities were related to Re-I, suggesting that this treatment may also be considered when surgery is not feasible, but prospective studies with larger population are needed in this setting. A multivariate analysis is ongoing to identify tumor, patient, and primary treatment variables that could correlate with worse clinical outcomes and may require intensified treatments.

DP14

STEREOTACTIC BODY RADIOTHERAPY IN LOCALLY ADVANCED PANCREATIC CANCER: A MULTICENTER RETROSPECTIVE ANALYSIS ON 125 PATIENTS (PAULA-1)

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Aims. Stereotactic body radiotherapy (SBRT) is a modern treatment technique based on high-precision image-guided delivery of ablative doses with a short overall treatment time. SBRT seems particularly effective in locally advanced pancreatic cancer (LAPC), promoting optimal integration with chemotherapy (CHT) while minimizing its interruptions or delay. Aim of this multicenter retrospective observational study was to assess local control (LC), distant metastasis free survival (DMFS), and overall survival (OS) of LAPC patients treated with SBRT +/- CHT.

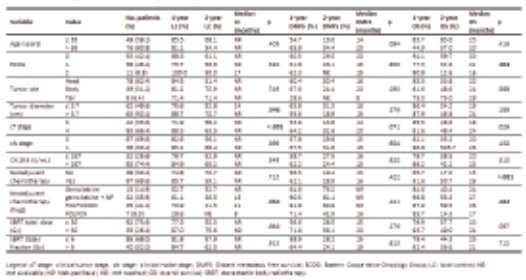
Methods. Patients treated between 2012 and 2022 with SBRT +/- CHT in 15 Italian centres were selected from a large DB of LAPC. Neoadjuvant CHT regimens included gemcitabine (14.9%), gemcitabine+Nab-paclitaxel (35.9%), FOLFIRINOX (41.2%), and FOLFOX (8.0%). Median total dose and dose/fractionation were 30.0 Gy (range: 18.0-67.5 Gy) and 6.0 Gy (range: 3.9-10.0 Gy), respectively. Median tumor diameter was 3.7 cm (range: 1.2-8.7 cm). Survival curves were calculated by Kaplan-Meier method. A Cox regression model was fitted for multivariable analysis.

Results. We analysed 125 LAPC patients. Median follow-up was 17 months (range: 3-92 months). Median OS was 23 months with 40.8% 2-year OS rate. Median LC was not reached with 60.1% 2-year LC rate. At univariate analysis (Table 1), patients with cT4 ($p<0.001$), tumor diameter > 3.7 cm ($p=0.038$), treated with total doses ≥ 30.0 Gy ($p=0.012$), and with modern CHT regimens as FOLFIRINOX ($p=0.014$) had statistically significantly prolonged LC. Patients with ECOG-PS=0 ($p=0.004$), treated with neoadjuvant CHT ($p<0.001$), and particularly with gemcitabine+Nab-placlitaxel ($p=0.042$),

had prolonged OS. At multivariable analysis tumor diameter >3.7 cm was confirmed to be a significant predictor of improved LC (HR: 0.42, 95%CI 0.19-0.93, p=0.034) and improved OS (HR: 0.48, 95%CI 0.25-0.90, p=0.022), respectively. cT4 tumor stage (HR: 0.34, 95%CI 0.15-0.77, p=0.010) and novel CHT regimens such as gemcitabine+Nab-placlitaxel or FOLFIRINOX (HR: 0.34, 95%CI 0.15-0.77, p=0.010) were independent predictors of improved OS.

Conclusions. The combination of SBRT and modern CHT regimens is effective in LAPC, with significantly improved OS. Our analysis confirms our previous data on the correlation between larger and cT4 LAPC with prolonged OS. Future studies are needed to explain these paradoxical findings.

Table 1.



DP15

STEREOTACTIC RADIOTHERAPY (SRT) WITH SIMULTANEOUS INTEGRATED PROCTECTION (SIP) PLANNING STRATEGY TO MANAGE UPPER ABDOMINAL LESION WITH CRITICAL OVERLAP WITH VISCERAL ORGANS: PRELIMINARY RESULTS OF A PROSPECTIVE STUDY

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Aims. One of the challenges of stereotactic radiotherapy (SRT) is to manage lesions near or abutted to bowel, duodenum and stomach. Treating such lesions with effective doses is difficult, given the intrinsic radiosensitivity of the organs and the consequent risk of severe and life-threatening toxicities. This study was designed to investigate if deliberated dose-reduction strategy consisting in tailoring dose in the area of overlap between PTV and critical organs at risk (simultaneous integrated protection, SIP approach) is safe while maintaining effectiveness.

Methods. This is a prospective, single arm, observational study. Inclusion criteria were tumor abutment with duodenum, stomach or jejunum, dose prescription reaching at least a biologic effective dose (BED) of 70Gy (alpha/beta 10 for the tumor), per-protocol dose constraints were: (near) maximum dose, D2cc and D20cc to duodenum, stomach or small bowel were 38Gy, 32Gy and 24 Gy. Primary endpoint were 1 year freedom from local recurrence (FFLR) and acute-late toxicity.

Results. From December 2019 to January 2022 88 patients were enrolled. Of the 47 patients treated on the pancreas, 33 patients presented with locally advanced pancreatic cancer, 11 with single pancreatic metastasis from clear cell carcinoma and 3 patients affected by single metastasis from colon cancer. The other 41 patients were treated on paraduodenal or perigastric lymph-nodes, adrenal gland and liver lesions.After a median FU of 15 months, 14 pts (15.9%) experienced an in-field recurrence. Median FFLR resulted not reached with one and two years FFLR of 88.2% and 71.2%, respectively. In 8 cases, recurrence occurred in SIP area while in 6 cases the recurrence was in a high dose area. Concerning toxicity, one case of G4 acute toxicity occurred (splenic abscess), one case of acute G3 toxicity (duodenal stenosis) and 13 cases of G2 toxicity mainly represented by emesis and dyspepsia. No grade 3 or worse late toxicity occurred, two case of G2 toxicity was registered, consisting in recurrent cholangitis.

Conclusions. SRT with SIP planning strategy is safe and effective for the treatment of upper abdominal lesions with critical anatomical relationship with duodenum, jejunum and stomach, local relapses seems to be similarly distributed in SIP and high dose areas. The pre-determined per protocol coverage objectives ensured consistency in planning and results, that are similar to those achieved with SRT for treating less critical districts.

DP16

RE-IRRADIATION FOR RECTAL CANCER RECURRENCES USING PENCIL BEAM SCANNING PROTON THERAPY: A SINGLE INSTITUTIONAL EXPERIENCE

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Aims. Rectal cancer (RC) is a common malignancy, with approximately 800,000 worldwide new cases per year. Although the use of adjunctive pre- or postoperative radiation/chemoradiation therapy has reduced the incidence of local recurrence rectal cancer (LRRC), 4 % to 13 % of patients still experience recurrence in the pelvis. Salvage treatment often is performed with radiation ther-

apy. However, it presents risk of late complications given the radiation sensitivity of nearby organs and tissues of the abdomen and pelvis. Proton therapy (PT), thanks to the typical dose fall-off of the Bragg peak, could minimize the risk of side effects compared to conventional photon therapy. Based on this background we report our institutional experience on re-irradiation with PT for rectal cancer recurrences.

Methods. Between 2014 and 2022, 16 patients (pts) were analyzed, including 6 pts with rectal recurrence (37.5%) and 10 pts with pelvic recurrence (62.5%). Median age at re-irradiation was 64 years (range, 46-84 years) and median Karnofsky Performance status was 90 (range, 70-100). The median reirradiation dose was 50 GyRBE (range, 39.6-50.4 GyRBE). Median time between first radiotherapy and re-irradiation with PT was 49 months (range, 15-166 months). All patients were treated with PBS-PT, typically with 2 or 3 lateral/lateral - posterior fields with single-field optimization technique, with some cases using a multiple-field optimization. Median PTV (planning target volume) was 334 cc. The primary outcome measure was local control (LC). Secondary outcomes included overall survival (OS) and treatment-related toxicity.

Results. All patients completed the treatment without breaks. No G≥3 acute toxicities were reported, except a case of G3 ureteral stenosis (6%). Four patients (25%) experienced grade < 3 late toxicities including grade 2 pain (12%), grade 2 fatigue (6%), grade 1 erythema (6%) and grade 1 constipation (6%). An improvement of their symptoms experienced was noted in 30% of the cases. After a mean follow-up of 3.6 years (range, 0–7 years) 1-year and 3-year LC were 80 and 69%, respectively. 1-year and 3-year OS were 94% and 60%, respectively. No difference in terms of LC and OS if we compare rectal recurrence and pelvic recurrence.

Conclusions. PT as re-irradiation for locally recurrent rectal cancer seems to be a safe and valid treatment with an acceptable rate of morbidity of surrounding healthy tissue and good local control.

DP17

STEREOTACTIC RADIOTHERAPY FOR LIVER METASTASES: A LARGE POOLED REAL-WORLD ANALYSIS

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Aims. A large pooled real-world analysis of liver metastases treated by stereotactic radiotherapy (SBRT) was carried out.

Methods. The clinical and dosimetric data of patients who underwent stereotactic radiotherapy for liver metastases from several tumors were collected and analyzed in terms of efficacy and toxicity profile. In particular, the Local Control (LC), Distant Metastases Free Survival (DMFS), Disease-Free Survival (DFS), Overall Survival (OS), and Next Systemic Therapy Free Survival (NESTFS) rates were analyzed.

Table 1. Patients characteristics.

Patients	119
Lesions	156
Lesions Burden	
None	28
1-5	58
6-10	3
>11	27
Liver Segment	
1	4
2	9
3	1
4	22
5	17
6	22
7	9
8	20
More than one liver segment	51
Equipment	
LINAC	96
MRI-LINAC	60

Results. Data of 119 patients (M/F: 49/70), accounting for a total of 156 hepatic lesions, that were treated between March 2006 and February 2023 in two Italian centers were evaluated. The patients' median age was 67 years old (36-92) and 47 (39.4%) patients had at least one comorbidity, mainly cardiovascular ones (31.1%) and diabetes (6.7%). The main primary tumors were colorectal (36.1%) and breast (16.3%) ones. The majority of the lesions could be defined as induced (28.8%) or repeated oligoprogressive (17.9%) metastases. 104 lesions were treated with more than one daily fraction and 50 Gy in 5 fractions (32.7%) was the most used fractionation. Among the 52 radiosurgery treatments, 28 Gy in a single fraction (19.2%) was the most represented schedule. The median Gross Tumour Volume was 6.3 cc (0.1-151.2), the median Planning Tumour Volume was 23.3 cc (2.7-207.8), and the median liver volume was 1319.7 cc (727.8-2421.2). More details on patient and lesion characteristics are reported in Table 1. At the time of analysis, the treatment response was evaluable in 153 lesions, reg-

istering a complete response in 28.8%, partial response in 17.0%, stable disease in 34.0%, and progressive disease in 20.2% of the patients. Actuarial LC, DMFS, DFS, OS, and NESTFS at one year were 69.9%, 27.1%, 24.6%, 83.9%, and 53.1% respectively; while actuarial LC, DMFS, DFS, OS, and NESTFS at two years were 57.9%, 21.1%, 19.2%, 67.3%, and 40.4% respectively. As per the toxicity profile, we registered only 2 acute toxicity cases higher than grade 2 (2 Grade 3 and 2 Grade 4 liver toxicities), while only 6 late toxicity cases were higher than grade 2 (1 Grade 4 bone toxicity and 5 G3 liver toxicity).

Conclusions. Stereotactic treatment for liver metastases seems to be a safe and promising option in terms of LC. Moreover, one year after the treatment at least 50% of the patients were free from the start of a new systemic line.

DP18

ROLE OF ABLATIVE REGIMEN AND PRIOR CHEMOTHERAPY IN LIVER METASTASES TREATED WITH SBRT

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Aims. SBRT has emerged as a therapeutic option in the ablative treatment of liver metastases. There is wide heterogeneity of clinical scenarios, both in terms of fractionation and technique, so the aim of this work is to evaluate the effects of SBRT to assess whether there are predictors for OS, LC and PFS.

Methods. Among the 88 patients with liver metastases treated from 28/01/2019 to 14/12/2022, we included the 62 for whom radiological follow-up was available. Patients were treated either with fiducial based real time tumor tracking (CK) or abdominal compression VMAT. Clinical and treatment-related data were analysed. Survival analysis was performed.

Results. Of the 62 patients, 25 were oligometastatic (OM) and 41 oligoprogressive (OP); 24 had metastases of breast origin, 17 of colorectal origin and 21 had other histologies; 44 were chemo-naive or at first-line chemotherapy and 18 were multi-chemotherapy treated (>1 line). Seventeen patients had VMAT treatment and 45 CK treatment. SBRT was delivered in 3-5 fractions for a DTF of 30-60 Gy. Median BED was 95.05 Gy with 39 patients treated with BED > 100Gy. Median OS, LC and PFS were 21 months, 21 months and 7 months respectively. 6 months OS, LC and PFS were 86%, 80% and 57% respectively while 1 year OS, LC and PFS were 69%, 71% and 31% respectively. OS was correlated with chemotherapy exposition (p 0.0301), multi-treated patients with systemic therapy (second line or more) have worse outcomes. LC was correlated to BED >100 Gy (p 0,031, HR 0,4); LC is 41 months and 21 months respectively for BED >100 Gy and <100Gy. PFS was associated with BED >100 Gy (p 0,002, HR 0,4) and chemotherapy exposition (p 0.0002), both proved independently correlated at MV analysis (p 0,014 and p 0,0028 respectively). No differences were found in terms of treatment outcome for technique , OP/OM disease and primary histology.

Conclusions. Liver SBRT have good oncological outcomes in both OP and OM disease, particularly in not-heavily chemotherapy-treated patients. Independently of primary tumor, the use of dose intensive regimen (BED >100Gy) have better outcomes. Furthermore the use of abdominal compression assisted VMAT was not inferior to fiducial based real time tumor tracking CK.

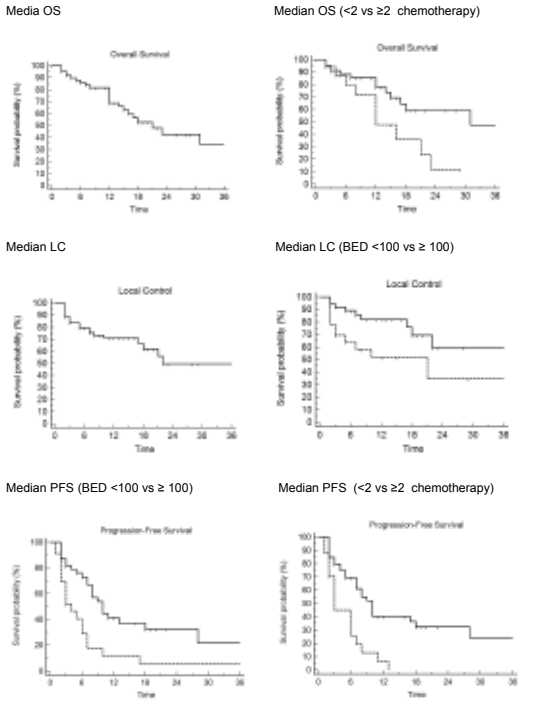

Figure 1.

DP19

FOCAL RADIOTHERAPY FOR OLIGO-PROGRESSIVE PLEURAL MESOTHELIOMA: FINE-TUNING THE OPTIMAL DOSES

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Aims. There is growing evidence of the role of focal radiotherapy in the treatment of selected patients (pts) with oligo-progressive pleural mesothelioma (PM). The optimal doses of radiation in this setting are not defined.

Methods. We retrospectively enrolled pts treated with stereotactic body radiation therapy (SBRT, defined as >5 Gy per fraction) on pleural lesions for oligo-progressive PM (defined as <= 3 lesions detected at CT scan). They were divided in a group treated with "intermediate dose" SBRT (i-SBRT, total dose 30-36 Gy/ 5-6 fractions) and a group receiving "high dose" SBRT (h-SBRT, total dose 45-50 Gy / 4-8 fractions). No concomitant systemic therapy was administered. Local control (LC) and toxicity (according to CTCAE 4.0) were the co-primary endpoints of the study. Time to further systemic therapy (TFST), progression free survival (PFS) and overall survival (OS), all measured from the first day of SBRT, were the secondary endpoints.

Results. From 06/2014 to 09/2022, 23 pts were treated on 25 pleural lesions, 15 and 8 with i-SBRT and h-SBRT, respectively. The median biologically effective dose (BED) calculated with an alfa/beta of 3 was 90 Gy (range 90-116 Gy) for i-SBRT group and 160 (range 144-240) for h-SBRT group. The median planning target volumes (PTVs) were 83.6 cm^3 (range 13.9-347.1) for i-SBRT and 59.9 cm3 (range 22.4-446.4) for h-SBRT (p=0.99). After a median follow up of 13.3 months from SBRT (range 3-37 months), 6-mo, 1-yr and 3-yr LC were 100%, 100% and 80% for i-SBRT pts, and 100%, 100% and 67% for h-SBRT pts (p=0.94). A radiological complete response was achieved in 5/15 (33.3%) and in 2/8 pts (25%) in i-SBRT and h-SBRT groups. No severe toxicity was reported for i-SBRT pts, while in 3/8 h-SBRT pts (37.5%) G2 (2 pts) and G3 (1 pt) acute and late chest wall pain was registered. Overall median TFST, PFS and OS were 12.0, 8.2 and 38.0 months; no significant differences in TFST, PFS or OS were found between i-SBRT and h-SBRT groups in univariate analysis.

Conclusions. SBRT for oligo-progressive PM is safe and feasible in selected pts. Intermediate SBRT doses (total dose 30-36 Gy / 5-6 fractions) were equally effective but safer than higher SBRT doses.

DP20

GENETICALLY-BASED COX-NTCP MODELS FOR LATE TOXICITY AFTER PROSTATE CANCER RADIOTHERAPY

B. Avuzzi[1], T. Rancati[1], E. Gioscio[1], M. Massi[2], N. Rares Franco[2], A. Cicchetti[1], B. Rosenstein[3], P. Seibold[4], D. Azria[5], A. Choudhury[6], D. De Ruysscher[7], M. Lambrecht[8], E. Sperk[9], C. Talbot[10], A. Vega[11], L. Veldeman[12], A. Webb[10], P. Zunino[2], A. Paganoni[2], F. Ieva[2], A. Manzoni[2], S. Gutierrez[13], S. Kerns[14], A. Dunning[15], R. Elliott[6], C. West[6], C. Claude[4]

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Aims. An international, prospective cohort study recruited prostate cancer patients (pts) in 8 countries (4/2014-3/2017). It was aimed at multinational validation of clinical/dosimetric/genetic risk factors that predict late toxicity following radiotherapy (RT). We propose a Cox-NTCP models for late toxicity including genetic information a polygenic risk score (PRS) that incorporates SNP-SNP interactions (PRSi).

Methods. 1808 pts were enrolled. Involved centres used standardised data collection. Grade≥1 (G1+) rectal bleeding, Grade≥2 (G2+) rectal bleeding, G2+ urinary frequency and G1+ haematuria were considered as separate endpoints. Studied dosimetric descriptors included rectum/whole bladder/bladder neck DVHs and dose-surface-histograms (DSHs). A pool of 43 SNPs associated with late RT toxicity from the literature was tested, and a deep sparse autoencoder method identified the SNPs affecting the toxicity risk at 2 year follow-up (F-up). A new method for accounting for SNP-SNP interactions (PRSi) was developed; the PRSi shows which SNPs and alleles are included, whether they affect the risk of toxicity and their combined effects. (Figure 1). NTCP models were based on Cox regression, allowing inclusion of F-up time and censoring.

Results. 1482 pts had long-term F-up (median 24 mos, 75th perc 60 mos). 75% pts had conventional fractionation, 25% hypofractionation. 70% pts had VMAT, 12% IMRT, 18% 3DCRT. 30% had post-prostatectomy RT, 32% pelvic RT and 72% hormone therapy. Toxicity crude rates were 18% G1+ rectal bleeding, 5% G2+ bleeding, 5.7% G2+ urinary frequency, 8.5% G1+ haematuria.

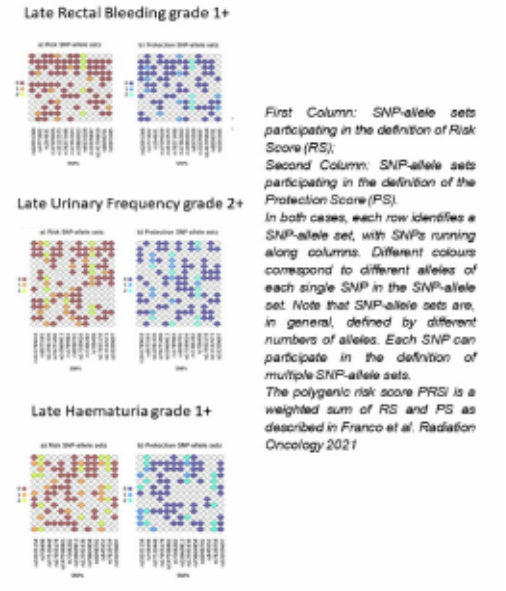

Figure 1.

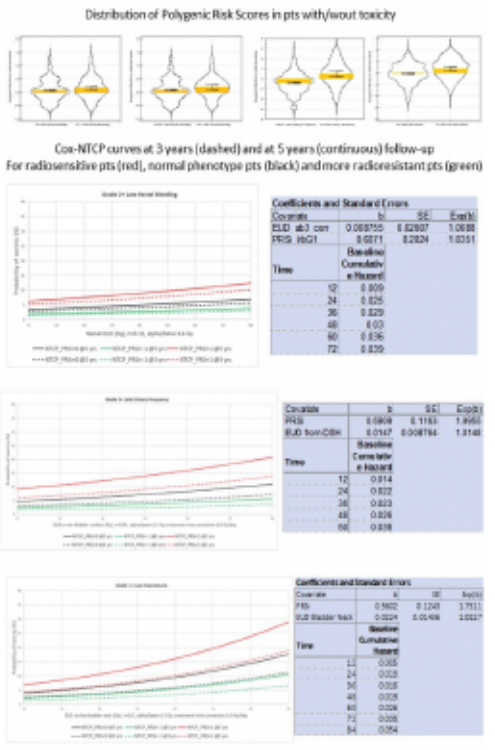

Figure 2.

The previously defined PRSi (at 2 yrs) were still associated to toxicity in the long term. For rectal bleeding the best dosimetric descriptor was the rectal EUD from DVH, for urinary frequency it was the whole bladder EUD from DSH, while for heamaturia the bladder neck EUD from DSHs. All doses were collected for fractionation using the linear quadratic model and alpha/beta ratios derived from maximum likelihood fit. The developed Cox-NTCP models are presented in Figure 2.

Conclusions. The present analysis showed for the first time the benefit of adding PRSi Cox-NTCP prediction models. These models allow both a patient-specific tailoring of prediction and accounting of F-up time. All models were based on a large modern multicenter prospective cohort with long term standardised F-up.

Fundings. REQUITE: European Union's 7th FP GA 601826, RADprecise: ERAPerMed Network (ERAPERMED2018-244)

DP21

ABRUPT TRIAL: RADIOTERAPIA ABLATIVA IN SINGOLA SEDUTA NEL CARCINOMA PROSTATICO ORGANO-CONFINATO A PROGNOSI SFAVOREVOLE

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Aims. To investigate early gastrointestinal (GI) and genitourinary (GU) side effects in patients with organ-confined unfavorable prostate cancer (PCa) following Single-Dose Ablative Radiation Therapy (SDART).

Methods. Twenty-five patients included in the prospective clinical trial "ABRUPT" (NCT04831983) were treated with a single fraction of 24 Gy to the whole prostate with urethra sparing in association with androgen deprivation therapy (ADT), as per standard of care. The treatment was delivered on Linac platform with Volumetric Modulated Arc Therapy (VMAT) and a real-time prostate tracking system. Side effects were evaluated with CTCAE_v5 scale. IPSS score and Quality of Life (QoL) metrics assessed with EORTC questionnaires QLQ-PR25/-C30 were also measured. In addition, multi-parametric MRI was performed before SDART (time 0), one-hour post-SDART (time 1), and 3-month after treatment (time 2).

Results. Median age was 77 years (range 62-84) and median iPSA level was 7,8 ng/ml (range 3,88-18,27). With a median follow-up of 10 months (range 3-22) only one patient experienced a major (G3) GU toxicity, while none of them developed a ≥G2 GI toxicity. Two instances of G2 GU toxicity were recorded. Median IPSS showed a

transient decline at 3 months, before gradually returning at baseline levels. At the same timepoints, a worsening in the QoL (83 *vs* 67) and urinary domains (8 *vs* 17) was documented, while no significant changes were observed thereafter. Bowel domains remained unchanged. A 24% reduction in the median prostate volume was observed, from 33.7 cc (range 10-59) at time 0 to 27 cc (range 8,5-48) time 2. At time 2, all patients showed a radiological response at MRI. At last follow up, all patients were found b-NED (nine patients ADT-free).

Conclusions. SDART irradiation of the whole prostate with urethra sparing and organ motion control was feasible and well tolerated in patients with organ confined unfavorable PCa. Long term results are awaited to confirm these findings.

DP22

STRILL: A PHASE I TRIAL EVALUATING STEREOTACTIC BODY RADIOTHERAPY (SBRT) DOSE ESCALATION FOR REIRRADIATION OF INOPERABLE LUNG LESIONS

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Aims. Few data are available on the role of SBRT reirradiation for isolated recurrences after initial thoracic SBRT; moreover, possibility of delivering a second course of ablative dose RT (BED ≥ 100 Gy) is even less studied. Based on this background, we designed a prospective phase I study to evaluate the maximum tolerated dose (MTD) of SBRT for thoracic re-irradiation. Dose limiting toxicity was defined as pneumonitis ≥ G3.

Methods. From May 2020 to October 2022, patients candidate to thoracic reirradiation with SBRT were proposed for study enrolment. The radiation treatment was delivered with 3 possible schedules, with a dose escalation design from 30 Gy in 5 fractions up to 50 Gy in 5 fractions. Dose was prescribed to Target mean ensuring that more than 98% of PTV will receive 95% of prescribed dose. The primary end point was the definition of the maximal tolerated dose (MTD) of SBRT for thoracic re-irradiation. Dose limiting toxicity was pneumonia ≥ G3. Secondary end points were local control, progression free survival, overall survival, acute and late toxicities other than dose limiting toxicity.

Results. 15 patients were ultimately enrolled. Patients and disease characteristics are shown in Table 1. Median patients age at SBRT time was 72 years. No cases of pneumonia ≥ G3 occurred in any of our patients cohort. Only one patient developed pneumonia G1 6 months after treatment. 3 patients developed acute toxicities that included dyspnea G1, cardiac failure G3 and chest wall pain. One patient developed G3 late toxicity with an acute coronary syndrome. Neither acute nor late toxicities ≥ G2 were developed by patients receiving the higher dose scheduled of 50 Gy in 5 fractions. Local response to SBRT was PR in 7 patients, SD in 7 patient and PD in 1 patient. After a median follow up of 21 months (range 3.6-29.1 months), 6 patients (40%) had a local relapse. Distant relapse occurred in 5 patients (33.3%). At last follow up, 6 patients died, all but two due to progressive disease.

Conclusions. SBRT dose escalation for thoracic reirradiation is an effective and well tolerated option for patients with inoperable lung lesions after a first thoracic RT with acceptable acute and late toxicities. No dose limiting toxicity was seen during the study. Anyway, a phase II trial is needed to better define efficacy of SBRT at high doses.

Table 1. Patients and disease characteristics.

Features	Patients (n)	Percentage (%)
SEX		
Male	11	73%
Female	4	27%
SMOKING HISTORY		
Never	2	13%
Former	9	60%
Current	4	27%
COMORBIDITIES		
0	3	20%
1	11	73%
>1	1	7%
PULMONARY COMORBIDITIES		
No	13	87%
BPCO	2	13%
CARDIAC COMORBIDITIES		
No	5	33%
Hypertension	8	53%
Atrial fibrillation	3	20%
Heart failure	1	7%
Acute coronary Syndrome	1	7%
PRIMARY CANCER SITE		
Lung	10	67%
Larynx	2	13%
Rectum	1	7%
Sarcoma	1	7%
Unknown	1	7%
PRIMARY CANCER HISTOLOGY		
Adenocarcinoma	8	53%
Squamocellular carcinoma	5	33%
Synovial sarcoma	1	7%
Epithelial NOS	1	7%
PRIMARY CANCER TREATMENTS		
Surgery	6	40%
Systemic therapy	8	53%
Radiotherapy	9	60%
FIRST RT ON TARGET LESION TYPE		
SBRT	12	80%
Hypofractionated RT	2	14%
Conventional RT	1	7%
OVERLAP		
In site	6	40%
50%	9	60%
PS AT SBRT		
0	9	60%
1	6	40%
SBRT TOTAL DOSE IN 5 FRACTIONS		
30 Gy	5	33%
40 Gy	5	33%
50 Gy	5	33%

DP23

RE-IRRADIATION FOR INTRAPROSTATIC RELAPSE AFTER CURATIVE PROSTATE CANCER RADIOTHERAPY: A REAL-WORLD ANALYSIS

E. Cammareri[1,2], G. Corrao[1], M. Zaffaroni[1], M.G. Vincini[1], D. Zerini[1], S. Clobiaco[1,2], S. Luzzago[5], F.A. Mistretta[5], S. Alessi[4], F. Ceci[2,3], G. Petralia[2,4], G. Musi[5], F. Cattani[1], O. De Cobelli[5], G. Marvaso[1], B.A. Jereczek Fossa[1,2]

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Aims. Aim of the present study is to evaluate the safety and effectiveness of re-irradiation for local relapse on patients who received RT as primary treatment for prostate cancer (PCa).

Methods. Patients who received radical RT (external beam RT (EBRT) or brachytherapy) and with evidence of isolated intraprostatic disease at MRI or PET choline were retrospectively considered for study inclusion. Salvage re-EBRT was delivered with image-guided RT (RapidArc®, VERO® and CyberKnife®).

Results. A total of 84 patients, with a median age at salvage re-EBRT of 75 years, were included in the present analysis. A total of 19 patients received 25Gy/5fx, while 40 received 30Gy/5 fx and 25 received 35 Gy/7 fx. Median pre-salvage SBRT prostate-specific antigen (PSA) was 4.1 ng/ml. A total of 22 (26.2%) patients received concomitant hormone therapy. The intraprostatic disease was assessed by PET choline or MRI in 80 patients (95.2%) and 57 patients (67.0%), respectively. A total of 63 (75.0%) patients received partial prostate irradiation (only the visible lesion was treated), while 21 received treatment on the whole prostate. Median GTV was 17.2 cc. At a median follow-up of 38 months, 57 patients (68%) experienced a biochemical progression, with a median time to progression of 14 months. Biochemical recurrence-free survival rates at 1- and 2-year were 73.4% and 45.3%, respectively (Figure 1). Clinical progression was observed in 47 patients (56%). Among them, 13 had both intraprostatic relapse and distant metastasis, 7 developed only distant metastasis and 27 had only intraprostatic relapse. Among the 20 patients who developed distant metastasis, two had only lymphnodal lesions, 13 had only bone lesions, 3 had both (2 missing). Among the 40 intraprostatic relapse, 12, 20 and 8 were observed in the 25Gy, in the 30Gy and in the 35Gy groups, respectively. One G2 acute GU event was registered. Considering maximum toxicity during the treatment, three G > 3 late GI events (two solved at last FU) and six G > 3 late GU events (three solved at last FU) were reported.

Conclusions. Salvage re-EBRT for isolated intraprostatic relapse of PCa could represent a safe and effective treatment with an adeguate patients selection. Further studies should be focused on the identification of the ideal prescription dose and suitable patients.

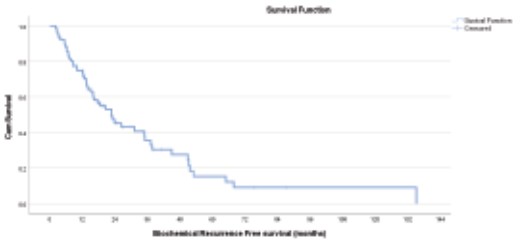

Figure 1.

DP24

SAFETY AND EFFICACY OF RADIOLIGAND THERAPY WITH 177LU-PSMA IN A PATIENT WITH METASTATIC PROSTATE CANCER

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Aims. Prostate-specific membrane antigen (PSMA) is a cell surface protein highly expressed in nearly all prostate cancers, with restricted expression in some normal tissues. Lutetium 177 prostate-specific membrane antigen-617 (^{177}Lu-PSMA-617) delivers beta-particle radiation selectively to PSMA-positive cells and surrounding microenvironment, representing a promising theragnostic treatment for metastatic castration-resistant prostate cancer (mCRPC). This radioligand therapy has been associated with encouraging biochemical and radiographic response rates, reduced pain and low toxicity in multiple early-phase studies involving patients with progressive mCRPC after standard therapy. In this abstract, we report the experience of the first patient treated with ^{177}Lu-PSMA-617 in our centre within the compassionate use program.

Methods. A 71-year-old man with mCRPC progressing after antiandrogen, multiple chemotherapy lines, taxane and platino based, and external beam radiotherapy, was treated with ^{177}Lu-PSMA-617 in our institution until January 2023. He presented in December 2021 with PSMA-positive metastatic lesions determined with gallium-68 (68Ga)–labeled PSMA-11 (68Ga-PSMA-11)

PET–CT imaging. He received six cycles of ^{177}Lu-PSMA-617, starting in March 2022. Activity administered was 7.4 GBq every 6 weeks when possible. The 2nd and the 6th and last cycle were delayed respectively due to failure in drug production and Sars Cov2 infection, plus protocol-permitted standard care.

Results. The patient reported marked biochemical and imaging response, improvement in clinical status and skeletal pain. At the end of the treatment almost no toxicity was registered except for mild dry mouth. Renal function maintained normal several months after therapy, only mild lymphocytopenia was reported during the treatment and resolved three months after its conclusion. In Figure 1. PSA values trend since the treatment was started. In Figure 2 68GA-PSMA imaging pre-treatment and after 4th and 6th cycle are presented. In a later control, during follow-up, the response appeared maintained.

Conclusions. The theragnostic concept applied to targeting PSMA offers an advantage for patients with treatment-refractory prostate cancer by a precise and personalised "see what you treat" option. Our case confirms how ^{177}Lu-PSMA-617 may have a significant role improving biochemical and structural disease control in mCRPC with PSMA expression, without significant toxicity.

Figure 1. PSA value trend.

DP25

IMPACT OF WHOLE-BRAIN RADIATION THERAPY ON NEUROCOGNITIVE FUNCTIONS, HEARING AND ALOPECIA: A SYSTEMATIC REVIEW AND META-ANALYSIS ENDORSED BY THE PALLIATIVE CARE AND NEURO-ONCOLOGY STUDY GROUPS OF THE ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY (AIRO)

D. Pezzulla[1], F. Maurizi[2], L. De Cicco[3], V. Borzillo[4], F. Beghella Bartoli[5], A. Viola[6], F. Gregucci[7], E. Clerici[8], I. Desideri[9], A. Guerini[10], B. Diletto[11], C. Scarigni[12], C. Delli Paoli[13], E. Bonzano[14], S. Lillo[15], F. Pastore[5], S. Longo[5], A. Zamagni[16], A. Ciabattoni[17], A. Argenone[18], A. Cacciola[19], S. Colombo[14], E. Scipilliti[4], G.C. Mazzola[20], L. Bergamaschi[11], E. D'Ippolito[21], L. Dominici[8], S. Chiesa[5], V. Pinzi[17], R. Di Franco[4]

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Aims. We search the current literature on data regard-

ing the role of Whole-Brain Radiation Therapy (WBRT) on neurocognitive functions, hearing and alopecia, through the use of hippocampal-, cochlea-, and scalp-sparing respectively.

Methods. This systematic review followed the PRISMA recommendations. Prospective and retrospective studies with at least 5 patients were included in this analysis. The papers performing a cognitive or a scalp evaluation in patients treated with WBRT with Hippocampal Sparing using a control group were included in the meta-analysis.

Results. Regarding Cochlea-sparing, no citation was selected. 11 works were selected for hippocampal sparing: they were published between 2015 and 2021 and accounted for 753 patients treated with prophylactic WBRT or for metastases who underwent the sparing procedures. Neurocognitive functions were evaluated with a heterogeneous range of tests, with the HVLT-R, TMT A and B, Cowa test and MME as the most used ones. For Scalp-sparing, only 3 papers of the initial 160 ones were selected: one retrospective study and two prospective ones, published form 2014 to2015, accounting for a total of 65 patients. An important heterogeneity in terms of scalp definitions, CTVs, used techniques and doses, and the methods and scales used to evaluate the clinical efficacy of scalp sparing differ in each experience (The SALT score, the EORTC-QLQ-BN20, or a simple observational comparison) was observed. The metanalysis could be conducted only for the paper focusing on the hippocampal sparing procedures, with only 5 papers meeting the inclusion criteria. The heterogeneity of the studies was high (Cochran Q test 208.3, df 4, $p<0.001$, I2 index 98.08%, H2M index 51.08). For this reason, we opted for random effect models DerSimonian Leard (DL), Maximum Likelihood (ML), and Profile Likelihood (PL), which provided widely overlapping results, as can be seen from the forest plot (Figure 1).

Conclusions. A high heterogeneity in terms of hippocampal-, cochlea-, and scalp-sparing was registered among the studies; our findings indicate the need for further studies to explore this issue.in particular, although the data show an average protective effect of Hippocampal Avoidance on cognitive performance, the meta-analysis, based on the available studies, is unable to demonstrate its significance.

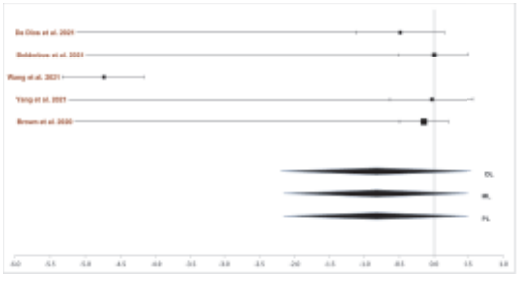

Figure 1.

DP26

FEASIBILITY STUDY BASED ON RADIOMICS AND MACHINE LEARNING FOR THE DEVELOPMENT OF PREDICTIVE MODELS FOR RESPONSE OF VESTIBULAR SCHWANNOMA TREATED WITH RADIOSURGERY

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Aims. To predict vestibular schwannoma (VS) response to radiosurgery, using machine learning (ML) algorithms based on radiomic features extracted from pre-treatment MR images.

Methods. Patients with *vs* treated with radiosurgery (12Gy/1 fraction or 18Gy/3 fractions) in two centers from 2004 to 2016 were retrospectively evaluated. Inclusion criteria were having contrast-enhanced T1-weighted MR images available before and at 24 and 36 months after treatment. Clinical, audiometric, and treatment data were collected at the same time points. Lesions were classified as stable, decreased, or increased according to the volume variation assessed on the pre- and post-radiosurgery MR images. Tumors were semi-automatically segmented and the pre-treatment MR images were standardized between centers through a multi-step preprocessing pipeline. For each patient, 851 radiomic features were extracted on the 3D segmented regions from the processed images and after wavelet transformation. We trained and tested 4 ML algorithms to predict the lesion increase at 24 and, separately, 36 months after radiosurgery, using a nested cross-validation scheme (outer loop: 5 folds; inner loop: 3 folds). During the training phase, feature selection was performed using Least Absolute Shrinkage Selector Operator (LASSO) and the selected features were used as input to separately build four ML classification algorithms. To overcome class imbalance during training, Synthetic Minority Oversampling Technique (SMOTE) was used. Finally, trained models were tested on the corresponding held out set of patients to evaluate balanced accuracy, sensitivity, and specificity.

Results. 108 patients, with a mean age of 61.4 years, treated with Cyberknife® were included. The Neural Network was the best algorithm for predicting the response at 24 months (average test set accuracy 73%, specificity 85%, sensitivity 60%) and 36 months (accuracy 65%, specificity 83%, sensitivity 47%).

Conclusions. Radiomics may predict vestibular schwannoma response to radiosurgery treatment and could be used to avoid long term follow-up as well as unnecessary treatment for the patients, whose therapy can be optimized and eventually changed for the chance of a better outcome.

DP27

IMPACT OF LIQUID BIOPSY IN PATIENT WITH GLIOBLASTOMA

F. Pasqualetti[1], S. Crucitta[2], A. Gonnelli[1], C. Trippa[1], P. Puccini[1], G. Gadducci[1], N. Giannini[1], M. Ruglioni[2], G.I. Luculli[2], M. Cantarella[1], V. Ortenzi[3], C. Scatena[3], A.G. Naccarato[3], R. Danesi[2], M. Del Re[2], F. Paiar[1]

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Background. Since circulating free DNA (cfDNA) represents a useful tool to detect molecular alterations and depends on tumor characteristics, its detection in gliomas is captivating. The present study evaluates the correlation of the IDH1 mutation assessed in cfDNA with survival and other clinical characteristics in glioma patients treated with postoperative radio-chemotherapy.

Methods. Samples of the blood of glioblastoma patients older than 18 years and treated with radio-chemotherapy (60 Gy with temozolomide) were collected between 2015 and 2018. CfDNA was obtained during follow-up and extracted from plasma. IDH1 p.R132H mutation analysis was performed on a digital droplet PCR. A statistical analysis was performed to investigate the prognostic power of such mutation and any association with clinical features. Sixty-seven patients were enrolled. The present project has been approved by the Pisa Ethics Committee, Comitato Etico Area Vasta Nord Ovest: 2015-787. Survival analyses were performed using the Kaplan-Meier method, and differences were compared using the log rank test. Hazard ratios (HR) and 95% confidence intervals (CI) were obtained using Cox's proportional hazard model.

Results. A promising concordance between IDH1 status in tissue and plasma was found (p=0.0004). Moreover, the presence of the IDH1 mutation was associated with a longer median OS in tissue (138.8 months vs. 25.6, p<0.0001) and cfDNA (116.3 months *vs* 35.8, p = 0.016). A univariate Cox regression analysis found a significant association between IDH1 mutation, both in tissue and cfDNA, age, tumor grade and OS. No statistically significant association between the IDH1 mutation and tumor grade was found (p=0.07).

Conclusions. This study shows that liquid biopsy is a useful tool for brain tumors and can be further implemented to detect molecular alterations. The IDH1 mutation detected in liquid biopsy constitutes an important prognostic biomarker in patients with different types of gliomas and is associated with OS.

DP28

SALVAGE BREAST CONSERVING SURGERY AND RE-IRRADIATION WITH INTRAOPERATIVE ELECTRONS FOR RECURRENT BREAST CANCER: A MULTICENTRIC ITALIAN STUDY OF 109 PATIENTS

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Aims. There is a growing interest toward a second breast conserving surgery with partial breast re-irradiation (re-PBI) for local recurrence (LR) after quadrantectomy and whole breast irradiation for primary breast cancer (BC) in lieu of salvage mastectomy (SM). To minimize the toxicity of adjacent organs at risk, intraoperative radiotherapy with electrons (IOERT) may represent a viable choice.

Materials and Methods. A database to collect data on national basis regarding re-PBI with IOERT was set up in the years 2016-2018 upon the joint initiative of two AIRO Study groups. The outcome of such patients was recently updated, providing a long-term follow-up (FU).

Results. From 8 Italian centres, 109 patients were analyzed and described in Table 1. At a median FU of 8.5 years, there were 48 events, resulting in a disease-free survival of 81.3% and 53.5% at 5 and 10 years, respectively. The cumulative incidence of 2nd LR was 12.2% at 5 years and 32.3% at 10 years. Regarding the site of the 2nd LR, 15/ 31 (48.3%) were in the same site as the 1st LR. The management of the 31 2nd LR consisted in SM (n.24), ri-quadrantectomy (n. 5), none surgery (n.2). Six patients developed distant metastases, leading to a cumulative incidence of 0.9% at 5 years and 5.8% at 10 years.

At a median FU of 11.7 years, 23 (21.1%) deaths occurred, of which 15 (13.8%) related to BC. At 5 and 10-years, overall survival was 95.2% and 88.3%, respectively, while BC specific survival were 98% and 94.5%. Regarding late toxicity, the maximum grade of side effects throughout the FU (median, 5.2 years) was considered and available for 89/109 subjects. Grade ≥2 side effects were as follows: 43.5% fibrosis (18.9% Grade 3), 6.7% breast pain, 35.5% retraction/atrophy, 44.9% radiological liponecrosis. Cosmesis evaluation was available only for 57 patients, who reported it as good/excellent in 64.2% of the cases.

Table 1. Clinical and histopathological characteristics of the 1st LR.

Characteristic		Patients (N=109)
Interval between primary BC and 1st LR, median years (min-max)		11.1 (2.4-27.7)
Age at 1st LR, median (min-max)		62 (40-81)
Site of 1st LR, N. (%)	*Primary quadrant*	45 (41.7)
	Other quadrant	63 (58.3)
	Missing	1
Type of surgery, N. (%)	*Quadrantectomy alone*	62 (56.9)
	Quadrantectomy + axillary investigation	47 (43.1)
pT (cm), median (min-max)		0.9 (0.3-3.0)
pN, N. (%)	*0*	42 (38.5)
	1-3	5 (4.6)
	X	62 (56.9)
Grade, N (%)	*G1*	10 (10.4)
	G2	60 (62.5)
	G3	26 (27.1)
	Missing	13
Molecular Subtype, N. (%)	*Luminal A*	44 (43.6)
	Luminal B (Ki67≥20%)	38 (37.6)
	Luminal B (HER2 positive)	9 (8.9)
	HER2 positive	2 (2.0)
	Triple negative	8 (7.9)
	Missing	8
IOERT Dose (Gy), median (min-max)		18 (12-21)
Applicator size (cm), median (min-max)		4 (3-6)
Electron energy (MeV), median (min-max)		8 (4-10)

Conclusions. Considered that the 1st LR presented in median a favorable profile (small size and long interval from the primary BC), the 2stLR free survival was lower than expected. The cumulative incidence of 2stLR was almost the double compared to other reports and very much the same as modern series of selected patients undergoing repeat quadrantectomy without re-PBI. Fibrosis was higher than that described in the dedicated literature, although the rate of cosmesis reported by patients as good/excellent was quite high.

DP29

HYPOFRACTIONATED RADIOTHERAPY UP FRONT TO ADJUVANT CHEMOTHERAPY IN N POSITIVE BREAST CANCER. PRELIMINARY REPORT ON ACUTE TOXICITY

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Aims. Hypofractionated radiotherapy (AH-RT) has become a new advantageous standard of care in breast cancer (BC). Conventionally adjuvant radiotherapy (A-RT) is delivered after adjuvant chemotherapy (A-CT) which has been lengthened with new drugs combinations . In the meanwhile AH-RT has been shortened in 15 or 5 fractions (frs). We started a mono-institutional prospective study on AH-RT in upfront to A-CT in high-risk nodal positive breast cancer to assess toxicity and survival outcomes. Here in an interim analysis on acute toxicity.

Materials and Methods. In 2022 a mono-institutional study started to assess feasibility of AH-RT given in upfront to A-CT in high risk nodal positive BC patients (pts). Up to now 45 pts have been enrolled. BCS in 30 pts and mastectomy in 15 pts were included. AH-RT-15 consisted of 2.67 Gy/fr/40.05 Gy (SIB 3,2 Gy/fr/48 Gy) while AH-RT-5 on alternate days was 5.7 Gy/fr /28.5 Gy (SIB 6.4 Gy/fr/ 32 Gy)and 5.4 Gy /fr /27 Gy on nodal areas . RT started after 45 mean days from surgery (30-55). AH-RT-15 frs was given to 28 pts. Supraclavicular area (SVC) and internal mammary chain (IMC) in 10 pts, chest wall (CW) in 5 pts were treated. AH-RT-5 fr (8 SVC area and 5 CW) was delivered to 17 pts. A-CT long course was defined on the basis of Oncotype, molecular phenotype and nodal involvement and started after 10 mean days (8-15) RT off. Follow up was conducted after 2 weeks off RT, 1 month, 3-6-9 months during chemotherapy. Acute toxicity was scored according CTCAE v5 for skin, pulmonary and cardiac adverse events. Pearson's covariance multivariate analysis was conducted to assess as significant prognosticators for skin / lung/heart acute toxicities the AH-RT 5/15 frs arms and chemotherapy ($p < 0.005$).

Results. At 9 months mean follow up, no significant differences in toxicity were found between the different RT arms. G2 skin toxicity was experienced in 8 % of pts with SIB and 5 % without SIB. G1-G2 skin toxicity and dysphagia were recorded in pts treated on SVC(3%). Skin G3 toxicity in 1 pt during the first cycle of Taxane. Pneumonitis G2 occurred in ICM pts in the Taxane and TDM1 arms (3%). Multivariate analysis confirmed no significant effect for CT and AH-RT arm for skin /lung acute toxicities ($p=.077$) and irradiated volumes ($p= .065$)

Conclusions. AH-RT upfront to A-CT seems safe with a low acute toxicity prophile before long course A-CT without differences between the 2 AH-arms. Longer follow-up is needed.

DP30

IMPLEMENTATION OF ULTRA -HYPOFRACTIONATED ADJUVANT RADIANT TREATMENT WITH THE H-VMAT SIB HYBRID TECHNIQUE FOR BREAST CANCER:PRELIMINARY REPORT OF ACUTE TOXICITY

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Aims. The purpose of the study was to evaluate the toxicity of an ultra-hypofractionated radiotherapy treatment with the H-VMAT-SIB hybrid (+Deep Inspiration Breath Hold) technique in the adjuvant setting of breast cancer (BC).

Methods. Inclusion criteria were: T1-T3 invasive BC, no or limited axillary involvement, clear margins, age ≥ 45 years. Patients received adjuvant radiotherapy as follows: 26 Gy to the whole breast and 30 Gy to the tumoral bed in five fractions over 1 week after breast-conserving surgery. LimpiAD (@Aileens Pharma s.r.l.) cream or foam 2 times a day on the whole irradiated gland for 21 days starting from the first day of radiotherapy was prescribed as supportive therapy. The acute and late cutaneous and subcutaneous toxicities, as well lung toxicity, were assessed subjectively using the CTC-AE v.5.0 scale and objectively in terms of skin elasticity percentage and melanin levels with a dedicated device (Cutometer® dual MPA). The evaluation of the photographic documentation was carried out on the basis of the consensus scoring method as described by Haviland et al. Cosmetic results were evaluated by Harvard scale and quality of life questionnaires (EORTC QLQ-C30, EORTC-QLQ-BR23) before and 6 months after treatment.

Results. From June 2022 to June 2023, 27 BC patients completed the ultra-hypofractionated radiotherapy treatment and were enrolled in the study. Median age was 69 (45-82) years and median body mass index was 25 (18.4-36). Most of the BC patients were T1 (92.6%), while the remaining ones were T2 (7.4%). The axillary status was negative in 100% of the patients. At the end of the ultra-hypofractionated radiotherapy treatment, no severe toxicity were reported. Twenty-one of the 27 patients had mild (Grade 1) and limited at the skin level toxicity. In details 13 had erythema (2 brisk, 11 faint), 2 moist desquamation, 12 skin hyper pigmentation, and 6 had pruritus. The cumulative acute toxicity data resulted lower than figures reported in the available literature.No lung or subcutaneous toxicities were registred. Due to the short follow-up of the study no data on cosmetic results or quality of life will be reported here.

Conclusions. In our preliminary experience the ultra-hypofractionated whole breast RT with the H-VMAT-SIB hybrid technique and LimpiAD cream/foam as supportive therapy was successful recording a remarkably mild acute toxicity. In order to assess late toxicity and cosmetic results, a longer follow-up is needed.

DP31

VENTRICULAR TACHYCARDIA ABLATION THROUGH RADIATION THERAPY (VT-ART): A WIDE COHORT MULTICENTER ANALYSIS OF EFFICACY AND HOMOGENEITY OF APPROACH

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Aims. Ventricular Tachycardia Ablation by Radiation

Therapy (VT-ART) for ventricular tachycardia (VT) is promising. Definitive data on efficacy are lacking. Most of the available case series account for limited number of patients -pt- (ranging 5-20). Defining the best RT procedure is also an issue. Aim of this multicenter study is to evaluate VT-ART's homogeneity and efficacy on a large cohort.

Methods. We collected pt undergone to VT-ART for refractory VT, within a spontaneous network among Centers having performed preliminary experience for limited series, outside clinical trials. No restriction about pt selection and VT-ART treatment administration were applied. Collected variables focused on both treatment efficacy and procedural homogeneity.

Results. Six Italian Centers collaborated, enrolling 21 pt. Not each of the data required by the promoting Center were available for all the sub-series, depending on the center's trend for default data collection. Based on the shared variables: range of recruitment was September 2019-February 2023; all pt were male; mean pt age was 69,7 years (range, 52-87). Pretreatment mean left ventricular ejection fraction was 33% (range22-50). All pt underwent at least one radiofrequency catheter ablation. Linac dedicated to SBRT was used in 11/21(52,4%) pt; 6/21 (28,6%) used MRgRT; 4/21 (19%) used conventional Linac. In 7/21 (33,4%) free breathing 4D simulation, and in 12/21 (57%) a gated breath hold (deep inspiration) was performed. Target delineation procedure varied among Centers. Although choosen references for constraints were similar among centers, the applied ones ranged 1-7 different guidelines. The mean CTV volume of the was 71,3 cc (range 8.9-238.5). The mean PTV margin provided was 3,3 mm (range 3-5). For all pt, SBRT was performed with a dose of 25 Gy in single fraction; prescription isodose was 97% in 1/21, 95% in 3/21, 94% in 1/21, 80% in 15/21 pts, 75% in 1/21(mean 87,5%). PTV mean Dose was 27,6 Gy (23,4-29,7). Briefly, each of the 6 RT Centers applied its IGRT inner rule; online monitoring was performed through 4D gating control in all cases adding peculiar approaches in 2/6 Centers.

Conclusions. The presented series is one of the largest collected. Feasibility of VT-ART seems confirmed. High homogeneity in dose prescription is confirmed. Still relevant differences on details of delineation, treatment planning and procedural settings are reported. For brevity further details will be specified at the conference.

Poster

P001

IMMUNOTHERAPY (IT) OR TARGETED THERAPY (TT) COMBINED WITH STEREOTACTIC RADIOTHERAPY (SRT) FOR MELANOMA BRAIN METASTASES (BM): PRELIMINARY RESULTS FROM A MULTICENTRE RETROSPECTIVE STUDY ON BEHALF OF AIRO NEURO-ONCOLOGY (NO) GROUP

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Aims. Despite guidelines for melanoma patients with asymptomatic BM would suggest to defer local therapy until the evidence of progression in favour of IT (Ipilimumab and Nivolumab) or TT (Dabrafenib and Trametinib), there is a lack of randomized evidence for oligo-BM. To define efficacy and toxicity of IT or TT with SRT, including radiosurgery (SRS) or hypo-fractionated SRT (HF-SRT), for melanoma BM in a multicentre retrospective study on behalf of AIRO NO Group.

Methods. patients with melanoma BM receiving SRT + IT or TT (within 28 days) treated in 6 Italian Centres were preliminary analysed.

Results. 81 melanoma patients with 167(median 1; range, 1-12) BM received concurrent SRT + IT or TT. Median age and median PS were 63y (27-85) and 0(0-2), respectively. 38(47%) patients developed BM during TT or IT (oligo-progressive patients), while 43(53%) developed BM without an active treatment (oligo-recurrent patients); 67(82.5%) received upfront SRT (i.e. at the time of radiological evidence of BM), while 14(17.5%) delayed SRT (i.e. at the evidence of brain progression after upfront TT or IT). 43(53%) patients had controlled extracranial disease at the time of brain progression. 60(74%) received LINAC-based SRT, the others Cyberknife. 62(76,5%) patients underwent SRS with a prescribed median dose of 24Gy(15-24), the remaining 19(23,5%) HF-SRT with a median dose of 25Gy(21-35) in 3/5fractions. Median volume of treated lesions was 1,93cc(0,16-8,48). All patients received IT or TT within 28days of SRT (median time 10 days), 54(67%) received IT, 27(33%) TT. At a median follow-up of 17months (6-94,) 44(54%) patients developed local recurrence on at least one treated lesion after a median time of 14months (3-68), 38(47%) patients had intracranial progression outside the treated lesions after a median time of 10months

(3-53). 30(37%) experienced extracranial progression. 5,11,and 3 patients developed G1,G2, and G3 radionecrosis(RN), respectively. No case >G3RN was observed. At the time of analysis 28(34,5%) died.

Conclusions. Despite the retrospective nature, our data support the feasibility of the combination of SRT+IT or TT, showing efficacy and good tolerability (only 3% of patients developed G3 RN). We disagree with the interpretation that IT or TT alone approach should be considered as the first-line therapy in asymptomatic oligo-BM melanoma patients, suggesting that combined approach of IT or TT+SRT should be considered the first choice in this setting of patients.

P002

STEREOTACTIC ABLATIVE RADIOTHERAPY AND DURVALUMAB: THE BACKBONE OF UNRESECTABLE LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER PATIENTS UNFIT TO CONCURRENT CHEMO-RADIOTHERAPY -RIB OF START-NEW-ERA TRIAL

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Aims. Several real world experiences have been reported safety and effectiveness of Durvalumab after concurrent or sequential chemo-radiotherapy (ChT-RT) in locally advanced non-small cell lung cancer (LA-NSCLC) patients. There is a lack of data after sequential ChT-hypofractionated RT. In single arm phase 2 trial (Clinical trials.gov NCT05291780) we assessed local control (LC) and safety of stereotactic ablative radiotherapy (SAbR) in unresectable LA-NSCLC patients unfit for concurrent chemo-radiotherapy (ChT-RT) (1). Here we report clinical outcomes of SAbR in LA-NSCLC patients treated with radical-intent based on PACIFIC trial.

Methods. Between December 31, 2015 and January 31, 2023 77 LA-NSCLC patients were enrolled. 43 (56%) fit patients received neoadjuvant ChT and 16 (21%) received Durvalumab. The tumor volume included primary tumor (T) and any regionally positive node/s (N). The co-primary study endpoints were LC and safety.

Results. The median age was 73 years (range, 52-78). Histology was adenocarcinoma (ADC) and squamous cell carcinoma (SCC) and in 9 (60%) and 6 (40%), respectively. The stage was IIIA, IIIB and IIIC in 7 (44%), 6 (37%) and 3 (19%) patients, respectively. Median prescribed dose was 45 Gy (range, 40-50) and 40 Gy (35-50) in 5 daily fractions to T and N, respectively. After a median follow-up of 20 months (range, 9-67), 4 (25%) patients had experienced local recurrence (LR) at a median time of 13 months (range, 7-34). The median LR-free survival (FS) was 34 months (95% CI, 14 to 34). The 1-, 2- and 4- year LR-FS rates were 92±8%, 72±14% and 48±22%, respectively. At last follow-up, 12 (75%) patients were alive. Median overall survival (OS) was 50 months (95% CI, 31-55). The 1, 2, and 4-year OS rates were 92±5%, 70±8% and 51±9%, respectively. 4 (27%) patients developed distant progression (dP). The median dP-FS was not reached (95% CI, 14 to not reached). The 1, 2, and 4-year dP-FS rates were 100%, 50±19% and 50±19%, respectively. The pattern of disease recurrence was distant and local in 4 and 3 patients, oligo-metastatic disease recurrence in 6/7 patients. Two (13%) discontinued Durvalumab due to esophageal and lung G3 toxicity.

Conclusions. SABR and immunotherapy can be the backbone of patients unfit to concurrent ChT-RT. Our early outcomes would suggest the feasibility of using this approach in LA-NSCLC patients unfit for concurrent ChT-RT.

Reference

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P003

DAILY ADAPTIVE WORKFLOW (W) FOR MR_GUIDED RADIOTHERAPY (MRGRT) WITH UNITY® (U®) FOR HEAD&NECK (HN) AND GLIOBLASTOMA (GBM) PATIENTS TREATED WITH RADIO-CHEMOTHERAPY (RT-CHT)

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Aims. Implement better w to treat pts and obtain biological markers (BMs) is challenge of first months after U® arrival. Describe the MRgRT w for HN and GBM pts, where daily Adapt to Shape (ATS) and Adapt to Position (ATP) are performed.

Methods. From Sep 2022 to May 2023 116 pts had RM simulation (RMs). 43 were treated using U®. Medical, technic and physic phases (Mp,Tp and Pp) are identified. Mp: pts selection; MR's consent; OAR/target contouring for offline (o_l_p) and day_by_day (d_b_d) plan, approval of o_l_p and d_b_d plans; clinical evaluation during/after RT; interpretation of BMs. Tp: pts position, setup input within R&V system; scanning and treat-

ing; Pp: OAR mean density evaluation, density propagation to MR, plan template selection, o_l_p calculation, second check and transfer to R&V, pre-treatment measurement, d_b_d plan optimization and checks.

Results. 21 and 22 pts with HN and GBM were respectively treated; CHT were respectively Cisplatin and Temozolomide. Automated contouring (AC) 9 HN_CT atlases were created with Deep Learning Models and manual recontouring (Mp); 2 Air cavities and 2 Bone levels and low_density tissue were created (Pp). AAPM TG263 was utilized over 38 structures with a numerical prefix specifying the priority for creation of synthetic CT (sCT)(Pp). AC decreased contouring times and lowered errors in the creation of sCT. Contours are propagated to the reference MRs and targets are delineated (Mp). IMRT o_l_p is calculated on MRs, using densities obtained by AC (Pp); it is always used as reference during d_b_d treatment (Pp). Reference and back-up plan with Helical Tomotherapy (HT) is calculated (Pp). Multicriterial Optimization-based plans is competitive with HT (Pp); use of cost function weights block reduce a HN plan to <1min. GBM cases achieve planning faster and more automated con-vergence for lower complexity. Daily MR is acquired (Tp) to assess shifts and adaptive strategy (Mp). ATS strategy is mostly utilized for better OAR/target control and planning scorecards (M/Pp). For small corrections ATP can be used. More sequences can be acquired to evaluate OARs/target (Tp). The RT_session take 60 and 35 min for HN and GBL pts respectively (M/P/Tp). The dose accumulation proved that daily ATS deviates minimally from the initial o_l_p.

Conclusions. Daily ATS w for HN/GBM cases has proven its feasibility in terms of daily accuracy as well as procedural times. Preliminary clinical and biological data are going to be analyzed.

Figure 1: HeadNeck and Glioblastoma MRgRT WorkFlow

Figure 1.

P004

EFFEECTIVENESS OF RADIOTHERAPY ON DELAYING TERAPEUTIC SWITCH IN PRIMARY OR SECONDARY IMMUNO-REFRACTORY METASTATIC PATIENTS : PRELIMINARY RESULTS FROM A SINGLE CENTRE RETROSPECTIVE STUDY

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Aims. To investigate whether radiotherapy could provide some clinical benefits for patients with metastatic oligoprogressive solid tumours who displayed an acquired (AR) or innate (IR) resistance on Immunocheckpoint inhibitors (ICI).

Methods. Patients with metachronous oligoprogressive disease (≤5 metastatic sites) treated in our Institute between January 2019 and December 2022 were identified retrospectively. The patients were stratified by drug-resistance (AR *vs* IR) according to the time of developing resistance. Time to switch (TTS)was the primary endpoints. The secondary endpoints included were : post-radiotherapy first progression free survival (prf-PFS), Local Control (LC) ,Overall Survival (OS) and treatment related-toxicities. Furthermore, abscopal effect have been hypothesized. Kaplan Meier method was performed for survival analysis.

Results. Among 91 patients with oligoprogressive disease , 31 patients with 80 lesions met criteria for inclusion (Table 1). The most common primary sources of oligoprogressive sites were the lung cancer (45,16%, N=14) and the Merkel cell carcinoma (22,58%, N=7). The most common oligoprogressive sites were the brain, followed by lymph nodes, the adrenal gland and the lung (Figure 1). Concomitant radiation therapy was administered to a total median dose of 30 Gy (range 18-63.8) in 5 fractions (range 1-12). 70,96% of patients (N=22) received one course of radiotherapy, while 29,04% (N=9) were administered with two or more courses prior to switch systemic therapy. 21 patients developed AR while 10 IR. The median TTS among AR *vs* IR patients were 30.5 *vs* 12 months. 2-years LC and pr-PFS were 100% and 63,64% among IR patients *vs* 80% and 90% in AR patients respectively. At the time of the analysis 6 patients (4 IR and 2 AR) switched systemic therapy and 2 died following poli-progression disease. Overall, only 5 patients experienced in- field recurrence within 12 months from the end of radiation treatment. Regardless of radiation dose we did not observe ≥ G3 acute or late treatment-related toxicity. Radio necrosis as late side effect after brain stereotactic radiotherapy has occurred in 2 patients. Although abscopal effect has been hypothesized, we were

not able to record it.

Conclusions. Our preliminary results seems to confirm that the integration of radiotherapy and ICI might allow the continuation of systemic therapy beyond progression with a subsequent benefit in term of clinical outcomes even in IR patients.

Table 1. H: histology; ICI: immunocheckpoint inhibitors; RT: radiation therapy; M: merkel cell carcinoma; L : lung cancer; U: urothelial cancer; B: breast cancer, Me: melanoma; H: hypopharyngeal carcinoma; O: oropharyngeal carcinoma; A: avelumab, N: nivolumab; P: pembrolizumab; At : atezolizumab; VMAT: volumetric modulated arc therapy, SRS: stereotactic radiosurgery; SBRT: stereotactic body radiotherapy; FSRT :fractionated stereotactic radiotherapy.

H	Sex	Age	ICI	RT technique (1°course)
M	F	80	A	VMAT
M	F	85	A	VMAT
M	M	81	A	VMAT
M	F	65	A	SBRT
M	F	61	A	VMAT
M	M	61	A	SBRT
M	M	70	A	SBRT
R	M	59	N	SBRT
R	M	71	N	SBRT
R	M	53	N	Lattice
L	M	50	N	SRS
L	M	58	P	SBRT
L	M	55	P	SRS
L	M	67	A	SBRT
L	M	77	P	SBRT
L	M	55	P	SBRT
L	M	75	P	SFRT
L	M	68	N	Lattice
L	M	49	N	SBRT
L	M	54	At	SRS
L	M	76	P	Lattice
L	M	69	N	SRS
L	M	58	P	Lattice
L	M	80	P	Lattice
U	F	84	P	VMAT
U	M	66	A	SBRT
B	F	61	At	SRS
Me	M	59	N	SBRT
Me	M	73	N	FSRT
H	M	65	N	SRS
O	F	58	P	SBRT

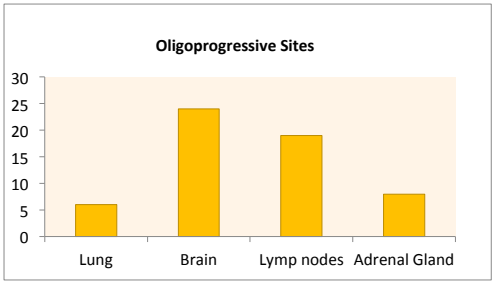

Figure 1.

P005

EFFICACY AND TOLERABILITY OF STEREOTACTIC RADIOTHERAPY IN ASSOCIATION WITH BEVACIZUMAB IN OLIGOMETASTATIC, OLIGOPERSISTENT AND OLIGORECURRENT GYNAECOLOGICAL CANCER: A CASE SERIES

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Aims. Scarce data are available on the safety of combining stereotactic radiotherapy (SBRT) with modern targeted therapy in oligometastatic, oligopersistent and oligorecurrent gynaecological tumors. The aim of this report was to analyse the results of our preliminary experience with SBRT and bevacizumab in a cohort of oligometastatic gynaecologic cancer patients.

Methods. Seventeen patients (30 lesions), were included in the analysis. Fifteen patients had an ovarian cancer, 2 had a cervical tumor. Nine patients were previously treated with more than one systemic regimen. Fourteen patients received bevacizumab before SBRT: the last administration of the anti VEGF was done 1 month before SBRT in 3 patients, 2 months before in 12 patients and 3 months before in 2 patients, while 3 patients started bevacizumab 3 months after SBRT. Five of the patients who received bevacizumab before SBRT, started it again within the first month after the radiation treatment. Stereotactic radiotherapy was delivered as first radiotherapy treatment in all but 2 patients. Nine lesions were treated with an MRI guided technique. Up three to five consecutive daily fractions were delivered on 20 nodal and 10 parenchymal lesions. Doses were all prescribed at specific isodose (80%) and ranged from 25.5 Gy in 3 fractions to 50 Gy in 5 fractions according to the site of metastases and constraints to organ at risk.

Results. Complete clinical response was achieved in 11/30 lesions (36,6%), while partial response was documented in 16/30 lesions (53.3%); stable disease was observed in 2/30 lesions (6.6%) while progression was shown in 1/30 lesion (3.3%). The overall response rate was 90%. With a median follow-up of 13 months (range 4-59 months), 13/17 patients (76,5%) experienced local control of disease. Only two patients experienced acute toxicity: 1 patient had a G1 diarrhoea and 1 patients had

a G1 headache. None of the seventeen reported late toxicities. There was no difference in quality of life scores between the data collected before stereotactic radiotherapy and the first follow-up evaluation.

Conclusions. Fractionated stereotactic radiotherapy administered with a short interval from bevacizumab is well tolerated and effective. Further studies of stereotactic radiotherapy in association with this target therapy are warranted in the challenging setting of oligometastatic, oligorecurrent and oligopersistent gynecological tumors.

P006

SYNERGISTIC EFFECT OF STEREOTACTIC RADIOTHERAPY AND IMMUNOTHERAPY: AN ITALIAN MULTICENTRIC RETROSPECTIVE EXPERIENCE

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Aims. To evaluate the oncologic outcome, toxicity and prognostic factors associated with outcome of the combined treatment with Immune Checkpoint Inhibitors (ICIs) and Stereotactic Radiotherapy (SRT) in patients with metastatic disease from different primary malignancies.

Methods. A retrospective multicenter cohort of metastatic patients treated with ICIs and SRT for oligometastatic (OMD) or oligoprogressive disease (OPD) was performed. Descriptive statistics was used to evaluate patient and treatment related features. Progression-Free Survival (PFS) and Overall Survival (OS) were analyzed using Kaplan-Meyer curves and log rank testing. The cumulative incidence of local recurrence (LR) and Therapy Switch (TS) were estimated through the Kaplan-Meier method according to the Fine-Gray model. Toxicity was evaluated through CTCAE v 5.0 scale.

Results. Between 2014 and 2022, 27 patients were treated with SRT to 53 lesions for OMD or OPD during ICIs. Initial diagnosis was melanoma, lung cancer, renal cancer and head and neck cancer in 10 (37%), 12 (44%), 4 (15%) and 1 (4%) patients respectively. Irradiated metastatic lesions were in brain, lymph nodes, lung and and others in 32 (60%), 9 (17%), 7(13%) and 5(9%), respectively. After SRT, patients were followed for a median follow up of 11.3 months. One-year PFS and OS were 39.5% and 73%, respectively. Median PFS was 8.2 months and median OS was 18.3 months. Median TS-FS was 10.2 months, with an average Time to Treatment Switch (TTS) of 11 months for all patients who changed systemic therapy and an average TTS of 31.5 months for patients who underwent SRT two or more times for oligoprogressive disease. Therapy switch was made in ten patients due to progressive disease, leading to a cumulative incidence of 42.5% (95% CI: 20.0%-63.5%) at 36 months after SBRT. Only four patients experienced treatment related toxicity (grade 1 to 3).

Conclusions. The combination stereotactic radiotherapy and immunotherapy is safe and allows to postpone the initiation of a new line of systemic therapy of about 11 months with a very favorable toxicity profile. Results in terms of survival are encouraging. Further research is needed to evaluate the optimal integration between immunotherapy and local therapies and SRT in particular as well as to identify predictive biomarkers. We aim at understanding the role of systemic inflammation biomarkers in this scenario.

P007

RETROSPECTIVE MULTICENTRIC TOXICITY ANALYSIS OF RADIOTHERAPY CONCURRENT WITH ERIBULIN IN METASTATIC BREAST CANCER PATIENTS

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Aims. Since its approval in 2011, eribulin has been extensively used for the treatment of metastatic breast cancer (mBC). Nonetheless, up to date only one retrospective experience has been published regarding the combination with radiotherapy (RT). In the context of a larger retrospective study assessing the safety of combining RT with systemic treatments, we planned this analysis to evaluate the toxicity profile of RT concurrent with eribulin.

Methods. We retrospectively analyzed female mBC patients treated with RT concurrently (allowed interval between last drug administration and RT 5 half lives) with

eribulin between 01 January 2006 and 28 February 2021 at three Institutions (ASST Spedali Civili di Brescia, CROB di Rionero in Vulture, Azienda Ospedaliera di Perugia).

Results. We identified 22 patients with mBC with the following characteristics: 86% ductal and 14% lobular carcinoma, 59% ER positive, 14% HER-2 positive, grade 2 47% grade 3 53%. Median age at RT was 60.5 years, median ECOG PS was 1 and were mostly heavily pretreated as 73% of patients received previous hormonal treatment (median 2 lines) and 100% previous chemotherapy (median 3 lines, range 2-6 lines). Treated lesions were 49: 24 (49%) localized in the spine, 10 (20%) in the brain, 5 in the pelvis, 5 in the skull, 3 in the ribs, one in the extremities and one pathologic lymphnode. The most used radiotherapy fractionation was 20 Gy in 5 fractions (20 lesions, 41%), followed by 30 Gy in 10 fractions (16 lesions, 33%); 6 lesions were treated with a single-fraction regimen (8-24 Gy), 6 lesions in a 3-fraction schedule (24-30 Gy) and one with 55 Gy in 20 fractions. The only grade 2 toxicity possibly due to radiotherapy recorded during treatment was fatigue in one patient (5%), while grade 1 toxicity consisted in pain flare (20% of patients), neurologic toxicity (14%), fatigue (9%), esophagitis (9%), pharyngodynia (9%), nausea (9%), tinnitus (5%) and dermatitis (5%).

Conclusions. Safety of radiotherapy concurrent with eribulin was excellent, with no reports of severe noonhematologic toxicity. Larger studies are awaited to confirm this preliminary data.

P008

INTRODUZIONE DELLA RADIOTERAPIA NEI PAZIENTI CON CARCINOMA A CELLULE DI MERKEL METASTATICO CON OLIGOPROGRESSIONE DURANTE AVELUMAB : UNO STEP EFFICACE CONTRO L'IMMUNORESISTENZA PRIMARIA E SECONDARIA?

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Aims. To investigate the ability of radiotherapy (RT) to prolong progression-free sur-vival (PFS) and to report treatment-related toxicities among oligoprogressive metastatic Merkel cell carcinoma (mMCC) patients on avelumab.

Methods. We retrospectively collected clinical data on mMCC patients who underwent radiotherapy for limited progression on avelumab. Patients were categorized as primary or secondary immune refractory depending on the time of onset of resistance to immunotherapy (at the first or subsequent follow-up visits after avelumab initiation). Pre- and post-RT PFS were calculated. Overall survival (OS) from the first progression treated with RT was also reported. Radiological responses and toxicities were evaluated according to the irRECIST criteria and RTOG scoring system, respectively.

Results. Eight patients, including five females, with a median age of 75 years, met our inclusion criteria. The median gross tumor and clinical target volumes at first progression on avelumab were 29.85 cc and 236.7 cc, respectively. The treatment sites included lymph node, skin, brain, and spine metastases. Four patients received more than one course of RT. Most patients were treated with palliative radiation doses (mainly 30 Gy in 3 Gy/day fractions). Two patients were treated with stereotactic RT. Five/eight patients were primary immune refractory. The objective response rate at the first post-RT assessment was 75%, whereas no local failure was reported. The median pre-RT PFS was 3 months. The pre-RT PFS was 37.5% at 6 months and 12.5% at 1 year. The median post-RT PFS was not reached. The post-RT PFS was 60% at 6 months and 1 year. The post-RT OS was 85.7% at 1 year and 64.3% at 2 years. No relevant treatment-related toxicity was observed. After a median follow-up of 18.5 months, 6/8 patients are still alive and continuing on avelumab therapy.

Conclusions. Adding radiotherapy to mMCC patients with limited progression on avelumab seems to be safe and effective in prolonging the successful use of immunotherapy, regardless of the type of immune refractoriness.

P009

PRACTICAL CONSIDERATIONS FOR THE IMPLEMENTATION OF A SURFACE GUIDED RADIATION TREATMENT (SGRT) PROGRAM.

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Aims. With multiple studies supporting the use of surface guided radiation treatment (SGRT), we evaluated practices that could inform effective implementation of a SGRT program.

Methods. Using a context-focused realist methodology, an advisory committee of interprofessional clinicians identify challenges in implementing an SGRT program.

SGRT does not use ionizing radiation, provide a real-time motion monitoring of the patient surface throughout the whole treatment fraction. The beam can be held if parts of the patient's surface deviate from the reference position based on the planning CT set-up or if the calculated isocentric deviations exceed a certain threshold. To take advantage of SGRT, a well-structured clinical implementation is recommended. It should be led by a core multidisciplinary team, consisting of Radiation Oncologists, Radiation Therapists and Medical Physics experts.

Results. a workflow for the SGRT implementation with C RAD Catalyst Sentinel System has been developed at our Radiation Oncology Unit. The Catalyst System consists of a camera paired with a certain software. It offers patient tracking, both before and during treatment, integrated in the typical clinical workflow. The system has three main assisting functions: patient setup and positioning, intra-fraction motion detection, and respiratory gating. Our workflow for SGRT implementation for daily treatment first of all consists of training of a smaller, specialized group before expanding to a broader cohort of staff. Dedicated protocols were created for each steps: step 1- CT simulation with Sentinel. Step 2 - Catalyst Pre treatment planning, Step3- Catalyst treatment with continuos surface monitoring and comparison of reference with live surface and beam hold if patient moves outside surface tolerance. Image-Guded RT (IGRT) is a very useful tool to detect SGRT inaccuracies and it should be used in a complementary manner. All team members should principally be familiar with each step of the workflow. Team communication, thorough documentation, and standardized nomenclature can reduce system errors.

Conclusions. Using a realist approach, we identified practical considerations for the implementation of an SGRT program. The realist methodology provided an effective framework to explore the factors that may contribute to effective implementation within different contexts.

P010

THE IMPACT OF LATE TREATMENT TOXICITY ON QUALITY OF LIFE IN A COHORT OF PATIENTS TREATED WITH LOW-DOSE RATE (LDR) INTERSTITIAL BRACHYTHERAPY FOR PROSTATE CANCER: CONGRUENCE BETWEEN PATIENT PERCEPTION AND CLINICAL EVALUATION

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Aims. to assess differences between clinical evaluation and subjective patient perception of the impact of late genitourinary (GU) and gastrointestinal (GI) toxicity on quality of life (QoL) in a cohort of patients undergoing low-dose-rate brachytherapy (LDR-BCT) as exclusive treatment for localized prostate cancer. This study is part of Clinical Outcome of Radiotherapy Treatment in Azienda Toscana Nord-Ovest (CORTATNO) research project funded by Tuscany Region.

Table 1. Clinical and QoL data (prostate LDR-BCT).

Patient ID	Age	Date of LDR-BCT	iQoL score	1y-QoL score	1y-GU toxicity (CT-CAE v5.0)	1y-GI toxicity (CT-CAE v5.0)
1	68	2015	0	0	0	0
2	69	2015	1	0	0	0
3	68	2015	1	2	0	0
4	69	2015	0	1	0	0
5	77	2015	1	1	0	0
6	69	2016	1	1	0	0
7	67	2016	0	0	0	0
8	76	2016	1	2	0	0
9	71	2016	1	3	0	0
10	63	2016	2	2	1	0
11	77	2016	0	0	0	0
12	72	2016	3	2	1	0
13	66	2016	3	3	1	1
14	73	2016	3	3	0	0
15	55	2016	0	0	0	0
16	75	2016	2	4	1	0
17	72	2017	4	2	2	0
18	75	2017	5	3	0	0
19	75	2017	0	1	0	0
20	53	2017	0	2	1	0
21	69	2017	0	0	0	0
22	70	2017	0	0	0	1
23	76	2017	0	5	0	0
24	68	2017	1	1	0	0
25	71	2018	0	0	0	0
26	76	2018	1	1	0	0
27	64	2018	0	1	1	0
28	67	2019	0	0	0	0
29	70	2019	1	1	0	0
30	74	2019	1	1	0	0
31	63	2020	1	1	0	0
32	59	2020	1	1	0	0
33	69	2020	2	3	0	0
34	63	2020	2	2	0	0
35	74	2021	1	1	0	0

LDR-BCT: low dose rate brachytherapy; **(i)QoL**: (initial) quality of life; **GU:** genitourinary; **GI:** gastrointestinal

Methods. International Prostate Symptoms Score (IPSS) and International Index of Erectile Function (IIEF) values from 35 patients treated with I-125 permanent intra-prostatic seeds implantation (145 Gy total target dose) for low- and favorable intermediate-risk prostate cancer between January 2015 and June 2021 were extrapolated. Data of baseline and 1y-post-LDR-BCT self-administered questionnaires were recorded and compared to the GU and GI toxicity (CT-CAE v5.0) reported at the 1y-follow up visit with a focus on QoL tools (0: delighted; 1: pleased; 2: mostly satisfied; 3: equally satisfied/dissatisfied; 4: mostly dissatisfied; 5: unhappy; 6: terrible). Pre-planning ultrasound and 1-month post-implant CT dosimetry, clinical and morpho-functional parameters with known or suspected impact on the subject were also collected.

Results. Table 1 summarizes population outcomes object of the study. We found only 1 (3%) case of G2 1y-urinary toxicity (no ≥G3 cases), but corresponding better post-implant QoL than the baseline; 1 (3%) patient had contemporary G1 GU and GI toxicity, but no changes in QoL perception. There was no ≥G2 late rectal toxicity. No erectile dysfunction complained. Median initial QoL score was 1 (0-5), median 1y-QoL score 0 (0-5). No

changes in pre-/1y-post-implant patients perception were reported in 23 (66%) of cases, slightly worsening but still satisfactory QoL in 5 (14%) patients, disabling worsening QoL in 4 (11%) and improvement in 4 (11%) of them, respectively. Of note, severe worsening of QoL score after LDR-BCT was associated with few or none of GU/GI reported symptoms.

Conclusions. Despite the low toxicity rates, which confirmed LDR-BCT to be a safe therapeutic option for localized prostate cancer, patient reported outcomes revealed some level of distress and impairment that was misunderstood at the follow up interview. Validation of our findings on large series is warranted to set up integrated, well tolerated, patient-tailored strategies for the management of prostate cancer.

P011

THE INFLUENCE OF PERMANENT MARKS ON ONCOLOGICAL PATIENTS IN FOLLOW-UP: UNDERSTANDING THE PSYCHOLOGICAL AND SOCIAL IMPACT FOR IMPROVED WELL-BEING

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Aims. The purpose of this study was to evaluate the psychological and social impact of permanent marks on oncological patients in follow-up, such as surgical scars or tattoos performed for radiotherapy (RT).

Methods. During follow-up check-ups, we administered a questionnaire about body image (BI) using the EORTC Quality of Life Study Group Body Image scale, which included 4 brand new questions specifically related to the impact of tattoos, making a total of 13 questions.

Results. From September 2022 to February 2023, a population of 500 patients with different tumor types (51.8% male and 48.2% female), with a mean age of 68 years (range 34-89 years) was evaluated. All patients completed the questionnaire. More than 32% of patients believe that their body has undergone changes due to cancer treatments, and in 21.4% to 25.4% of cases, a reduction in physical and sexual attraction is reported. This discomfort is related to surgical scars in 22.4% of patients. Our study shows that 9% of patients feel physically less attractive due to RT tattoos, and 6.8% of patients reported being influenced in the way they dress or experiencing general discomfort when looking at themselves naked in the mirror. Globally, the preference for RT without permanent tattoos was reported in 17% of patients. A global dissatisfaction over Body Image was reported by 37.1% of women and 7.4% of men. In the whole group, physical and psychological discomfort caused by permanent tattoos was reported in 14.2% of women and 1.3% of men. In a subgroup of 132 women aged 35-65 with thoracic tumors (breast, lung, thymoma) the percentage arises to 58.3%; moreover in this group 18.2% of cases refer that they feel less attractive because of tattoos and the preference for radiotherapy without permanent tattoos was reported in 29.5%.

Conclusions. This study revealed that permanent marks, such as surgical scars and tattoos for radiotherapy, have a psychological and social impact on oncological patients. The study underscores the importance of addressing patients' body image concerns and exploring alternative approaches to enhance their well-being during follow-up.

P012

PREDICTORS OF EARLY AND LATE DYSPHAGIA AND IMPACT ON PATIENTS QUALITY OF LIFE (QOL) AFTER INTENSITY-MODULATED RADIOTHERAPY (IMRT) FOR NASOPHARYNGEAL CANCER

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Aims. The aim of our study was to investigate the value of pre-treatment neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as predictors of inflammation and their correlation with early and late dysphagia in patients diagnosed with nasopharyngeal carcinoma (NPC) treated with combined chemotherapy (CT) and intensity modulated radiotherapy (IMRT).

Methods. We enrolled 13 patients (8 men and 5 women, mean age 56 years) pT2-3 N0-1 M0 with NPC who underwent CT and IMRT from 2015 to 2020. The pretreatment evaluation included: physical examination, blood tests, nasopharyngeal laryngoscopy, magnetic resonance imaging (MRI), brain, chest and abdomen computed tomography. The post-treatment dysphagia was assessed with the Sydney Swallow Questionnaire (SSQ) and objectified through FEES (flexible endoscopic evaluation of swallowing). Pre- and post- treatment, 6 months, 1 and 3 years follow-up (FU) Perceived Dysphagia Scores and DOSS scores were evaluated.

Results. Out of 13 pts enrolled, mean NLR was 1.98 and mean PLR ratio was 184,68. After investigation at 3 years FU, 11 out of 13 pts reported different DOSS levels of dysphagia: 5 pts had mild dysphagia (level 5), 3 pts Mild–moderate (level 4), 3 pts moderate (level 3). We also found a significant relationship between a high NLR and PLR and low DOSS and high NLR and high SSQ score.

Conclusions. This evaluation, carried out early at the end of the treatment, could make it possible to determine the risk of dysphagia, allowing patients to be stratified into different risk classes and, depending on the class, an early speech therapy and nutritional rehabilitation program could be undertaken to improve survivors QoL.

P013

IMPACT OF WEIGHT LOSS AND PAIN IN QUALITY OF LIFE FOR RADIOTHERAPY OF PATIENTS WITH HEAD AND NECK CANCER

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Aims. Expected weight loss and the pain planned therapeutic program plays a key role in oncological care and treatment effectiveness in Head-Neck Cancer (HNC) patients. We aimed to determine the impact of worse pain during RT has been associated with worse treatment tolerance, weight loss, and worse quality of life (QoL). This work explored the relationship between pain control, weight loss, and QoL in a short group of patients receiving RT for HNC.

Methods. We considered between November 2019 and March 2021, 50 patients treated with radiotherapy for locally advanced HNC. Patients had RT dose > 60 Gy, ECOG 0-2. Analgesia was prescribed in accordance with the WHO Pain Ladder, but the extended-release opioid option was limited to microsphere oxycodone. QoL was assessed with the Brief Pain and nutritional risk (BMI)

Results. Responses were available from participants at 1 month post-RT and at 3 months post-RT . During RT treatment, the BMI positively correlated with pain control. In addition, worst pain correlated with amount of pain interfering with enjoying life as well as with the ability to eat solid foods. To 1 and 3 months post-RT , the pain was significantly associated with change in ability to enjoy life due to pain. At 3 months post-RT, change in worst pain negatively correlated with overall ability to enjoy life and ability to eat solid food. Change in BMI correlated with change in relief with pain medication at 1-3 month post-RT. No significant difference in pain relief was noted when considering men *vs* women.

Conclusions. Response to pain medication is associated with change in weight during and shortly after completion of RT. Pain levels were significantly correlated with QoL, particularly the ability to enjoy life and eat food at both 1- and 3-months post-RT.

P014

EVALUATION OF URINARY MORBIDITY IN PATIENTS TREATED WITH STEREOTACTIC BODY RADIATION THERAPY AFTER TRANSURETHRAL RESECTION OF THE PROSTATE

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Aims. Stereotactic body radiation therapy (SBRT) has now reached such levels of evidence on efficacy and toxicity that it can be considered a primary treatment option for selected patients. However, some grey areas remain regarding the use of (SBRT) in patients who have undergone transurethral resection of the prostate (TURP) due to the lack of data in this specific population. Although TURP is not a criterion for exclusion from treatment with the SBRT technique, this patient population has likely been underrepresented due to the potential risk of toxicities related to the previous surgery and the theoretical increase in the risk of urethral stricture.

Methods. Between 2019 and 2022, we treated 20 patients with the SBRT technique for localized prostatic disease with a history of previous TURP. Treatment was delivered using a linear accelerator with a dose of 36.25 Gy delivered in 5 fractions without urethral dose-sparing planning. Exclusion criteria included severely symptomatic pre-treatment urinary function and TURP performed within the last six months. Urinary toxicities were assessed according to the Common Terminology Criteria for Adverse Events v 4.0 rating scale. In contrast, the urinary quality of life data was evaluated using the International Prostate Symptom Scoring (IPSS). A Wilcoxon signed-rank sum test was used to determine if there was a statistically significant increase or decrease in IPSS between time points.

Results. The median age was 78 years (range 61-85). The mean follow-up was 26 months (12-38 months). Grade 2 toxicities occurred in 15 patients (75%), necessitating pharmacological therapy, including corticosteroids, anticholinergics, antimuscarinics or 5- alpha-reductase.

There were no acute toxicities Grade >2 toxicities. The baseline IPSS scores had a low mean value of 7 (ranging from 2 to 10), indicating mild to moderate symptoms. At one month, there was a statistically significant deterioration in the urinary quality of life compared to the baseline. However, it returned to comparable values observed before radiotherapy at three months.

Conclusions. SBRT treatment in patients with prior TURP was well tolerated. Low-grade acute toxicities, manageable with supportive therapies, did not significantly affect the quality of life over time. However, the relatively short follow-up period needs to provide conclusive information on chronic toxicities.

P015

QUALITY OF LIFE IN ELDERLY PATIENTS WITH HEAD AND NECK CANCER ONE YEAR AFTER TREATMENT

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Aims. The multidisciplinary evaluation of head and neck cancer patients who are candidates for radical treatments has improved their oncological outcomes. Managing elderly patients remains difficult and increasingly important, needing to balance the benefits of radical treatments with their associated morbidities that can impact their quality of life.

Methods. Seventy-six elderly patients (with age >70 years) who were candidates for multimodal radical treatments with head and neck carcinoma (in the oral cavity, pharynx or larynx) were requested to complete the European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire and EORTC Head and Neck Cancer Quality of Life Questionnaire prior to treatment. Forty-five patients completed the questionnaire throughout the 3, 6 and 12-month follow-up period. Patients were also assessed using the G8 scale and, depending on the results, with a multidimensional geriatric assessment.

Results. At three months, the patients reported increased difficulty in eating due to various causes (such as dental problems, pain, or xerostomia. However, at 6 and 12 months, the quality of life was comparable to the baseline, with no statistically significant differences, even among patients with a G8 score greater than or equal to 14, indicating increased frailty.

Conclusions. The treatment did not affect the patient's quality of life who completed the questionnaires. The evolution of treatments has undoubtedly positively impacted the reduction of toxicity and the comprehensive care provided by multiple specialists who are, therefore, able to implement specific therapeutic and supportive protocols tailored to each patient. The evaluation in a multidisciplinary team made up of professionals also dedicated to supportive therapies, including dentists, geriatricians, and nutritionists, can contribute to the implementation of strategies dedicated to the management of the side effects and establishment of an optimal support network of the patient in his treatment path that can predict and anticipate the patient's needs. Patients also considered more frail maintained a quality of life comparable to the pre-treatment at one year.

P016

IHELP PROJECT (PERSONALISED HEALTH MONITORING AND DECISION SUPPORT BASED ON ARTIFICIAL INTELLIGENCE AND HOLISTIC HEALTH RECORDS)

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Aims. This project is financed under the Horizon 2020 Research and Innovation Framework Programme: GRANT AGREEMENT NUMBER 101017441 — iHELP. The main aim is the acquisition of PREMs (Patient Reported Experience Measures) and PROMs (Patient-Reported Outcome Measures),using portable monitoring tools during multimodal therapies and follow-up period in patients with pancreatic/prostate/anal cancer,using a dedicated app and wearable technologies (wristband) as data collection tools that can be integrated into the EHR.Primary endpoint is to investigate the role of real-world data in predicting treatment toxicity, assessing patients' QoL and analyzing survival outcomes.

Materials and Methods. Patients aged over 18 years,with pathologically established pancreatic/prostate/anal canal cancer and indication for radiotherapy treatment are included.EORTC QLQ-C30 and specific dedicated questionnaires (QLQ-PAN26,AN27,PR25) are periodically submitted to the patient via a mobile application during radiotherapy treatment and the initial follow-up period.Data regarding motor activity,energy consumption, heart rate, sleep and oxygen saturation are measured

through the use of IoT.Demographic, clinical and laboratory data, overall survival and disease-free survival are also collected.The mobile application is Healthentia, an eClinical solution, certified as a Class I medical device, GDPR-compliant and ISO27001 (FAGGS BE/CA01/1-72378) that facilitates the optimisation of clinical trials by accelerating trial processes.Within the iHelp study, the Healthentia mobile application is used to deliver questionnaires that are displayed on the mobile application at given times. In addition to standardised questionnaires, the application also allows the monitoring of symptoms of interest selected by the clinician and/or patient.

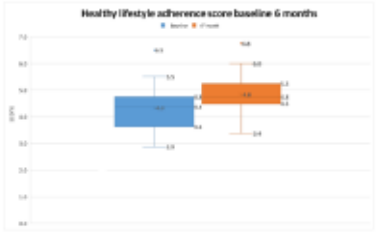
Results. For AI algorithms, data are continuously recorded by the IoT and may provide a solid basis for identifying reliable predictors of toxicity and aggravation risk. Toxicity is assessed according to the NCI-PRO-CTCAE™ ITEMS-ITALIAN Version 4.0.The artificial intelligence and machine learning models used in the project include classical statistical models up to Deep Learning techniques, both with regression and classification functions.

Conclusions. This model based on predictions provided by AI can be useful for the assessment of patients with an indication for radiotherapy to prevent possible toxicities and for the early identification of high-risk patients.

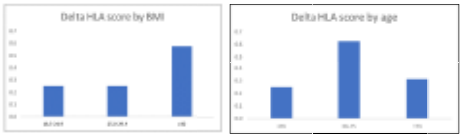
a)

Variable	N.	ALL, n (%) 198	IG, n (%) 94	CG, n (%) 104
ISUP group	1	29 (14.6)	16 (17)	13 (12.5)
	2	55 (27.8)	30 (31.9)	25 (24)
	3	47 (23.7)	20 (21.3)	27 (26)
	4	25 (12.6)	11 (11.7)	14 (13.5)
	5	16 (8.1)	9 (9.6)	7 (6.7)
	missing	26 (13.1)	8 (8.5)	18 (17.3)
Smoking habits	Smoker	31 (15.7)	16 (17)	15 (14.4)
	Former smoker	86 (43.4)	41 (43.6)	45 (43.3)
	Never smoker	72 (36.4)	34 (36.2)	38 (36.5)
	missing	9 (4.5)	3 (3.2)	6 (5.8)
PSA (ng/ml)	Median (IQR)	1.08 (4.82)	1.12 (4.97)	0.94 (4.72)
BMI (kg/m²)	Median (IQR)	27.9 (5.7)	28.5 (5.6)	27.6 (5.9)
WHR	Median (IQR)	1 (0.1)	1 (0.1)	1 (0.1)
Heart rate (bpm)	Median (IQR)	73 (16)	73 (14.3)	72 (17.5)
Glycemia (mg/dl)	Median (IQR)	97 (19.5)	98 (20)	95 (19)
Triglyceride (mg/dl)	Median (IQR)	102 (62)	104 (61)	99 (67)
Total cholesterol (mg/dl)	Median (IQR)	189 (46)	186 (38)	196 (47)
HDL cholesterol (mg/dl)	Median (IQR)	51 (15)	49 (14.0)	52 (14)
LDL cholesterol (mg/dl)	Median (IQR)	113 (34.5)	105 (38)	124 (50)
RT treatment		ALL, n (%)	IG, n (%)	CG, n (%)
Curative treatment		109 (55.1)	54 (57.4)	55 (52.9)
Adjuvant/salvage RT		41 (20.7)	25 (26.6)	16 (15.4)
ADT		68 (34.3)	35 (37.2)	33 (31.7)

b)



c)



List of abbreviations: BMI: body mass index; HLA: healty lifestyle adherence; ISUP: international society of urological pathology; PSA: prostate specific antigen; WHR: Waist to Hip Ratio.

Figure 1. Summary of patients baseline characteristics and treatment (a); HLA score at baseline and at 6 months (b); change in HLA score according to BMI and age at recruitment (c).

P017

AN UPDATE OF MICROSTYLE STUDY: A RANDOMIZED CONTROLLED TRIAL ON LIFESTYLE AND INTERACTION WITH MICROBIOTA IN PROSTATE CANCER PATIENTS UNDERGOING RADIOTHERAPY

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Aims. To report preliminary data from MICROSTYLE study, a clinical trial for prostate cancer (PCa) patients (pts) undergoing RT designed to investigate whether changes towards a healthy lifestyle are able to modify microbiome, improve quality of life and decrease the side effects of RT.

Methods. According to the study protocol 300 PCa pts undergoing adjuvant/salvage or curative RT will be recruited in two comprehensive Italian Cancer Centers. Pts will be randomized in two arms: Intervention Group (IG) and Control Group (CG); the ones allocated to the IG will receive personalized counseling on diet and exercise to improve overall lifestyle (LS) and reduce eventual RT-related toxicities. Primary outcome will be assessed after 6 months by measuring the change in healthy LS adherence (HLA) score. The score will be calculated according to the World Cancer Research Fund recommendations and will range from 0 to 7 (minimal to maximal adherence). Intestinal microbiome composition will be evaluated trough fecal samples analyses. According to the cross-over design, the CG will cross to the IG after 6 months.

Results. Recruitment started on October 2021 and to

date, 198 pts have been enrolled (94 in the IG and 104 in the CG) with a median age at recruitment of 70 years, and a total of 485 fecal samples were collected. Baseline characteristics of pts are reported in Figure 1a. One-hundred and fifty pts completed the RT course with no grade (G) >3 gastrointestinal (GI) acute toxicities reported and only 2 genitourinary (GU) >G3 toxicities observed among both arms. The HLA score resulted significantly higher at 6 months (data available for 47 pts) respect to baseline (median HLA 4.4 *vs* 4.8, $p < .0001$, Figure 1b). When pts were stratified according to BMI at baseline, pts with a BMI ≥ 30 had a greater increase in HLA at 6 months. While, when stratified by age, pts aged 66-75 resulted the ones with a major change in HLA score (Figure 1c). At 12-month FU (data available for 27 pts) all pts are alive with no evidence of disease and only one GI >G3 late toxicity was reported.

Conclusions. This innovative trial proposes a LS intervention during RT, which includes dietary and physical activity counselling, as well as monitoring changes in microbiome and serum biomarkers. The promotion of healthy LS will be started before initiation of standard care, to achieve long lasting impacts, control side effects, coping with feelings of anxiety and depression and improve RT effectiveness.

P018

ADJUVANT RADIOTHERAPY FOLLOWING OPEN PARTIAL HORIZZONTAL LARYNGECTOMY (OPHL): LONG-TERM TOXICITIES AND FUNCTIONAL OUTCOMES

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Aims. Our objective was to conduct a retrospective evaluation of outcomes, including results, toxicity, and quality of life, in patients with laryngeal cancer who underwent partial laryngectomy followed by postoperative radiotherapy (PORT).

Methods. Between 2018 and 2023, we retrospectively analyzed 30 patients diagnosed with glottic or supraglottic squamous cell carcinoma (Table 1). These patients underwent either supraglottic laryngectomy (OPHL1 = n 18) or supracricoid laryngectomy (OPHL2 = n 12) along with ipsilateral or bilateral neck dissection at our institution (data are summed in Table 2). PORT was administered for cases with pT4 NX, pTX pN1-3, positive margins, pT3 with extraglottic extension, and other pathological risk factors such as Perineural Invasion and Lymphovascular Invasion. All patients were treated using SIB-IMRT (VMAT), optimizing the plan to respect a constraint dose for constrictor muscles of 55Gy as Mean Dose. The prescribed radiation dose was 60 Gy to the remaining larynx (Neolarynx) and positive node levels, 66 Gy in the presence of positive margins or extracapsular node extension (ENE+), and 54 Gy to elective node levels. We compared the toxicities observed at the end of treatment, using CTCAE 5.0 scale, with those reported at the last follow-up (FUP). Laryngeal edema was evaluated using RTOG scale (Table 3).

Table 1. Population characteristics.

	Clinical	Pathological		Clinical	Pathological
T1	2	0	N0	14	14
T2	6	6	N1	7	4
T3	20	23	N2	7	6
T4	2	1	N3	2	6

Table 2. Type of surgeries.

OPHL1	18
OPHL2	12
Ipsilateral Neck Dissection	13
Bilateral Neck Dissection	17

Table 3. RTOG edema scale.

Grade	Description	No of Patients
0	None	17 (57%)
1	Hoarseness, slight arytenoid edema	5 (17%)
2	Moderate arytenoid edema, chondritis	7 (23%)
3	Severe edema, severe chondritis	1 (3%)
4	Necrosis	0

Results. Nineteen (63%) patients were treated with exclusive radiotherapy while 11 (37%) patients were treated with concurrent chemoradiotherapy. All patients successfully completed the treatment without interruptions, except for one patient who had a 4-day interruption. Mean follow-up was 34.8±18.1 months. Acute toxicity included mucositis (G1-G2: 50% of patients), dysphagia (G1-G2: 73%, G3: 3%), skin toxicity (G1-G2: 73%, G3: 3%), xerostomia (G1: 43%), and weight loss (G1-2: 20%). At the last follow-up, patients experienced xerostomia (G1-G2: 43%), dysphagia (G1-2: 43%), and laryn-

geal edema (Table 3) evaluated during fibroscopy (G1-2: 40%, G3: 3%). One patient (3%) required a gastrostomy 4 years later while no patient was tracheostomy-dependent at the last follow-up. Overall survival (OS) was 90%, 3 patients died from other causes. Disease free survival (DFS) was 83%; no local recurrence of disease was observed during the FUP, although 2 patients had metachronous lung cancer.

Conclusions. Postoperative radiotherapy to the neck following partial laryngectomy does not have a significant impact on local acute and chronic morbidity. However, careful treatment planning for radiotherapy is essential as well as longer FUP is needed.

P019

EVALUATION OF ACUTE FATIGUE CANCER-RELATED IN ELDERLY BREAST CANCER TREATED WITH OR WITHOUT REGIONAL IRRADIATION: OUR EXPERIENCE

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Aims. Breast cancer patients receiving adjuvant radiotherapy (RT) benefit from local control. Regional nodal irradiation (RNI) also improves outcomes in breast cancer (BC) patients. Cancer-related fatigue (CRF), a persistent state of severe exhaustion, is a common side effect of these treatments, especially in older women. We evaluated and compared acute CRF in elderly BC patients with and without regional nodal irradiation (RNI).

Methods. A total of 52 elderly breast cancer patients (≥75 years) treated with adjuvant radiotherapy (RT) between 2020 and 2022 were assessed for QoL and CRF using the FACIT F questionnaire before treatment (T1) at the end of radiotherapy (T2), and three months post-RT (T3). The FACIT-fatigue (FACIT-F) questionnaire is a subscale of the original FACIT-general questionnaire, focusing on fatigue assessment. Thirty patients received whole breast irradiation (WBI) (40.05 Gy, 15 fractions) after surgical resection, while 22 patients received RNI and WBI (50 Gy, 25 fractions). The mean age in the group treated with only WBI was 82 years, and in the RNI+WBI, 80 years old. Patients treated with RNI had higher stages (stages II and III) and received neoadjuvant or adjuvant chemotherapy.

Results. Fatigue at T1 was more severe in patients receiving chemotherapy before RT. All patients experienced CRF. For patients without RNI, the fatigue severity increased from T1 to T2, returning to baseline at T3. Instead, the scores remained constant over time for patients treated with RNI.

Conclusions. Patients undergoing adjuvant radiotherapy for breast cancer can develop CRF influenced by previous treatment (e.g. chemotherapy). In our small cohort, the incidence of fatigue is higher baseline in patients who have received previous chemotherapy. The addition of RNI does not seem to be correlated with a significant CRF.

P020

PELVIC INSUFFICIENCY FRACTURES AFTER PELVIC NODAL IRRADIATION: A MONO-INSTITUTIONAL CASE SERIES

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Aims. Pelvic insufficiency fractures (PIF) are a well-known but under-estimated late effect of pelvic radiotherapy (RT). The aim of our analysis was to assess clinical characteristics of patients (pts) diagnosed with symptomatic PIF who have received pelvic RT as part of their definitive treatment.

Materials and Methods. Clinical and morphological (CT or pelvic MRI) characteristics of 13 pts with 22 reported symptomatic PIF treated at our Institution between May 2008 and July 2021 were analyzed. Primary tumor was gynaecological in 7 pts, prostatic in 2 pts, anal in 2 pts, rectal in 2 pts. All patients received pelvic RT with a median dose of 50.4 Gy (46.2-74.2) in 28 median fractions (18-38). According to Pickhardt et al, who assessed CT attenuation Hounsfield Unit (HU) threshold to identify osteoporosis, HU were retrospectively recorded with a single oval over the trabecular bone in the L5 vertebral body on pre- and post-RT CT scans. The correct position in the middle of the vertebral body was double checked in the axial view. According to Berger-Groch et al, the pattern of appearance was defined as osteoporotic with HU values lower than 100 (6 pts), osteopenic with 100-150 HU (5 pts) and with normal bone density more than 150 HU (2 pts). Then, in pre-RT CT scan, punctual bone density on the fracture site was recorded. Patient characteristics are reported in Table 1.

Results. Median follow-up was 4.5 years (1.8-14.9). Median time between end of RT and PIF was 18.9 months (6.0-137.7). All pts experienced pelvic pain with a median VAS score of 6 (5-9). In 3 pts the evaluation of post-RT bone density was not possible in absence of any post RT CT scan. From the imaging analysis, no significant differences or evident trends emerged in median L5 bone

pre- and post-RT density, suggesting that bone density reduction was not a risk factor for PIF. Similarly, in a random sample of different bone points in the pre RT CT scan, the site of PIF did not always correspond to the lowest bone density area.

Conclusions. Oncological therapies often have a negative impact on bone density. The use of simulation CT to detect osteopenia/osteoporosis is a promising way to identify these conditions without increasing the diagnostic burden in cancer patients. A larger sample size and further analysis are needed to identify potential risk factors for PIF.

Table 1. Patient's characteristics.

N° pt	Age	Sex	Histology	BMI	RT dose (Gy)	Latency period (months)	N° of PIF	HU L5 pre-RT	HU L5 post-RT	HU PIF site	Maximal dose site of PIF (Gy)
1	57	F	Rectal cancer	22.48	64.8	8.99	1	145	70	129	48.1
2	67	F	Anal cancer	19.53	46.2	110.48	3	84	\	\	\
3	72	F	Rectal cancer	28	68.4	44.36	1	143.2	128	106	30.4
4	74	F	Cervical cancer	18.3	52.5	18.74	1	65.2	139	27	62
5	74	F	Cervical cancer	15.92	50	11.14	3	52.9	46	12-42-68	35-31-36
6	49	M	Prostate cancer	23.66	71.4	136.69	2	143.6	\	\	\
7	79	F	Endometrial cancer	25.3	50.4	19.07	3	79.3	12.3	60-72-136	43-43-32
8	80	F	Endometrial cancer	20.2	50	12.93	1	39.3	8.7	32	39
9	74	F	Cervical cancer	21.63	50	6.25	1	142	39.7	42	51
10	70	F	Endometrial cancer	28.6	50	14.98	1	109	153	14	46
11	58	M	Anal cancer	24	68.4	9.36	2	112	67.3	110-115	56-56
12	64	F	Ovary cancer	17.78	50.4	22.02	2	50.8	154	42-41	32-30
13	78	M	Prostate cancer	22.86	74.2	17.29	1	113	\	\	\

P021

A NEW STRATEGY TO IMPROVE QUALITY OF LIFE: DAILY ONLINE ADAPTIVE RADIOTHERAPY IN PROSTATE CANCER

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Aims. Radiation therapy (RT) is standard procedure in Prostate Cancer (PCa) treatment. Currently, inter- and intra-fraction set-up errors and daily anatomical changes, such as organ position and shape modifications, may determine a decrease of treatment efficacy because of variations of delivered dose to the target. Daily Online Adaptive Radiotherapy (do-ART) is an innovative technique that has been introduced to optimize treatments and minimize potential deviations in dose delivering. The aim of study is to assess the impact of do-ART in prostate cancer treatment in terms of quality of life.

Figures 1 and 2.

Methods. Data included patients treated for Pca from July 2021 to September 2022. All patients were subjected to Intensity Modulated RadioTherapy (IMRT) with a radical intent, a total dose of 67.5 Gy in 25 fractions was dispensed. The EORTC QLQ-C30 and PR-25 questionnaires were administered to all patients at the beginning of RT,

during the second week of treatment and at the end.

Results. Fourty-nine patients were enrolled: 17 (35%) were subjected to do-ART, 32 patients (65%) underwent a non-do-ART. Patients' age was included between 55 and 85 years, with a median age of 74 years. During the second week of treatment, the PR-25 questionnaires were administered and differences between the two groups were evidenced, including both functional and symptomatic aspects. Regarding functional domain, a better sexual functionality was reported for do-ART (59 *vs* 8 percentage points), while as regards for symptoms, worse urinary (28 *vs* 24) and bowel treatment-related symptoms (29 *vs* 16) were described in non-do-ART patients (Figure 1). At the end of treatment, the analysis of QLQ-C30 and PR-25 questionnaires showed a higher Global Health Status (74 *vs* 69) and was confirmed a favorable trend in do-ART patients (Figure 2).

Conclusions. Daily Online Adaptive Radiotherapy should be implemented as standard treatment for Pca, because, compared to non-adaptive treatment, could determine the optimization of dose delivering and may improve the quality of life. Further studies are still necessary to determine the benefits of do-ART in PCa patients.

P022

PROKLAMA CT-RT TO IMPROVE RECTAL PREPARATION IN PATIENTS SCHEDULED FOR PELVIC RADIOTHERAPY

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Aims. An empty rectum is an important condition in pelvic radiotherapy (RT) to reduce local toxicity and geographic missing, and the rectal gas has a significant effect in target displacement. The progressive increase of radiation induced inflammation may compromise optimal rectal preparation. PROKLAMA CT-RT (Geophyt srl, Novi Ligure, Italia) is a food supplement based on: seaweed Klamath, prebiotic elements and various lactobacilli. These components have anti-inflammatory, analgesic, prebiotic and laxative activity. Furthermore, one of the actions of this supplement is to reduce the amount of intestinal gas which is particularly useful in this type of treatment. In this prospective study we prophylactically prescribed Proklama CT-RT to patients (pts) scheduled for pelvic RT.

Methods. From 2/2023 to 5/2023, Proklama CT-RT (one sachet per day) was prophylactically prescribed from the first day of RT to a cohort of 15 pts (6 female and 9 male) treated with pelvic RT at our Institute. Primary tumors were: prostate cancer in 9 pts (60%), cervical cancer in 4 pts (26 %), anal canal cancer in 1 patient (6.5%), and bladder cancer in 1 patient (6.5%). Cervical, anal, and bladder cancer patients received concomitant chemotherapy. Fourteen pts underwent RT to the primary tumor site and pelvic lymph nodes, delivered with helical intensity modulated RT (12pts=80%) or volumetric modulated arc RT (2 pts=14.5%). One patient (6.5%) was treated with prostate robotic stereotactic RT. To assess the efficacy of Proklama CT-RT, we evaluated: subjective symptoms reported by pts, presence of rectal gas on Megavoltage/Kilovoltage computed tomography (CT) scans of daily Image Guided RT (IGRT), the need to use the catheter to correct rectal filling, fiducial rigid-body deformation due to the gas transit for the robotic SBRT technique.

Results. All pts experienced grade ≤2 intestinal toxicity (diarrhea, abdominal discomfort/pain). However, none of them presented improper rectal condition and needed rectal filling correction procedures throughout the course of RT. This evidence is significant compared to our clinical practice data, which highlighted a 13% rate of rectal catheter use before RT delivery. The treatment was completed, without any interruption, in 100% of pts.

Conclusions. In our experience the use of Proklama CT-RT improved treatment compliance, tolerance and precision. A larger cohort of pts and a prospective randomized study would be required to confirm these findings.

P023

LET'S IMPROVE TOGETHER: RECEPTION AND COMUNICATION IS OUR GOAL; OUR JOB IS TO TAKE CARE OF THE PATIENT AND HIS FAMILY

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Since February 2022, the oncological radiotherapy service of the University Hospital of the Arcispedale S. Anna in Ferrara has hosted a psychological listening point for patients and their families. The project was born from the will of the current Director Dr. A. Stefanelli and Dr. D.A. Lombardo psychologist former nurse now retired. The need was felt, in the oncological-radiotherapy context in the broadest sense, to have as a tool to help patients in their radiotherapy experience-path. The adaptation of the patient to the disease and to the treatments also depends on the relational and communicative approach with the treating team. The attitude adopted is

to maintain a cautious, humble and self-reflexive orientation. The clinical reference model developed (George L. Engel) combines the individual dimension of mental distress with the family and relational ones, trying to prevent psychological disorders with reactive onset. The approach concerns the taking charge and analysis of all the dimensions of the patient and her loved ones. The specificity of the "Listening Point" consists in addressing the person (patient) whose psychological discomfort does not depend primarily on a psychopathological disorder but is generated by the traumatizing situation of the diagnosis of "tumor" and/or oncological treatments. Counseling, based on communication skills, does not represent a psychotherapeutic moment, but support in times of crisis. The offer of the psychological support service is offered to patients from the time they take charge of Radiotherapy.Subsequent moments can then also be identified, i.e. during therapy or in control follow-ups. Patients can ask for an interview even in particularly critical phases such as in the relapse of the disease, in poor adherence to treatments or in stress management. The possibility of a dedicated clinic in the service structure itself was useful, where it was possible to set up a relaxing environment with paintings and floral images of animals, green plants and perfume diffusers. During the first interview with the patient, a simple data collection form is filled in, with the necessary characteristics of confidentiality and comfort. In subsequent meetings, if deemed useful, the patient, or even the family members, can be asked to fill in the "DISTRESS THERMOMETER" form which, if repeated over time, can be used to verify the clinical course. During the subsequent interviews, other tests can be administered, to detect the need for diagnostic insights, with specific forms or structured interviews, to be sent to psycho-oncology clinics. Thirty patients with ten family members were interviewed in 2022 and support interviews carried out in 2022 varied from a minimum of three to a maximum of fifteen. The access times to the clinic are distributed over two mornings and one afternoon for a total of 22 hours per week. In the course of taking charge of these patients and their families, importance was given to narrative skills that allow understanding, interpreting and giving clinical relevance to the patients' narratives. These skills have made it possible to identify and specify the individual path through the disease and all its clinical, individual and social complications. In fact, patients attribute meaning to themselves and to the world around them by developing real narratives of their own experiences and personal experiences. Each narration has implicit and explicit contents full of meaning, which aim to transmit certain contents. We were able to see how the oral and written self-narration of one's lives and experiences improved the insight of the cancer patient, favoring an adaptive response to the treatment and to the sequelae of the disease.

P024

FAIR-AC (FATIGUE IN RADIOTHERAPY AND ACUPUNTURE): A PHASE III MULTICENTRIC RANDOMIZED CONTROLLED TRIAL ON BREAST OR PROSTATE CANCER PATIENTS TREATED WITH RADIOTHERAPY. PRELIMINARY RESULTS

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Aims. Acupuncture (A) had a marked effect on fatigue (F) in cancer patients (pts), regardless of concurrent anti-cancer treatment, particularly among breast (BC) and prostate cancer (PC) patients. FAIR-AC (FAtigue In Radiotherapy and ACupunture) is a phase III multicentric randomized controlled trial that evaluates the actual incidence of F in Italian BC and PC pts treated with radiation therapy (RT), and the role of A on F mitigation during RT treatment.

Methods. 400 consecutive pts affected with BC both after breast conservative surgery or mastectomy who will be referred for postoperative RT, and 200 consecutive pts affected with PC, referred for definitive or postoperative RT to three Radiation Oncology Units in Tuscany were planned to be enrolled in FAIR-AC trial. Stratification is made according to adjuvant and neo-adjuvant chemotherapy (CT) in BC patients, and to concomitant androgen deprivation therapy (ADT) in PC patients. Randomization (ratio 2:1) is used. In Arm 1 patients are treated with "standard care", in Arm 2 with "standard care+A". Specific and validated questionnaires investigate F and QoL.

Results. Between February 2022 and May 2023 175 patients were enrolled (105 BC and 70 PC), randomized and their clinical data collected on a customized web-based platform. 90 patients were assigned to the standard arm and 85 to the experimental arm. Breast conservative surgery was performed in 87% of BC patients. Most cases were T1-2 (87%), N0 (45%), luminal A subtype (48%), received adjuvant endocrine treatment (74%) and moderately hypofractionated breast 3DCRT (72%), for only 22% bed boost was planned. 54% of PC had high risk disease, 19% intermediate risk and 27% low risk. VMAT/

IMRT with IGRT was planned and RT volume encompassed prostate and seminal vesicles in all pts, standard doses and fractionation were prevalent. The study is still on-going and actively recuiting; the preliminary analysis, limited to BC patients (only 1 PC patient so far has reached the end of treatment) shows a significant effect of acupuncture in reducing fatigue in the experimental arm. Acupuncture's tolerance profile is optimal and no relevant adverse events have been signaled.

Conclusions. A is a safe and well tolerated treatment. If these results will be confirmed in the definitive analysis, it might be offered outside of clinical trials to prevent and reduce F to all BC and PC patients planned for RT. Definitive results might be available in a two years' time.

P025

MUSIC AND ANXIETY IN PATIENTS UNDERGOING RADIATION THERAPY (MUSA-RT)

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Objectives. This study aims to explore the role of music listening as a potential tool for assessing stress and anxiety in patients undergoing radiotherapy treatment. Validated questionnaires, namely the STAI-S Anxiety Scale and Symptom Distress Thermometer (SDT), were utilized for this purpose.

Methods. The music therapy (MT) approach employed in this study involved daily sessions of Music Listening (ML) during radiotherapy, with each session lasting approximately 10-15 minutes throughout the entire radiotherapy cycle. The music selection, primarily ambient 'soundscape' music, was curated and developed by the Music Therapist Lyz Cooper. The study encompassed two treatment groups: Control Arm A: Patients in this group did not listen to music but followed the evaluation protocol. Experimental Arm B: Patients in this group listened to a random playlist designed to induce calmness and relaxation during the radiotherapy sessions. All patients underwent weekly assessments using the STAI-S and SDT questionnaires.

Results. The preliminary findings of the trial involved the enrollment of 65 patients, with 33 patients assigned to the Control Arm A and 32 patients assigned to the Experimental Arm B. At baseline, there were no significant differences in STAI-S and SDT scores between the two groups ($p>0.05$). However, over the course of radiotherapy, a notable difference emerged, with the Experimental Arm B demonstrating significantly lower scores in both STAI-S ($p:0.008$) and SDT ($p:0.016$) compared to the Control Arm A.

Conclusions. The potential utilization of ML throughout the radiotherapy treatment warrants further investigation in patients undergoing radiotherapy. We believe that a comprehensive analysis upon completion of the enrollment process will shed more light on the benefits associated with this approach.

P026

OZONETHERAPY IN COMBINATION WITH STEREOTACTIC RADIATION THERAPY IN PATIENT WITH INOPERABLE PANCREATIC CANCER

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Aims. Pancreatic cancer is one of the most malignant tumors of the digestive tract with poor prognosis. 5-years survival rate was less than 10%, due to drug and radiation resistance. Stereotactic radiation therapy (SBRT), in combination with chemotherapy, was an alternative treatment for patient with inoperable pancreatic tumors (locally advanced and metastatic disease). Oxygen-ozone (O2/O3) therapy is an emerging integrative treatment of several clinical disorders and ischemic syndromes. The aims of the study was to evaluate the clinical and radiological effects of ozonetherapy in association to SBRT and Chemotherapy in pts with inoperable pancreatic cancer.

Methods. From January 2022 to May 2023, 3 pts were recruited into this study (2M and 1F), the median age was 62 years (range 55-72). All 3 pts were treated on the primitive pancreatic lesion with dose of 36 Gy (isodose of 70%) in 3 fr, 2 pts of this had a secondary liver metastasis treated with dose of 37.5 Gy (isodose of 67%) in 3 fr. The PTV delineation was performed on CT-MRI fusion to limit normal tissue toxicity. The VMAT treatment was delivered by 6MV Linac. Active Breathing Coordinator was used for taking in account respiratory organ motion. CBCT was employed to control patient setup before each fraction. dADC and sb1000 MRI sequences were analyzed before and after 1-3-6 months the end of SBRT. Toxicity was recorded according to CTCAE v.4.02 and radiological response was described according to RECIST criteria. O2/O3therapy consisted in rectal administration of high dose and concentration, such as 4 consecutive days per week for 3 months, alternating with 3 months of suspension.

Results. The 3 and 6-month cumulative incidence of gastrointestinal toxicity (duodenal perforation, gastric or duodenal ulcer) was not statistically significative and our analysis also showed a highly significant positive effect on pain relief for all treated pts. A reduction of Diffusivity index was registred in all cases.

Conclusions. The addition of O2/O3 therapy to RT treatment has shown to have advantages on local disease control, to reduction the adverse effects also in association with chemotherapy and finally on the reduction of pain symptoms. Unfortunately in this moment there are not enough studies in literature to support the efficacy of these integrated therapies which can justify greater adherence to these therapeutic protocols, however this promising association need to be tested in prospective trials.

P027

HYALURONIC ACID IN THE MANAGEMENT OF URINARY TOXICITY DURING EXCLUSIVE RADIOTHERAPY FOR PROSTATE CANCER: RESULTS OF A PILOT STUDY

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Aims. To evaluate the efficacy of Jalurost Oral Gel containing low molecular weight Hyaluronic Acid (200 mg) in reducing acute genito-urinary toxicity (GU) in patients with radiation-treated prostate cancer with curative intent.

Methods. 30 patients affected by prostate cancer who underwent exclusive radiation treatment of the prostate and seminal vesicles, with moderate hypofractionation (70.2Gy/ 2.7 Gy in 26 fractions) and volumetric technique were enrolled. All patients were randomized into two groups: the JOG Group was treated orally with 1 Jalurost Oral Gel sachet/day from the first radiotherapy session up to 3 months; the Control Group (CTR) started symptomatic treatment only in case of urinary toxicity (as per internal protocol).

The symptomatology was evaluated through:

- RTOG/EORTC SCALE (Radiation Toxicity Grading) compiled at the start of treatment (V02), at the end of each week of radiation treatment (v03-v08), after 3 months (v10) and after 6 months (v11)
- IPSS (International Prostatic Symptoms Score) completed at recruitment (V01), at the end of the radiation treatment (V08), after 3 months and after 6 months.

Results. The maximum toxicity (GU) reported during treatment was grade G2 in both groups. The number of patients with G0, G1 and G2 toxicities is shown in the table. In particular, the JOG group showed a reduction of G2 in all phases of the treatment compared to the CTR group. This reduction, evaluated by means with an independent non-parametric statistical tests, was statistically significant at V6 (p=0.016) and 3 months after the end of treatment (p=0.044).

Conclusions. The Jalurost Oral Gel administration at the start of exclusive radiotherapy treatment in prostate cancer has been shown to be effective in reducing acute and sub-acute urinary toxicity.

Table 1.

RTOG		v02	v03	v04	v05	v06	v08	V10 (3 mesi)	V11 (6 mesi)
G2	JOG	0	0	1	1	1	3	0	0
	CTR	0	1	2	2	5	6	0	0
G1	JOG	3	7	9	10	10	11	9	6
	CTR	5	11	12	13	10	9	14	6
G0	JOG	12	8	5	4	4	1	6	7
	CTR	10	3	1	0	0	0	1	6

P028

EFFICACY OF EYE MOVEMENT DESENSITIZATION AND REPROCESSING (EMDR) THERAPY FOR ANXIETY AND DEPRESSION IN ONCOLOGICAL PATIENTS DURING RADIOTHERAPY

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Aims. Fear of cancer treatments and results are the greatest problems with which cancer patients have to deal. High levels of fear are characterized by intrusive thoughts about cancer-related events and re-experiencing these events, avoidance of reminders of cancer, similar to post-traumatic stress disorder (PTSD). Eye Movement Desensitization Reprocessing (EMDR) therapy is an integrative psychotherapy approach that has been used for trauma treatment. EMDR therapy focuses on images and memories, reducing PTSD, fear and anxiety, The aim of the present study is to evaluate of the effectiveness of EMDR in patients received radiotherapy.

Methods. According to our institutional care management, all patients receiving RT were prospectively enrolled to receive charge-free assessment of their cognitive, emotional and physical states and psycho-oncological support during treatment. For the whole population who accepted the psychological support during RT, a descriptive analysis was reported, to evaluate anxiety, depression and distress, the Hospital Anxiety Depression Scale (HADS), Distress Thermometer (DT) were used. To evaluate post-traumatic stress symptoms, the Impact of Event Scale-revised (IES-R) was used.

Results. From July 2020 to May 2023, 1145 cases were evaluated during RT with structured psycho-oncological interviews for a median of 3 sessions (range 2–5).

During their first psycho-oncological interview, all the 1145 patients experienced the assessment of anxiety, depression and distress levels with the following results concerning the HADS-A and -D scale, 50% of cases (574 patients) and 30% of cases (340 patients) reported a pathological score more than 8, concerning the DT scale, 60% (687 patients) reported a pathological score more than 4. Twenty-one patients out 1145 received EMDR approach with a median of 4 psychological visits (range 3-5) during RT and 2 visits during follow-up. 7/21 were male (33.3%) and 14 female; 8 suffered from breast cancer (38%), 5 from gynecological caner (23.8%). In terms of anxiety and depression a reduction between baseline and follow-up was reported (median HADS-A and -D of 10 versus 8 and 7 versus 6, respectively). Median DT were 15 versus 13; median IES-R 73 versus 52.

Conclusions. The results seem promising for EMDR therapy as a potentially effective treatment for PTSD. Further research is recommended.

P029

PRELIMINARY EVALUATION OF FLASH ELECTRON RADIOTHERAPY IN THE TREATMENT OF UVEAL MELANOMA

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Aims. Uveal melanoma is the most common type of ocular disease in adults. The treatment possibilities can range between organ-conservative techniques and organ-removal approaches, depending on the overall tumor dimensions. Surgery was the first approach to ocular melanoma treatment and involved the complete removal of the organ. Other possible treatments are the Plaque Brachytherapy, Charged Particle Therapy using mainly proton beams, and Stereotactic RadioTherapy (SRT). Several studies have demonstrated the efficacy and safety of organ-conservative therapies in the limited disease over an organ-removal approach, especially regarding the improvement of the overall quality of life after treatment. The principal aim of this study is to preliminary verify the possibility of using FLASH electron Radiotherapy as an alternative treatment modality to localized uveal melanoma.

Methods. The Flash effect is proven to spare normal tissue while having the same biological effect on tumoral tissue, mainly from *in vivo* studies. The first step in this work is the dose deposition simulation using a Monte Carlo (MC) algorithm which simulates the ElectronFlash (EF) machine situated in our center. This LINAC is for research use only and can deliver high-energy electrons (7MeV-9MeV) to the target in both FLASH (>40Gy/s up to 5000Gy/s) and conventional (2Gy/min) regimes. Some tests were conducted on the Ebt3-gafchromic films and flashDiamond detector to verify the MC simulations and for the dosimetric assessment of the electron beam.

Results. From the analysis performed on the EF emerged a good agreement (gamma passing rate 95% @3%,3 mm) between the MC simulations and the dose distribution measurements. That result made possible to develop a calculation tool to simulate the dose distribution on the target, starting from the patient CT scan and the beam quality parameters.

Conclusions. Our work aims to study the possibility of introducing a new clinical intervention to treat uveal melanoma. At this preliminary stage, the MC simulation of the electron beam and the dosimetric assessment of the machine output have been performed. The next steps of the work will concern the study of the sparing effects generated by the FLASH effect in an RBE planning, and a quantitative comparison based on advanced statistical techniques between the DVH obtained with our FLASH treatment and that of the standard techniques, in particular SRT.

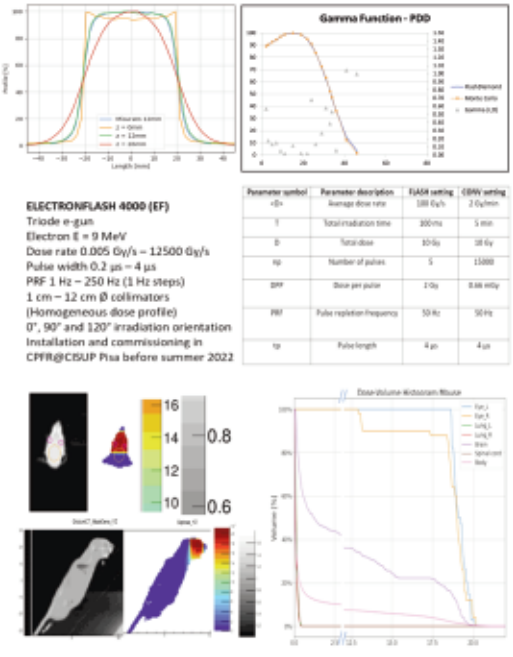

Figure 1.

P030

A CASE REPORT OF ACUPUNCTURE IN A METASTATIC YOUNG WOMAN

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Introduction. Complementary therapies can play an important role in the management and assistance of the oncological patient both in the support phase during conventional therapies and in the management of symptoms in the metastatic patient; the best known approaches of these methods are acupuncture and other oriental medicines, homeopathics, music therapy. Aim of this study is to report a case of a young metastatic breast cancer patient treated with acupuncture.

Materials and Methods. An interesting case that has come to our observation is that of a 40-year-old patient, suffering from advanced breast cancer, who underwent demolitive surgery followed by chemotherapy and radiotherapy in 2021. In July 2022 the patient went into bone and visceral progression and in October of the same year domiciliar best supportive care where proposed due to the impossibility (due to medical conditions) of continuing active treatment. The patient was dyspneic with a permanent need for oxygen; she also presented pain in the spine and partly in the pelvis with an average VAS score of 8 and functional limitation. No further radiotherapy was proposed as the patient was not in the clinical conditions to allow it to be performed. She was evaluated to perform complementary therapy for palliative purposes.

Results. In addition to administering homotoxicological remedies with a draining intent, acupuncture therapy was provided with 45-minute sessions with a weekly shortage. Four acupuncture session were performed. In addition to the local painful points (ashi points), some unblocking ones (TSRI), the use of the distinct meridians (of the lung) and the curious ones (DAI MAI) was used. After the first sessions, an immediate reduction in pain (VAS2) was observed immediately after removal of the needles. Moreover, it was observed that the patient was able to partially suspend the oxygen therapy for 12 ours and on average of 3 days. The respiratory benefits were also observed after two more acupuncture sessions. The patient then died 15 days after the last session.

Conclusions. Complementary therapies, such as acupuncture, can play a role also in palliative setting for pain and dyspnea control when other therapies are controindicated.

P031

CLINICAL OUTCOME AND TOXICITY PROFILE OF HYPOFRACTIONATED RADIOTHERAPY (HYPORT) IN ELDERLY PATIENTS WITH PANCREATIC CANCER: A SINGLE-RETROSPECTIVE STUDY

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Aims. Pancreatic cancer is a challenging disease to treat, especially in elderly patients (pts). HypoRT has gained attention as a potential treatment approach. This retrospective study aims to evaluate the feasibility and safety of HypoRT in elderly pts with pancreatic cancer.

Methods. We retrospectively analysed outcomes of patients aged ≥80 years, treated at our institution for pancreatic adenocarcinoma from July 2017 to October 2022. HypoRT was administered using volumetric modulated arc therapy. Acute and late toxicities were recorded and graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 scale.

Results. We analysed 30 patients aged ≥80 (range 80-89) years treated with HypoRT:

- Six patients received neoadjuvant radiotherapy exclusively and subsequently underwent surgical resection. The radiation doses were either 50 Gy or 40 Gy in 5 fractions.
- Twelve patients underwent neoadjuvant chemo-radiotherapy. The radiation dose range was 50-40 Gy in 5 fractions for 6 pts, 37.5 plus a boost of 67.5 in 15 fractions for two patients, and 30 Gy in 10 fractions for two pts. Of these 12 patients, 2 patients underwent surgery.
- Twelve patients underwent HypoRT exclusively. The range of radiation doses utilized in this subgroup was: 50-40 Gy in 5 fractions for 4 pts, 25-30 Gy in 5 fractions for other 4 pts, 1 received a dose range of 37.5 plus a boost of 67.5 Gy in 15 fractions and other 2 pts received 30 Gy in 10 fractions.

Acute gastrointestinal (GI) toxicities (nausea, vomiting, abdominal pain, diarrhoea and cholangitis) were distributed in 5, 6, and 2 events of Grade 1, Grade 2, and Grade 3, respectively. No >3 Grade were recorded. Regarding late toxicity, only 2 Grade 3 events (cholangitis) were recorded in the entire cohort. With a median follow-up of 12 months (1-60 months), 9 pts died, 21 pts still

alive: 8 with disease progression, 4 stable disease, and 1 with non evidence of disease. Seven pts were lost at follow-up.

Conclusions. Based on our experience, HypoRT appears to be a safe and well-tolerated treatment option for elderly pts with pancreatic cancer. Thus, HypoRT should be offered also to elderly patients.

P032

FEASIBILITY OF LINAC-BASED FRACTIONATED STEREOTACTIC RADIOTHERAPY FOR ELDERLY PATIENTS WITH MULTIPLE BRAIN METASTASES

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Aims. Linac-based fractionated stereotactic radiotherapy (fSRT) is increasingly used to manage patients with multiple metastases. This retrospective cohort study aimed to evaluate safety and feasibility for linac-based fSRT in elderly patients with multiple brain metastases (BMs).

Methods. From January 2021 and April 2022, elderly patients over 70 y-o with BMs were treated with Linac-based fSRT and SRS. Volumetric modulated arc therapy with Hyperarc were performed for all patients.

Results. Thirty-one elderly patients and 175 BMs were treated:. 17 out 80 patients (55%) were male and 14 were female, median brain mets were 6 (range 2-16). Primary tumors were as follow: 26% breast, 45% lung, 12% melanoma. Median PTV in cc was 9 (0.5-62cc). Median dose was 24Gy (range 18-25) in 3 fractions (range 3-5). No acute side effects were reported. Seven patients (22,5%) reported a progression of disease out of field and 6 patients underwent to a second course of stereotactic radiotherapy for the new brain metastases (median 6 lesion, range 3-10). One patient out 6 underwent to another course of brain fSRT (median brain mets 11).

Conclusions. It seems reasonable to use linac-based fSRT in elderly patients with multiple BMs due to the high feasibility and safety. Second and third stereotactic RT could be proposed in selected elderly patients without increasing side effects. Surely, robust data are needed.

P033

MANAGEMENT OF PATIENTS WITH CARDIAC IMPLANTABLE ELECTRONIC DEVICES (CIED) UNDERGOING RADIOTHERAPY (RT) A CUSTOM ROAD INSIDE A RADIATION ONCOLOGY CENTRE

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Aims. We created a custom road inside our radiation oncology centre for the management of patients with CIED receiving RT, to realize a structured multidisciplinary approach and apply a consensus document from Associazione Italiana Aritmologia e Cardiostimolazione (AIAC), Associazione Italiana Radioterapia Oncologica (AIRO), Associazione Italiana Fisica Medica (AIFM).

Methods. A Radiation oncology specialist and a health physicist dedicated were individualized in our team to management of patients with CIED underwent to radiotherapy. The physician created a check list of questions to ask to the patients at first examination and of the document necessary for cardiologic evaluation. The health physicist is dedicated to the elaboration of the radiotherapy plan considering the recommendations of the AIAC/AIRO/AIFM consensus document and estimate the dose to the device. Then they interfaced with the electrophysiologist specialist of our hospital to evaluate risk class for each patient with CIED who needed radiotherapy and apply the guidelines mentioned. For each patient the operational indications to follow during treatment and the evaluations to be carried out by the patients, were reported on medical record.

Results. From December 2018 to March 2023, 23/6000 (0,3%) patients with CIED were submitted to radiotherapy. Median age was 78 years (range, 63-89), 4 patients with defibrillator and 20 with pacemaker, 5/23 (22%) were at intermediate and 18/23 (78%) were at low risk based on AIAC/AIRO/AIFM consensus. All patients underwent to radiotherapy with energy ≤ 6MEV and dose to CIED was ≤ 2 Gy. Site of disease were head and neck, thorax, abdomen, and pelvis in 5, 10 and 8 patients, respectively. Radiotherapy techniques were 3-dimensional, volumetric arc therapy, brachytherapy in 4, 15 and 3 patients respectively. No adverse cardiologic event, no CIED malfunctions were registered during radiotherapy course. Each patient followed a personalized multidisciplinary approach with a team dedicated to the management of patients with CIED.

Conclusions. The incidence of patients with CIED undergoing radiotherapy is very low, most patients are at low risk of malfunctions. A custom road inside the radia-

tion oncology centre ensures a multidisciplinary approach for each patient and greater quality assurance of the radiotherapy treatment.

P034

BUILDING AN ONCOGERIATRICS SERVICE: THE SUPERO GROUP'S EXPERIENCE AT GEMELLI ISOLA CANCER CENTER

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Aims. Providing dedicated pathways for elderly patients including frailty assessment is advocated by national and international oncology guidelines. In the acquisition of a new Cancer Center, a geriatrician with expertise in oncology was added to the staff. The purpose of our study is to evaluate, in a center that previously did not have an oncogeriatrician, what type of patients are sent to the service, frailty status, treatments performed and tolerance.

Methods. The oncogeriatric service was open to out and inpatients aged 75 years or older belonging to the Cancer Center. For each patient we collected: tumor histology, staging, oncological treatments, comorbidities, symptoms, socio-housing situation, reason for oncogeriatric visit. Each patient received a comprehensive geriatric assessment (CGA) that included tools for functional autonomy, physical performance, cognitive performance, nutritional status, quality of life. At the end of treatment, at 1 month and at 3 months, patients were re-tested by same tools to check for any changes in physical and cognitive performance, autonomy and quality of life. Data on any reported toxicities were also collected.

Results. From January 2023, 97 patients were evaluated; the average increase in the number of visits performed for each month was 45% compared to the previous month; avarage age is 80 years old. 68% of patients underwent pre-treatment CGA while 32% of patients were evaluated only after treatment start for support during toxicity or during hospitalization for acute events. Among patients evaluated with pre-treatment CGA 23% were fit, 18% vulnerable, 38% frail. The most prevalent diseases were: prostate (42%), colorectum and anus (25%), and breast (12%). 39% of patients received radiation therapy alone; 30% hormone therapy; 10% concomitant radiochemotherapy; and 10% received chemotherapy alone. The remaining 11% were sent to palliative care or follow-up. The vast majority of patients (88%) were followed up during treatment with supportive oncogeriatric visits. 20% of patients completed treatment while 65% of patients are still undergoing it. 12% of patients were sent to palliative care or died; only 3% of patients discontinued the prescribed treatment due to toxicity.

Conclusions. The oncogeriatrics service quickly became part of the cancer center's clinical practice. We are observing very good treatment tolerance of patients followed, with a very low percentage of patients discontinuing treatment started.

P035

HYPOFRACTIONATED RADIATION THERAPY WITH TEMOZOLOMIDE FOR ELDERLY PATIENTS WITH GLIOBLASTOMA: AN INSTITUTIONAL EXPERIENCE

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Aims. Glioblastoma (GBM) is a very poor-prognosis brain tumor. To date, maximal excision followed by radiochemotherapy in 30 fractions, is the standard approach. Limited data are present in the literature about hypofractionated radiotherapy (hypo-RT) in elderly patients with GBM. Thus, this retrospective study was conducted to evaluate efficacy and toxicity of hypo-RT with simultaneous integrated boost (SIB) in association with temozolomide (TMZ) in this setting of patients.

Methods. Elderly GBM patients (over 65 yeras old) underwent surgery (complete, subtotal or biopsy) followed by SIB-hypo-RT and concomitant/adjuvant TMZ. The prescription dose was 40.05 Gy (15 fractions) with a SIB of 52.5 Gy (3.5 Gy/fraction) on surgical cavity/residual/macroscopic disease. Volumetric modulated arc therapy was performed. Concomitant temozolomide (75 mg/mq/die) and adjuvant chemotherapy (TMZ 150-200 mg/mq/5 days q 28) were administered. Overall survival (OS) and progression-free survival (PFS) were estimated using the Kaplan-Meier method.

Results. From January 2021 to April 2023, 35 patients were treated. The median age and KPS were 70 years (range 65-82) and 60%, respectively. At the median follow-up time of 15 months (range 7-24), median overall survival and progression-free survival were 12 months and 6 months, respectively. No acute or late neurological side effects of grade ≥ 2 was reported during RT. Grade 3-4 hematologic toxicity occurred in three cases.

Conclusions. HF-RT may offer equivalent outcomes and reduce treatment in elderly GBM patients

P036

STEREOTACTIC BODY RADIOTHERAPY FOR OLIGOMETASTASIS TO THE LUNG IN ELDERLY PATIENTS

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Background. Surgical treatment is considered a radical treatment for patients with lung oligometastases but many patients were considered medically inoperable. Stereotactic body radiotherapy (SBRT) is an accepted treatment for lung oligometastases in medically inoperable patients. Many elderly patients are inoperable owing to age and comorbidities and SBRT is a useful therapy for these patients. SBRT offers excellent local control though with the risk of higher toxicities than in younger populations. We report our institutional experience with the use of SBRT for lung metastases in patients ≥75 years old.

Materials and Methods. We retrospectively evaluated the data of consecutive patients treated from 01/2021 to 01/2023 aged ≥75 years with lung oligometastatic lesions. SBRT was administered with radical intent. The radiation treatment was delivered on a linear accelerator (TrueBeamTM, Varian Medical System). A vac-lock bag was used for patient immobilization in the supine position. Deep inspiration breath hold technique, respiratory gated technique or evaluation of slow CT were used for SBRT planning and to manage respiratory motion. GTV was delineated on PET-FDG or TC with contrast. PTV was created adding 3-5 mm of margin to GTV depending on the breath control used technique. Volumetric Modulated Arc Therapy with Image-guided radiotherapy using cone-beam CT were used for treatment. Treatment toxicities were analyzed using CTCAEv4 scales during treatment and follow-ups.

Results. 45 lesion in 35 patients were included; median age was 78 years (range, 75-88), median KPS was 70% (range, 90-60%). Oligo-recurrence primary sites were: lungs, 18; colorectal, 16; head and neck, 2; breast, 2; hepatobiliary tumors, 6; and others, 1. The median SBRT dose was 40 Gy (range, 25-54 Gy) administered in a median of 5 (range, 3-6) fractions. Median follow-up was 9 months (range, 3-20). All patients completed SBRT with no acute G3-5 toxicities. G1 toxicities included: fatigue in 18 patients, asymptomatic (radiographic) pneumonitis in 3, and mild dyspnea in 23 patients. G2 radiation pneumonitis occurred in 1 patient.

Conclusions. In our Institutional experience lung SBRT for oligometastasis was feasible in patients aged ≥ 75 years achieving minimal toxicity. For elderly patients SBRT is extremely safe with very low acute toxicity rates (no >G2 toxicity). Patients ≥75years remain excellent candidates for ablative-intent SBRT.

P037

HORMONE THERAPY AND ADJUVANT ULTRA-HYPOFRACTIONATED RADIOTHERAPY FOR ELDERLY BREAST CANCER PATIENTS: OUTCOME, TOXICITY AND COSMESIS

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Aims. Moderate hypofractionation Radiotherapy (RT) with 15–16 fractions of 2.6– 2.7Gy has been accepted as the standard of care for whole breast external treatment after surgery. The FAST-Forward randomized trial showed that ultrahypofractionation (5 fractions) results in non-inferior local control rates and similar adverse event profile when compared to standard RT and it has been approved by the European Society for Radiotherapy and Oncology Advisory Committee in Radiation Oncology Practice consensus. Aim of our analysis was to evaluate outcome, cosmesis and acute toxicity of early stage breast cancer patients > 70 years treated with adjuvant once-weekly ultra-hypofractionated radiotherapy and hormone therapy.

Methods. From January 2022 to May 2023, thirty-six elderly hormone receptor-positive patients with early stage breast cancer were treated with postoperative RT. All patients received hormonal therapy. RT was administered with an Elekta Versa HD linear accelerator giving a total dose of 26/30 Gy in 5 fractions over one week (5.2/6 Gy per fraction) to the whole breast with or without concomitant boost. Acute toxicity was assessed using the Radiation Therapy Oncology Group (RTOG) scale. Early-late toxicity was assessed using the Late Effects Normal Tissue Task Force Subjective, Objective, Management, and Analytic scale (LENT-SOMA); cosmesis was assessed at last follow-up, using Harvard criteria.

Results. All patients were >70 year-old with a range between 70 and 88 years and they all were treated with surgery and hormone therapy. Pathological staging was pT1 for 80.5% and pT2 for 19.5% of patients. Nodal status and margin status were negative for all patients. Excellent, good, fair and poor outcome was recorded for all patients according to physician evaluation. Excellent or good cosmesis were observed in 91.6% of patients, 8.4% of patients reported fair cosmesis, and no poor cosmesis was registered. Maximum acute skin toxicity

within 6 months after RT was G2 in 2.8% of patients while G1 acute toxicity was observed in 8.3% of patients and G0 toxicity in 88.9% of patients. No other acute toxicities were observed. At the last follow-up all patients were alive and free of any event.

Conclusions. Our analysis showed that weekly ultra-hypofractionated whole breast RT seems feasible and effective, representing a valid alternative to long RT schedules or no treatment for elderly patients at low risk of relapse. Cosmesis was good and toxicity was acceptable allowing a reduction of treatment time led to high patients' satisfaction and compliance.

P038

CONCOMITANT CHEMORADIATION THERAPY IN RADIATION ONCOLOGY UNIT: DOES IT MAKE THE DIFFERENCE?

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Aims. Radiation therapy unplanned interruptions have a negative impact on the success of treatment and pose a challenge for radiation oncologists. Concomitant chemotherapy during radiotherapy can negatively impacts on toxicities, causing interruptions or prolongation of the overall radiation treatment time. The aim of this study is to investigate if performing concurrent RT-CHT at the same center may play a role for better management of interruptions during radiotherapy.

Methods. We evaluated the interruptions in 40 patients (9 F, 31 M, median age of 73) with head-neck cancer, treated from January 2021 to January 2023. 20 patients underwent concurrent RT+ CHT within radiation oncology unit (Arm A), while 20 patients were treated in radiation therapy unit and oncology unit (Arm B). Radiation therapy was delivered in daily fraction of 2 Gy followed by sequential boost (18 patients), or daily fraction of 2.2 Gy with SIB (22 patients). 11 received induction with cisplatin 100 mg q21. It has been investigated how many patients completed RT-CHT treatment in the expected time (≤49 days), how many patients completed RT-CHT treatment beyond the expected time due to interruptions and how many patients interrupted RT-CHT without reaching the expected dose.

Results. In the Arm A, 17 pts concluded the treatment course in time, without any interruptions. Only 3 patients interrupted RT-CT for toxicity. Of these patients, 1 patient who received induction chemotherapy before RT-CHT, completed the treatment course beyond the expected time of 49 days. In the Arm B, 12 patients concluded the treatment course in time without any interruptions. 3 pts completed the treatment beyond the expected time of 49 days, 2 of them receved induction chemotherapy before RT-CHT and interrupted concurrent chemiotherapy at 1° and 3° cicle. 5 pts did not completed the treatment, not reaching the prescription dose (Table1).

Conclusions. Despite the small number of patients evaluated, it is clear that performing RT-CHT in the same center has a positive impact on the overall duration of radiotherapy treatment. Furthermore, even if it is beyond the scope of this study, it can be presumed that less interruption can positively impact clinical outcomes and treatment efficacy.

Table 1.

40 pts			
Dose reached: 33 pts		Dose not reached: 7 pts	
29 < 49 days	4 > 49 days	2 Arm A	5 Arm B
17 Arm A + 12 Arm B	1 Arm A / 3 Arm B		

P039

SHARED OPTIMIZATION, BETWEEN RADIOTERAPY UNIT AND MEDICAL PHYSICS UNIT, OF THE TERAPEUTIC PATHWAY: CREATION OF MANAGEMENT AND RECOVERY TOOL FOR PROLUNGED INTERRUPTION OF THE RADIATION TREATMENT

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Aims. To describe the necessary operations to determine the assessment of additional fractions in relation to those scheduled in the initial program, in case of long interruption.

Methods. In the contest of D.Lgs.101/2020 implementation, we developed a tool to calculate the recovery of missed BED (Biologically Effective Dose) duo to prolonged treatment interruption. The BED model is summarized in Table 1. Three spreadsheets have been drawn up

for: 1) Single prescription with or without concomitant boost; 2) two-sequential-step treatment (First Step and Sequential Boost), with interruption in the first step; 3) two-sequential-step treatment with interruption in the sequential boost. The Physician chooses the spreadsheet and collect treatment data by identifying the radiobiological benchmarks related to the site of disease. In our experience this has been made relying on the leading bibliographic reference (Table 2).

Table 1. (Bed Model).

Model	$BED = n * d * \left[1 + \frac{d}{(\alpha/\beta)}\right] - \frac{\ln 2 * (T - T_{delay})}{\alpha * T_{eff}}$
Parameters	n = number of fractions d = dose per fraction [Gy] α and β =linear-quadratic radiobiological parameters T = overall treatment time, including week-ends and treatment interruptions [days] T_{eff} = average doubling time of clonogenical cell population [days] (Note: this is the average time of cellular repopulation, not the tumour volume doubling time) T_{delay} = kick-off time [days], i.e. the time after which the cellular tumor repopulation starts. For a time t<T_{delay}, the tumor cellular repopulation is assumed equal to zero
References	Dale et al (Br J Radiol 2000; 73(872):893-4) Dale et al (Clin Oncol 2002; 14(5):382- 93)

Table 2. (Bibliographic Reference).

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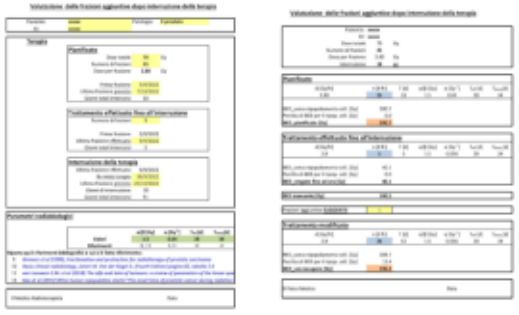

Figure 1. (Spreadsheet).

They will add: 1) personal details of the patient; 2) data of radiotherapy prescription; 3) radiobiological benchmarks: A/B (Gy), A (Gy-1), Teff (d), Tdelay (d). For SIB, the appraisal for each prescription will be performed using spreadsheet 1; for sequential boost, the evaluation will be performed using spreadsheets 2 and 3 (Figure 1). The Expert in Medical Physics will then calculate the BED according to the radiobiological model (Table 1), and will fill in the spreadsheet by entering: 1) planned BED; 2) administered BED so far; 3) missing BED; 4) suggested additional fractions; 5) BED with recovery doses. The value entered in the suggested additional fractions box must be such that the new total BED (BED with recovery doses) matches or at least balances the planned BED. Thereafter, the Physician will evaluate and accept what is suggested and proceed to modify the prescription by adding the number of fractions needed.

Results. This computational tool made it possible to assess in real time the need to reschedule the treatment of patients with prolonged suspensions of radiotherapy; this facilitated the optimization of treatments from a radiobiological point of view by avoiding under- or overdoses; moreover, rescheduling the patient in a timely manner also allowed optimizing the management of slots at the accelerators, avoiding lengthening waiting lists.

Conclusions. With a view to optimal patient management, this tool showed excellent potential from both a clinical and management point of view, having a positive impact in the quality of the patient's pathway in radiotherapy.

P040

QUALITATIVE STUDY ON DIVERSITY, EQUITY, AND INCLUSION WITHIN RADIATION ONCOLOGY IN EUROPE

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Purpose. Organizational culture plays a major role in prioritizing diversity, equity, and inclusion (DEI) objectives by aligning individual values of employees with organizational values. However, effective strategies to create an inclusive organizational culture, in which these values are aligned, remain unclear. The European Society for Radiotherapy and Oncology (ESTRO) launched a qualitative study, as a follow-up of the previous project on DEI that highlighted low levels of inclusion and work engagement among radiation oncology (RO) professionals in Europe. The aim of the present study was to gain an understand_ing of how DEI could be improved within RO departments by creating a more inclusive organizational culture.

Methods and Materials. A qualitative research study was conducted by enrolling RO professionals from 4 selected European countries through an open call on the ESTRO platform. Respondents who completed an online survey and met the inclusion criteria, such as experiencing low DEI levels at work, were invited for an online semistructured interview. Interview transcripts were analyzed thematically with an abductive approach via concepts in relation to "DEI," "work engagement," "organizational culture," and "professional values."

Results. Twenty-six eligible respondents from Great Britain, Italy, Poland, and Switzerland were interviewed. The thematic analysis identified cases in which limited engagement at work emerged when the personal values of RO professionals conflicted with dominant organizational values, hampering DEI. Three conflicts were found between the following personal versus orga_nizational values: (1) self-development versus efficiency, (2) togetherness versus competition, and (3) people-oriented versus task-oriented cultures.

Conclusions. Awareness of how organizational values can conflict with professionals' values should be raised to improve inclusion and engagement in the workplace. Additionally, efforts should be focused on tackling existing power imbalances that hamper effective deliberation on organizational- versus personal-value conflicts

P041

GENDER EQUITY/EQUALITY IN AIRO: A RETROSPECTIVE ANALYSIS OF TEN YEARS (2012-2022) ON BEHALF OF AIRO

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Aims. Diversity, Equity, and Inclusion (DEI) in the medical workforce improve patient care and innovation. Transparency helps identify gaps, measure performance, and develop an action plan.

Methods. AIRO's directive council (nDC) created a task force to analyze DEI, focusing on gender equality. The governance and scientific activity of AIRO and academic careers in Italian Radiation Oncology were analyzed. A modified matrix was used to analyze the variation of different variables. Data were extracted from AIRO's proceedings and registry of members. A rate of 40 % for both females (F) and males (M) is considered by the EU Council as a parity threshold. The ratio M/F measured gender equality for the different variables ($\geq 0.6 \leq 1.5$ = parity; not computable = no F).

Results. Management positions, Disease Study Groups coordinators (cDSG) and members are elective; nDC selects Scientific Committee (SC)'s components. The SC, DSG and nDC propose relators/moderators to the national congress.

1. Table 1 reports the gender of AIRO members for each year (y) (mean F 57%, M 43%: ratio M/F=0.75).
2. Members of SC were mostly M in the first 5 y; from 2018 F increased (range 29-33%).
3. cDSG were M 58.6% and F 41.4% in the first 5 y; M 49.5% and F 50.5% in the other six.
4. 10/11 AIRO's presidents were M. In the nDC M were the majority in all y; in 2022 F were 43%. The coordinators of Regional Groups were M from 2012-2015; F ranged 18-40% from 2016 to 2022 (40% in 2022). F cDSG ranged 29-43% in the first 5 y and 33-67% in the last 6.
5. 102 papers were published on behalf of AIRO. 92/204 authors were F. In the last 5 y the M/F ratio considering only the first authors was < 1.5, reaching values < 0.6 in 2 y; the M/F ratio for the last authors

was <1.5 only in 2022-2023.

6. Moderators to the Congress: F ranged 14,9-26,4% in the first 5 y and 26,5-50% in the last (50% in 2022). Relators show the same trend: 25,8-33,8% and 37,4-56,3 respectively in the first 5 and last 6 y.
7. In 2023 F were 8/18 and 5/16 respectively associate and full professor (ratio M/F 1,25 and 2,2).

All the M/F ratios are summarized in Table 1.

Conclusions. This analysis shows that while F are the majority in scientific activities, the gender gap is evident within Society's governance organs. There is a slow increase in F involved in different decisional roles in Society. Further analyses are necessary to understand the reason for these results, and the causes of the gap and improve F's involvement in all Society aspects.

Table 1. Number and percentage of females and males between AIRO members per year and M/F ratio for all the considered variables.

	AIRO's members %		President	nDC*	cDSG*	cRG*	SC*	Authors*		Relators*	Moderators*
	F	M						first	last		
2012	55,58	44,42	M	4,5	**1,3**	nc	14	0	nc	2,68	5,86
2013	54,76	45,24	"	2,6	2,5	nc	6	5	nc	2,2	3,8
2014	54,94	45,06	M	2,3	0,4	nc	"	**0,67**	nc	1,95	4
2015	54,80	45,20	M	"	**1,25**	nc	"	0	1	2,76	2,86
2016	58,19	41,81	"	5	2	2,33	7	**1,5**	1,5	1,95	2,79
2017	56,43	43,57	"	5	**1,2**	2,66	"	0,5	2	1,54	1,83
2018	38,54	61,46	M	8	**0,83**	1,75	2,5	**1**	2	**1,43**	1,58
2019	59,35	40,65	"	6	"	"	"	**1**	2,33	**0,78**	2,77
2020	63,41	36,59	M	"	2	4,5	2	0,33	**1,29**	1,53	2.05
2021	62,74	37,26	"	2,5	"	"	**1,3**	**0,63**	4,17	1,68	**1**
2022	62,42	37,58	F	**1,3**	0,5	**1,5**	2	**1**	**0,8**	**1,4**	**1,26**
2023	63,48	36,52						0,4	0,4		

Males M; Females F; Ratio M/F(*); ratio nc: not computable; (") the same; nDC: national Directive Council; cRG: coordinator Regional Group; cDSG: Disease Study Group coordinator; SC: scientific commission; bold text: ratio ≥ 0.6 ≤ 1.5 = parity

P042

A LITERATURE REVIEW OF PEDIATRIC CANCER PATIENTS SUPPORTING IMPROVED ACCESS TO PALLIATIVE RADIOTHERAPY

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Background. Palliative radiotherapy (RT) is safe and effective in relieving symptoms of adult cancer patients with advanced cancer as demonstrated by several trials. Conversely, palliative RT is less commonly used in pediatric cancer patients being its efficacy and tolerability less known. Therefore, the aim of this literature review is to summarize the available evidence on the efficacy and safety of palliative RT in this setting.

Material and Methods. A narrative review was conducted in order to identify studies on pediatric palliative RT. A search on PubMed of papers published from January 2000 to April 2023 was carried out. The primary outcome was symptomatic response while the secondary end-points was radiation-induced toxicity. The quality of evidence of the selected studies was performed using the Scottish Intercollegiate Guidelines Network (SIGN) guidelines.

Results. Overall, 13 papers were selected and of all of them reported on retrospective studies. The total number of included patients was 1528. Median age ranged between 4.0 and 17.9 years (median: 9.2 years). The most frequently treated symptom was pain (20-80%), followed by dyspnea and neurological disorders. The symptom relief rate, reported in 10 papers, ranged between 44.0% and 89.6% (median: 66.8%). Nine papers reported toxicity, with 3.1% and 2% median rates of grade 1-2 and grade ≥ 3 adverse events, respectively. The level of evidence was scores as 2+ in all papers.

Conclusions. This review confirms that pediatric palliative RT has been poorly investigated. However, the few available studies, albeit with a low level of evidence, show efficacy and safety results completely similar to those recorded in adult patients. This result justifies renewed efforts to overcome the current logistic-organizational and cultural barriers to the use of palliative RT in this setting, as well as the design of prospective studies able to properly define its role.

Table 1.

P043

FACING THE CLIMATE CHANGE: IS RADIOTHERAPY AS GREEN AS WE WOULD? A PRELIMINARY ANALYSIS

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Aims. This study aims to develop a conceptual "score" using data from a historical patient cohort to estimate the treatment footprint in radiation oncology.

Methods. We included patients who received radiotherapy between 2017 and 2021, excluding 2020, and provided valid research consent. To calculate the carbon footprint, we converted daily fractionation into a 2-Gy-factor. Patients were categorized based on their origin, distinguishing between those from the Lombardia region and those from outside. For patients from outside Lombardia, we estimated half of them with a carbon footprint of 140 Kg, equivalent to a return flight ticket from Rome to Milan. Assuming that the remaining half of the population used train transport (40 Kg), we calculated an average carbon footprint of 90 Kg per patient. The impact of transportation to and from the facility was not considered, given the minimal effect of public transport. For patients from Lombardia, we estimated the carbon footprint based on a hypothetical distance of 20 Km from our institute, considering the proximity of other radiation oncology departments, equal to 10 Kg of CO_2 per journey by car (20 Kg for a round trip). Train travel was not factored in due to its negligible impact and was considered as 0. Taking the average trip journey into account, we calculated a carbon footprint of 10 Kg of CO_2 per fraction.

Results. We included a total of 6,306 patients in our study. Out of these, 2,952 patients (46.81%) were categorized as regional patients, with an average carbon footprint of 142.94 Kg of CO_2 per treatment (interquartile range [IQR]: 13 - 397). The remaining patients were classified as non-regional, and their average carbon footprint was estimated to be 109.12 Kg of CO2 per treatment (IQR: 93-125.25). In Table 1, we conducted an analysis of fractionations, presenting the data divided by extra-regional patients (E) and regional (R) patients for each year.

Conclusion. Our study is a hypothetical attempt to make an estimation of the Carbon Footprint of the impact of a single treatment of Radiotherapy. We will focus to evaluate the real distance of the patients from our center and their CO_2 produced, also depending on pre-treatment imaging and the kind of treatment to establish a real-life model that could be applied to assess the impact of the carbon footprint in radiation oncology.

Table 1.

Number of fractions	2017	2018	2019	2021	Total
<= 5 Fr	15,02%	10,77%	10,61%	8,85%	45,24%
E	7,90%	5,11%	5,38%	3,96%	22,34%
R	7,12%	5,66%	5,23%	4,88%	22,90%
> 15 FR	7,48%	3,24%	3,27%	2,73%	16,71%
E	3,20%	1,22%	1,46%	1,06%	6,95%
R	4,28%	2,01%	1,81%	1,67%	9,77%
6-15 Fr	12,31%	10,42%	7,98%	7,34%	38,04%
E	6,17%	5,06%	3,74%	2,55%	17,52%
R	6,14%	5,36%	4,23%	4,79%	20,52%
Total	34,81%	24,42%	21,85%	18,92%	100,00%

P044

ULTRASOUND (US) EVALUATION OF BLADDER FILLING IN PELVIC RADIOTHERAPY

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Aims. To evaluate if assessing bladder filling in patients undergoing pelvic radiotherapy (RT) using a portable US probe prior to imaging with ionizing radiation (CT/CBCT) may reduce machine-time and exposure to ionizing radiation due to unnecessary IGRT imaging, while optimizing the workflow in the delivery phase.

Methods. Between February and March 2022, we collected daily data about bladder filling of 40 consecutive patients undergoing pelvic RT for prostate, rectal or gynecological malignancies, using a portable ultrasound probe ("GE-Vscan Extend"®). Measurements were taken in two different moments: before the simulation CT or before the delivery of RT. During the CT phase, the purpose was twofold:

1. To verify the correlation between the value measured by the US probe and that estimated by the TPS on the CT images, after the contouring of the bladder;
2. To identify an acceptable bladder filling threshold value, considered adequate after performing the CT scan.

During the delivery phase, the purpose was to optimize bladder filling before therapy. Indeed, bladder volume was monitored by the US scan until its value was near the TPS volume (+/- 10%).

Results. During the CT phase we evaluated 30 patients; in 90% of them, we found that the bladder vol-

ume estimated by US was slightly inferior to the volume calculated based on CT. For each patient, we calculated the percentage difference between US and CT volumes. This average difference was 10,68% (range 1,9%-54,4%): in 16 measurements the variation was below 10%, in 7 it was between 10% and 20% and in only 7 measurements was >20% (these values were more frequent at the beginning of the study probably due to the operator learning curve). During the delivery phase, we evaluated 10 patients, each for 12 fractions. A total of 164 US measurements were performed, 44 more than the 120 planned US scans, as scans had to be repeated because of inadequate bladder volume, suggesting that a total of 44 MVCT or CBCT were saved by prior intervention with US.

Conclusions. The US measurements of bladder volume prior to treatment planning CT/IGRT may reduce the execution of unnecessary IGRT scan, reducing patient exposure to imaging-based x-ray dose as well as machine time. Though this procedure operator-dependent, appropriate training and calibration of the system may dramatically improve the workflow in situations where optimal bladder filling is essential.

P045

DISPARITIES IN CERVICAL CANCER STAGE AND OUTCOMES: DOES PLACE MATTER?

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Background. Social/demographic inequalities in cancer survival are known. However, evidence on this topic in patients residing in Italy is lacking, despite the significant immigration flows registered in the last decades. Therefore, the purpose of this preliminary study is to analyse any differences in stage and outcome in patients with locally advanced cervical cancer (LACC), who underwent chemoradiation plus brachytherapy boost, between patients of Italian and foreign origin.

Materials and Methods. The following data were extracted from the database of a single centre observational study on LACC (FIGO IB-IVA): age, BMI, FIGO stage, tumor diameter, local control (LC), disease-free survival (DFS), and overall survival (OS). These parameters were compared between Western European (including Italian) and patients of different geographical origins.

Results. One hundred and seventy-three LACC patients were included in this analysis: 132 Western European (including Italian), 30 Eastern European, 6 African, 3 South American, and 2 Asian. The results of the study are shown in Table 1. The comparison of Western European and other origin patients showed a significantly younger median age (49 *vs* 58 years; p<.001) in the latter, but non-significantly different outcomes in terms of BMI, FIGO, tumor diameter, LC, DFS, and OS.

Conclusions. The results of this analysis did not show significant differences in terms of tumor size and stage at diagnosis and survival outcomes between Western European patients and subjects of different origins. However, it should be emphasized that this result refers only to patients who accessed the Italian national health service. In particular, considering the large number of residents in our region of Bengalese, Filipino and Chinese origin, the rate of Asian LACC patients (4.9% of non-Western Europeans) treated in our center is surprisingly low.

Table 1. Results.

Ethnic origin	No. Patients (%)	Median age, years (range)	p	Median BMI (range)	p	FIGO stage III-IV (%)	p	Tumor diameter (mm)	p	LC (5y) %	p	DFS (5y) %	p	OS (5y) %	p
West Europe	132 (76.3)	58 (28-85)	<.001	24.0 (16.4-45.0)	.582	75/132 (56.8)	.722	46 (20-147)	.503	82.9	.623	66.6	.714	70.9	.930
Other countries	41 (23.7)	49 (27-73)		24.2 (18.2-31.2)		22/41 (53.7)		47 (21-74)		79.5		65.7		69.8	

Legend: BMI: body mass index; DFS: disease free survival; FIGO: International Federation of Gynecology and Obstetrics; LC: local control; OS: overall survival

P046

ADOPTING THE ISO STANDARD METHODOLOGY IN THE IMPLEMENTATION OF A PROSTATE CANCER CLINICAL PATHWAY FOR PATIENTS TREATED WITH STEROTACTIC BODY RADIATION THERAPY USING HYDROGEL SPACER AND FIDUCIAL MARKERS: A COMMUNITY CASE STUDY

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The implementation of clinical pathways is a priority in the oncology field, especially when different health professionals and hospital divisions are involved. Clinical

pathways aim to guarantee efficiency and safety of the treatment process in compliance with legal requirements. An accurate process modeling and the definition of specific skills and responsibilities are the first steps in the implementation of a clinical pathway. A number of ISO standards can provide useful guidance in this regard. We describes the experience conducted at our institute in the implementation, by means of ISO 9001, ISO/IEC 19510 and ISO 31010 standards, of a clinical pathway for prostate cancer patients candidates to radiation therapy with sterotactic technique (total dose 36.25 Gy in 5 fractions) using hydrogel spacer and intraprostatic fiducial markers. After definition of the working team, the care pathway was designed based on expected process efficiency outputs, related key process indicators, as well as identification of potential risks and mitigation actions using the FMEA analysis. Each of these steps was managed in paperless through a Business Process Management framework. The established clinical pathway was tested in 98 patients treated between August 2020 and December 2022. Only one incident report related to a potential event (with no effect) was recorded; 4 cases of no hydrogel spacer/fiducial marker insertion (near miss), 6 of CT re-planning and 13 of patient re-setup for inadequate bladder/rectal preparation were reported. In the period analyzed, there was a 32% reduction of the pathway duration, while the single fraction time was in line with the available resources. Although this is a time-consuming method requiring a good knowledge of ISO standards, it has allowed for the implementation of an efficient and safe clinical pathway, which may also trigger further improvement actions. In addition, this operating method has provided a better organizational knowledge and an increased awareness of potential risks on the part of the professionals involved. The integration of a "facilitator" role, such as a department Quality/Project Manager, would be particularly helpful especially for the implementation of complex clinical pathways.

P047

REFERRAL PATTERN TO PALLIATIVE RADIOTHERAPY IN ITALIAN PATIENTS WITH ADVANCED CANCER: A SUBANALYSIS ON 534 PATIENTS FROM THE MULTICENTRIC ARISE-1 STUDY.

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Background. Pain is one of the most common symptoms among cancer patients, occurring in 75-90% of patients with advanced tumors. Radiotherapy (RT) is an effective treatment in this setting. However, evidence on the RT referral pattern in symptomatic patients is lacking. Therefore, the aim of this subanalysis of our prospective observational multicenter study (ARISE-1) was to evaluate the adequacy and efficacy of analgesic therapy in patients referred for palliative RT.

Materials and Methods. In this analysis we included 534 patients complaining of pain from 13 Italian RT Departments. RT aims and patients and pain characteristics were recorded, using a data collection sheet, during the first visit. A Pain Score was defined with values from 0 (no pain; NRS: 0) to 3 (severe pain; NRS: 7-10). An Analgesic Score was defined with values between 0 (no

pain medication) and 3 (use of strong opioids). To score the pain management adequacy we used the Pain Management Index (PMI), calculated by subtracting the Pain Score from the Analgesic Score. A PMI score < 0 indicates patients with inadequate analgesic therapy.

Results. Patients complained of cancer-related pain, non-cancer pain, and mixed pain in 71.2%, 6.0%, and 22.8% of cases, respectively. Patients were not taking analgesic therapy in 15.0% of the cases while 34.0% of them were taking non-opioid drugs. In addition, 51% of patients were under weak or strong opioids. PMI was < 0 in 28.0% of cases. Moreover, most patients with PMI ≥ 0 complained of moderate to severe pain. Overall, the rate of patients with adequate and effective therapy was only 33% (Table 1).

Conclusions. Ideally, palliative RT should be used to prevent pain from reaching levels worsening the quality of life and to avoid the need for opioid medications, given their side effects. Instead, this analysis showed a very high rate of patients candidates for palliative RT with inadequate or ineffective pain therapy, suggesting that patients are referred too late to RT. Therefore, together with the concept of "early palliative care", the approach of "early" or at least "timely palliative radiotherapy" should be promoted.

Table 1. Results.

		Number	(%)
Gender			
	Male	315	59.0
	Female	219	41.0
Age, years			
	≤ 70	327	61.2
	71-80	135	25.3
	> 80	72	13.5
ECOG-PS			
	0	15	2.8
	1	206	38.6
	2	176	33.0
	3	114	21.3
	4	23	4.3
Tumor stage			
	Metastatic	490	92.0
	Non Metastatic	44	8.0
Type of Pain			
	Cancer Pain	352	71.2
	Non-cancer Pain	30	6.0
	Mixed Pain	112	22.8
Pain score			
	(NRS: 0)	0	58	11.0
	(NRS: 1 – 4)	1	156	29.0
	(NRS: 5 – 6)	2	208	39.0
	(NRS: 7 – 10)	3	112	21.0
Analgesic score			
	(No therapy)	0	81	15.0
	(Analgesics)	1	182	34.0
	(Weak Opioids)	2	104	19.5
	(Strong Opioids)	3	167	31.5
Pain Management Index			
	< 0	151	28.0
	≥ 0	383	72.0

P048

RADIATION ONCOLOGY UNDER THE MICROSCOPE: SHEDDING LIGHT ON EFFICIENCY AND OPTIMIZATION THROUGH PROCESS MINING IN A HIGH-FLOW DEPARTMENT

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Aims. The aim of the study is to utilize process mining techniques to assist healthcare professionals in discovering, monitoring, and enhancing processes by leveraging real-world data collected daily. The goal is to prototype and visualize workflows accurately, analyzing the key events in patient treatment journeys in a high-flow Radiation Oncology department, to discover pitfalls or chances for optimization.

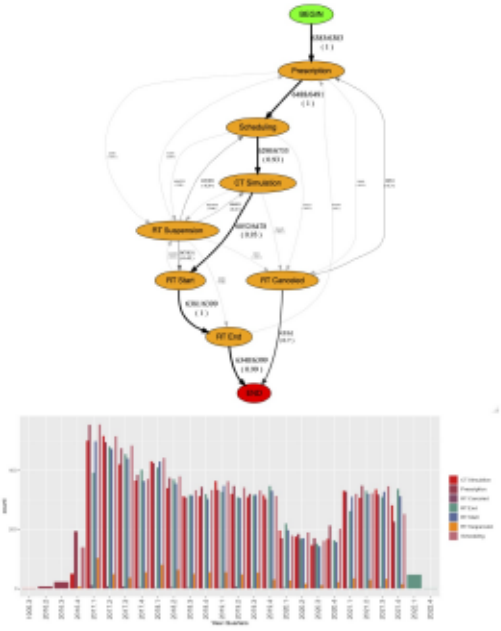
Methods. All patients who provided research informed consent and were scheduled for radiotherapy treatment between 2017 and 2021 at our department were included in this study. We developed a custom script to refine and convert data from our institutional database into an event log, identifying the significant events that represent the patient care pathway. These events included the first consultation, scheduling, CT simulation, and the start and end of treatment, as well as treatment suspensions and cancellations, categorizing the underlying causes. The process mining analysis was performed using pMineR v.046, and the Kruskal-Wallis test was used to identify time differences among priority groups.

Results. The study encompassed a total of 34,049 events, which corresponded to 6,383 treatments administered from January 1, 2017, to December 31, 2021. The primary treatment pathway was identified and visually presented in Figure 1, where the significant events were represented by bold arrows. A time-space analysis was conducted, considering the events per year quarters. Each event transition was carefully examined to detect any bottlenecks and assess the overall impact of individual transitions on the complete workflow. The median time difference for event transitions between patients who experienced treatment suspensions and those who did not was found to be statistically significant ($p<0.05$). Notably, the impact of suspensions on the time duration was significant for specific cancer types, such as Breast cancer ($p<0.05$), GI ($p<0.05$), Metastasis ($p<0.05$), H&N ($p<0.05$), further stratifying per main reason for suspension.

Conclusions. Our study clearly highlights the signif-

icance of implementing a process mining methodology, as it provides valuable insights into the actual workflow, enabling health-workers to implement effective mitigation strategies and optimize the patients' care path.

Figure 1.



P049

WHAT IF COVID-19 HADN'T EXISTED? A HYPOTHETICAL ANALYSIS TO ASSESS THE IMPACT OF COVID-19 ON A HIGH-FLOW RADIATION ONCOLOGY DEPARTMENT

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Aims. The outbreak of the COVID-19 pandemic has posed numerous challenges to healthcare systems worldwide, impacting various medical specialties, including radiation oncology departments. This study aims to investigate the impact of COVID-19 on a radiation oncology department and explores a hypothetical scenario of how the department would have operated without the pandemic, utilizing process mining and predictive models.

Methods. This study includes all patients who provided research informed consent and were scheduled for radiotherapy treatment between 2017 and 2021 at our department. We compared the actual data collected during the pandemic with simulated data from a hypothetical COVID-free period, generated by a machine learning model trained on real data before the 08/03/202. The density and the volume of treatments were used as units of comparison. The analysis was conducted using R v 4.2.2 and the pMineR v.046 library.

Results. The study analyzed a total of 34,409 events, corresponding to 6,383 treatments administered from January 1, 2017, to December 31, 2021. Our analysis reveals significant changes in patient flow and resource utilization, which coincide with the outbreak of the Sars-CoV-2 pandemic and subsequent lockdown measures implemented in Italy (from 08/03/2020 to 16/01/2021). The data from this period accounts for only 63,2% of the prescription events observed in the preceding period of the same duration, indicating a substantial decrease in the utilization of radiotherapy services during the pandemic. We stratified the treatments into priority ranks, demonstrating a reduction in attended treatments, in particular for elective treatments (Table 1). Furthermore, we analyzed the pathologies primarily affected by the decrease in treatment volume, finding that GU, Thorax, H&N, Breast pathologies as well as metatastasis were the most affected.

Conclusions. This study enhances our understanding of the consequences of COVID-19 in radiation oncology departments and provides insights for future healthcare crises. Further analysis will be conducted to better stratify the population and understand the factors contributing to the variation in treatment volumes during the pandemic e post-pandemic period.

Table 1.

Priority	Expected patients	Patients during covid	Real volume after Covid
1	117	117	226
2	582	365	670
3	313	148	307
4	141	90	100

P050

ABSTRACT WITHDRAWN

P051

AUTOMATIC SEGMENTATION IN PELVIC RADIOTHERAPY: IMPLEMENTATION AND EVALUATION OF FOUR AUTOMATIC TOOLS IN OARS CONTOURING FOR CERVICAL CANCER AND PROSTATE CANCER

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Aims. In this study, 4 automatic segmentation (AS) tools were evaluated in OAR contouring in cervical (CC) and prostate cancer (PC) treatment. The first one is an atlas-based model named Simultaneous Truth And Performance Level Evaluation (STAPLE (ST)), the second is a conventional machine learning-based model as a random forest (RF), and the last 2 are deep learning-based tools (DL), MVision (MV) and LimbusAI (LI)).

Methods. A mono-institutional consecutive series of 40 CC and 40 PC structure sets (SS) were retrospectively selected. Twenty CC and 20 PC SS (testing) were auto-segmented by ST, RF, MV, and LI and compared, setting manual contouring as the Gold-Standard. AS times have been registered. Performances have been tested by comparing the resulting 200 sets by means of the Dice Similarity Coefficient (DSC), the Hausdorff Distance (HD), and the Distance-to-Agreement Portion (DAP), i.e. the percentage of automated contours standing 1 mm-, 3 mm-, and 5 mm-far from the manual Gold-Standard (DAP_{1mm}, DAP_{3mm}, DAP_{5mm}). The Wilcoxon test has been performed to assess statistical significance.

Results. The median CC AS time per structure set was 21.9 min, 21.0 min, 0.7 min, and 1.1 min for ST, RF, MV, and LI, respectively. PC AS time was 1.8 min and 2.5 min in MV and LI, respectively, and about 20 min were required for RF and ST. In CC, rectum and bladder DL results showed a significantly increased DSC (e.g., MV *vs* ST: DSC_{Rectum}+34.4%, $DSC_{Bladder}$+20.2%). In PC, DL registered a smaller and not statistically significant DSC increase (e.g., MV *vs* RF: DSC_{Rectum}+0.3%; LI *vs* RF: $DSC_{Bladder}$+6.0%). DL performances were confirmed at the DAP comparison (e.g., in CC bladder DAP_{3mm}: MV 74.5%, ST 27.1%). In both sites, all algorithms showed excellent DSC values for femoral heads contouring. Bowel bag AS showed its dependence on cranial extension (Table 1). Contouring limitation to the manual cranial extension confirmed DSC increases (*e.g.* MV DSC_{BB} = 0.67 *vs* DSC_{BBcorr} = 0.88).

Conclusions. DL-based AS outperformed ST and RF algorithms and the strong time reduction could suggest an easier introduction in RT workflow, possibly automatizing its running in the background. An on-going study is collecting the correction times needed by 3 senior radiation oncologists to validate the AS SS. This further AS validation would confirm its cost-benefit ratio freeing up resources to facilitate patients' access to healthcare.

Table 1.

Bladder	CC	PC
ST	0.79 [0.43 – 0.94]	0.91 [0.70 – 0.97]
RF	0.90 [0.60 – 0.97]	0.87 [0.63 – 0.96]
MV	0.95 [0.89 – 0.98]	0.91 [0.91 – 0.98]
LI	0.94 [0.79 – 0.98]	0.93 [0.86 – 0.98]
Rectum		
ST	0.64 [0.35 – 0.76]	0.84 [0.74 – 0.87]
RF	0.77 [0.47 – 0.89]	0.87 [0.75 – 0.90]
MV	0.86 [0.11 – 0.93]	0.87 [0.74 – 0.92]
LI	0.83 [0.75 – 0.92]	0.86 [0.74 – 0.91]
Left FH		
ST	0.94 [0.80 – 0.96]	0.94 [0.87 – 0.96]
RF	0.95 [0.82 – 0.97]	0.95 [0.88 – 0.97]
MV	0.95 [0.81 – 0.97]	0.91 [0.84 – 0.94]
LI	0.94 [0.77 – 0.95]	0.89 [0.83 – 0.94]
Right FH		
ST	0.94 [0.66 – 0.96]	0.93 [0.87 – 0.97]
RF	0.96 [0.92 – 0.97]	0.94 [0.89 – 0.96]
MV	0.95 [0.84 – 0.97]	0.90 [0.86 – 0.95]
LI	0.95 [0.90 – 0.96]	0.88 [0.83 – 0.95]
Bowel Bag		
ST	0.83 [0.61 – 0.92]	/
RF	0.87 [0.71 – 0.93]	/
MV	0.88 [0.74 – 0.94]	/
LI	0.81 [0.55 – 0.91]	/

Table 1 – Performance comparison of automatic contouring tools in terms of Dice Similarity Coefficient (DSC) in cervical cancer (CC) and prostate cancer (PC) cases. Median and range values are reported. (ST=STAPLE, RF=Random Forest, MV=Mvision, LI=LimbusAI, FH=Femoral head).

P052

QUALITY IMPROVEMENT IN HEALTHCARE: APPLICATION OF FAILURE MODE AND EFFECT ANALYSIS IN A RADIATION THERAPY DEPARTMENT

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Background. Administering radiation therapy delivery for women affected by breast cancer is a complex process at high risk of error. Failure mode and effect analysis (FMEA) is a tool that permits the proactive identification of possible failures in complex processes, provides a basis for continuous improvement and identify failures before they happen and prioritise remedial meas-

ures. To examine the hazards associated with the process of radiation therapy delivery for women affected by breast cancer, we performed a proactive risk-assessment analysis.

Figure 1.

Materials and Methods. With a multidisciplinary team, composed of radiation oncologist, medical physicists, nurses, technicians and administrative staff, we analyzed the process inherent in the management of patients with breast cancer in the radiotherapy department. The phases of the process and the actors involved have been defined. The FMEA analysis was then applied with the identification of the risks in the various stages of the process and the subsequent assessment of the severity, probability and predictability of the events. Finally, for the highest risks, the necessary improvement actions to be applied were identified.

Results. A total of 85 potential risk modalities were identified, of which 18 were high risk. For the latter, the necessary improvement actions and the respective execution managers have been defined. After a set time, the FMEA analysis was repeated for the high-risk activities with evaluation of the implementation of the actions identified.

Conclusions. FMEA is an effective and reliable method to proactively examine complex processes in the radiotherapy department. FMEA can be used to highlight the high-risk subprocesses and allows these to be targeted to minimize the future occurrence of failures, thus improving patient safety and streamlining the efficiency of the radiotherapy department.

P053

PRELIMINARY ANALYSIS OF RADIONCOVID STUDY: EVALUATION OF THE CONSEQUENCES OF COVID-19 OUTBREAK ON ITALIAN RADIATION ONCOLOGY CENTERS AND THEIR PATIENTS

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Methods. Patients with ongoing or planned anticancer treatment at 20 Italian Radiation Oncology Centers were included in the study retrospectively from February 03,2020 to December 31,2020 and prospectively from January 01,2021 to May 31,2021. Confirmed cases were defined as patient with a positive real-time polymerase chain-reaction (RT-PCR) test.Anonymized data were collected using a dedicated online database, assessing demographic and clinical features.

Results. A total of 41039 patients were treated or had a planned treatment in the study period. Overall 123 patients had a COVID-19 diagnosis confirmed by RT-PCR during active treatment (group A) and 99 patients had a confirmed diagnosis before antineoplastic treatment start (group B). The global incidence of Covid-19 across patients with active or planned treatment in this period was 0.54% (groups A+B) and 0.30% considering only patients with a positive RT-PCR performed while already on active treatment (group A). Considering the sum of group A and group B, a total of 60 patients developed severe Covid-19 and a total of 45 patients died as a consequence of the infection, leading to an incidence of 0.15% and 0.11%, respectively. The number and incidence of total and severe Covid-19 cases and death likely due to Covid-19 divided by month are summarized in Table 1. Among the 123 patients with Covid-19 diagnosis while already on active therapy, 46 cases (37.40%) required temporary treatment suspension, 40 cases

(32.52%) definitive suspension and 37 patients did not necessitate suspension and continued treatment while positive. No toxicity increase likely associated with Covid-19 was described. As for the 99 patients with a Covid-19 diagnosis before treatment start, 53 (53.53%) experienced temporary delay (median 18.5 days, mean 25.6 days), 20 (20.20%) definitive treatment suspension and 26 (26.26%) no delay; in 9 subjects (9.09%) RT was performed while positive.

Conclusions. although mortality was high within patients with active or planned anticancer treatment diagnosed with COVID-19, the majority of the patients recovered and completed the planned therapy. Moreover, the global incidence of death due to COVID-19 or severe COVID-19 cases over the whole population treated was extremely low and decreased over time.

P054

MORE THAN FIVE DECADES OF PROTON THERAPY: A BIBLIOMETRIC OVERVIEW OF THE SCIENTIFIC LITERATURE

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Aims: Aim of this study is to provide a comprehensive bibliometric analysis of the current status and trends in scientific literature that have appeared in the field of proton therapy (PT).

Methods. The literature on PT from 1946 to 2022 in the Scopus database was searched. The research strategy included the following keywords: proton AND radiotherapy AND cancer/tumor in title, abstract, and/or keywords. The open-source R Studio's Bibliometrix package and biblioshiny (version 2.0) software were used to assess the annual production and growth rate, top-sources and authors, top contributing countries, and collaboration among countries. As far as the analysis of keywords and trends is concerned, the 2002-2022 period was considered.

Results. A total of 7,183 documents, mainly articles (n = 4716, 66%) and reviews (n = 1494, 21%), were collected from 1054 sources and 20,506 authors. Of these, roughly 80 % (n = 5711, 79.5%) were produced in the last 15 years (2008-2022), in which the mean annual growth rate was 13%.

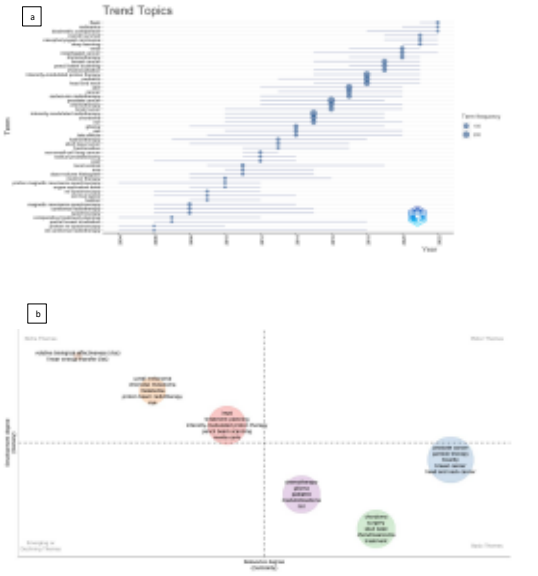

Figure 1. a: thematic evolution of keywords (2002-2022); blue dots: top-three proton therapy associated keywords for each year; the line indicates the time-span in which the keyword was hot topic as well; b: thematic map (2002-2022). This graph allows the identification of the hot topics (higher values of centrality and density) in the upper-right quadrant, the basic topics (higher values of centrality and lower values of density) in the lower-right quadrant, the peripheral topics (lower values of centrality and density) in the lower-left quadrant, and the niche topics (lower values of centrality and higher values of density).

Considering the corresponding author's country, 79 countries contributed to literature; the USA are the top contributor, with 2795 (39%) documents, of whom 84% as single-country publications (SCP), followed by Japan and Germany, with 528 and 521 documents of whom 93% and 65% SCP. Among all considered documents, 21% were publications with authors from at least two countries. Considering the themes subanalysis (2002-2022), a total of 6,647 documents were analyzed; among all keywords used by authors, top three were Radiotherapy (n = 1393, 21% of documents), Prostate cancer (n = 304, 5%), and Intensity-modulated radiotherapy (n = 286, 4%). Among disease types, prostate cancer is followed by chordoma, head & neck, and brain tumor. Change in trend themes demonstrated the fast evolution of hotspots in PT; among the most recent trends (Figure 1), the appearance of Flash, Radiomics, Relative Biological Effectiveness (RBE), Linear Energy Transfer (LET), hypofractionation, and treatment planning deserves to be highlighted.

Conclusions. Results of the present bibliometric analysis showed that PT is an active and rapidly increasing field of research. Themes of the published works encompass the main aspects of its application in clinical practice and the continuing technological advances.

P055

CAN ARTIFICIAL INTELLIGENCE REDUCE COSTS AND SPEED UP PROCESSES IN RADIATION ONCOLOGY?

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Aims. The delivery of radiation therapy requires a lengthy process from patient visit to treatment. This process involves numerous medical professionals, all connected by sophisticated software. The overall cost of a radiation therapy department to society is high. Today, the growing interest and concern about the use of artificial intelligence (AI) in medicine and healthcare has become the focus of interdisciplinary scientific research, policy debates, and societal engagement. In particular, in radiation oncology (RO), AI could potentially transform this medical specialty because of its heavy reliance on digital computing and computer software.

Methods. We searched PubMed, Scopus, and Web of Science databases using the search terms (Artificial Intelligence OR Machine Learning OR Deep Learning AND Radiotherapy) between December 2012 and December 2022. The search yielded a total of 106 scientific articles, all in English and freely available. Their geographic distribution was the following: 38 (36%) Americas, 29 (27%) Europe, 35 (33%) Asia, 4 (4%) Australia-Oceania, 0 Africa. Type of items dealt with were as follows: Segmentation 46 (43%), treatment planning 19 (18%), imaging 15 (14%), adverse events 7 (6%), dosimetry 5 (5%), RT process 21 (20%). These last 21 studies, aimed at improving RT processes, were reviewed in detail.

Results. Autosegmentation of Organs at risk (OARs) has shown significant time savings. Planning Target Volume (PTV) segmentation is more complex than segmentation of OAR due to heterogeneity of target shape, size, and location, and is therefore still at an early stage. In High-precision treatment procedures such as stereotactic body ablation RT often requires hours or even days of human labor in planning. AI also plays a role in radiotherapy imaging, treatment delivery, and quality assurance. Some works also address the role in radiomedicine.

Conclusions. Artificial intelligence and machine learning can improve the overall efficiency of processes at RT by reducing human intervention, supporting decision making, and efficiently performing tedious, repetitive tasks. This improvement could allow radiation oncologists to reallocate resources and focus on tasks such as patient counseling, education, and research, especially when resources are limited.

P056

A COMPUTATIONAL TOOL TO DEAL WITH INTERRUPTIONS IN RADIOTHERAPY TREATMENTS

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Good clinical practice dictates that radical radiation therapy (RT) treatment courses should not be interrupted. However, RT treatment interruptions commonly occur, determining prolonged overall treatment time (OTT). The effects of OTT on the therapeutic efficiency of RT, extensively discussed in the literature, vary considerably depending on several factors, including tumor type, tumor characteristics, extent of delay and the radiation schedule. In general, accelerated repopulation of RT-surviving tumour cells during these protracted intervals is responsible for the inferior results of the treatment. However, despite several formats for performing radiobiological compensations, pragmatic and non-radiobiologically justified approaches are often recommended. Driven by these considerations, we faced this issue by presenting a "homemade computational-tool" for rapidly calculating the dose per fraction ideally needed to compensate for prolonged OTT and the feasibility of its use in terms of toxicity and compliance with dose constraints. By implementing this tool, the radiation oncologist will always have the freedom to update and access a detailed library with the most recent literature regarding treatment interruptions, K-factors and trigger times for different tumor populations. On the other side, the physicist will be helped in his works by the following instruments. The calculation of a new plan dose as a function of the desired number of fractions (not strictly equal to the initially planned treatment) and the delivery dose rate. This feature will allow an instantaneous choice of the best option, considering the hospital ward availability and patient necessities. Visualization of the planned DVH before treatment interruption and its final correction under the hypothesis of a slight change in OAR volume. A mathematical tool thought to analyze the OAR Dose-Volume statistics. During the poster session, a PC demonstration of the device working with an Android version will be given.

P057

ADVANCED PROTON THERAPY APPROACHES: A MULTICENTER HIGH-QUALITY DATA REGISTRY. STUDY PROTOCOL

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Aims. Paucity and low evidence level data on proton-therapy (PT) represent one of the main issues for the establishment of solid indications in the PT setting. Aim of the present registry is to provide a tool for systematic, prospective, harmonized, and multidimensional high-quality data collection to promote knowledge in the field of PT with a particular focus on the use of hypofractionation.

Methods. All adult patients with any type of oncologic disease (benign and malignant disease) who will be eligible for PT at our Institute, will be included in the present registry. Three levels of data collection will be implemented. **Level 1**: Clinical research (patients outcome and toxicity, quality of life and cost/effectiveness analysis). **Level 2**: Radiological research (radiomic and dosomic analysis as well as biological modelling). **Level 3**: Translational research (tumor specimens, biological fluids will be collected for either biological biomarkers or genomic data analysis). A summary of collected data and possible research lines is provided in Figure 1.

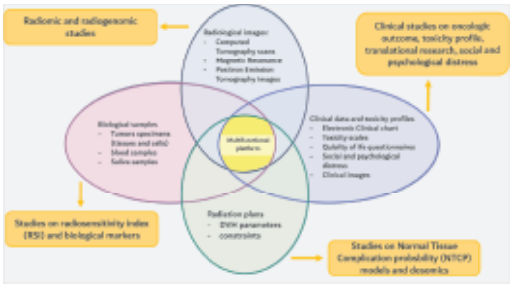

Figure 1. A schematic representation of data collected in the proton registry platform.

Results. The registry will start the recruitment in October 2023. It will be multicentric prospective data collection Registry with our Institute as Coordinator Center. The expected number of enrolled patients is 2000.

Outcome Measures. Primary: Treatment efficacy (Tumor response rate, Progression Free survival, Overall Survival). Secondary: Toxicity Profile (collected by CTCAE V5), Quality of Life (collected by internationally validated questionnaires *e.g.* EORTC, FACT-H&N, MDADI), Costs analysis.

Platform. An on cloud platform will collect all data in a centralized data storage. The study protocol has been approved by ethical committee and is going to be registred on clinical trial.gov. Additional PT facilities (equipped with IBA Proteus®ONE or Proteus®PLUS technologies) are planned to join the registry data collection. Moreover, the registry will be also fully integrated in international PT data collection networks.

Conclusions. The importance of generation of high-quality data for PT is of paramount importance for building solid scientific evidence and individuating patients who could really benefit from PT. In this scenario, the present multicentric and multi-source prospective registry may substantially foster the research endeavor at leading cancer research institutions worldwide.

P058

PROTECTIVE EFFECTS OF GRAPE SEED EXTRACT ON RADIATION-INDUCED MUCOSITIS: A PRE-CLINICAL STUDY

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Aims. The study investigated the efficacy of grape seed extract (GSE), derived from grape pomace, as a protective agent against mucosal stress caused by ionizing radiation and bacterial infections.

Methods. GSE was analyzed using high-performance liquid chromatography (HPLC-DAD) and nuclear magnetic resonance (NMR). 6-well plates containing inserts with human intestinal epithelial cells (Caco-2) treated with lipopolysaccharide (LPS), GSE or LPS+GSE, were irradiated with a flat and symmetric (± 2%) 40x40 cm2 X-Rays radiation field and a dose rate of 3Gy/min at a room temperature. Cells were irradiated with 2 Gy per day up to a maximum of 10 Gy. The analysis of the irradiated material was performed at the total doses of 0 Gy (control condition, sham), 2, 4, 6, 8, and 10 Gy. Every sham sample underwent the same enviromental and mechanical stress, except for the radiation exposure. Epithelial barrier integrity was assessed using fluorescein isothiocyanate-dextran, ROS production was measured by adding 2′,7′-dichlorodihydrofluorescein diacetate using a Tecan reader. Experiments were performed twice in triplicates.

Results. HPLC-DAD and NMR revealed that GSE contained 70% of procyanidins and 24 other metabolites. Co-treatment with GSE prevented epithelial barrier damage in LPS-treated cells (5.215 *vs* 0.3407; $p<0.05$). Irradiation increased intestinal permeability in both Caco-2 cells without LPS treatment (3.64 *vs* 0.441; $p<0.05$) and LPS-treated cells (25.5 *vs* 2.42; $p<0.05$), while GSE treatment significantly reduced this damage in both conditions (25.5 *vs* 2.04; $p<0.05$ and 38.87 *vs* 2.675; $p<0.05$ respectively). LPS and irradiation increased ROS production, but GSE treatment mitigated these effects. Moreover, LPS significantly increased ROS production in Caco2 cells (12,9 *vs* 104; $p<0.0001$) and GSE treatment significantly prevented this damage (104 *vs* 11.3; $p<0.0001$). Irradiation increased ROS production in LPS-treated cells (3056 *vs* 362; $p<0.0001$) and also in this case GSE treatment was able to reduce ROS production due to irradiation (502 *vs* 357; $p<0.0001$). This beneficial effect was observed also in LPS treated cells and then exposed to irradiation (3056 *vs* 681; $p<0.0001$) (Figure 1).

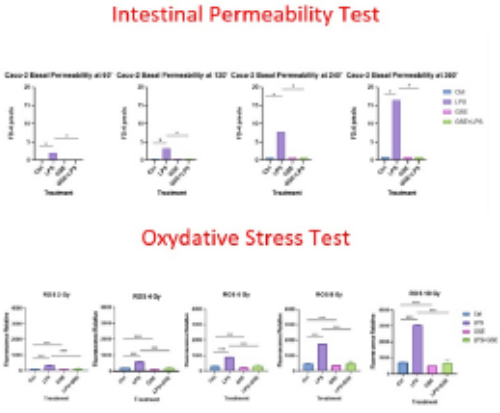

Figure 1.

Conclusions. GSE demonstrated the ability to protect intestinal epithelium from damage and reduce ROS production caused by LPS and ionizing radiation in an *in vitro* model. Further studies are needed to understand the mechanisms behind radiation-induced mucositis and GSE's antioxidant potential in prevention and clinical application.

P059

NON-MALIGNANT PAIN IN CANCER PATIENTS: PREVALENCE AND ADEQUACY OF MANAGEMENT IN 2104 SUBJECTS EVALUATED IN RADIOTHERAPY DEPARTMENTS. A SECONDARY ANALYSIS OF THE ARISE-1 MULTICENTER OBSERVATIONAL TRIAL

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Aims. Pain prevalence is high in cancer patients. Furthermore, also non-malignant pain (NMP) is frequent in this patients due to age, comorbidities, and treatment-related side-effects. Very few studies have been conducted on patients with NMP during radiotherapy (RT). Therefore, we planned a sub-analysis of a multicenter observational study (ARISE) evaluating the adequacy of pain management during RT using the Pain Management Index (PMI). Aim of this study is to evaluate the adequacy of pain management in patients reporting NMP.

Methods. Data on gender, age, ECOG-PS, aim of RT,

primary cancer, and tumor stage were collected during the normal setting of 13 Italian RT departments. A Pain Score was defined with values between 0 (no pain; NRS: 0) and 3 (severe pain; NRS: 7-10). An Analgesic Score was defined with values between 0 (no pain medication) and 3 (use of strong opioids). The PMI was calculated by subtracting the pain score from the analgesic score with negative values indicating poor pain management.

Results. Four hundred fifty-six patients (21.7%) reported NMP. Among them, the PMI value was <0 (inadequate pain management) in 71.5 % of cases. The risk of PMI<0 was significantly higher in NMP compared to cancer-related pain (OR: 2.630; 95%CI: 1.879-3.683; p<0.001). Patients were referred to curative and palliative RT in 91.2% and 8.8% of cases, respectively. Patients undergoing curative and palliative RT showed PMI<0 in 72.3% and 62.5% of cases, respectively. Moreover, patients with non-metastatic disease and subjects with metastases had PMI<0 in 72.5% and 64.4% of cases, respectively. Specifically: i) of patients with mild NMP (Numeric Rating Scale, NRS: 1-4) 100% were not taking analgesics; ii). of patients with moderate NMP (NRS: 5-6) 38.3% were not taking analgesics and 61.7% were taking non-opioid medications; iii) of patients with severe NMP (NRS: 7-10) 33.3% were not taking analgesics, 54.5% were taking non-opioid analgesics, and only 12.2% were taking opioid medications. The following parameters were significantly (p<0.05) correlated to NMP with PMI<0: female gender, better ECOG-PS score (ECOG-PS=1), and breast cancer.

Conclusions. This analysis confirms a non-negligible prevalence of NMP in cancer patients. Furthermore, most of these patients have inadequate pain management. This result suggests that physicians pay little attention to non-cancer-related symptoms in cancer patients and therefore the need for a more patient-centered approach.

P060

USE OF KARIOSYTE• IN THE PREVENTION AND TREATMENT F MUCOSITIS IN HEAD AND NECK CANCER PATIENTS UNDERGOING RADIOTHERAPY

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Aims. This observational study aims to assess the effectiveness of Kariosyte®, a concentrated solution containing antioxidant substances such as Epigallocatechin-3-gallate and Beta-Caryophyllene, in preventing and treating oral cavity lesions caused by chemoradiation therapy (CRT). The study also evaluates its impact on nutritional intake in patients undergoing CRT for head and neck cancer (HNC).

Methods. Between December 2022 and May 2023, we included 26 patients (aged 18 years or older) with HNC (T1-4, N0-3). The patient cohort consisted of 12 (49%) oral cancer, 6 (25%) laryngeal cancer, 6 (21%) pharyngeal cancer, and 2 salivary gland cancer cases (5%). Of these patients, 10 received curative CRT, 2 received curative radiotherapy (RT) alone, 4 received adjuvant CRT, and 10 received adjuvant radiotherapy alone. The patients were randomly assigned to two treatment arms: 13 patients in arm 1 and 13 patients in arm 2. In arm 1, all patients were instructed to maintain excellent oral hygiene and use Kariosyte® three times a day throughout the entire duration of RT and for up to 15 days after treatment completion. In arm 2, patients were advised to maintain excellent oral hygiene, and Kariosyte® was introduced only when oral mucositis reached or exceeded grade 1 severity based on the Common Terminology Criteria for Adverse Events (CTCAE) scale version 5.0.

Results. None of the patients from either treatment arm discontinued RT. In arm 1, by the end of treatment, 4 patients (18%) developed grade 2 (G2) mucositis, and 2 patients (5%) developed grade 3 (G3) mucositis. The median incidence of mucositis occurred at week 3 of treatment, with a median radiation dose of 30 Gray (Gy). In arm 2, 8 patients (35%) presented with G2 mucositis and 5 patients (19%) with G3 mucositis at week 2 of treatment, with a median radiation dose of 20 Gy. All patients were able to continue RT and maintain a regular oral diet.

Conclusions. The combination of using Kariosyte® upfront along with good oral hygiene practices demonstrates efficacy in reducing and preventing severe acute oral mucositis during RT treatment in HNC. This approach enables patients to maintain a regular oral diet and continue RT without interruption.

P061

SYSTEMATIC SCHEDULING OF FOLLOW-UP VISITS AFTER PALLIATIVE RADIOTHERAPY: IS IT USEFUL? PRELIMINARY RESULTS OF A MONOCENTRIC EXPERIENCE

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Aim. After palliative radiotherapy (RT), patients are frequently referred to primary care providers. However, these patients may require progressive adaptations of supportive therapy and, in particular, of analgesic therapy. Additionally, in case of insufficient symptomatic response, re-irradiation may be indicated. Finally, it is not uncommon, in patients with multiple metastases, together with the symptomatic response of the irradiated site, the appearance of new symptoms in different sites. Therefore, in our center, we planned a specialist follow-up service dedicated to patients undergoing palliative RT. The purpose of this report is to analyze the preliminary results of this experience.

Material and Methods. Since February 2023, we have been running a follow-up outpatient clinic for patients treated with palliative RT for symptom relief, managed by a radiation oncologist (RO) with experience in palliative and supportive care. During the visits, the symptomatic response and toxicity after RT are systematically analyzed. In addition, the RO systematically evaluates the need for adjustment of pain management and treatment of other symptoms, the need for re-irradiation in the same treated site, or for irradiation of new symptomatic sites. In patients in poor general conditions and/or residing far from our hospital, it is offered the possibility of performing a telephone interview with patient and caregivers instead of the outpatient visit.

Table 1. Results.

	number	%
All patients	53	100
All visits	74	100
Contact performed by		
Medical examination in the hospital	52	70.3
Phone	23	31.1
Adaptation of pain management	16	21.6
Planned re-irradiation at the same site	2	2.7
Planned irradiation in a different site	7	9.5
Patients with pain	27	36.5
Pain Management Index < 0 (inadequate pain management)	5	6.8
Patients with others symptoms	21	28.4
Relief of treated symptom	43	58.1
Toxicity (grade 1-2)	13	17.6
Deceased	6	8.1

Results. From February to May 2023, 74 follow-up visits were performed. The results of the analysis are shown in Table 1. Out of 74 visits performed, 5 patients with inadequate pain management were identified and, overall, pain management was adapted to the changing symptoms in 16 subjects. In addition, re-irradiation to the same site or irradiation of new symptomatic sites was planned in 2 and 7 patients, respectively. Overall, an adjustment of drug therapy or RT strategy was performed in 33.8% of subjects.

Conclusions. The preliminary results of the activity of a follow-up clinic dedicated to patients undergoing palliative RT showed the possibility of early intervention on emerging or residual symptoms in over one third of subjects. The continuation of our study will allow us to provide more reliable data on the usefulness of this service.

P062

WHICH PATIENTS IRRADIATED TO THE PELVIS COULD BENEFIT FROM PROBIOTICS AND NUTRITIONAL SUPPLEMENTS? A POOLED ANALYSIS OF OBSERVATIONAL CLINICAL TRIALS TO ESTABLISH A CURRENT BENCHMARK AND A PREDICTIVE MODEL

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Aims. Gastrointestinal (GI) acute toxicity (AT) is a known limitation of radiotherapy (RT) in pelvic cancers. Therefore, the use of probiotic and antioxidant dietary supplementation has been proposed for these patients. However, the utility of these treatments should be validated in prospective clinical trials. This would require benchmark data on AT in patients irradiated with modern RT techniques. Furthermore, these studies should be directed to patients with high risk of GI AT. Therefore, there is a need for preliminary studies to identify these patients' categories. Therefore, the aim of this analysis is to define the risk of GI AT in patients irradiated to the pelvis with modern RT techniques and to identify high-risk categories.

Methods. For the purposes of this analysis, data regarding GI AT (RTOG scale) were collected in all patients enrolled in our center, in the period October 2022 - April 2023, in prospective observational studies on pelvic RT (prostate, rectal, anal, uterine, and cervical cancers) delivered with Volumetric Modulated Arc Therapy. Overall AT rates were calculated and the impact on AT of

a number of parameters (gender; age; mesorectal, obturator, external iliac and inguinal lymph nodes irradiation; concurrent chemotherapy) was evaluated using the chi square test.

Table 1.

Table 1: Acute toxicity rates and impact of patient and treatment data. Statistically significant p-values are shown in bold.

			GASTROINTESTINAL TOXICITY GRADE				
		TOT	G0	G1	G2	G3	p
All patient		83	45 (51.8%)	28 (33.7%)	11 (13.3%)	1 (1.2%)	
Gender	M	39	20 (51.3%)	14 (35.9%)	5 (12.8%)	0	0.801
	F	44	23 (52.3%)	14 (31.8%)	6 (13.6%)	1 (2.3%)	
BMI	<30	69	33 (47.8%)	24 (34.8%)	11 (15.9%)	1 (1.4%)	0.282
	≥30	14	10 (71.4%)	4 (28.6%)	0	0	
Concurrent chemotherapy	no	49	32 (65.3%)	14 (28.6%)	3 (6.1%)	0	0.011
	yes	34	11 (32.4%)	14 (41.2%)	8 (23.5%)	1 (2.9%)	
Prophylactic nodal irradiation	no	32	13 (91.7%)	3 (8.3%)	0	0	0.029
	yes	71	32 (45.1%)	27 (38%)	11 (15.5%)	1 (1.4%)	
Mesorectal irradiation	no	82	37 (39.7%)	33 (33.9%)	4 (8.9%)	0	0.002
	yes	21	6 (28.6%)	7 (33.3%)	7 (33.3%)	1 (4.8%)	
External iliac nodes irradiation	no	40	27 (67.5%)	11 (27.5%)	2 (5%)	0	0.024
	yes	43	16 (37.2%)	17 (39.5%)	9 (20.9%)	1 (2.3%)	
Inguinal nodes irradiation	no	73	41 (56.2%)	28 (38.4%)	4 (8.2%)	0	<0.001
	yes	10	2 (20%)	2 (20%)	5 (50%)	1 (10%)	
Dose to the pelvic nodes	0 Gy	32	30 (71.4%)	4 (28.6%)	0	0	0.634
	≤50 Gy	56	23 (41.1%)	24 (42.9%)	8 (14.3%)	1 (1.8%)	
	>50 Gy	15	8 (53.3%)	4 (26.7%)	3 (20%)	0	
BED α/β 10 to the pelvic nodes	0 Gy	32					0.758
	≤50 Gy	64	28 (43.8%)	26 (40.6%)	9 (14.1%)	1 (1.6%)	
	>50 Gy	7	3 (42.8%)	2 (28.6%)	2 (28.6%)	0	
Boost (GTV or tumor bed)	0 Gy	4					0.349
	≤68 Gy	49	22 (44.9%)	17 (34.7%)	9 (18.4%)	1 (2%)	
	>68 Gy	30	18 (60%)	10 (33.3%)	2 (6.7%)	0	
BED α/β 10 of the boost	0 Gy	4					0.161
	≤72 Gy	48	22 (45.8%)	18 (33.3%)	9 (18.8%)	1 (2.1%)	
	>72 Gy	31	18 (58.1%)	11 (35.5%)	2 (6.5%)	0	

Results. Overall, 83 patients were included in the analysis (Table 1). The rate of grade 1, 2, and 3 AT was 33.7%, 13.3%, and 1.2%, respectively. The following parameters were found to be significantly related to the AT rate: concurrent chemotherapy (p: 0.011), prophylactic nodal irradiation (p: 0.029), mesorectal irradiation (p: 0.002), external iliac nodes irradiation (p: 0.024), Inguinal nodes irradiation (p: <0.001) (Table 1). By combining these risk factors (RF), a simple predictive model of grade ≥ 2 AT was developed: LOW RISK (0-2 RF, AT: 6.5%), HIGH RISK (3-5 RF, AT: 38.1%).

Conclusions. "Modern" pelvic RT produces low rates of significant AT. A predictive model of AT was developed and will be validated with a subsequent cohort of patients to be recruited in the period April 2023 - April 2024. The definitive results of this study will allow us to define the ideal patient population to test innovative supportive therapies based on probiotics and nutritional supplements.

P063

ARE WE LOOKING AT THE PATIENT OR JUST AT THE TUMOR? UNEXPECTEDLY HIGH RATE OF CANCER PATIENTS WITH NON-MALIGNANT PAIN: A LITERATURE REVIEW

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Aim. A holistic care should include attention to all patient needs and symptoms, regardless of their origin. Instead, some studies suggested a high incidence of non-malignant pain (NMP) and frequent poor management of NMP in cancer patients. However, this topic has been investigated in only a few studies and, currently, specific guidelines for NMP management in cancer patients are lacking. Therefore, the aim of this literature review is to collect the available evidence on the incidence and management of NMP in cancer patients.

Materials and Methods. We conducted a literature review selecting in PubMed the papers reporting incidence and/or management of NMP in cancer patients, without time limits and using various combinations of terms such as "non-malignant pain" and "non-cancer pain". Given the lack of homogeneity of methodology and setting across the analyzed papers, we did not perform a quantitative analysis (meta-analysis) but only a qualitative description of characteristics and results of the selected reports (Table 1). In most studies, the adequacy of pain management was analyzed with the Pain Management Index (PMI), calculated by subtracting the pain score from the analgesic score. A negative PMI value indicates inadequate analgesic prescription.

Results. Based on the inclusion criteria, 13 papers were selected: 12 reporting on prospective studies and one on a retrospective study. The total number of patients with pain was 17,974. NMP prevalence rates ranged from 4.9% to 55.4% (median: 30.0%). Eight studies analyzed the adequacy of pain management showing poor management (PMI<0) in 71.5-91.4% of cases. Furthermore, opioid therapy of NMP was recorded in 12.2% and 49.0% of subjects in two studies. Finally, one study reported significantly worse NMP management compared to cancer-related pain (p<0.001).

Conclusions. Our review confirms a non-negligible prevalence of NMP in cancer patients. Furthermore, NMP was significantly undertreated pharmacologically. Therefore, this finding suggests that clinicians underestimate non-cancer-related symptoms in cancer patients and hence the need to improve attention to all patient-reported symptoms.

Table 1.

P064

EFFICACY OF A PROPOLIS AND HYALURONIC ACID BASED MOUTHWASH IN PREVENTING RADIATION-INDUCED MUCOSITIS IN LOCALLY ADVANCED HEAD AND NECK CANCER

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Aims. To evaluate the efficacy of a mouthwash (fructose, PVP, Propolis, hyaluronic acid, sodium xsal, aroma, sodium benzoate, potassium sorbate, water, green tea 95%, EGCG, b-caryophyllene, fluid extract of Syzygium aromaticum), in preventing radiation-induced mucositis in locally advanced head and neck cancer patients.

Methods. Patients were treated with concurrent chemoradiotherapy (CRT) or exclusive radiotherapy(RT). Every patient received mouthwash from the beginning of CRT/RT until the first follow-up. Patients underwent a weekly clinical exam with assessment of mucositis according to CTCAE (vers. 5.0) and with weight monitoring. Patients were also evaluated 3 weeks after the end of RT.

Results. To date, 10 patients were enrolled. Median age was 70. Four (40%) completed the protocol and were evaluated at 3 weeks follow up. Six patients are still on treatment. Grade 2 toxicity occurred in 2/10 patients (20%) and it was detected at the third week of treatment. No patients experienced grade 3 toxicity. Two PEG patients had a mean weight gain of 5 kg. Seven patients lost an average 2,4 kg and one remained stable. One patient discontinued CRT for 15 days due to bacterial pneumonia requiring hospitalization.

Conclusions. The mouthwash was well tolerated and delayed mucositis that was induced by CRT or RT, allowing for continued treatment for locally advanced head and neck cancer.

P065

SEGMENTATION WITH DEEP NEURAL NETWORKS IN IDH MUTATED GRADE 4 ASTROCYTOMA AND GLIOBLASTOMA TO PREDICT PATTERNS OF RELAPSE: A MULTICENTER AND MULTIAPPROACH ANALYSIS

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Aims. The aim of our study is to develop a predictive algorithm of relapse disease based on clinical data and deep neural networks, in order to personalise loco-regional treatment for patients with high grade glioma (HGG).

Methods. We initiated a retrospective multicenter study of HGG patients, from 2009 to 2021, at 3 French medical centers, participating in a national funding for artificial intelligence in oncology clinical practice (AI.DReAM project). Clinical and MRI pre-radiotherapy (RT) and relapse data, RT data, disease-free survival (DFS), and overall survival (OS), are being collected. A team of expert radiation oncologist is currently identifying disease volumes on pre-RT and relapse MRI. The deep neural network, for automatic HGG segmentation, in both time points is under development. Relapse patterns were differentiated by MRI into local (lR) and disseminated (dR) and we started evaluating relapse patterns based on the intersection between the relapse area and the

95% isodose line RT and the distance between the CTV and the relapse volume. As a preliminary study phase, we conducted univariate analysis with the chi-squared test and multivariate analysis with logistic regression to identify only clinical predictors of dR.

Results. A total of 976 patients' data were collected. In this preliminary analysis, we evaluated data from 203 patients: 70% were male, 28% were > 69 yrs. 16.7% of the patients had disseminated disease at diagnosis. The temporal lobe was the most frequent site (54.6%), while 26.6% of the patients had a deep location. 43% of the patients underwent total tumor resection while 36% had only biopsy. MGMT methylation was observed in 34% of the patients. The median RT dose was 60 Gy [33 Gy-72 Gy]. 98.5% of the patients received Temozolomide along with RT. The median DFS was 7 months, while the median OS was 17.6 months [3 to 92 months]. Univariate analysis showed a correlation only between initial disseminated and bi-hemispheric disease and dR (p=0.015 and p=0.012, respectively). Multivariate analysis did not show any correlation between our data and dR.

Conclusions. Preliminary results of our study did not show an association between the analyzed data and dR. Currently, imaging analyses of the first 600 patients (pre-RT and relapse MRI) are ongoing using deep neural networks, and subsequently, the relapse prediction algorithm will be tested on the complete cohort. The results will be presented at the congress.

P066

CONTRIBUTION OF RADIOMICS FOR PREDICTING OVERALL SURVIVAL IN PATIENTS WITH HIGH-GRADE GLIOMAS WITH SUBTOTAL RESECTION - APPLICATION TO A MULTICENTRE COHORT

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Aims. The objective of this study is to use radiomic analysis of multiparametric MRI combined with clinical data in patients with high-grade gliomas (HGG) who underwent subtotal resection (STR) to identify a predictive signature of survival (OS).

Methods. We initiated a retrospective multicenter study of HGG patients, from 2009 to 2021, at 3 French medical centers, participating in a national funding for artificial intelligence in oncology clinical practice (AI.DReAM project). Clinical and pathological data, pre-radiotherapy (RT) and relapse MRI, were collected. A deep learning algorithm was used to generate three tumor subregions based on the international BraTS challenge 2020: label 1 representing the tumor necrotic part, label 2 corresponding to T2/FLAIR hypersignal, and label 3 indicating the gadolinium-enhanced region. The cohort was divided into a training set of 189 patients and an independent test set of 48 patients. A repeated 10-fold cross-validation was performed to ensure the robustness of the model on the training set. Survival stratification was based on the median OS in months within our cohort. The Pyradiomics library was used for radiomic feature extraction. An XGBoost architecture was selected to build the final model, including 312 radiomic features per segmented volume (104 features per MRI sequence) and 14 clinical variables.

Results. A total of 976 patients were initially included in the study; however, for this preliminary analysis, only patients who underwent STR with automatic segmentation were considered, resulting in a sample size of 237 patients. Among these patients, 82% were wild-type IDH and 8.4% exhibited MGMT methylation. The area under the ROC curve (ROC-AUC) for survival prediction based on radiomic and clinical parameters alone were 0.61 and 0.60, respectively, in the validation test. Combining radiomic variables with clinical variables showed slightly higher performance with a ROC-AUC of 0.67 in cross-validation and 0.64 in the validation test.

Conclusions. In this study, we obtained a generalizable estimate of OS using radiomics. At the upcoming congress, we will present comprehensive data on the entire study cohort, further stratified based on the extent of resection and residual volume. This expanded analysis will involve an increase in the number of labels up to 10 and will incorporate manual contouring performed by a team of experienced radiotherapists, as well as a deep neural network to help the segmentation.

P067

STEREOTACTIC RADIOTHERAPY FOR BREAST CANCER BRAIN METASTASES: OUTCOME EVALUATION AND PROGNOSTIC FACTORS ASSESSMENT

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Aims. Breast cancer (BC) is the second most common cause of brain metastases (BMs). The incidence of brain metastases is increasing due to the longer overall survival related to modern systemic therapies (STs) and the greater use of MRI able to detect also small lesions. Despite availability of new STs, in cases of limited number and/or volume of BMs, local treatment remains the mainstay: radiosurgery (SRS) or hypofractionated radiosurgery (HSRS) exclusive or after surgery. We evaluated the clinical outcomes of a large series of BM-BC patients treated in our center using SRS, in terms of Local control (LC). Brain distant failure (BDF), progression-free survival (PFS) and overall survival (OS) were analysed too.

Methods. For target definition and organs at risk delineation, post contrast T1MRI were acquired and basal CT scan was used for radiotherapy planning after coregistration. Different total doses and fractionation were delivered: 24-25Gy/1fraction, 20Gy/1fraction, 32Gy/4fractions, 30Gy/5fractions, according to tumor size and location, and 27-30Gy/3 fraction in cases of adjuvant HSRS after surgery

Results. From October 2004 to August 2022, 169 patients, for a total of 504 BMs treated were evaluated. Patients and treatment characteristics are reported in Table 1. The median follow-up time was 24 months for the whole cohort and 54 months for alive patients. Median LC time was not reached, 1, 3 year LC rates were 91.2%, and 79.5%, respectively. The median time, 1, 3 year BDF were 15 months, 44.3%,76.8%. Median time, 1, 3 year PFS were 16 months, 53.6%,33.5%. Median time, 1,3 year OS from radiotherapy were 39 months, 74.8%, 51.8%, and it improved by the starting a ST after the BM treatment at both univariate and multivariate analysis [p=0,0010]. Molecular profile, interval time until BM diagnosis, systemic therapy after SRS were observed as conditioning outcome.

Conclusions. To our knowledge this is the largest series of BM-BC treated with SRS. Satisfactory local control has been obtained conditioning survival. A careful assessment of prognostic factors and multidisciplinary evaluation are mandatory for the optimal therapeutic approach.

Table 1. Patients and treatment characteristics

Median Age at BC diagnosis 48 years old		
	n of patients	%
Molecular profile		
Luminal A	22	13%
Luminal B	35	21%
HER2	82	48%
Triplo negativo	30	18%
Status at the diagnosis		
Localized	108	64%
Metastatic	61	36%
of which		
1 Organs	29	48%
2 Organs	10	15%
3 Organs	15	25%
4 Organs	4	7%
5 Organs	3	5%
Median interval time from diagnosis to BM: 42 months		
Median age at BM diagnosis: 54 years old		
Number of BM lesions		
1 lesion	90	53%
from 2 to 5 lesions	65	38%
from 6 to 10 lesions	11	7%
> than 10 lesions	3	2%
Extracranial disease during BM treatment		
No extracranial disease	34	20%
Extracranial disease	135	80%
of which		
1 Organs	41	30%
2 Organs	44	33%
3 Organs	29	21%
4 Organs	17	13%
5 Organs	4	3%
Brain Metastases treatment		
Surgery	48	28%
RT alone	121	72%
of which		
HSRS	27	22%
SRS	94	78%
Systemic treatment after local BM treatment		
No	31	18%
Yes	138	82%

P068

THE MULTIDISCIPLINARY METHOD TO DISTINGUISH TRUE TUMOUR PROGRESSION FROM PSEUDOPROGRESSION IN HIGH GRADE GLIOMA VIA THE SYSTEMIC INFLAMMATORY MARKERS

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Aims. To identify the role of serum inflammatory markers and T1-gadolinium volume (T1GV) post-radiotherapy (RT), in the multidisciplinary approach to differentiate true tumor progression (TTP) from pseudo-progression (PsP) in high-grade glioma (HGG) patients.

Methods. A retrospective cohort of HGG (WHO 2021) from 2015 to 2021 was enrolled, based on pattern of PsP or TTP within 6 months and simultaneous blood testing. Clinical, instrumental, and therapeutic data were collected at diagnosis, treatment and within 6 months after RT. Treatment's response was assessed according to modified RANO criteria; volumetry of suspected progression was performed on T1G and FLAIR. Blood tests analysed neutrophil/lymphocyte ratio (NLR), systemic immune-inflammatory index (SII) and systemic inflammatory response index (SIRI). Any association between clinicopathological factors and progression was analysed by Chi-square and Fisher's exact test. Differences between groups in continuous variables were assessed by independent sample-T test or Mann-Whitney U test. Due to an existing multicollinearity in the common multivariate regression model between the variables "NLR" and "SII index", two further separate binary regression models were set up, whereby in the "Multivariate Model NLR" the SII index was not considered and in the "Multivariate Model SII index" the NLR was not included. A Cox regression analysis was conducted to assess the impact of PsP- and TTP-related factors on overall survival (OS).

Results. 16 out of 39 patients showed PsP and 23 TTP. NLR, SII and T1GV were higher in TTP than in PsP (respectively 4.7 *vs* 2.8, p= 0.002; 890.5 *vs* 546.5, p = 0.009; and 11.7 cm^3 *vs* 2.2 cm3, p<0.001). Further differences between the two groups are reported in Table 1.

Table 1. Differences between patients with pseudoprogression and progression disease (N=39).

		Pseudoprogression (N = 16)	Progression (N = 23)	p
Gender	Female	7 (43.8%)	9 (39.1%)	0.77
	Male	9 (56.3%)	14 (60.9%)	
MGMT methylation	No	9 (56.3%)	14 (60.9%)	0.77
	Yes	7 (43.8%)	9 (39.1%)	
T1 gadolinium volume (cm^3)		3.6 ± 4.49	19.8 ± 25.21	<0.001*
		2.2 (0.1 - 13.9)	11.7 (0.2 - 94.4)	
Platelets		199.7 ± 70.99	212.7 ± 88.12	0.62
		196.5 (82.0 - 323.0)	209.0 (52.0 - 481.0)	
Neutrophils		4.5 ± 2.55	5.9 ± 2.39	0.061
		4.1 (1.8 - 10.3)	5.5 (1.9 - 10.1)	
Lymphocytes		1.4 ± 0.62	1.1 ± 58	0.18
		1.3 (0.5 - 2.5)	0.8 (0.3 - 2.0)	
Monocytes		0.5 ± 0.22	0.7 ± 0.44	0.51
		0.5 (0.3 - 1.1)	0.7 (0.0 - 2.0)	
NLR		4.1 ± 3.72	7.3 ± 7.26	0.002*
		2.8 (1.1 - 16.0)	4.7 (2.8 - 36.1)	
SII index		915.5 ± 1215.34	1511.0 ± 1615.33	0.009*
		546.5 (152.0 - 5157.0)	890.5 (397.5 - 7538.9)	
SIRI		2.1 ± 2.26	5.8 ± 8.17	0.06
		1.5 (0.7 - 9.9)	3.3 (0.8 - 36.1)	

Any association between the clinicopathological factors and the presence of progression were analysed by Chi-square and Fisher's exact test. Differences between group in continuous variables were assessed by independent sample-T test or Mann-Whitney U test, as appropriate.

A multivariate "NLR" regression model showed NLR (OR 7.9, 95%CI: 1.4 to 45.3, p=0.020) and T1GV (OR 3.0, 95%CI: 1.4 to 6.7, p=0.007) as predictors of PSP; whereas the "SII model" confirmed the effect of T1GV [OR 2.7, CI 95% 1.3 to 5.5, p=0.006)] and SII [OR 4.2, 95%CI: 1.1 to 15.3, p=0.030]. The OS was significantly worse in TTP compared to PsP [HR 3.97, 95%CI: 1.59 to 9.93, p=0.003]. At multivariate analysis other factors didn't impact the OS.

Conclusions. Higher NLR, SII and T1GV showed good sensitivity and specificity to differentiate between PsP and TTP. Further studies with larger cohorts are needed to evaluate the inclusion of inflammatory indixes and volumetry in the differentiation diagram of PsP from TTP.

P069

ASSESSMENT OF POST-RADIOSURGERY RESPONSE FOR INTRACRANIAL MENINGIOMA: UPDATE ON TYPE OF ANALYSIS AND CUT-OFF VALUE

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Aims. Defining both a threshold of progression and the optimal endpoint for clinical trials on radiation therapy for benign meningioma is difficult. In fact, the growth rates of meningiomas are variable, overall survival (OS) is often very long, and progression-free survival (PFS) requires long-term follow-up. To assess radiation response various strategies have been evaluated. Although most of the published studies describe the used criteria for control assessment, there is no uniform definition. On the other hand, the more reliable criteria used to evaluate other tumor types, including high-grade glioma or metastases, do not seem to be suitable for meningioma evaluation. Volumetric analysis of MRI imaging has been proposed as the most appropriate method for detecting change in slowly evolving brain tumors. In this scenario, we analyzed this method in post-radiosurgical intracranial meningiomas as part of a prospective clinical trial. The primary aim of the present study was to validate a volumetric assessment method after fractionated radiosurgery (f-RS) treatment of benign intracranial meningiomas. Secondary aims were evaluation of a cut-off to define progression, stable or partial response and volumetric response after f-SRS.

Methods. To validate the volumetric assessment, we appraised Δ values of volume variations. To evaluate tumor response, a volumetric analysis has been performed by means of co-registration of each follow-up MRI on baseline MRI and contouring of the lesion on each post-treatment MRI.

Results. Overall, 118 patients were considered eligible for the purpose of the volumetric analysis. After a mean time of follow-up of 86.5 months ([SD 17], median 84, range 60–120 months) the median reduction in tumor volume was -26%. Baseline volumes were similar in each group (p=0.092), and final volumes were significantly

larger in tumors that progressed ($p < 0.001$) using a ΔV of 20% as a cutoff for progression. The 20% ΔV became significantly different by 10 months, with continued diversion up to 36 months. Moreover, we calculated a new cut-off for response-to-treatment definition by means of Gaussian mixture model and frequency band clustering, in order to find a cut-off for standardizing evaluation.

Conclusions. Our results suggest quantitative volumetric assessment of tumor response to f-RS may help clinicians to better understand early response profiles and provide a valuable tool for patient management following f-RS for meningiomas.

P070

IDH1 MUTATION DETECTED IN LIQUID BIOPSY IS ASSOCIATED WITH SURVIVAL OUTCOME IN GLIOMA PATIENTS

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Background. Since circulating free DNA (cfDNA) represents a useful tool to detect molecular alterations and depends on tumor characteristics, its detection in glioma is challenging. This study evaluates the correlation between the IDH1 mutation in cfDNA with survival and clinical characteristics in glioma patients.

Methods. Samples blood of glioma patients were collected between 2015 and 2018. CfDNA was extracted from plasma and IDH1 p.R132H mutation analysis was performed on a digital droplet PCR. Statistical analysis was performed to investigate the prognostic power of such mutation and any association with clinical factors. Sixty-seven patients were enrolled. The present project has been approved by Pisa Ethics Committee, Comitato Etico Area Vasta Nord Ovest: 2015-787. Survival estimates has been performed using the Kaplan-Meier method, and differences will be compared using the log rank test. Hazard ratios (HR) and 95% confidence intervals (CI) has been obtained using Cox's proportional hazard model.

Results. A concordance between IDH1 status in tissue and in plasma was found (p=0.0004). The presence of the IDH1 mutation was associated with longer median OS in tissue (138.8 months *vs* 25.6, p<0.0001) and cfDNA (116.3 months *vs* 35.8, p=0.016). A univariate cox regression analysis found a significant association between IDH1 mutation both in tissue and cfDNA, age, tumor grade and OS. No statistically significant association between IDH1 mutation and tumor grade was found (p=0.07).

Conclusions. This study shows that liquid biopsy is a useful tool in brain tumors to detect molecular alterations. IDH1 mutation detected in liquid biopsy constitutes an important prognostic biomarker in patients with different types of gliomas, being associated to OS.

P071

RELATIONSHIP BETWEEN BRAIN LOCATION AND DEVELOPMENT OF RADIONECROSIS AFTER BRAIN FRACTIONATED STEREOTACTIC RADIOTHERAPY

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Aims. Radionecrosis is a late radiation damage with a variable percentage of incidence ranging from 5 to 26%. Its etiology is multifactorial. The aim of this study is to map the incidence of RN (symptomatic and asymptomatic) in patients treated with fractionated brain stereotactic radiotherapy (FSRT) and evaluate whether some brain areas are more susceptible to radiation damage.

Methods. In this retrospective observational descriptive study we included patients treated in our institution with stereotactic radiotherapy (FSRT) from March 2015 to July 2021. Radiological radionecrosis was assessed by two neuroradiologists. They reviewed for each patient all MRI performed (pre and post FSRT) with particular sequences (T1 s, T1 c+, T1 post-contrast, T2, T2/Flair, DWI ADC) and defined as radiological RN the central core of the stereotreated lesion surrounded by an area of edema, resulting in the typical "cut green pepper" ("swiss cheese" or "soap bubble). Moreover they mapped all the radionecrosis, using a radiological atlas iMAIOS. We defined as symptomatic patients those who needed corticosteroid therapy or, being refractory to cortisone therapy, started anti-VEGF therapy or underwent surgical removal of necrosis. We also recorded dosimetric data

(dose/volume of treated lesions, volume of irradiated normal brain, number of treated lesions, cumulative intracranial volume of disease) and clinical data (previous treatments, concomitant systemic therapy, primary tumor).

Results: we included 75 patients for a total of 208 brain metastases; the median total dose was 27 Gy (range min.12Gy-27Gy) delivered in 3 fractions. The total incidence of asymptomatic radiological RN was 17,8% and the incidence of symptomatic radionecrosis was 4.8%. Topographic distribution of radiological radionecrosis was as follows: 29. 7% subcortical region, 24,1% deep periventricular region, 21,2% cerebellum, 20.0% brainstem). The site of brain metastasis was correlated with symptomatic radionecrosis (cerebellar: p= 0.006; deep periventricular region: p=0.005), not with asymptomatic (p=NS). Dosimetric factors were associated with the risk of developing radiological radionecrosis (volume of lesion: p= 0.02, and cumulative intracranial volume: p= 0.04).

Conclusions. Cerebellar and deep ventricular sites of brain metastasis resulted associated with a greater incidence of symptomatic radionecrosis revealing a particular susceptibility to radiation induced damage.

P072

HYPOFRACTIONATED VERSUS CONVENTIONALLY FRACTIONATED RADIATION THERAPY WITH TEMOZOLOMIDE FOR PATIENTS WITH GLIOBLASTOMA: AN INSTITUTIONAL EXPERIENCE

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Aims. Hypofractionated radiation therapy (HF-RT) schedules may have radiobiological, patient convenience and healthcare resource advantages over conventionally fractionated radiation therapy (CF-RT) in glioblastoma (GBM). We report outcomes of GBM patients treated with HF-RT and CF-RT.

Methods. From January 2021 to April 2023, patients with IDH-wildtype GBM treated with HF-RT (52.5Gy/15 fractions) or CF-RT (60Gy/30 fractions)were selected. Volumetric modulated arc therapy were performed for all patients. Concomitant temozolomide (75mg/mq/die) and adjuvant chemotherapy (TMZ 150-200 mg/mq/5 days q 28) were administered. Overall survival (OS) and progression-free survival (PFS) were estimated using the Kaplan-Meier method.

Results. Ninty-nine patients were treated (HF-RT:53, CF-RT:46). For both HF-RT and CF-RT groups, median age was 65 and 54 years and median KPS was 70%. All patients received concurrent/adjuvant temozolomide. No acute or late neurological side effects of grade ≥ 2 were reported during RT. Grade 3-4 hematologic toxicity occurred in five cases. At 12 months median follow-up (range 2-28), median OS was 14 months for HF-RT and CF-RT (p NS), and median PFS was 6 and 8 months, respectively.

Conclusions. HF-RT may offer equivalent outcomes and reduce treatment burden compared to CF-RT in GBM patients. Surely, robust data are needed to change the standard approach

P073

ANALYSIS OF A COHORT OF PATIENTS WITH HIGH GRADE GLIOMA TREATED WITH POST-OPERATIVE RADIOTHERAPY AND TEMOZOLOMIDE: EVALUATION OF INTEGRATED MORPHOLOGICAL AND METABOLIC IMAGING (MRI AND AMINOACID PET) IN THE PLANNING PROCESS

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Aims. To evaluate prognostic value of morfological, metabolic and dosimetric parameters in a cohort of patients (pts) with high grade glioma (HGG) treated with adjuvant Radiotherapy (RT) and Temozolomide Chemotherapy (TMZ), in which the morphological Imaging of postoperative MRI was integrated with FluorEthyl-l-Tyrosine (FET) PET during the radiation therapy treatment planning process.

Methods. In the planning process, MRI and FETPET were co-registered on the CT scan using the registration

algorithms of MIM (version 7.2.5). CTV was delineated according to ESTRO-ACROP guidelines based on the postoperative post-contrast T1w MR images but it also encompassed the postoperative metabolic abnormalities on the FET-PET images. Maximum tumour-to-brain ratios (TBRmax), SUVmax, Volume-Based PET Parameters, and dosimetrics data were calculated. Survival analysis was performed by Kaplan-Meier method. We used log rank test and Cox proportional hazards model in evaluating the prognostic value of analyzed parameters.

Results. We retrospectively assessed 32 pts (15 males and 17 females, median age 54 y) with histopathologically confirmed HGG (18,7% WHO grade 3; 81,3% WHO grade 4) treated with postoperative RT-TMZ, from November 2020 to April 2022. Clinical and pathological characteristics were collected. Median follow-up was 13.4 months (m), median OS and PFS were 16,2 m and 12.15 m, respectively. In the univariate analysis, WHO grade 4 (p .005), age >50 y (p .039), IDH-wildtype status (p .034), TBRmax >4.02 (p .0001), Metabolic Tumor Volume (MTV) > 40245 mm^3 (p .0003), MTVmax > 12963.5 mm^3 (p .0001), and VGTV57 Gy <99% (p .0001) were independent prognostic factors of poor OS. All these factors, as well as the evidence of residual disease on MRI (p .015), and VPTV57 Gy <96.4% (p .03), were correlated to worse PFS.

Conclusions. Our analysis confirmed the prognostic value of grading and mutational status of HGG. Interestingly, FET-PET parameters and an optimal coverage of target volume influenced OS and PFS. Further analysis are needed to validate the usefulness of FET PET parameters in the RT planning, in order to improve the clinical outcomes of pts with HGG.

P074

EFFECTIVENESS AND SAFETY OF NON-COPLANAR MONOISOCENTER MULTIFRACTION RADIOSURGERY FOR MULTIPLE BRAIN METASTASES

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Background. Synchronous irradiation of multiple brain metastases (mBMs) by means of Multifraction Stereotactic Radiosurgery (mfSRS) represents a challenge due to complex dose delivery process. Aim of the present study was to evaluate long-term outcomes of mfSRS for mBMs, using an innovative mono-isocenter non-coplanar technique.

Methods. Patients with mBMs, good performance status (ECOG ≤ 2), and life expectancy > 3 months, treated with mfSRS from 2019 to 2021 at our Institution, were retrospectively evaluated. For radiotherapy planning, a mfSRS VMAT plan was generated with 5 non-coplanar arcs using HyperArcTM(Varian Medical System, Palo Alto, US). Primary endpoints were local progression-free survival (LPFS) and intracranial progression-free survival (iPFS).

Table 1. Patients and lesions characteristics

Patients, n		67
Treated BMs, n		399
Sex, n (%)	Female	43 (64.2)
	Male	24 (35.8)
Age, median (range)		61 (30-80)
Primary tumor histology, n (%) *	Lung (NSCLC)	37 (55.2)
	Breast	17 (25.4)
	Melanoma	10 (14.9)
	Others	3 (4.5)
Extracranial disease, n (%) *	Present	45 (67.2)
	Absent	22 (32.8)
BM presentation, n (%) *	Metachronous	47 (70.2)
	Synchronous	20 (29.8)
Intracranial BM site, n (%)	Supratentorial	311 (77.9)
	Infratentorial	80 (20.1)
	Brainstem	8 (2.0)
Previous brain RT, n (%) *	No RT	62 (92.5)
	mfSRS	2 (3.0)
	WBRT	1 (1.5)
	WBRT + SIB	2 (3.0)
Total mfSRS courses, n (%) *	1	37 (55.2)
	2	18 (26.9)
	3	9 (13.4)
	4	3 (4.5)
Mean treated BMs, n (range) °		3 (1-16)
Dose and fractionation, n (%)	24 Gy/3 fractions	156 (39.1)
	27 Gy/3 fractions	192 (48.1)
	30 Gy/5 fractions	23 (5.8)
	Other	28 (7.0)
GTV, cc, median (range) ^		0.2 (0.1-19.8)
IPTV, cc, median (range) °		5.1 (0.3-108.7)

BMs: brain metastases; NSCLC: non-small cell lung cancer; RT: radiotherapy; mfSRS: multifractionated stereotactic radiosurgery; WBRT: whole-brain RT; SIB: simultaneous integrated boost; BMs: brain metastases; GTV: gross tumor volume; IPTV: cumulative intracranial planning target volume.
* per patient
° per mfSRS course
^ per lesion

Results. A total of 67 patients accounting for 399 brain metastases were analyzed. Non-small cell lung cancer (NSCLC) (55.2%), breast cancer (25.4%) and melanoma (14.9%) were the most frequent histologic types. The median number of treated metastases for mfSRS course was 3 (range 1-16), and the median lesion (GTV) and intracranial cumulative target volume (iPTV) were 0.2 cc (range 0.1-19.8) and 5.1 cc (range 0.3-108.7), respectively. With a median follow-up (FU) time of 10.5 months (range 0.8-36.4), the overall local control (LC) rate was 75.5%, with a 1- and 2-year LPFS of 72.2% and 65.6%, respectively. Median iPFS after first mfSRS course was 6.9 months (95% CI 4.5-11.9), and 30 (44.8%) patients received repeated mfSRS courses (range 2-4) for intracranial progression (IPD). Salvage whole-brain radiotherapy (WBRT) was used in 5 (7.4%) patients. At multivariate analysis, number of treated lesions (≥5) and histology (melanoma) correlated with LC and iPFS (HR 4.59 [95% CI 1.48-14.24]; p=0.008 and HR 3.05 [95% CI 1.13-8.23]; p=0.009) respectively. Radiological signs of radionecrosis or hemorrhage occurred in 1.6% of treated lesions; no other acute or late grade ≥3 toxicities were reported. The median overall survival (OS) of the entire cohort was not reached (95% CI 19.6 months-NE), with a 1- and 2-year OS of 76.7% and 60.7%, respectively.

Conclusions. Multifraction Stereotactic Radiosurgery with mono-isocenter non-coplanar technique represents an effective treatment option for selected

patients with mBMs. Considering the high local control rate and the excellent toxicity profile, it appears to be an attractive approach compared with WBRT, especially in the context of a multimodal patient management.

P075

LEXICOGRAPHC OPTIMIZATION-BASED PLANNING FOR SINGLE AND MULTIPLE BRAIN METASTASIS RADIOSURGERY WITH COPLANAR ARCS

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Aims. This study validated a not yet commercially available fully-automated lexicographic optimization planning system (LOps) for single (SL) and multiple lesions (ML) intracranial stereotactic radiosurgery (SRS).

Methods. Forty-four consecutive SRS plans (21 Gy/1 fx) delivered between November 2019 and August 2022 were retrospectively selected and automatically re-planned by LOps: 25 of them has 1 lesion, 13 had 2 lesions, 4 had 3 lesions, and 2 had 4 lesions. An a-priori assigned priority list, Wish List (WL), was used to define the sequential LO: 4 patients (tuning) were necessary to tune each WL, for SL-plans (SLp) and ML-plans (MLp). While in manual plans (MP), the arc setup is freely chosen, the WL was tuned to use 2 coplanar arcs of 140° and 360° for SLp and MLp, respectively. A target coverage as high as possible was requested, with at least 80% of the prescription dose covering 99% of the PTV. The main criteria for SLp approval was a brain V_{12Gy}<10 cm^3. In MLp this criterion can be overcome to get the minimum target coverage. The remaining 36 SRS plans (21 SL and 15 MLp) were automatically re-planned (testing). Testing plans were compared in terms of dose-volume constraints, conformality, and monitor units (MUs). Statistical significance was assessed by performing the Wilcoxon test and delivery accuracy was verified by pre-treatment QA.

Results. WLs-tuning took 3 days. Overall MP and automatic MCc time can be estimated at 8 hours and 3 hours, respectively. Statistically significant increases in SLp and MLp target coverage (GTV_D98%: +3.0% SL, +5.7% ML, PTV_D98%: +4.4% SL, +13.4% ML) and conformity index were registered. Automatic plans showed acceptably higher median brain V_{12Gy} (SL: MP 7.2 cm^3, SLp 7.6 cm^3; ML: MP 8.7 cm^3, MLp 10.3 cm^3). The SLp registered a lower median MU number (-4.2%) while MLp were obtained with a higher median number of MU (+9.8%). This not statistically significant difference did not affect gamma passing rates.

Conclusions. The novel LOps produced high-quality clinically acceptable SRS SL and ML plans with coplanar arcs significantly reducing the overall planning time from about one working day for one MP to about 3 hours for one automatic plan. Together with comparable OAR sparing, the target coverage was significantly increased and the plan deliverability was preserved. Here presented planning times and dosimetric results suggest the possibility to treat SRS patients from CT simulation to plan delivery in a one-day session.

P076

REPEATED HYPERARC RADIOSURGERY FOR RECURRENT INTRACRANIAL METASTASES AND DOSIMETRIC ANALYSIS OF INTRACRANIAL PATTERN OF RECURRENCE

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Aims. Stereotactic radiosurgery (SRS) is an effective treatment in the management of multiple brain metastases (BMs). Furthermore, mono-isocentric techniques allow the delivery of multiple stereotactic courses, in the event of intracranial failure. Nevertheless, limited data on the effectiveness and toxicity have been reported, as well as details on failure pattern. Aim of this study is to evaluate effectiveness and safety of multiple HyperArc courses and the pattern of progression in patients affected by BMs with intracranial progression.

Methods. Between June 2017 and January 2022, 56 patients were treated to 702 BMs with 198 (range 2-8) HyperArc courses in case of exclusive intracranial progression. Primary tumor was lung 26 (46.5%), breast (32%), melanoma 8 (14%), and other 4 (7.5%). BM site was: supratentorial 529 (75%), infratentorial 160 (23%), brainstem 13 (2%). The primary end-point was the overall survival (OS), secondary end-points were intracranial progression-free survival (iPFS), toxicity, local control (LC), neurological death (ND), and WBRT-free survival. Site of progression into specific treatment isodoses (0, 1, 2, 3, 5, 7, 8, 10, 13, 15, 20, and 24 Gy) was registered.

Results. The 1-year OS was 70%, and the median was 20.8 months (17-36). At the univariate analysis (UVA) BED>51.3Gy and non-melanoma histology sig-

nificantly correlated with OS. The median time to iPFS was 4.9 months, and the 1-year iPFS was 15%. Globally, 324 new BMs occurred after the first HA cycle in patients with extracranial disease controlled. 95% of them occurred within the isodoses range 0-7 Gy as follows: 105 (0 Gy), 57 (1 Gy), 51 (2 Gy), 50 (3 Gy), 36 (5 Gy), 7 (7 Gy) (p=0.00). Clinical toxicity was represented by headache 4 (7.1%), and radionecrosis 2 (0.28% of treated metastases). One- and 2-year LC was 90% and 79%, respectively. At the UVA BED>70 Gy and non-melanoma histology were significant predictors of higher LC. The 2-year WBRT-free survival was 70%. At the last follow-up 12 patients deceased by ND (median time 17.4 months).

Conclusions. Intracranical relapse can be safely and efficaciously treated with repeated HyperArc, with a possible survival improvement. Diffuse dose by volumetric RT might reduce microscopic disease also at relatively low levels, potentially acting as a virtual CTV. Neurological death is a relatively rare event in this population. Systemic treatment and extracranial disease should be considered in the decisional workflow.

P077

DOSIMETRIC AND CLINICAL ANALYSIS OF SINGLE-ISOCENTER LINAC-BASED RADIOSURGERY FOR BRAIN METASTASES USING COPLANAR ARCS

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Aims. To investigate the efficacy of linac-based stereotactic radiosurgery (SRS) and fractionated stereotactic radiosurgery (fSRS) treatments using single-isocenter coplanar FFF-VMAT technique for both single and multiple brain metastases (BM).

Methods. Seventy patients (129 BM) were treated with 15-21 Gy in 1 (n=59) or 27 Gy in 3 (n=11) fractions. PTV was defined by a 2 mm isotropic GTV expansion. Pre-treatment setup errors were corrected using CBCT and a robotic six-degrees-of-freedom couch. For each fraction, plans involving translational and rotational errors measured by post-treatment CBCT (Fx-plans) were recalculated. Dose parameters were compared between original and Fx-plans, by performing the Wilcoxon-Mann-Whitney test (alpha=0.05). The relationships of BM size, distance-to-isocenter and barycenter shift with the difference in target coverage were evaluated. Clinical outcomes were assessed using logistic regression and Kaplan-Meier analysis calculated from the end of treatment.

Results. The median single GTV and PTV volumes were 0.27 cc [0.01–10.48] and 1.05 cc [0.12–17.05], respectively. For multiple BM, the median distance-to-isocenter was 4.95 cm [0.89–7.52]. Plans were mostly optimized with two coplanar arcs (54%) or a single arc (29%). The median delivery time was 3.78 min [1.83 – 9.25]. The median post-treatment 3D error and maximum rotational error were 0.5 mm [0.1–2.7] and 0.3° [0.0–1.3], respectively. For single BM patients, the GTV D95% was never reduced by >5%, while PTV D95% reductions >1% occurred in only 11 cases (29%). For multiple BM patients, dose deficits >5% and >1% occurred respectively in 2 BM (2%) and 34 PTV (37%). Only one patient with single BM had a >5% increase in brain V12Gy. The dosimetric comparisons did not result statistically significant (p>0.05). The differences in target coverage showed a moderate-to-strong correlation only with the barycenter shift. At a median clinical follow-up of 8 months [1-37], a local failure of at least one treated BM occurred in 13 (19%) patients, and the 1-year and 2-year local control rates for all lesions were 93% and 89%, respectively.

Conclusions. The implemented workflow ensured no significant degradations of dose metrics due to residual setup and head motion errors for both single and multiple BM patients with this treatment technique. Along with the encouraging clinical outcomes, these findings warrant a reduction in the PTV margins and in the number of arcs at our institution.

P078

NEUROPATHIC PAIN TREATMENT FOR NEURALGIA TRIGEMINAL. THE RADIOSURGERY OPTION

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Aims. To evaluate the efficacy and safety of radiosurgery (RS) for patients with drugs resistant neuropathic pain for neuralgia trigeminal.

Materials and Methods. From august 2008 to February 2023 41 patients were treated with SRS for drug resistant neuralgia trigeminal. Radiosurgery was given with photon beam multiple arc therapy in a single fraction by linear accelerator with micro-multileafs collimator. Diagnostic MRI was co-registered with CT plan to delineate target volume and elaborate treatment plan. Three patients were lost to follow-up, 38 were evaluable. Clinical response to treatment was considered as complete or partial response, that is if pain was gone or reduced and patient stopped taking or reduced drugs, respectively. Clinical stability or progression was defined if pain was stable or progressed. Statistical analysis was

performed with Kaplan-Meyer method. Acute and late toxicity was scored with CTAEC scale.

Results. Median age was 66 years (range, 32-88), median KPS 90% (range, 80-100%), median PTV was < 0.1 cc, left side in 17 patients, right side in 24, median RS dose 70 Gy (range, 40-75). Six patients had neurovascular conflict and two of these were undergone to surgery before RS. Clinical response at 3 months was obtained in 31/38 patients (82%) particularly complete response and partial response in 16/38 (42%) and 15/38 (39%), respectively. Clinical stability in 6/38 (16%) and progression in 1/38 (3%) patients, respectively. After a median follow-up of 8,5 years (range, 0,3-13,5 years), clinical response was 92% +/- 4%, 71% +/-7%, and 53% +/- 9% at 1, 2 and 5 years, respectively; median time to onset of response was 3 months (range, 1-16 months), median duration of response was 62 months (range, 37-158 months). About clinical response at univariate analysis, there was a significant statistical difference for patients treated with dose < 70 Gy or ≥ 70 Gy (p=0,0036) in favour of higher dose. Moreover, achieving a complete response does not affect clinical response duration at univariate analysis. Patients without clinical response were re-irradiated in 4 cases after a median time of 5 years (range, 1-8 years), and 2 underwent to surgery. No acute toxicity was registered, only 1 patient (4%) developed hearing loss after 12 years as chronic toxicity.

Conclusions. RS is a therapeutic option efficacy and safety for neuropathic pain of neuralgia trigeminal. The dose administered at least 70 Gy is crucial to obtain a satisfying clinical response, and also prolonged response time.

Table 1. Patients characteristics.

Characteristics	Patients (n=4)
Gender	
Male	2
Female	2
Median age	56.8 (range 41-68)
Histology	
GBM NOS*	3
Anaplastic astrocytoma	1
Surgery	
Complete resection	3
Subtotal removal	1
Chemotherapy	
Concurrent and adjuvant TMZ	4

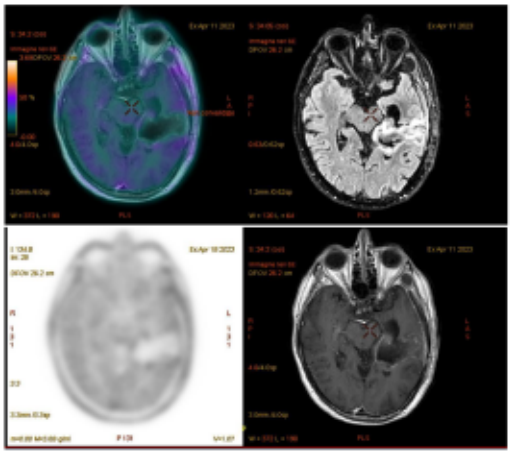

Figure 1. 18F-FET-PET and MRI.

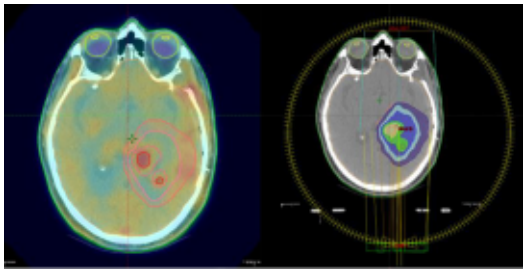

Figure 2. RT volume

All patients with contrast-enhancing MRI showing regions suspicious of non enhancing tumor underwent post-operative 18F-FET-PET prior to commencing radiotherapy. Radiotherapy target delineation with MRI and standard margins of expansion were employed in accordance with ESTRO-EANO guideline. The Gross Tumor Volume (GTV-RM) was defined as T1 contrast-enhancing tumour (for biopsy only patients) and/or resection

P079

INITIAL USE OF 18F-FLUOROETHYLTYROSINE POSITRON EMISSION TOMOGRAPHY (18F-FET PET) TO DOSE-ESCALTION RADIATION THERAPY FOR GLIOBLASTOMA

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Aims. To evaluate the impact of 18F-fluoroethyltyrosine positron emission tomography (18F-FET-PET) on radiotherapy planning for patients diagnosed with glioblastoma (GBM), presence of suspected non-enhancing tumors compared with standard magnetic resonance imaging (MRI) and dose-escaleted radiation therapy.

Methods. Patients with newly diagnosed, histologically confirmed glioblastoma aged ≥18 years were eligible.

cavity plus residual contrast-enhancing tumour, if present. 18F-FET-PET was used to create Biological Tumor Volumes (BTV) by encompassing FET avid regions in accordance with EANM/ESTRO guideline (Figure 1).

Target volumes included 54, 60, and 66 Gy in 30 fractions with a simultaneous integrated boost (SIB), and concurrent and adjuvant temozolomide for 6 months (Figure 2). 18F-FET-PET imaging was used to guide dose-escalated radiation therapy (DERT) and the volume increased with addition of 18F-FET-PET.

Results. 4 patients with GBM were treated with radiotherapy from December 2022 to May 2022 and all patients had demonstrable FET uptake. The median age was 56.8 years (range: 41-68 years). The baseline patient characteristics are described in Table 1. The median GTV-RM and BTV was 153.7 cc (range 75.3-185.1 cc) and 40.9 cc (range 40-62.8 cc), respectively. When 18F-FET-PET was utilized, there was a mean increase in volume from CTV-RM to BTVF by 20%, as the 18F-FET-PET uptake was often outside or at the margins of the GTV-RM.

Conclusions. In patients with GBM where the MRI demonstrates an area of suspected non enhancing tumor, 18F-FET-PET combined with MRI may help to clarify the nature of this region. This may result in improved radiotherapy target delineation, reduce the risk of potential geographical miss and dose-escaleted radiation therapy.

P080

SINGLE – ISOCENTER NON – COPLANAR STEREOTACTIC RADIOTHERAPY (HYPER ARC (HA)) FOR SINGLE OR MULTIPLE BRAIN METASTASES (BMS): UPDATED RESULTS OF A MONO – INSTITUTIONAL EXPERIENCE

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Aims. To analyze the clinical impact of HA technique in our series of patients (pts) treated for single or multiple BMs.

Methods. Pts with BMs and ECOG performance status 0 – 2 treated with HA technique were enrolled in the study; they were retrospectively evaluated as to overall survival (OS) from the end of radiotherapy to the last follow-up or death, and toxicity.

Results. 95 pts (49 males, 46 females) accounting for 255 BMs, treated at our institution from March 2019 to December 2022, were reviewed. Primary tumor histology was NSCLC in 29 pts, SCLC in 4, breast in 17, melanoma in 16, kidney in 8, colon in 5, pancreas in 4, prostate in 2, cardias in 1, thoracic esophagus in 1, base of tongue in 1, adult medulloblastoma in 1, endometrium in 1, bladder in 1, germinoma testis in 1, parotid in 1, rectum in 1, thymic carcinoma in 1. Median age at the time of BM diagnosis was 65 years (range 24-83). The average number of metastases in each treatment (Tx) was 2.7 (range 1-12). A single BM was present in 44 among the 95 pts, multiple BMs in 51 pts. The average diameter of the greatest lesion in each Tx was 1.9 cm (range 0.2-5.5). In 5 Tx, the surgical bed was one of the targets. The GTV encompassed the macroscopic contrast enhancing lesion on T1-MRI and was assumed to be equal to the CTV. The PTV was obtained from the GTV plus an isotropic margin of 2 mm. Dose prescription was 27 Gy in 3 fractions (Fx) or 21 Gy in single Fx, related to the size of the lesion and brain localization. All 5 surgical cavities were treated with 27 Gy in 3 Fx. 20 Tx were a 21-Gy single-Fx treatment; among them, the average diameter of the greatest lesion was 0.9 cm (range 0.2-2). 75 Tx consisted in 27 Gy in 3 Fx; the average diameter of the greatest lesion was 2.2 cm (range 0.3-5.5). MRI follow – up was available for all patients; among them, 48 pts had a stable disease, 6 pts an increasing size of the treated lesion, 35 pts an onset of new lesions, 6 pts both. In the whole series, after an average follow-up of 14 months (range 1-47), median OS was 11 months (range 1-47). As to the most frequent histologies, median OS was as follows: NSCLC 13 months (range 1-39), SCLC 12 months (range 3-13), breast 12 months (range 4-43), melanoma 6 months (range 1-38), kidney 6 months (range 3-37), colon 8 months (range 3-27), pancreas 10 months (range 1-27). Patients did not develop G2-G3 toxicities.

Conclusions. HA technique proved to be safe and tolerable in our series. Outcome data are encouraging, even with pts with large and multiple BMs.

P081

LOCALLY ADVANCED SKULL BASE MENINGIOMAS TREATED WITH CONVENTIONALLY FRACTIONATED RADIATION THERAPY: A DOSIMETRIC COMPARISON BETWEEN CYBERKNIFE AND INTENSITY MODULATED PROTON BEAM DELIVERY

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Aims. A dosimetric comparison of intensity modulat-

ed proton therapy (IMPT) and photon Cyberknife therapy (CK) for locally advanced skull base meningiomas (SBM) not amenable to extreme hypofractionation due to violation of constraints of surrounding critical structures.

Methods. Ten cases of locally advanced SBM identified at two institutions (IRE and CNAO) were planned using the same planning objectives: D95%>=95% for the clinical target volume (CTV), D0.035cc <55Gy for brainstem, optic nerves and chiasma planning risk volumes, Dmean <45Gy for the cochlee, V7.3Gy<40% and Dmean<30Gy for the hippocampus. A conventional fractionation scheme of 54 Gy in 27 fractions was used in all cases. Starting from a common set of contoured structures, plans were run blindly at IRE and CNAO for CK and for protons, respectively. CK plans were generated on the Accuray Precision system ver.3.2 and calculated with the Monte Carlo (MC) algorithm. Pencil beam scanning IMPT plans were optimized with the MC engine of the RayStation treatment planning system v.11B with 2-3 non-coplanar beams. Relative Biological Effectiveness was set to a constant value of 1.1. Normal tissue complication probabilities (NTCP) were estimated using the formulas described by Gondi for delayed recall, Dutz for fatigue, memory impairment and cochlea toxicity, De Marzi for hearing loss and Lee for tinnitus. Comparison between plans was performed with the Wilcoxon paired test.

Table 1.

		Cyberknife - Median (range)	Proton – Median (range)	p
CTV	D95%	52.84 Gy (52.05-53.63)	52.41 GyRBE (51.97-53.21)	0.074
	V95%	99.11% (98.11-99.93)	99.17% (97.78-99.99)	0.76
	D0.035cc	106.8% (106.2-108.6)	106.6% (105.3-107.1)	0.72
	Dmean	54.85 Gy (54.5-55.23)	54.03 GyRBE (53.95-54.17)	0.059
	CI	1.12 (0.87-1.71)	1.14 (0.77-1.54)	0.33
	HI	1.07 (1.06-1.08)	1.06 (1.05-1.07)	0.10
Brainstem	D0.035cc	54.17 Gy (10.68-55.20)	53.17 GyRBE (4.93-56.30)	0.29
	Dmean	27.57 Gy (2.49-40.56)	15.11 GyRBE (0.15-32.75)	0.005**
Optic chiasm	D0.035cc	52.78 Gy (35.71-54.05)	53.13 GyRBE (42.60-54.34)	0.96
Ipsilateral optic nerve	D0.035cc	52.16 Gy (35.25-53.99)	52.65 GyRBE (27.71-54.91)	0.33
Contralateral optic nerve	D0.035cc	34.61 Gy (10.60-52.61)	42.89 GyRBE (1.22-53.83)	0.29
Ipsilateral cochlea	Dmean	38.75 Gy (2.43-46.61)	45.12 GyRBE (0.02-53.96)	0.29
Contralateral cochlea	Dmean	6.98 Gy (0.90-35.57)	4.16 GyRBE (0-39.95)	0.80
Bilateral hippocampus	Dmean	12.78 Gy (3.05-14.95)	16.10 GyRBE (0.72-24.07)	0.059
	V7.3Gy	34.56% (1.05-49.77)	55.29% (2.31-65.57)	0.037**
	D0.035cc	51.67 Gy (24.53-54.47)	51.69 GyRBE (33.15-52.83)	0.96
	Dmean	4.09 Gy (1.81-16.97)	4.67 GyRBE (0.01-15.55)	0.76
Brain-CTV	D0.035cc	56.26 Gy (54.11-57.81)	55.96 GyRBE (53.34-60.58)	0.88
	Dmean	6.56 Gy (2.49-11.87)	4.28 GyRBE (2.51-9)	0.007**

Results. The dosimetric data of CTV and OARs are reported in Table 1. On average, the planning objectives were respected with both approaches, except for the hippocampus V7.3Gy which was 34.56% in the CK plans and 55.29% in the PT plans (p=0.037). NTCP analysis revealed that CK and PT were comparable for all the toxicities investigated, except for memory impairment≥G2 at 24 months, which was inferior in the CK plans (17.4% versus 18.2%, p=0.014), and fatigue≥G1 which was inferior in the IMPT plans (34.8% versus 33.5%, p=0.028).

Conclusions. Although with a limited cohort, our study shows that fractionated Photon based treatment with CK is a reasonable alternative to IMPT for the treatment of locally advanced SBM.

P082

ADJUVANT TREATMENT FOR RESECTED BRAIN METASTASES (BMS): RADIOSURGERY (SRS) *VS* HYPOFRACTIONATED STEREOTACTIC RADIOTHERAPY (HSRT). A SINGLE-CENTER SERIES UPDATE

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Aims. Post-operative SRS and HSRT are effective and safe approaches commonly used to treat BMs. We analyzed our patient's series to explore the rate of local control, the risk of leptomeningeal diffusion as well as the risk of brain radiation necrosis in both single fraction (SRS) and multi fraction (HFSRT) approaches in the setting of post-operative radiosurgery for brain metastases.

Methods. We retrospectively analyzed clinical, dosimetric and radiological data of 71 patients (pts) who underwent partial or total resection for BM and adjuvant SRS or HSRT with Cyberknife (CK) from April 2011 to May 2020 at our Institution. Survival and local control were correlated to both clinical and dosimetric data. Pts with prior whole brain irradiation (WBRT) or leptomeningeal disease (LMD) were excluded.

Results. The main represented histologies were breast and non-small cell lung cancers. Twenty-nine pts underwent SRS (14-20 Gy in single fraction), 42 HSRT (21-24 Gy in 3 fractions). The cumulative 1-year local control (LC) rate and progression free survival (PFS) were 78.5% and 87%, respectively. Four events of late brain radiation necrosis (RN) were registered, all G2 graded according to CTCAE v.5. The median overall survival (OS) was 47 mo, with a 12-mo OS rate of 83%. A 20% rate of LMD was reported; the type of surgical resection of the BM (piecemeal *vs* en-bloc), and the inclusion or exclusion of the surgical corridor leading to the cavity in PTV volume did not show a statistically significant correlation with the onset of LMD. A better trend for PFS emerged for pts with a waiting time from surgery to CK ≤ 45 days *vs* > 45 days (p=0.07). PTV volume, dose prescription, fractionation and histology seemed not to affect LC, nor OS. A DS-GPA score ≥ 3 *vs* < 3, an extracranic (EXC) disease at CK absent or oligometastatic *vs* present not oligometastatic, and an EXC disease at last follow up stable *vs* in progression were found to be

significantly correlated with a better OS (p=0.0000, p=0.02, p=0.0009, respectively).

Conclusions. We can confirm that both SRS and HSRT are effective and safe approaches in the adjuvant setting of resected BMs; dose prescription and fractionation must be selected according to PTV volume. With regards to OS, they are a valid alternative to WBRT. Further data are needed to better assess the role of target delineation, waiting time from surgery to SRS, and systemic therapies in order to improve pts outcomes.

P083

REAL LIFE DATA OF REGORAFENIB IN RECURRENT GLIOBLASTOMA: A MONOCENTRIC RETROSPECTIVE SINGLE CENTER EXPERIENCE

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Background: in the randomized phase 2 REGOMA trial, regorafenib (REG) showed promising activity in recurrent glioblastoma (GBM) patients (PTS); subsequently, in Italy the National Health System has permitted the reimbursement of the REG as second-line. We report our monocentric experience.

Materials and Methods. we retrospectively collected data from recurrent GBM PTS enrolled in our center from Dec 2020 to Apr 2023. Major inclusion criteria were: histologically confirmed diagnosis of glioblastoma according to WHO 2016 and relapse after Stupp treatment, Karnofsky performance status (KPS) from 50% to 100%, good organ function. REG was administered at standard dose of 160mg/die for 3 weeks on/1 week off. Brain MRI was performed within 14 days before starting regorafenib and every 12 weeks, subsequently. Primary endpoint was OS; secondary endpoint was PFS. CTCAE v. 5 for adverse events (AE).

Results: We collected data from 26 recurrent GBM PTS: median age was 57.5ys (IQR 21.0-76.0), 65% male, KPS was 80-100% in 24 (92%), 22 PTS (84.6%) underwent surgery, 14 PTS (53.8%) undertook steroids at baseline. MGMT was methylated in 16 PTS (61.5%), IDHwt in 22 PTS (84.6%), while IDH was not available for 2 PTS (7%). Median follow-up was 17 months (IQR 6-28). The median of REG cycles per patient was 5.7 (IQR 2-20). Grade 3-4 AE were reported in 3 (11.5%) PTS: 2 PTS had to permanently discontinue REG, 1 PT had reduction and delayed therapy due to AE. Only one PT voluntarily withdrew from therapy. 12 (46%) PTS received third-line therapy. In April 2023, 23 PTS (88%) had died. No death was treatment-related. Median OS was 22.7ms (95% CI 10-71), median PFS was 12.9ms (95%CI 5-43).

Conclusions. According to our experience, the use of REG in the second line improved OS and PFS in PTS with recurrent GBM with acceptable toxicity and good tolerability.

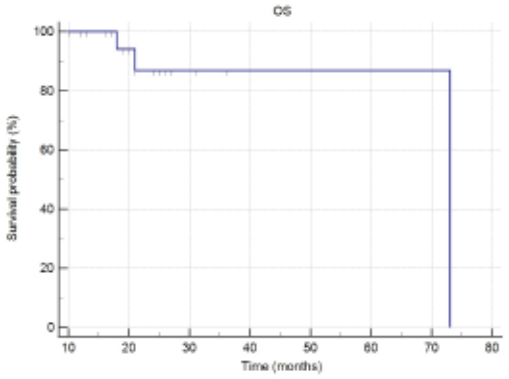

Figure 1.

P084

MONO-INSTITUTIONAL EVALUATION OF RESPONSE, CLINICAL OUTCOMES AND OF A NEW PROGNOSTIC INDEX IN BRAIN METASTASES PATIENTS TREATED WITH STEREOTACTIC RADIOTHERAPY

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Aims. In order to personalize the best treatment regimen, an easy-to-perform Prognostic Score could be useful to guide treatment decisions. The aim of the study is to evaluate the clinical outcomes of the SRT and the Comprehensive Prognostic Index (CPI).

Methods. We retrospectively analyzed 83 patients treated with SRT for brain metastases between 2015 and 2022. All patients had a KPS score ≥ 70. The histological type of the primary lesion, extent of extracranial metastatic disease and the characteristics of brain metastases were collected. Overall survival (OS) and local control (LC) were determined. The CPI was calculated according to Stankiewicz et al.1 and patients were divided in 4 group in terms of scores: 1 (0-1 points), 2 (2-3 points), 3 (4-5 points) and 4 (≥6 points). The responses were divided in complete (CR) and in partial (PR) response and ana-

lyzed with LC. The OS was compared to CPI in order to verify the prognostic value of the index. Treatment outcomes were evaluated using Kaplan–Meier analysis. A P-value less than 0.05 was considered statistically significant.

Results. The median age was 63 years old. Non–small cell lung cancer (47%) and breast cancer (29%) represented the most common primary tumors. 26% of patients had uncontrolled systemic metastatic disease. The median number of treated brain metastases was 1,5 lesions per patient. The most used RT schedule was 27 Gy (9 Gy/day). The median follow-up was 12 months. 60% of patients obtains achieved a lesion response of which 50%, a complete response. The 1-year and 2-year OS rates were 51%, and 39%, respectively. The median time for response was 4 months. The 1-year and 2-year LC rates were 58%, and 39%, respectively. Figure 1 shows that CR patients had a better and longer LC compared to PR patients (97% *vs* 25%, p<0,001). In terms of prognostic value of CPI, it was showed that Group 4 had a 5-times higher risk of lower OS compared to Group 1 (p<0,001) whereas Group 2 and 3 had 3-times higher risk (p=0,05 and p=0,02 respectively).

Conclusions. SRT was able to guarantee a good OS and LC in most patient for the ability to obtain a lesion response. In our setting the use of CPI showed to be an easily applicable tool with an optimal prognostic value to guide treatment decision.

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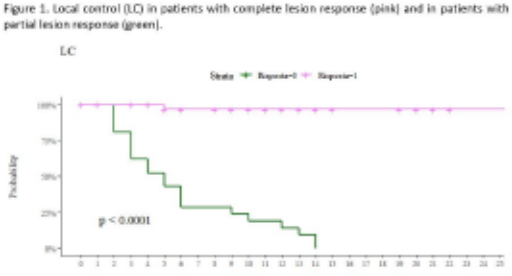

Figure 1.

P085

SCALP-SPARING PROTON THERAPY IN YOUNG ADULT PATIENTS WITH BRAIN TUMORS: EARLY COSMETIC OUTCOMES

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Aims. Radiation-induced alopecia (RIA) is one of the most common and emotionally troublesome effects resulting from brain tumor radiation therapy (RT). Proton therapy (PT) is considered a promising RT treatment modality for brain tumors (BT). However, the higher entry dose of the spread-out Bragg peak may represent a disadvantage, thus causing concern over a possible increase in skin adverse effects, such as hair loss. In our previous analysis [Palma G et al. 2020], permanent RIA was registered in 19% of patients (pts) treated with PT for BT. D2% scalp dose (cut-off of 48 Gy) was the only variable predictive for permanent RIA. Aim of the study is to report preliminary cosmetic outcomes in young adults treated with PT plan optimization aiming the scalp dose sparing.

Methods. Between January 2021 and March 2022, 12 young (< 40 years) pts (2 male, 10 female) received PT for BT (3 meningiomas, 9 lower grade gliomas). Target was in very close proximity (≤ 5 mm) of the scalp in all pts. Prescribed dose ranged between 54 and 59.4 Gy with standard fractionation. Once the requested target coverage was reached, a further plan optimization was accomplished to achive a scalp D2% ≤ 48 Gy. Cosmetic outcomes (both subjective and objective) were prospectively assessed during and after radiotherapy. RIA was graded according to the Common Terminology Criteria for Adverse Events version 4 for acute (≤90 days after RT), late (>90 days after RT) and permanent (persisting for >12 months after RT) injury.

Results. Scalp sparing (without target uncoverage) was achieved in all the pts. In 8 pts the goal was reached with a single-field optimization technique. In 4 pts, intensity-modulated optimization was necessary to achieve the scalp sparing. During radiotherapy grade 2 RIA with a subjective fair score was registered in all pts. At six months after the completion of PT grade 0 and 1 RIA with a subjective excellent and good cosmetic score were registered in 17% and 83%, respectively. At last follow-up (> 9 months) grade 0 and 1 RIA with a subjective excellent and good cosmetic score were registered in 67% and 33%, respectively. No pts experienced permanent grade 2 RIA.

Conclusions. PT with scalp sparing plan optimization seems feasible. Early cosmetic outcomes seems superior to institutional historical controls but need to be confirmed in a large prospective pts population.

P086

EVALUATION OF PATTERN OF RECURRENCE FOLLOWING POSTOPERATIVE BRAIN CAVITY STEREOTACTIC RADIOSURGERY OF BRAIN

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Aims. Brain metastases (BM) account for more than half of all newly diagnosed intracranial malignancies.

Surgical excision is a valuable treatment option, especially in case of symptomatic lesions. Since patients who undergo surgical resection of a BM have a 50-60% risk of local relapse within the next 6-12 months, postoperative radiosurgery (SRS) to the surgical cavity has become the standard of care, supported by data from two randomized trials showing decreased risk of neurocognitive decline compared to WBRT and improved local control compared with observation. We report our experience on patients with newly-diagnosed BM treated with radical surgery followed by SRS with the aim to evaluate patterns of local recurrence.

Methods. We retrospectively collected data from consecutive patients treated with SRS to the surgical cavity in our center between November 2018 and February 2023. Patients who experienced intracranial disease progression from surgery to initiation of SRS were excluded. Local (infield) and distant (out of field) treatment failures were defined on the basis of magnetic resonance. Kaplan-Meier curves were generated for local, distant and leptomeningeal recurrence free survival (LRFS, DRFS, LeRFS).

Results. Twenty-five patients for a total of 35 cavities were treated with either Gamma Knife (GK) or CyberKnife (CK) after surgical resection. Patients baseline characteristics are summarized in Table 1. Eight out of 25 patients received concomitant SRS to synchronous BM for a total of 10 lesions. The median prescription dose was 19 Gy (range 12-25) at a median isodose line (IDL) of 70% (range 50-83.5) with a median of 1 fraction (range 1-5). Local, distant or leptomeningeal recurrence occurred in 3, 6 and 3 patients, respectively. Nine patients died, for a median PFS and OS of 11 and 14 months, respectively. After a median follow up of 11 months, median LRFS, DRFS and LeRFS were 11, 9 and 11 months, respectively. No significant association between surgical cavity volume and LRFS, DRFS and LeRFS was detected. No significant impact of primary tumor histology (melanoma, ovarian and renal cell carcinoma *vs* others) on LRFS or DRFS was found.

Conclusions. Findings from our analysis confirm the efficacy of SRS as postoperative treatment for newly-diagnosed BM, irrespectively of total cavity volume and primary tumor histology. This information will aid in the development of comprehensive treatment strategies with potentially improved outcomes for patients with BM.

Table 1. Baseline characteristics of 25 patients with first-diagnosed BMs treated with surgery and SRS.

	Median (range) or Number (%)
Number of patients	25
Number of BMs	35
BM treated: -1 -≥2	 17 (68%) 8 (32%)
Sex: -male -female	 9 (36%) 16 (64%)
N. of patients with age at BMs diagnosis ≤ 65 years	18 (72%)
Karnofsky performance status scale (KPS) <0	22 (88%)
Primary tumor: -breast -NSCLC -kidney -G.I -Ovary -melanoma -others	 4 (16%) 9 (36%) 1 (4%) 2 (8%) 3 (12%) 3 (12%) 3 (12%)
Extracranial metastasis at BMs presentation	13(52%)
Controlled extracranial disease at BMs diagnosis: -Yes -No	 20 (80%) 5 (20%)
Concomitant systemic therapy	5 (20%)
RT technique -Gammaknife (GK) -Cyberknife (CK)	 12 (48%) 13 (52%)

P087

EVALUATION OF MIM AUTOCONTOURING SOFTWARE FOR BRAIN ORGANS-AT-RISK SEGMENTATION

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Aims. Accurate segmentation of organs at risk (OARs) is critical for optimal treatment planning in brain radiotherapy. This study aimed to evaluate the role of MIM, an autocontouring software, in the segmentation of brain OARs. Three datasets were compared: contours generated solely by MIM, contours generated by MIM and subsequently modified manually, and contours manually drawn by experts.

Methods. The study included a total of 23 patients undergoing brain radiotherapy. OARs, including optic nerves, chiasm, lens, brainstem and cochlea, were contoured using three approaches: MIM autocontouring,

MIM autocontouring with manual modification, and manual contouring by experts. The accuracy of OARs volumes was assessed using the Dice Similarity Coefficient (DSC). The DSC values were compared between the three contouring methods using the paired t-test. Statistical significance was set at $p<0.05$. Time-saving effects were also evaluated.

Results. The initial MIM-generated contours demonstrated acceptable segmentation of the brain OARs. However, subsequent manual modifications significantly improved the accuracy and conformity of the contours. The manual modifications accounted for anatomical variations and subtle boundaries that may have been missed by the automated software. Quantitative analysis revealed a reduction in volume discrepancies when comparing the manually modified MIM contours with the expert-drawn contours (see table). The time-saving effect was observed in the contouring process using MIM software (average time: 6 minutes, range 2-10) compared to manual contouring (average time: 28 minutes, range 20-40).

Conclusions. MIM autocontouring software provides a valuable starting point for brain OARs segmentation in radiotherapy treatment planning. However, manual modifications by experienced clinicians are necessary to achieve optimal accuracy. A combined approach, utilizing automated software and expert knowledge, is recommended to achieve reliable and accurate OARs segmentation in brain radiotherapy. This study emphasizes the importance of integrating automated tools with manual intervention to ensure high-quality treatment planning.

Table 1.

	DSC (mean ± std dev)		
OAR	Manual vs MIM	Manual vs MIM refined	MIM refined vs MIM
Brain	0,98 ± 0,02	0,98 ± 0,02	1 ± 0
OpticNerveR	0,69 ± 0,08	0,67 ± 0,08	0,97 ± 0,09
OpticNerveL	0,69 ± 0,08	0,67 ± 0,09	0,95 ± 0,06
CochleaR	0,43 ± 0,16	0,42 ± 0,17	0,97 ± 0,1
CochleaL	0,43 ± 0,18	0,43 ± 0,19	0,98 ± 0,13
Gland_Lacrimal_R	0,54 ± 0,27	0,54 ± 0,27	1 ± 0,01
Gland_Lacrimal_L	0,54 ± 0,25	0,54 ± 0,25	1 ± 0,02
Lens R	0,72 ± 0,09	0,72 ± 0,1	0,98 ± 0,09
Lens L	0,68 ± 0,09	0,68 ± 0,09	0,96 ± 0,06
EyeR	0,87 ± 0,04	0,87 ± 0,04	1 ± 0
Eye L	0,89 ± 0,03	0,89 ± 0,03	1 ± 0
Lobe Temporal R	0,94 ± 0,04	0,94 ± 0,04	0,99 ± 0,03
Lobe Temporal L	0,94 ± 0,04	0,94 ± 0,04	1 ± 0,01
Pituitary	0,45 ± 0,27	0,45 ± 0,27	1 ± 0
SpinalCord	0,76 ± 0,1	0,76 ± 0,1	1 ± 0
Optic Chiasm	0,1 ± 0,16	0,44 ± 0,2	0,29 ± 0,33
Brainstem	0,87 ± 0,03	0,88 ± 0,04	1 ± 0

P088

DEVELOPMENT AND VALIDATION OF A FAST NEUROCOGNITIVE ASSESSMENT TOOL IN ADULT PATIENTS AFFECTED BY GBM IDH WT GRADE 4 CANDIDATE TO ADJUVANT RADIATION-CHEMOTHERAPY

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Aims. Neurocognitive function assessment is essential in glioblastoma (GBM) patients. However, several tools are available, and in clinical practice, physicians need a quick and practical assessment. We hypothesized to use a clock drawing test (CDT) as a rapid screening tool and to evaluate its sensitivity level, we compared it with the mini mental state examination (MMSE). We also administered a questionnaire on the percieved neurocognitive function (FACT-Cog survey). The primary outcome is to evaluate whether the CDT can be superimposed on other tests already used in literature to assess cognitive framework of patients affected by GBM. The secondary outcome is to evaluate if neurocognitive assessment correlates with overall survival, compliance and progression-free survival.

Methods. 100 patients will be enrolled in 6 months, with a new diagnosis of GBM, and undergoing adjuvant radiation-chemotherapy within 7 days. Each patient will undergo a neuropsychological evaluation. The assessment timing is before adjuvant treatment starts, at the end of treatment and at three months.

Results. The study started in May 2023, and currently five patients with GBM were enrolled (median age: 55 years). We first used the CDT and then administered the MMSE to validate the CDT result, taking about 10 minutes. In only 1/5 cases, the CDT result was not correlated with MMSE (CDT 1/3; MMSE 26.2/30), while in 4/5 cases we found an agreement between the CDT and MMSE results. From the analysis of the FACT-Cog survey, we also found an agreement between the patient's perceived neurocognitive functions in the last seven days and the documented tests. Moreover, 5/5 patients stated

that any found problems (such as difficulty concentrating or remembering) significantly impacted their quality of life. Only in 1/5 cases the caregiver's perceptions of the patient's neurocognitive functions were discordant thought the patient's; in particular the caregiver had a worse perception of the neurocognitive patient's status.

Conclusions. Cognitive functioning evaluation should be included among the standard clinical endpoints in treating adult neuro-oncology patients. We think developing and validating an efficient and quick neurocognitive assessment tool could be helpful in clinical practice to establish neurocognitive function.

P089

SINGLE-ISOCENTER LINAC-BASED RADIOSURGERY FOR BRAIN METASTASES USING COPLANAR ARCS

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Aims. To report clinical outcomes and identify predictive factors associated with improved treatment results in linac-based stereotactic radiosurgery (SRS) and fractionated stereotactic radiosurgery (fSRS) using single-isocenter coplanar FFF-VMAT technique.

Methods. Between March 2020 and June 2022, 70 patients with 129 brain metastases (BM) were retrospectively included. Patients received either 15-21 Gy in a single fraction (n=59) or 27 Gy in three fractions (n=11). Post-treatment MRI scans were used to assess local control (LC). Kaplan-Meier analysis was performed to evaluate in-field progression-free survival (ifPFS), brain progression-free survival (bPFS), and overall survival (OS) rates. Log-rank test and logistic regression analyses were carried out to identify predictive factors associated with better outcomes.

Results. The population consisted of 33 females and 37 males, with a median age of 66 years [30-85]. Lung (44%) and visceral (47%) were the most frequent tumor histology and extracranial metastases site, respectively. The median follow-up period was 8 months [1-37]. The 1-year and 2-year LC rates for all lesions were 93% and 89%, respectively, with 13 (19%) patients experiencing local recurrence in at least one treated BM. The median ifPFS was 7.8 months, while the corresponding 1-year and 2-year rates were 80% and 72%, respectively. The median bPFS was 3.9 months, with 1-year and 2-year bFPS rates of 40% and 20%, respectively. The same features for OS were 13 months, 52%, and 29%, respectively. Lung primary tumor histology and extracranial controlled disease were significantly associated with increased OS (log-rank P=0.050 and P=0.015, respectively) and bPFS (log-rank P=0.017 and P=0.015, respectively). No statistically significant differences (P>0.05) in clinical outcomes were found for number of treated lesions, total target volume, and systemic therapy. Patient age and gender showed borderline significant correlations with bPFS (P=0.055) and ifPFS (P=0.060), respectively. At multivariate analysis, lung primary tumor histology was independently related to brain progression (OR 0.35; 95% CI, 0.12–0.98; P=0.043).

Conclusions. Linac-based SRS treatments with single-isocenter coplanar FFF-VMAT technique were feasible and resulted in encouraging clinical outcomes, comparable to other treatment approaches involving multiple non-coplanar arcs or dedicated machines. Further analyses are ongoing to confirm these findings.

P090

WHAT IS THE BETTER THERAPEUTIC STRATEGY FOR DISTANT RECURRENT GLIOMA? OUTCOME AND PROGNOSTIC FACTORS EVALUATION IN A RETROSPECTIVE SERIES

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Aims. Distant recurrent glioma is a rare condition. A possible correlation has been postulate with original tumor location in close proximity to the subventricular zone. To date a standard of care is missing. Aim of this retrospective analysis was to investigate outcome of patients (pts) with distant recurrent glioma treated with radiation therapy (RT), with or without chemotherapy (cht).

Methods. Adult pts with distant recurrent glioma have been evaluated. Histological diagnosis has been reclassified according to the 2021 WHO Classification of CNS tumors. Distant progression treatment strategies included RT alone, RT concurrent with CHT (RT-CHT), RT followed by CHT. For RT planning, target delineation was defined on simulation CT scan and brain MRI co-registered into the image workstation of Brainlab

Results: From 2015 to 2023, 35 distant recurrent glioma pts have been evaluated. Histological diagnosis was: glioblastoma in 27 pts, astrocytoma grade 3 IDH-mutant in 6pts, and astrocytoma grade 2 IDH-mutant in 2pts. Location of primary tumor was in subventricular zone in all cases: 16 pts developed only distant recur-

rence, 19 both local and distant recurrence. Median interval time (IT) between diagnosis and distant recurrence was 22 months (mth) (range 5-49); 8 cases had distant recurrence within 12mth, 17 cases between 13 and 24mth, and 10 cases ≥ 24mth. Regarding treatment strategy, 10pts (29%) received RT alone, 6pts (17%) received RT-CHT, 11 (31%) received RT followed by sequential CHT, 8 (23%) received concurrent RT-CHT followed by sequential CHT. Median RT dose was 45Gy in 15 fractions (range 30-50 Gy in 5-20fr). Median follow up time was 36mth (range3-97). Median overall survival (OS) time, 6 mth,1,2-year OS rates from diagnosis were 33mth (95% CI 30-36), 100%, 94.3%±3.92, 70.0%±7.9, respectively. Median OS time, 6 mth,1,2-year OS rates from distant recurrence were 10mth (95% CI 7-12), 75.4%±7.6, 26.2%±7.9, 0%. On univariate, and multivariate analysis, prognostic factors impacting OS were IT between diagnosis and first recurrence, and treatment performed. Indeed, median OS time were 6mth (95% CI 2-10) for IT ≤ 1year (P= 0.0363), 17mth (95% CI 8-12), 10mth (95% CI 7-12), 6mth (95% CI 8-12) for RT alone, RT and concurrent RT-CHT followed by sequential CHT, concurrent RT-CHT without sequential CHT, respectively (P < 0.0001).

Conclusions. Our results suggest that RT alone could be a feasible and effective treatment option for distant recurrent gliomas.

P091

COMPLEX MENINGIOMA TREATED WITH FRACTIONATED GAMMA KNIFE VERSUS HELICAL IMRT/VMAT: COMPARISON OF TWO TECHNIQUES

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Purpose. To compare fractionated stereotactic radiotherapy with Gamma Knife (fGK) versus helical IMRT/VMAT for complex meningiomas in terms of outcomes and toxicity in a consecutive cohort of patients treated in a single institution. Analysis for prognostic factor identification were performed.

Materials and Methods. Patients treated for meningiomas between 2015 and 2017 (radiologically or histologically diagnosed) with fGK in 3 fractions or conventionally fractionated helical IMRT/VMAT were retrospectively analyzed. Ten out of 110 patients were lost to follow-up and excluded from the analysis, those remaining were divided in two groups. Group 1 included 49 patients treated with fGK (Gamma Knife Perfexion™, Elekta, Stockholm, Sweden) in 3 fractions to a median total dose of 21Gy (16.5-27Gy) prescribed at the 50% isodose of the GTV (with no margins). Group 2 included 51 patients who underwent helical IMRT/VMAT with TomoTherapy® (Accuray, Maddison, WI, USA) or RapidArc™ (Varian, Palo Alto, CA, USA) in 27 (25-30) fractions to a median prescription dose of 50.4Gy (46.8-60Gy). CTV was obtained with an isotropic expansion of 3-5mm –from the GTV, then other 4-5 mm were added to obtain PTV. Median GTV was 4.14 cc (IQR: 1.79-10.55), while median PTV was 11.69 cc (IQR 65.5-147.66). Biologically equivalent dose (BED3) prescribed, considering α/β=3 for meningioma, was 70Gy (IQR 70) in group 1 and 80.64 (IQR: 77.76-90) in group 2.

Results: Median follow-up was 68 months (IQR: 46.48 – 80.69), male to female ratio was 1:2.45 in patients cohort. The median age at diagnosis was similar in the two groups: 53.16 years (IQR: 46.34 – 61.15) and 61.46 years (IQR: 47.67 – 69.35) in group 1 and 2, respectively. The median progression-free survival (PFS) was 67.31 months (IQR: 42.68 – 80.03), with 10 patients who experienced disease progression and 3 died due to this progression. Five-year overall survival (OS) and 5-year PFS were 93.87% and 91.84% in group 1 and 88.23% and 88.23% in group 2. Cox regression identified PTV (HR:1.01,95%IC:1–1.02 p-value 0.0039), BED_{3Gy} (HR:1.07, 95%IC:1.01-1.13, p-value 0.0285), and male gender (HR:8.82, 95%IC:1.83–42.51, p-value 0.0067), as prognostic factors for worse OS, nothing were found for PFS. Acute and late toxicity were reported in Table 1.

Conclusion. Both fGK and helical IMRT/VMAT ensured good results in terms of PFS, local control and acute toxicity. Higher PTV volume, BED_{3Gy} and male gender negatively correlated with OS.

Table 1.

Table 1. Acute and late Toxicity distribution and types.

GRADE	G0		G1		G2		G3		G4	
Acute Toxicity (51 vs 49 patients)										
TYPE	IMRT	fGK	IMRT	fGK	IMRT	fGK	IMRT	fGK	IMRT	fGK
Nausea	41 80.4%	49 100.0%	10 19.6%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%
Headache	43 84.3%	47 95.9%	7 13.7%	1 2.0%	1 2.0%	1 2.0%	0 0%	0 0%	0 0%	0 0%
Neurological Deficit	44 86.3%	48 98.0%	6 11.8%	0 0%	1 2.0%	1 2.0%	0 0%	0 0%	0 0%	0 0%
Others	27 52.9%	48 98.0%	18 35.3%	0 0%	6 11.8%	1 2.0%	0 0%	0 0%	0 0%	0 0%
Late Toxicity (51 vs 49 patients)										
	IMRT	fGK	IMRT	fGK	IMRT	fGK	IMRT	fGK	IMRT	fGK
Headache	49 96.1%	48 98.0%	1 2.0%	0 0%	1 2.0%	1 2.0%	0 0%	0 0%	0 0%	0 0%
Neurological Deficit	39 76.5%	45 91.8%	10 19.6%	2 4.1%	6 11.8%	1 2.0%	4 7.8%	1 2.0%	1 2.0%	0 0%
Others	32 62.7%	46 93.9%	9 17.6%	2 4.1%	10 19.6%	1 2.0%	0 0%	0 0%	0 0%	0 0%

P092

CLINICAL IMPLEMENTATION OF ROBUST IMRT-VMAT TREATMENT WORKFLOW FOR CRANIO-SPINAL RADIOTHERAPY IN MEDULLOBLASTOMA PATIENTS

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Aims. Assess the feasibility and the robustness of a radiotherapy treatment workflow for cranio-spinal (CSI) irradiation based on multi-isocentric volumetric modulated arc radiotherapy (VMAT).

Material and Methods. Seven patients affected by medulloblastoma, treated with cranio-spinal radiotherapy were retrospectively evaluated. A VMAT treatment plan template was developed with multiple-isocenters in the encephalon and upper and lower spine. The prescription dose was 36 Gy/18 fractions on rachis and encephalon plus a 18Gy boost on the cranial fossa. Patients were immobilized in head first supine position using a 5-point thermoplastic mask. To measure pre-treatment shifts kV Cone Beam CTs were acquired at each treatment session. Shifts ≥3mm were always corrected. A metric was setup for the evaluation of the robustness of plans *vs* real and systematic/stochastic isocenter shifts. In particular: volume of the CTV/PTV covered by 95% isodose, volume of PTV receiving 107% of prescription dose, maximum dose to the spinal cord, mean dose to the heart/kidneys, volume of each kidney receiving 30Gy, volume of both kidneys receiving 10Gy, volume of lungs receiving 20Gy were considered.

Results. Both dose accumulation and analysis have been performed with Elekta ProKnow DS software. The results compare real shift and stochastic/systematic shifts generated with a random process over spheres of radius of 2.5, 3.0, 5.0/3.0mm respectively. In general, coverage of CTV remains optimal for all shift values. The coverage of the PTV deteriorates significantly when 5mm stochastic/3mm systematic errors are considered. Dose to the OARs and in particular maximum dose to the spinal cord always remain within tolerance values.

Conclusions. Preliminary data demonstrate that the VMAT workflow for CSI irradiation promises to be feasible and robust regarding target coverage and critical organs sparing. Enlargement of patient cohort and dosimetric assessment of the results are advisable prior to implementating CSI-VMAT workflow in everyday clinical practice.

P093

RADIATION-INDUCED ALOPECIA IN PATIENTS WITH PRIMARY BRAIN TUMOR

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Aims. The aim of our study was to observe hair regrowth times in patients affected by brain tumors subjected to cranial irradiation, and to develop a dose-response relationship for the onset of alopecia, an important side effect that impacts on the quality of life of patients especially on a psychological level.

Patients and Methods. In this study were enrolled 26 patients with brain tumor, all female, aged between 25 and 76 years, treated with post-operative radiotherapy from 2018 to 2023. Radiotherapy technique was 3D-CRT (three-dimensional conformal radiation therapy) in 14 patients and the VMAT (volumetric modulated arc therapy) in 12 patients. Of the 26 patients, 7 were meningiomas, 2 oligodendrogliomas, 4 astrocytomas and 13 glioblastomas. Radiotherapy was associated with oral chemotherapy with temozolomide in 18 patients. During the treatment planning process, the scalp was drawn as an organ at risk, distinguishing the portion of the scalp located on the region ipsilateral to the surgical cavity, from the contralateral scalp region and giving a maximum dose cut-off of 4600 cGy and 3200 cGy. The alopecia was evaluated and divided into grade G1 (mild), grade G2 (moderate) and G3 (severe).

Results. The mean dose to the scalp ipsilateral to the treatment field was 2790 cGy. The patients were evaluated one month after the end of the radiation therapy and grade G1 alopecia was found in 10 patients (38%), grade G2 alopecia in 13 patients (50%) and grade G3 alopecia in 3 patients (12 %). In the follow-up three months after the end of the radiation therapy, complete resolution of the alopecia was found in patients with grade G1 and G2 and partial resolution in patients with grade G3. It was also found that the degree of alopecia was related to the technique used to perform the treatment. Of the 14 patients treated with the VMAT technique, none presented G3 alopecia, 50% G1 alopecia and 50% G2 alopecia. Of the 12 patients treated with the 3D conformal technique, 33% presented G1 alopecia, 58% G2 grade alopecia and 25% G3 grade alopecia.

Conclusions. Giving a cut-off of maximum dose to the scalp (OAR), we found a halving of hair regrowth times and absence of permanent alopecia. The dose-response relationship could provide a guideline for treatment planning by calculating the dose to the follicle and keeping it below the cut-off.

P094

COULD BLOOD TEST HAVE PROGNOSTIC VALUE IN GLIOMA PATIENTS? A MONO-INSTITUTIONAL RETROSPECTIVE STUDY

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Aims. Glioma are malignant brain tumors with low survival time after initial diagnosis so it is urgent to find easy-to-perform markers to predict the outcomes. The combinations of blood cells, such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), the lymphocyte-to-monocyte ratio (LMR), systemic immune inflammation index (SII) and systemic inflammation response index (SIRI) were demonstrated as effective prognostic indicators in many cancer patients. Our aim is to see if these combined ratios could have a prognostic value of survival time in glioma patients.

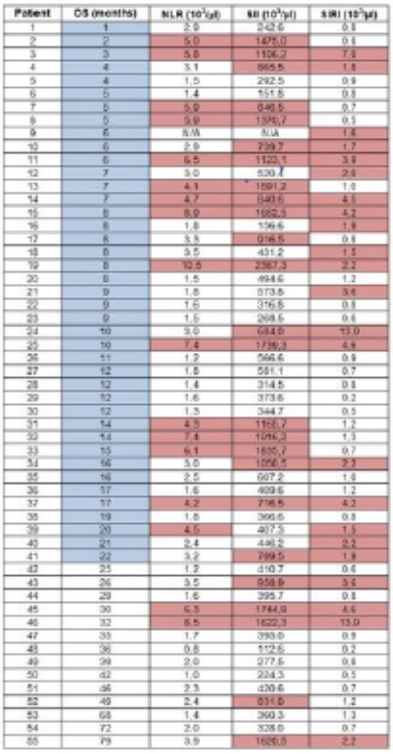
Methods. A retrospective study was carried out in patients with diagnosed glioma who underwent radiotherapy between January 2016 and December 2022. A 24-months cut off was set for overall survival (OS) in order to divide patients in two groups. The OS was defined as the interval between the diagnosis and death or, for patients still alive, between the diagnosis and their last follow-up. The expression of Ki-67 was categorized into two groups: low and intermediate (Ki-67 <30%), and high (Ki-67 ≥30%). Blood tests results were collected before starting radiotherapy. Hemoglobin, total white blood cells (WBC), neutrophils (N) platelets (P), lymphocytes (L) and monocytes (M) were collected. The NLR, the PLR, the LMR, the SII (P×N/L) and the SIRI (M×N/L) were calculated and compared to reference values.

Results. In our study, 55 pts were analyzed. The median age was 58 ± 13 years old. High-grade glioma were 80% of the analyzed group. Ki-67 ≥ 30% was registered in 80% for GBM. The median OS was 19 ± 18 months. All patients underwent radiotherapy and 54% of them received 60Gy (2Gy/fx). Temozolomide was given concomitantly to 80% of patients. Among blood variables, neutrophils were increased in 28% of patients. In 17 (31%) patients, NLR, SII and SIRI together exceeded the reference values (NLR >4x10^3/ µl, SII >655,5x10^3/µl and SIRI >1,43x10^3/µl). In 16 (37%), in 22 (51%) and in 26 (60%) of GBM patients, NLR, SII and SIRI were elevated, respectively. Regarding prognostic value, PLR and LMR did not show difference between groups; NLR, SII, SIRI values were increased in 15 (37%), in 20 (50%), in 25 (61%) of the patients with ≤ 2 years OS, respectively (Table 1).

Conclusions. Our analysis suggests that combined ratios of blood cells could have prognostic implications, in particular the SII and the SIRI and that they could increase the possibility of a personalized approach for glioma patients.

Table 1.

Table 1: Correlation between Overall Survival (OS) and combined of blood cells. In blue, OS < 24 months and in red, elevated values NLR, SII and SIRI.



Patient	OS (months)	NLR (10^3/µl)	SII (10^3/µl)	SIRI (10^3/µl)
1	1	2.9	2425	0.8
2	2	5.0	1475.0	0.8
3	3	5.8	1106.2	7.9
4	4	3.1	865.5	1.8
5	4	1.5	292.5	0.9
6	5	1.4	551.5	0.8
7	5	3.9	846.5	0.7
8	5	5.9	1376.7	0.5
9	6	N.A	N.A	1.6
10	6	2.9	739.7	1.7
11	6	6.5	1123.1	3.9
12	7	3.0	520.7	2.8
13	7	4.1	1891.2	1.0
14	7	4.7	840.6	4.5
15	8	8.9	1682.8	4.2
16	8	1.8	556.6	1.8
17	8	3.8	916.5	0.8
18	8	3.5	431.2	1.5
19	8	10.5	2367.3	2.2
20	8	1.5	494.6	1.2
21	9	1.8	573.8	3.6
22	9	1.5	316.5	0.8
23	9	1.5	268.5	0.6
24	10	3.0	684.0	13.0
25	10	7.4	1736.3	4.9
26	11	1.2	566.6	0.9
27	12	1.8	581.1	0.7
28	12	1.4	314.5	0.8
29	12	1.6	373.6	0.2
30	12	1.3	344.7	0.5
31	14	4.5	1165.7	1.2
32	14	7.4	1014.3	1.3
33	15	6.1	1835.7	0.7
34	16	3.0	1056.5	2.2
35	16	2.5	697.2	1.8
36	17	1.6	469.6	1.2
37	17	4.2	716.5	4.2
38	19	1.8	366.6	0.8
39	20	4.5	407.5	1.5
40	21	2.4	446.2	2.2
41	22	3.2	789.5	1.8
42	25	1.2	410.7	0.6
43	26	3.5	858.9	3.6
44	29	1.6	395.7	0.8
45	30	6.3	1744.0	4.6
46	32	8.5	1622.3	13.0
47	33	1.7	390.0	0.9
48	36	0.8	112.6	0.2
49	39	2.0	277.5	0.8
50	42	1.0	224.3	0.5
51	46	2.3	420.6	0.7
52	49	2.4	631.0	1.2
53	68	1.4	360.3	1.3
54	72	2.0	328.0	0.7
55	79	3.9	1626.0	2.2

P095

OUTCOME ANALYSIS AND PATTERNS OF RECURRENCE IN A SINGLE – ISTITUTION SERIES OF PATIENTS (PTS) WITH GLIOBLASTOMA (GBM)

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Aims. To evaluate patterns of recurrence and overall survival (OS) in a series of pts treated for GBM at our Institution.

Methods. From June 2016 to December 2022, 206 consecutive pts with GBM were treated. The majority of

pts underwent surgical resection followed by concurrent Temozolomide (TMZ) and localized radiotherapy (RT) (VMAT or Tomotherapy). GTV encompassed tumor bed and eventual residual tumor on contrast-enhanced (CE) T1 MRI; CTV was driven by a 2-cm expansion on GTV (including FLAIR abnormalities); PTV was driven by a 0.3-cm expansion from CTV. Standard RT course consisted in 60 Gy in 30 fractions (Fx); we delivered a hypofractionated RT course (40.05 Gy in 15 Fx) to elderly patients (70 or older) and to those with a poor prognosis. MRI images were analyzed and used to define three categories of recurrence: in-field if >80% of the recurrent tumor was located within the 95% isodose surface; marginal if 20-80% of the recurrent lesion was within the 95% isodose surface; distant if <20% of the recurrent lesion was within the 95% isodose surface.

Results. 206 consecutive patients were evaluated; of these 134 were male and 72 female. Median age at the time of first surgery was 61 (range 30-88). ECOG performance status in each pt was 0-2. 9 pts underwent biopsy, 19 pts a partial resection, 178 pts a gross total resection. Glioblastoma histology was confirmed in all pts. 160 pts underwent RT 60 Gy in 30 Fx plus concomitant TMZ; 46 pts received a hypofractionated RT schedule (40.05 Gy in 15 Fx) plus concomitant TMZ. 81 of the 206 pts relapsed: 83% in field, 7% marginal and 10% outfield. 17 out of the 81 pts underwent a second surgery followed by re-irradiation (reRT) and then a second line chemotherapy, 15 pts a reRT and then chemotherapy, 49 pts a second line chemotherapy only. ReRT doses ranged from 36 to 54 Gy in 18-27 Fx; GTV encompassed tumor or tumor bed (in case of resection) on CE T1 MRI; PTV was driven by a 1-cm expansion from GTV. No G2-G4 toxicities were observed in reRT pts. In the whole series, mean follow-up was 25 months (range 3-81). Median OS from the end of first RT was 16 months (range 3-81).

Conclusions. Our data in terms of OS are comparable to the ones of the literature. In case of relapse, reRT proved to be a valid option in terms of toxicity and efficacy. The predominantly in-field distribution of recurrences comforts us in applying the new guidelines which envisage a reduction in the expansion of GTV to CTV.

P096

ROLE OF THE CALCIUM INDEX SCORE IN ELDERLY PATIENTS WITH GLIOBLASTOMA TREATED WITH RADIO-CHEMIOTHERAPY

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Aims. Recent clinical evidence has shown that age and, especially, heart and brain comorbidities play a prognostic role in glioblastoma patients. Moreover, the role of comorbidities related to vascular disease is under investigation. On this basis, the present study aims to evaluate in a mono-institutional and retrospective manner a potential correlation between the calcium index score (CI) and the prognosis of glioblastoma patients treated with radiochemotherapy.

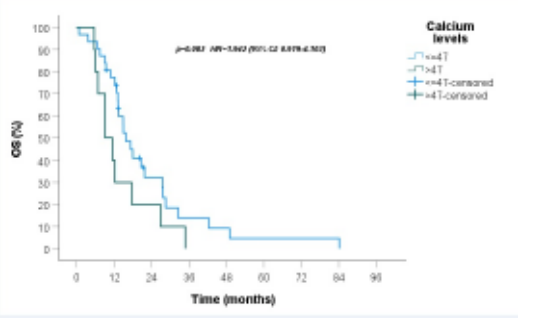

Figure 1.

Methods. We selected 95 patients older than 60 years and diagnosed with glioblastoma who were treated from 2015 to 2020 with postoperative radiochemotherapy. The primary endpoint was overall survival (OS) as measured from the diagnosis of glioblastoma. For quantification of the calcium burden, precontrast CT images with 2.5mm slice thickness were transferred to a dedicated workstation, and the Agatston score was computed semiautomatically using the Calcium Scoring Plugin of the open-source software Horos Project™, version 3.0 (https://horosproject.org). Agatston scores were categorized using the following cutoffs: 0 (none), 1-99 (mild), 100–399 (moderate), and ≥400 (severe). The mean value was identified; therefore, overall survival curves were calculated using the Kaplan–Meier method, while the log-rank test was applied to evaluate the differences between curves. Univariate survival analysis of the predictive continuous factors was performed, and the significant factors were subsequently dichotomized by the

quartile method. All the calculated categorical factors were subjected to Cox regression as a part of multivariate survival analysis (adjusting for surgery), using a stepwise method; a hazard ratio with a 95% confidence interval was indicated.

Results. Fifty-five patients were excluded due to the close relationship between the calcified arterial wall and the bony skull base, which prevented an accurate quantification of ICA calcifications. Forty-one patients were eligible for this analysis. OS median time considering all patients was 15 (IC 10-20). The mean value of the calcium index was 47 (median age 61, male/female 32/17, median OS 15). At the univariate analysis, OS median time in patients with CI≤47 or >47 was 16 (95%IC 12-20) and 9 (95%IC 4-14) months, respectively (p value was 0.082, HR 1.9 (0.9-4.1).

Conclusions. The data obtained indicate that IC could be further investigated as a prognostic biomarker in elderly GBM patients.

P097

HELICAL TOMOTHERAPY FOR LARGE-SIZE, COMPLEX-SHAPED INTRACRANIAL MENINGIOMAS

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Aims. Radiation therapy (RT) plays a major role in different settings of intracranial meningioma presentation according to feasibility and extension of surgical resection, grade and tumor dimension. Standard-fractionated RT is generally used for large-size meningiomas or lesions closed to critical organs at risk. Helical Tomotherapy (HT) allows high conformal dose-distribution also for complex-shaped lesions. Aim of this study is to present results of tolerability and efficacy of HT for RT treatment of large-size and complex-shaped intracranial meningiomas in a single-center experience.

Methods. A retrospective single-center study was performed. Clinical endpoints of the present study were RT acute an late toxicities, local control (LC), intracranial control (ICC) and overall survival (OS). Large-size, complex-shaped meningiomas were treated with HT at standard prescription dose of 54–60 Gy in 1.8–2.0 Gy fractions or lower RT-dosages in case of re-irradiation. Target volumes were defined using MRI imaging and Gross to Clinical Target Volume expansion was 3 mm. After HT patients (pts) were followed-up with clinical/physical evaluation and MRI every 3 months. Acute and late toxicity were defined according Common Terminology Criteria for Adverse Events scale, while LC, ICC, OS were extimated with Kaplan-Meyer method.

Results. From 2009 to 2022, 24 patients with large-size, complex-shaped meningiomas were treated with HT. Median age was 66 years (range 31-80), all patients had Karnofsky Performance Status (KPS) >= 70. Nine pts had skull-base locations, other pts had parafalcine and cortical meningiomas. Twenty-two pts (91.6%) underwent surgery with Simpson 4-5 grade resection. Two pts with inoperable meningiomas underwent definitive HT. Twelve pts had extra-cranial extension, and 10 pts were WHO grade II-III at diagnosis. Median follow-up was 21 months (range 1-162). No acute toxicity was assessed in 42 % of pts, mild toxicity was detected in 54% of pts with just 1 case of grade (G) 3 mucositis. Still, late toxicities were absent in 63% of pts, G1-G2 and G3 (1 case of hypopituitarism) were 33% and 4%, respectively). Three-year (y) LC , 3-y ICC and 3-y OS were 76%, 68% and 59% respectively. Recurrences after HT were inside RT field in 78% of cases (7/9 pts).

Conclusions. HT allowed a very good toxicities profile and clinical outcomes consistent with literature data for large-size, complex-shaped meningiomas with unfavourable risk factors.

P098

HYPOFRACTIONATED STEREOTACTIC RADIOTHERAPY AFTER HYPERBARIC OXYGEN THERAPY FOR RECURRENT HIGH GRADE GLIOMA

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Aims. Brain tumours, especially highly aggressive GBM with its necrotic tissue, are more likely to be affected by hypoxia. The presence of hypoxic cells in high-grade glioma (HGG) is one of major reasons for failure of local tumour control with radiotherapy (RT). The radiosensitivity of brain tumours could potentially be increased by performing hyperbaric oxygenation (HBO) before the RT session. We propose a new treatment to improve the efficacy of Hypofractionated Stereotactic Radiotherapy (HSRT) using HBO (HBO-RT) for the recurrent HGG (rHGG).

Methods. We enrolled 15 patients (aged >18 years) with diagnosis of rHGG. A total dose of 15-25 Gy was administered in daily 5-Gy fractions for 3-5 consecutive days after daily HBO. Each fraction was delivered up to maximum of 60 minutes after HBO.

Results. Median follow-up from re-irradiation was 28.5 months (5.3-56.8 months). Median PFS was 3.2 months (1.4-6.4 months), Six- and 12-month Progression-free survival was 40.0 % (95% CI: 16.5-62.8) and 10.0 % (95% CI: 0.8-33.5), respectively. Median overall survival of HBO-RT was 11 months (95% CI: 6.6-24.2). No acute or late neurologic toxicity >grade (G)2 was observed.

Conclusions. HSRT combined with HBO therapy appears to be feasible without serious toxicity and appears to be a promising treatment for relapsed high-grade glioma.

P099

FRAMELESS LINAC-BASED STEREOTACTIC RADIOTHERAPY (SRT) FOR VESTIBULAR SCHWANNOMA (VS): EVALUATION OF TOXICITY AND OUTCOME

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Aims. We document toxicity and outcome of a single fraction radiosurgery (SRS) or fractionated stereotactic radiotherapy (FSRT) on vestibular schwannoma (VS).

Methods. Patients (pts) diagnosed with *vs* are managed at the skull base clinic. They were evaluated according to their clinical presentation and tumor size. A 1 mm thickness CT-scan (pCT) was acquired while patients were in a supine position and secured with two different mask systems. Until September 2022, we used the BrainLab stereotactic mask, after that, we switched to the QFix Encompass system with HyperArc SRS workflow. Pts underwent a contrast-enhanced MR scan with 3D fast gradient echo T1-weighted sequences that were rigidly merged with pCT. The PTV resulted from the isotropic expansion (1-2 mm) of the GTV. VMAT plans were based on 6MV FFF non-coplanar beams. Treatment was delivered using the Varian-Siemens TrueBeam Stx platform.

Results. Between March 2021 and March 2023, we managed 25 VS. Symptoms at presentations included: hearing loss, tinnitus, imbalance, facial nerve palsy and trigeminal neuralgia. Four pts had prior surgery and were treated with SRT for recurrent VS. The median follow-up was 11 months. Ten patients were treated with SRS (12.5Gy/1fr) and 15 with FSRT. FSRT was delivered in 3 fractions for 11 pts (18Gy/3fr) and in 5 fractions (25Gy/5fr) for the last 4 pts. The total dose was prescribed to 95% of the volume. The median PTV volume was 1.1cc for SRS, 2.5cc for 3fr FSRT and 9.5cc for 5fr FSRT. The median dose to the PTV was 13.1Gy (1fr), 18.8Gy (3fr) and 25.8Gy (5fr) for the single and the multi-fractions radiosurgery, respectively. Cochlea Dmax(0.035cc) was: 11.4Gy (1fr), 18.2Gy (3fr) and 25.5Gy (5fr). The median Brainstem D1cc was 2.1Gy for the single fraction, 4.5Gy and 17.3Gy for 3 and 5 FSRT. At the time of treatment, 8 pts had functional hearing. One year after SRT, all pts maintained their hearing function despite almost half experiencing hearing decline. Four months after STR 76% of the pts had stable disease, 24% had increased *vs* size because of tumor inflammation. Seven pts had acute deteriorating symptoms, all but one were recovered one year after SRT. Nine pts (36%) reported acute Grade 1 and 2 toxicity, which required steroids. No Grade 3 acute toxicity events were recorded. Out of the 3 pts who developed radionecrosis one year

after SRT, only 1 exhibited symptoms.

Conclusions. Our findings regarding *vs* pts treated with SRT are in line with literature data.

P100

MANAGMENT OF GLIOBLASTOMA IN ELDERLY PATIENTS:SAFETY AND QUALITY OF LIFE

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Aims. Glioblastoma is characterized by a poor prognosis in the elderly, with a median survival of less than two years. Survival increases when chemotherapy is added to radiation therapy among patients 70 years.

Method. We analyzed the tolerance profile and quality of life of elderly patients treated in our center with glioblastoma treated with hypofractionated radiotherapy and concomitant temozolomide. The patients received either radiotherapy alone or radiotherapy with concurrent and adjuvant temozolomide.

Results. Twelve pts were analyzed from January 2020 to January 2023 (M/F: 7/5). The mean age is 75.5 years (65-87). Ten pts operated totally or sub-totally, and 8 pts had MGMT promoter methylation. Eight pts received hypofractionation radiotherapy (40 Gy in 15 fractions) alone, and five pts received hypofractionation radiotherapy with concurrent and adjuvant temozolomide. Overall survival was higher in patients who received temozolomide in addition to radiotherapy (21 months *vs* 15 months), as was progression-free survival (6 months *vs* 3.8 months). Quality of life was comparable in patients who received radiotherapy alone and those who received combined treatment and was analyzed using the EORTC QLQ-C30 questionnaires for cancer in general and the EORTC QLQ-BN2 questionnaire specific for brain tumors. In 8 pts, it was necessary to activate psychological support for the patient and caregivers. Hematological toxicity was found in 9 pts taking temozolomide and cortisone but was acceptable.

Conclusions. In our experience with elderly patients with glioblastoma, adding temozolomide to short-term radiotherapy confirmed an increase in overall survival compared to radiotherapy alone with acceptable safety profiles and tolerance.

P101

RESPONSE TO BEVACIZUMAB IN A PATIENT WITH CEREBELLAR RECURRENT HEMANGIOBLASTOMA

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Aims. We reported the efficacy of bevacizumab in recurrent hemangioblastoma with leptomeningeal spread of disease

Methods. We reported the case of 54- year old female patient , who underwent gross tumor resection of a right cerebellar mass in March 2011. The pathologist classified the lesions as hemangioblastoma grade I WHO. In July 2019 , following the appearance of neurological symptoms like dizziness and vomit, the patient was submitted to a brain MRI that showed recurrent disease in the IV ventricle . Afterwards the patient underwent second surgery with macroscopically complete resection of the tumor In March 2020, new neurological symptoms appeared and a Brain MRI showed the presence of multiple leptomeningeal nodular lesions. Considering the clinical and radiological progression, the patient started a first line of systemic therapy with Bevacizumab 10 mg/kg iv Q2W. After 6 cycles a brain MRI demonstrated a complete radiological response

Results. A complete radiological and clinical response was obtained with bevacizumab

Conclusions. Literature data report that hemangioblastoma seems to express high levels of vascular endothelial growth factor that drives the angiogenesis and tumor progression.[1] This case report shows the potential efficacy of anti VEGF Bevacizumab in hemangioblastoma patient with leptomeningeal spread of disease

Reference

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P102

STEREOTACTIC RADIOTHERAPY WITH HELICAL TOMOTHERAPY FOR BRAIN METASTASIS

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Aims. The role of stereotactic radiotherapy (SRT) for the treatment of brain metastases is well consolidated and supported by high level evidence in the literature. In the present study we report the outcomes of our mono-institutional experience of Helical Tomotherapy (HT)-based SRT for brain metastases

Methods. This study reports data collected from a retrospective series of patients with brain metastases treated with HT-SRT. Inclusion criteria were: KPS>70; life expectancy>6 months; ≤ 5 brain metastases; limited uncontrolled extracranial disease (up to 3 body metastases). Survival endpoints were assessed using Kaplan-Meier method and Cox regression for uni- and multi-variate analyses. Graphpad Prism was used for statistical analysis. Toxicity was prospectively collected using the CTCAE v5.0 criteria.

Results. From March 2018 to June 2022 a total of 64 lesions in 37 patients was treated with HT-SRT for a median total dose of 30 Gy (range, 28-30) in a median number of fractions of 5 (3-5). Median PTV was 2.66 cc (0.74-30.69cc). The most frequent primary histologies were NSCLC, colorectal cancer and breast cancer, respectively in 54%, 13.6% and 16.2%. Concurrent systemic therapy was administered in 56% of patients. With a median follow-up of 7 months (3-38), 1- and 2-years local control (LC) rates were 92,5% and 92,5%; at multivariate analysis, higher RT doses were predictive of improved LC (p=0.013). Similarly, higher RT doses were related to improved intracranial progression-free survival (IPFS) rates, although not reaching statistical significance. At multivariate analysis, LC was correlated to a better IPFS (p=0,01). Global IPFS rates were 56,75% and 51,35% at 1- and 2-years. Systemic progression-free survival rates were 51,35% and 48,64% respectively, without any predictive factor for improved outcomes at multivariate analysis. Overall survival (OS) rates were 54,05% and 40,54%, with uncontrolled extracranial disease and low RT doses related to worse survival outcomes. No severe adverse event reported.

Conclusions. HT-SRT resulted in promising initial results. Interestingly, higher RT doses showed statistical significance for improved outcomes in terms of LC and OS.

P103

CYBERKNIFE STEREOTATIC RADIOSURGERY FPR BILATERAL SCHAWANNOMAS IN PATIENT WITH NEUROFIBROMATOSIS TYPE 2

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Aims. Neurofibromatosis Type 2 (NF2) is an autosomal dominant. Patients with NF2 often harbor multiple central nervous system tumors. Bilateral vestibular schwannomas (BVS) are a hallmark of these disease and often result in progressive hearing loss, bilateral trigeminal and bilateral facial nerve function loss. Treatment strategy of BVS usually consist in microsurgery followed by radiation therapy (either single dose stereotactic radiosurgery (SRS) or fractionated stereotactic radiotherapy (FSRT)). Synchronous radiation treatment of BVS is challenging from a technical point of view because of the elevated risk of neurological toxicity associated. In this study we present the case of a patient affected by NF2 with BVS treated simultaneously with Cyberknife (CK) technology.

Methods. A 27-year-old man with a history of NF2 presented bilateral Schwannomas at VIII cranial nerve. Diagnostic brain MRI showed bilateral enhancing lesion in the internal auditory canal coupled with BVS (right 32x20x40mm, left 30x17x30mm). Traditional audiogram demonstrated bilateral sensorineural hearing loss. All other aspects of the neurological exam were intact. Patient had prior partial resection of right *vs* and then after 6 months he had partial resection of left one. The two bilateral residues of, respectively, 3.04cc left and 0.98cc right, were located close to the brainstem and were treated contemporarily with CK FSRT. The prescribed dose was 25Gy in 5 fractions (5Gy/fr/die) to the 79% isodose level with a coverage of both targets equal to 99% : the minimum dose delivered to the lesions was 2400cGy and the maximum dose was 3164cGy. Fractions were administered on consecutive days. After FSRT, the patient was clinically evaluated every 3-6 months.

Results. After a follow-up of 24 months , radiographic and clinical tumor control was reached. No new or worsening facial paresis developed during follow-up, consequently the facial nerve function preservation was obtained. At the last MRI, the residual tumors demonstrated shrinkage.

Conclusions. CK radiotherapy is a safe and an effec-

tive way of achieving local tumor control in patients with BVS even in patients with NF2 which are considered harder to control than sporadic vestibular schwannoma. The ability of CK to deliver high dose of radiation to small volumes with high conformality allowed to treat in the same session both lesions sparing the brainstem and thus avoiding neurological toxicities. Our patient experienced tumor control without additional toxicity. FSRT is a safe and effective treatment option for treating *vs* with tolerable toxicities.

P104

INDIVIDUAL MONITORING OF DOSIMETRIC CHANGES IN HEAD AND NECK ADAPTIVE PROTON THERAPY: ANALYSIS OF AN ADAPTIVE WORKFLOW

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Aims: Proton Therapy (PT) is sensitive to anatomical changes that may impact the planned dose distribution and the treatment quality. In non-adaptive treatment, robust anatomical planning might manage some anatomical changes with a potential decrease in plan quality. Adaptive strategies are recommendable, but they are technically and resource-demanding. Few studies reported the impact of individual monitoring of dosimetric changes occurring over PT treatment. In this study, we retrospectively evaluated head and neck (HN) patients treated for four years in our center, presenting the advanced workflow, based on monitoring by repeated computer tomography (CT) scans, implemented during the study.

Methods. Repeated CT scanning was performed on 201 patients to recognize dynamic anatomical changes during HN PT. The image-driven workflow we implemented includes in-room CT on-rails for image acquisition, automatic contouring using planning CT as atlas data, and fast dose computation on a Graphics Processing Unit by a Monte Carlo algorithm. Quality assurance (QA) of the automatic contouring was performed on seven patients (three with slimming and four with target modifications) by comparison with manual contouring under medical supervision. The time duration to perform each phase of the workflow was assessed. Finally, we calculated the number of patients who required replanning, identifying the causes for such an adaptive modification.

Results. Contours QA (Table 1) showed differences between the manual and automated process in only a few organs at risk (OAR), with dose differences in even fewer cases. The target needs always to be verified to identify progression/response. Table 2 reports the estimated time required to perform every workflow phase, with a total time of approximately 16-17 mins. Sixteen of the treated patients required treatment replanning for different reasons: variation in the filling of the nasal cavity, weight loss and slimming, change in the target volume, and consequent target under-dosage.

Conclusions. Start-of-the-art technology is mature for an affordable and time-efficient workflow,mostly automatized. Our data shows how anatomical changes requiring adaptive replanning occur in a small number of patients (8% of cases in our study). Reasons for replanning are different, and it is hard to model them all. Individual monitoring by repeated CT scans is an optimal strategy to select patients who require replanning in adaptive HN PT.

Table 1. Contours with observed differences between manual and automated contouring.

Contour	Cause of differences	Dosimetric impact	Adaptive replanning
CTV	Progression/Response	Yes	Yes
Eyes/Lens	Inter-fraction movement	Could be relevant	Only if critical*
Optic Nerves	Inter-fraction movement	Could be relevant	Only if critical*
Oral cavity	Slight inaccuracy (i.e. artifacts from dental implant)	Not relevant (<3 Gy)	No
Parotids	Slight inaccuracy	Not relevant (≤ 1 Gy)	No
Frontal/Temporal lobes	Inaccuracy in contouring due to unclearly anatomical boundaries	Can be relevant (≈4 Gy)	Only if critical*
Constrictor muscles	Slight inaccuracy	Not relevant (≤ 1 Gy)	No
**** Critical means that the dose to the OAR almost exceeds the maximal tolerance***			

Table 2_ Workflow time estimation

Procedure	Sub-procedure / Description	Estimated time (sec)	Operator
In-room CT acquisition	Couch movement	80 sec	Therapist
	CT acquisition	250 sec	Therapist
	Couch movement* Image transfer to TPS *	80 sec	Therapist
TPS Image loading	Load CT images into TPS	60 sec	Dosimetrist
Plan initialization	Creation of external contour, selection of calibration curve	200 sec	Dosimetrist
Image registration	Automatic rigid registration on the focused region of interest	40 sec	Dosimetrist/Radiation Oncologist
Automated CTV/OAR contouring	Atlas Based	120 sec	Dosimetrist/Radiation Oncologist
PTV/PRV contour propagation	Update of previously defined expansion	60 sec	Dosimetrist
Plan computation	1 beam-set	90 sec	Dosimetrist
	2 beam-set	90+30 sec	Dosimetrist
	3 beam-set	90+30+20 sec	Dosimetrist
** Performed contemporarily*			

P105

COMBINING HIGH-LET AND LOW-LET RADIATION FOR RADIORESISTANT SALIVARY GLAND AND SINONASAL CANCERS: PRELIMINARY OUTCOME RESULTS

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Aims: The combination of high-Linear Energy Transfer (LET) radiotherapy (RT) like carbon ions RT (CIRT) and low-LET RT, like photons or protons RT (PhT, PT) is an emerging approach to treat patients (pts) with radioresistant cancers. We aim to evaluate the outcomes of this mixed strategy with an up-front CIRT boost therapy followed by PhT or PT for a cohort of locally advanced salivary gland and sinonasal cancers (SGCs and SNCs).

Methods. A cohort of 78 pts with SGCs and SNCs unsuitable for radical or conservative surgery treated from June 2015 to June 2022 with CIRT boost followed by PhT (group 1) or PT (group 2) were included in this retrospective analysis. Patients' and tumor characteristics are shown in Table 1. Up-front CIRT boost was given to the High-Risk Clinical Target Volume (HR-CTV) and PhT or PT were delivered to Low-Risk CTV (LR-CTV). Target planning goals, OARs constraints and cumulative dose distributions were shared among radiation oncologists working at different centers. Differences in the two groups were explored by Mann-Whitney U test. Local Relapse Free Survival (LRFS) at 2-y was evaluated with the Kaplan Meier method and differences in PhT vs. PT, as well as in SGCs and SNCs, were investigated with Log-rank test (α=0.05).

Results: Adenoid cystic carcinoma was the most common histology in both groups. SNCs were more frequent in group 2. CIRT boost was delivered to all pts with a median total dose of 15 Gy RBE (3 Gy RBE/fr), (range: 9-24 Gy RBE). Median total dose was 54 Gy (range: 50 – 60) and 60 Gy RBE (range: 54 – 60) in PhT and PT groups, respectively with a statistically significant difference (p = .001). Group 2 had a smaller median HR-CTV compared to group 1 (p = 0.3). The median follow-up was 16.6 and 15.5 months for PhT and PT respectively. No statistically significant differences were reported in the 2-y LRFS (p=0.3) between the two groups: group 1 (97%, 95% CI: 90% -100%) and group 2 (86%, 95% CI: 74%-98%). Similarly, SGCs 2y-LRFS was not significantly different (p=0.6) in group 1 (96%, 95%CI: 88%-100%) and group 2 (86%, 95% CI: 77%-100%), while no comparison was performed for SNCs due to sample size issues. In both cohorts, toxicity profiles were acceptable.

Conclusions. Mixed-beam approach requires a timely coordination among centers. High LRFS were achieved by combining high-LET and different low-LET beam qualities, although future research is needed to optimize pts selection.

Table 1. Patients' and tumors' characteristics.

Patients' characteristics		
	Group 1 (n=32): CIRT + Photon	**Group 2 (n=46): CIRT + Proton**
Gender:		
▪ **Male (N, %)**	18 (56%)	26 (57%)
▪ **Female (N, %)**	14 (44%)	20 (43%)
Median Age (range)	55 (14-81)	58 (17-81)
Tumors' characteristics		
Salivary Gland Cancers (SGCs) (tot N pts)	27	26
▪ Adenoid cystic carcinoma (ACC)	15	17
▪ Trachea	3	-
▪ High grade non-ACC	8	8
▪ Low-grade non-ACC	4	1
Sinonasal Cancers (SNCs) (tot N pts)	5	20
▪ Undifferentiated Sinonasal Carcinoma (SNUC)	4	8
▪ Others (including intestinal type adenocarcinoma and mucosal melanoma)	1	12
Systemic treatment for SNCs	5	20
▪ Induction CT + RT-CT	4	3
▪ Induction CT	1	14
▪ Only RT-CT	-	-
▪ No CT	-	3*
HR-CTV SGCs and SNCs		
Range (cc)	14.81 – 759.03	17.98 – 182.64
Median (cc)	124.14	98.37
Mean ± SD (cc)	158.22 ± 135.64	117.67 ± 101.15

**1 Mucosal Melanoma, 1 Elderly patient, 1 refusal CT*

P106

IMMUNOTHERAPY-RELATED HYPOTHYROIDISM IS EXACERBATED BY PREVIOUS RADICAL RADIOTHERAPY: A MATCHED-COHORT ANALYSIS IN HEAD AND NECK CANCER

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Aims. Combined radiotherapy (RT) and immunother-

apy (IT) is a validated approach for head and neck squamocellular carcinoma (HNSCC) treatment. Hypothyroidism is a common side effect of both RT and IT. However no dosimetric or clinical parameters have been found to predict thyroid function outcomes and an eventual synergism between RT and IT in thyroid damage is not reported in literature. The aim of this study is to analyze the impact of RT in hypothyroidism risk in HNSCC patients treated with IT.

Methods. We retrospectively reviewed patients with HNSCC and divided them in 2 groups; patients treated with both RT and IT (RT-IT group) and patients treated with IT alone, or palliative RT with a total dose < 50 Gy (IT group). For all patients demographic and clinical data were noted. RT information, i.e. total dose, number of fraction, RT intent and dosimetric data i.e. mean thyroid dose (tDmean), thyroid volume (tVtot), the volume of thyroid receiving 50 Gy (tV50) and the volume of thyroid receiving 60 Gy (tV60) were recorded too. Occurrence or worsening of hypothyroidism (at least G1 according to CTCAE) and the relative levothyroxine dosage were noted too. Statistical analysis was conducted with MedCalc v20.013.

Results. We analyzed 57 patients, (31 males, 26 females). Median age at diagnosis was 70 years (48-96y). Twenty-seven patients were in RT-IT group, while 30 in IT group. The occurrence/worsening of hypothyroidism was observed in 11 patients in RT-IT group *vs* 5 patients in IT group. Between all patients, hypothyroidism was more frequent in age>70 years compared with younger ones (p=0.013). The need to prescribe levothyroxine or to increase the dosage was higher in the RT-IT group *vs* the IT group (p<0.001) and higher in patients who received any kind of neck RT compared to patients who did not receive any RT (p=0.017). A trend of an earlier onset of thyroid dysfunction was observed in RT-IT group compared with IT group (3 *vs* 5 months, p=0.8). Finally, in the RT-IT group, the occurrence/worsening of hypothyroidism was higher with the increase of tDmean (p<0.001), tV50 (p<0.001) and of tV60 (p=0.009).

Conclusions. In patients with HNSCC undergoing IT, the addition of RT increases the risk of developing or exacerbating hypothyroidism while also reducing the time interval for such an occurrence. Additionally, this risk is associated with the V50 and V60 to the thyroid. Therefore, it is important to provide proper counseling and monitor thyroid function during the follow-up of these patients.

P107

DOSIMETRIC AND NTCP ANALYSES FOR SELECTING PAROTID GLAND CANCERS PATIENTS TO PROTON BEAM THERAPY

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Aims. Malignant salivary gland cancers (SGCs) represent a rare disease and parotid gland represents the most common site. Intensity-modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT) are commonly used for the management of parotid gland cancers (PGCs). Despite the modern techniques, the IMRT/VMAT dosimetric advantage alone does not seem to be enough to overcome toxicities. In this scenario, intensity-modulated proton therapy (IMPT) represents a promising option for treatment-related morbidity reduction. The aim of this in silico study is to perform a dosimetric and a Normal Tissue Complication Probability (NTCP) analyses between Intensity Modulated Proton Therapy (IMPT) and Volumetric Modulated Arc Therapy (VMAT) in a cohort of patients (pts) with PGCs in a postoperative or radical setting.

Methods. From May 2011 to September 2021, thirty-seven PGCs pts treated at two Institutions were eligible. Inclusions criteria were as follows: pts aged ≥ 18 years old, diagnosis of PGCs candidate for PORT or definitive RT, presence of written informed consent for the use of anonymous data for research purposes. Organs at risk (OARs) were retrospectively contoured. Target coverage was defined as D95 > 98%. Six NTCP models were selected. NTCP profiles were calculated for each patient using an internally-developed Python script in RayStation TPS.

Results. 74 plans were generated. A 2 Gy dose per fraction was prescribed to High Dose-CTV (HD-CTV) for most plans (76%), with a median prescription dose of 66 Gy. Dose prescriptions to Low Dose-CTV (LD-CTV) ranged between 54 Gy to 58.1 Gy. Dose prescriptions to Intermediate Dose-CTV (ID-CTV) ranged between 63 Gy to 59.4 Gy. For proton plans dose was prescribed in Gy (RBE). A lower Dmean to the majority of OARs was obtained with IMPT *vs* VMAT with statistically signifi-

cance ($p < .05$). Dosimetric results are shown in Figure 1. Ten (27%) pts had a ΔNTCPx-p >10% for hearing loss and/or tinnitus: among them, 7 qualified for both endpoints, 2 pts only for hearing loss, and 1 for tinnitus. On the contrary, none of the patients were qualified for IMPT based on trismus, acute oral mucositis grade > 1.5, dysphagia and dysgeusia.

Conclusions. In the current study, IMPT showed a dosimetric advantage for most of all OARs over VMAT. Nearly one-third of pts resulted eligible for IMPT and they are the most likely to benefit in terms of prevention of hearing loss and tinnitus.

Figure 1. Dosimetric comparison between average mean doses to chosen OARs with VMAT and IMPT techniques. Abbreviations: PCM: pharyngeal constrictor muscles; IMPT: Intensity Modulated Proton Therapy; VMAT: Volumetric Modulated Arc Therapy.

P108

NRAS MUTATIONAL STATUS IN HEAD AND NECK MUCOSAL MELANOMA PATIENTS TREATED WITH CARBON ION RADIOTHERAPY: IS THERE ROOM FOR OUTCOME PREDICTION?

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Aims. To evaluate the impact of NRAS mutational status on oncological outcome in head and neck mucosal melanoma (HNMM) patients (pts) treated with carbon ion radiotherapy (CIRT).

Methods. Pts treated with CIRT after surgery or biopsy only for non-metastatic HNMM and available genetic profile information about NRAS gene were considered in the analysis. Data about oncological outcomes were prospectively collected and then retrospectively analyzed. Local Progression Free Survival (LPFS), Progression Free Survival (PFS), Distant Progression Free Survival (DPFS) and Overall Survival (OS) rates were calculated according to the Kaplan-Meier Method, and the impact of NRAS mutation was evaluated with Log-rank test and individually adjusted for the most relevant factors (surgery pre-CIRT, immunotherapy after CIRT, tumor (T) status and T stage) with Cox regression model (α=0.05).

Results. From June 2013 to September 2022, 56 consecutive pts received CIRT for HNMM at our institution. Information about NRAS genetic profile was available for 25 pts (44.6%). Among these 25 pts, 13 (52%) were male, 10 (48%) female; median age was 68 years. Primary tumor location was nasal cavity and paranasal sinuses in 23 and 2 pts, respectively. Tumor status was naïve and recurrent in 14 (56%) and 11 (44%) cases, respectively. Eighteen (72%) and 7 (28%) pts received surgery before CIRT or exclusive CIRT with radical intent, respectively. Thirteen (52%) pts had NRAS gene mutation, 12 (48%) were NRAS-wild type. CIRT was delivered with a prescription dose ranging from 64 to 68.8 Gy(RBE) in 16 fractions. Eighteen pts (72%) received immunotherapy after CIRT, mainly for distant progression during follow-up. After a median follow-up of 22.2 months, 2 year- LPFS, DPFS, PFS and OS rates were 79.5%, 36.2% and 21.8% and 84.7%, respectively. At Log-Rank univariable analysis, NRAS mutation showed a trend for better LPFS (p=0.085) and OS (p=0.065) (figure 1). Cox-regression analyses confirmed the trend (p<0.1) for OS, unless when NRAS mutation was adjusted for T stage.

Conclusions. NRAS mutated gene status provided a trend for better OS in pts treated with CIRT for HNMM. However, the small size, reduced number of events and heterogeneity of the pts sample as well as the short follow-up, make difficult to clearly interpret the data. Further studies (preferably multicentric and considering the whole gene profile for HNMM) are warranted to better define the potential prognostic role on clinical outcomes after CIRT.

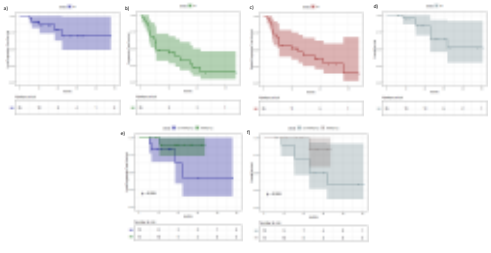

Figure 1. a) Local ProgressionFree Survival; b) ProgressionFree Survival; c) DistantProgressionFree Survival; d)OverallSurvival: e) Local ProgressionFree Survivalin NRAS mutatedvs NRAS wild type; f) OverallSurvivalin NRAS mutatedvs NRAS wild type.

P109

FRAILTY ASSESSMENT IN ELDERLY HNC PATIENTS: RETROSPECTIVE ANALYSIS AND OUTCOMES

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Aims. to evaluate how elderly HNC patients (pts) react to oncological treatment in relation to their initial health status through a frailty assessment index.

Methods. From June 2017 to May 2023 we retrospectively analyzed all elderly HNC pts over 65 years that received a comprehensive geriatric assessment and divided them into categories of fragility (fit, prefrail and frailty) prior to treatment and three months after according to Rockwood Frailty Index (FI). All pts underwent RT +/- systemic therapy. Primary endpoint was overall survival (OS) and secondary endpoint was acute G3 toxicity rate related to FI status.

Results. We enrolled 120 HNC pts with a mean age of 76ys (range 65-92). 17 pts (14%) were over 85 ys. Some of the features are shown in Table 1. Pts were classified according to FI as fit 21 (17%), prefrail 69 (58%) and frail 30 (25%) before oncological treatment. 54/120 pts (45%) received a corrective intervention. 65 pts (54%) received nutritional support. 14 (12%) have requested hospitalization, 85% of which were first evaluated as either prefrail or frail. Median OS for all pts were 12.7 months (range 0,13 – 62). Median OS of FI groups were respectively 19.4 (fit, range 2 - 62), 14.5 (prefrail, range 0.13 – 57) and 7.7 months (frail, range 0,5 - 57). 110/120 pts were evaluated for response. 76 pts achieved (63%) CR, 17 (14%) PR, 15 (12%) PD, 12 (10%) have not been evaluated or lost at follow up. To date 48 pts (40%) died: 25 (62%) for disease, 23 (38%) other cause. 8 pts died within 3 months of the end of RT, only 1 out of 8 was deemed "fit"; 81,5% of the pts who died within 6 months from RT end were either prefrail or frail. 78/120 pts had geriatric revaluation about 3 months after the end of RT. 51/78 pts (69%) did not change their assessment grade, 8 pts (14%) worsened their conditions, and 19 pts (33%) improved their status. 29 (24%) pts showed an acute G3 toxicity, and 75% of those patients were marked as either prefrail or frail at initial assessment.

Conclusions. Geriatric evaluation is a useful tool to better manage frailty in elderly HNC pts, though more data is necessary to understand its potential as a predictive factor for treatment response and toxicity. The prefrail category results suggest that those patients may require particular attention during local and systemic treatment planning and scheduling and in patient support. Further distinction of those pts in two different categories may lead to better treatment modulation.

Table 1.

FEATURES	N° (%)
RT OBJECTIVE	
ADJUVANT	23 (19%)
CURATIVE	91 (76%)
PALLIATIVE	6 (5%)
TREATMENT	
RT ONLY	73 (61%)
CONCOMITANT CETUXIMAB	25 (21%)
CONCOMITANT CDDP	18 (15%)
NEOADJUVANT CT	3 (2%)
CONCOMITANT CBDCA	1 (1%)
NUTRITIONAL INTERVENTION	
FOOD SUPPLEMENTS	19 (16%)
PARENTERAL NUTRITION	3 (2%)
PEG/NGT	6 (5%)
NONE	92 (77%)

P110

EARLY RESULTS OF RADIOMICIART TRIAL (NCT05081531): A PROSPECTIVE MONOCENTER STUDY OF MULTI-IMAGING ADAPTIVE RT FOR LOCALLY ADVANCED HEAD-NECK CANCER

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Aims. During the RT, patients with head and neck cancer (HNC) may develop significant anatomical changes. Re-planning with adaptive radiotherapy (ART) may ensure adequate dose coverage and sparing of organs at risk. Advanced imaging modalities play a role in the customization of the radiation treatment as shown the use of ART and radiomic. The early results of study show of evaluate of machine learning-based radiomic approach to predict outcome and toxicity of HNC patients treated with ART by CT, MRI and PET-scan.

Methods. Patients with locally advanced HNC treated with radical RT from October 2021 to October 2022 were analyzed. The target volumes were delineated on CT scan and adjusted on MRI and FDG-PET. The total dose was 66/60/54 Gy in 30 fractions with VMAT-SIB. For the whole sample, the 95% of the prescribed dose covered at least 95% of the PTV. At week 3 from RT start, CT simulation, MRI and FDG-PET were repeated for re-planning. The new plan started in week 4 (Figure 1). We performed the comparison of patients and disease characteristics between original plan and re-simulation (adaptive plan) on CT, MRI and FDG-PET. Univariate analysis was conducted for main patients and disease factors.

Results. At the time of analysis, 30 patients were enrolled. The most common site of primary tumor was oropharynx (63%) and HPV was found in 50% of patients. Stage disease was T4N1 in 47% of cases. All patients completed the radiation treatment as planned. Median GTV-T and GTV-N at baseline and at re-planning were 22 cc and 20 cc, and 5.7 cc and 5.5 cc, respectively. Between original plan and adaptive plan, the median difference (Delta) in volume of the ipsilateral parotid gland was 3 cc, and the median Delta of mean dose was 3.8 Gy. No relevant changes were described for contralateral parotid. At MRI analysis, the median absolute deviation of Delta-radiomics features was significantly associated with smoke ($p<0.05$), HPV presence ($p<0.005$) and primary tumor ($p<0.005$). At FDG-PET analysis, a significant difference was found for both SUVmax and SUVmean between baseline and interim scan for both GTV-T ($p<0.0001$) and GTV-N (p0.0005). Delta SUVmean of primary was related to gender ($p=0.006$) and HPV presence (p0.035).

Conclusions. The early results of study highlighted important differences between original RT plan and adaptive plan, combining both ART and radiomic analysis. However, it is necessary to wait an adequate follow-up to evaluate the benefit for survival and safety.

Figure 1.

P111

PROTON THERAPY ACHIEVES EXCELLENT TUMOR CONTROL AND PRESERVES QUALITY OF LIFE IN HEAD-AND-NECK PARAGANGLIOMAS.

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Aims. Paragangliomas (PGLs) are rare, slow growing tumour, however locally aggressive. Proton therapy (PT) can minimize the risk of radiation side effects preserving health related quality of life (HRQOL). The aim of this study is to report data of patients treated with Active Pencil Beam Scanning PT, early outcome, toxicity and impact on Quality of life (QoL) in terms of HRQOL scored by EORTC QLQ —C30 and EORTC H&N35.

Methods. 10 patients with 20 PGLs were irradiated. Patients completed Questionnaires before starting PT, at the end of PT and at every follow up. Four moments of treatment and follow up were analyzed: before starting (T0) and at the end of PT (T1), than after 3 months (T2) and after one year (T3). Toxicity was collected in according to Common Terminology Criteria Adverse Events (CTCAE) 5.0.

Results. All patients were treated with 50 GyRBE in 25 fractions of 2.0 GyRBE. At a median follow up of 4.5 years, local control was 100%. No acute or late toxicities > than grade 2 (G2) occurred. Questionnaires QLQ-C30 showed a general statistically significant trend in improvement from T0 to T3 for most of the items: reduction of pain (p-value <0.0001), appetite loss (p value <0.0039); fatigue improved both statistically ($p<0.0001$) and clinically, as physical functioning (p-value <0.018) and Global Health Status (p-value 0.0005). H&N 35 questionnaires showed an improving trend from T0 to T3 both statistically and clinically significant in speech and sticky saliva (p-value: 0.0002; p-value 0.00069 respectively), statistically significant for cough (p-value 0.0001). A clinical improvement at the limits of significance resulted also in social eating, painkillers, nutritional supplements and gaining weight. Dry mouth was both statistically and clinically worsened (p-value 0.0027) as weight loss but only clinically. No swallowing and speech impairment was detected, all the other items remained substantially unchanged.

Conclusions. Results of our study are promising, Pencil Beam Scanning PT seems to achieve optimal local control with an excellent toxicity profile and to preserve QoL.

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QUANTITATIVE EVALUATION OF DEEP LEARNING - BASED CONTOURING FOR ORGANS AT RISK IN CLINICAL HEAD AND NECK RADIOTHERAPY

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Aims. Accurately segmenting organs at risk (OAR) and target volumes is a crucial step in the radiation therapy workflow, but it can be highly time-consuming. Autocontouring tools aim to reduce workload, decrease inter- and intra- observer variability. The purpose of this study is to conduct a quantitative analysis of the manual adjustments on OAR contours performed by a deep learning (DL) commercial contouring tool to assess its clinical implementation for head and neck (H&N) treatments.

Methods. The structure sets of thirty consecutive H&N patients treated between March and May 2023, including the larynx, thyroid, brain, brainstem, mandible, left and right parotid glands, spinal cord, oral cavity, and esophagus were analyzed. The entire cohort was initially contoured using the LimbusAI (Limbus AI Inc., Regina, SK, Canada) deep learning (DL) commercial tool, and subsequently reviewed and manually edited by expert radiation oncologist for clinical use. The comparison between automated (AC) and clinical contours (CC) was performed using Dice similarity Index (DI) and Hausdorff distance-95% (HD), setting CC as reference.

Results. The AC process required approximately two minutes for each structure set. Comparing OAR volumes, brain, brainstem, mandible, and parotid glands demonstrated excellent agreement, with DI ranging from 0.97 to 0.99 and HD between 0.49 and 1.43 mm. The spinal cord, oral cavity, and esophagus exhibited slightly lower agreement, with DI of 0.97, 0.96, and 0.93, respectively, and corresponding HD ranging from 2.93 to 5.43 mm. On the other hand, larynx underwent the most extensive editing (Table 1), indicating a moderate level of agreement with CC.

Conclusions. This quantitative analysis demonstrated promising performance of the LimbusAI implementation in clinical H&N practice. The use of LimbusAI in clinical H&N practice can reduce the radiation therapy workload, since the majority of OAR structures have been successfully contoured within clinically acceptable parameters. However, it is necessary to emphasize the importance of careful manual review, and the impact of time for these manual corrections should be investigated. These preliminary findings will be validated on a larger patient population across different treatment regions. This validation will provide valuable insights about the integration of AI into routine clinical practice, ultimately enhancing efficiency and improving patient outcomes in radiation therapy.

Table 1. Performance comparison between Automated Contours and Clinical Contours in terms of Dice similarity Index and Hausdorff Distance - 95% in head and neck cancers. Mean values and standard deviations are reported.

Organ at Risk	Dice Index	Hausdorff Distance 95% (mm)
Larynx	0,85 ± 0,19	3,62 ± 4,45
Thyroid	0,96 ± 0,10	1,58 ± 2,61
Brainstem	0,99 ± 0,03	0,49 ± 0,95
Brain	0,99 ± 0,01	0,67 ± 1,33
Mandible	0,99 ± 0,02	0,53 ± 0,72
Parotid L	0,97 ± 0,05	1,20 ± 1,49
Parotid R	0,97 ± 0,04	1,43 ± 2,19
Spinal Cord	0,97 ± 0,10	2,98 ± 12,29
Oral Cavity	0,96 ±0,08	2,93 ± 3,66
Esopaghus	0,93 ± 0,17	5,43 ± 15,31

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PROTON BEAM RADIATION THERAPY FOR HEAD AND NECK ADENOID CYSTIC CARCINOMA

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Aims. Locoregional control (LC) in adenoid cystic carcinoma (ACC) is dose-dependent, initial results with particle therapy were promising. We report our experience with pencil beam scanning-proton theapy (PBS-PT) in 74/75 patients with pathologically confirmed adenoid cystic carcinoma (ACC) of the head and neck.

Methods. Treatment records of patients treated with (PBS-PT) between March 2016 and July 2022 were evaluated. Median age of patient was 54 years (range, 19-80 years). Thirty-eight patients were male and 36 were female. In 45 patients, tumors were located in major salivary glands (60,8%), in 14 patients in minor salivary glands (19%), in 4 patients in paranasal sinuses (5%), in 3 patients in cranial base (4%), the remaining (9, 12 %) were located in the pharynx (1), pterygopalatine fossa (2), lacrimal gland (2), nasopharynx (4). The numbers of R0, R1, and R2 surgical resection classification patients were 22 (29%), 35 (47%), and 18 (24%). 8 cases had received a previous irradiation with photons with a median dose of 63 Gy (range 45-70), the less time between the two irradiation was 12 months. 44 (59%) patients had perineural invasion, and 9 had neck node positive. Histology was ACC not otherwise specified in the majority of cases (57). The median total RT dose was 64 Gy (range, 45-74 Gy). Neck was irradiated only in case of node positivity all patients had cranial nerves irradiation. No one patient performed chemotherapy.

Results. Median follow-up period was 32,8 months (11-70 months). Treatment was well tolerated, most represented acute toxicities was cutaneous of grade 1 or 2, excepted for 17 patients, grade 3, the second was otitis in 11 patients grade 1 or 2, no toxicities more than G3 were observed. Most represented late toxicities was trisma in 13 patients all of G1. 1 patients reported carotid stenosis, 1 wound dejuice, 1 oronasal fistula, 2 cases of radionecrosis one of temporal lobes and one of the brain stem at 8 and 28 months respectively. No flap detachment were reported. Five patients (6%) had in field local relapse, 15 (20%) patients relapse at distance mostly in the bone or in the lung, only in one case a large metastasis was located in the liver. No patients developed neck recurrence.

Conclusions. High-dose conformal proton beam radiation therapy results in a very encouraging local control rate with a low toxicity profile in patients with adenoid cystic carcinoma of the head and neck. More follow up is necessary to confirm these results.

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STEREOTACTIC RADIOTHERAPY AND RADIOSURGERY VS FRACTIONATED RADIOTHERAPY FOR HEAD AND NECK PARAGANGLIOMAS

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Aims. Head and Neck paragangliomas (HNPGL) are rare, mostly benign, slow growing tumors. The aim of this study is to evaluate local tumor control and toxicity of radiotherapy (RT) treatments delivered at single Institution.

Methods. From 07/2002-01/2023 50 patients (pts) with 58 HNPGL were treated with RT. Eleven treatments were delivered by TomoTherapy® (Accuray, Maddison, WI) (TT), with a median dose of 50 Gy (45-60). Fractionated external beam irradiation was used to treat larger tumor volumes. Eleven treatments were delivered by Cyber Knife™ (Accuray, Sunnyvale, CA) (CK), with a median dose of 26 Gy (25-30), in a median of 5 (1-5) fractions, at a median prescription isodose of 78% (69-85). Thirty treatments were delivered by Gamma Knife Perfexion™ (Elekta, Stockholm, Sweden) (GK), with a median dose of 16 Gy (13-18); the median isodose line was 50%. Five of the 50 pts had multiples HNPGL, which were treated together. Local control (LC) was defined on MRI according RECIST criteria, while toxicity was assessed according to CTCAE v5.0 scoring system.

Results. Median Age was 60 years (28.5-89). Median PTV of lesions treated with TT was 51.135 cm^3 (8.1-444.1 cm^3), median PTV of CK lesions 33.98 cm^3 (8.52-70.68 cm^3), and median GTV of GK lesions 7.60 cm3 (0.36-24.60 cm^3). Median follow up was 68 months (2.2-180 months). Kaplan Meier estimates of local relapse-free survival was 97.2 %. One patient, treated with GK, experienced tumor progression and underwent a second GK, regaining LC. To perform a comparative toxicity analysis, volumes below 7cc have not been considered. Four pts (40%) treated with TT presented G2 acute toxicities: one mucositis, one erythema, one dysphagia and one xerostomia. Two pts (22.22%) treated with CK presented: pain G2 and dysphagia G2. One patient treated with GK experienced transient trigeminal neuralgia while another one experienced transient vertigo (11.76% of patients) (See Table 1). An improved neurological status was registered in 30 pts (60%), and 20 pts (40%) showed clinical stability. No patient experienced worsening of pre-existing neurological symptoms.

Conclusions. In our experience CK, GK and TT are effective and safe treatment options, with an excellent LC. Fractionated radiotherapy was prescribed for larger HNPGL volumes, and no difference was observed between treatments.

Table 1. Volumes and treatment techniques in HNPGL patients presenting toxicity.

Volume (cc)	Techniques	Toxicity
81	Tomotherapy	Mucositis G2
50.5	Tomotherapy	Xerostomia G2
29.9 (right) + 45.7 + 1.6 (left)	Tomotherapy	Erythema G2
50.5	Tomotherapy	Dysphagia G2
33.52 (right) + 39.83 (left)	CyberKnife	Pain G2
26.76	CyberKnife	Dysphagia G2
16.9	GammaKnife	Transient Vertigo
71	GammaKnife	Trigeminal neuralgia Transient

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HEAD AND NECK ADENOID CYSTIC CARCINOMA PATIENTS TREATED WITH PROTON BEAM THERAPY: OUTCOME AND TOXICITY

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Aims. To retrospectively analyze clinical outcomes and toxicity profiles of patients (pts) with head and neck (H/N) adenoid cystic carcinoma (ACC) treated with curative proton beam therapy (PBT) with at least 2 years of follow-up (FU).

Methods. Between February 2017 and June 2020, 53 patients (M/F = 20/33) with H&N ACC were treated with raster scanning PBT. No pts received previous RT. The following survival outcomes at 2 and 5 years- were estimated with Kaplan-Meier method: Local Relapse Free Survival (LRFS), Overall Survival (OS), Progression Free Survival (PFS), and Distant Metastasis Free Survival (DMFS). Univariable analysis was performed by means of Log-rank test (α=0.05) to evaluate the potential impact of the main sample characteristics. When appropriate, stratifications were based on the median values of the quantitative variables. Toxicity was evaluated according to the CTCAE v.4.0. Pts were followed up every three months after RT with clinical evaluation and MRI.

Results. Patients (pts) median age was 57 years (range 22-81 years). Tumour site was minor salivary gland in 34 (64%) and major salivary gland in 19 (36%) pts. In 49 (92%) pts treatment was at first diagnosis, 4 pts (8%) were treated after disease recurrence. Before PBT, 49 (92%) pts received surgery. Among these latter 27

(55%) pts reported positive margins (R1) and 11 (22%) pts received debulking surgery (R2) with a residual disease on pre-RT MRI. The prescribed total dose was 59.92-72 Gy(RBE) in 28-35 fractions, 5 fractions/week. With a median follow-up of 46 months (inter-quartile range 23 months), 2 years- LRFS, OS, PFS and DMFS were 88%, 96%, 73% and 73%, at 5 years- were 78%, 89%, 54% and 56%. At univariable analysis prognostic factors for OS were surgical marginal status before PBT (R1 resected patients had OS higher than R2 patients (p=0.015)), and GTV (P<0.001). At the end of treatment acute toxicity was reported as G1 in 4 %, G2 in 79% and G3 in 17% (mucositis and/or erythema). During FU the late maximum toxicity was G0 in 4%, G1 in 28%, G2 in 63% and G3 in 6%. Out of late G3 toxicity, 2 pts had ear impairment and 1 patient had eye disorders. No grade 4 or 5 acute and late toxicities were observed.

Conclusions. Postoperative RT is the main setting for H&N ACC. ACC management should be discussed in a multidisciplinary setting before delivering surgery. Although a longer FU is needed, no acute and late toxicity grade ≥G4 were observed.

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THE IMPACT OF IMPLEMENTING MULTIDISCIPLINARY TEAM CARE (MDT) IN MANAGING OF HEAD AND NECK CANCER (HNC) PATIENTS IN OUR CLINICAL EXPERIENCE

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Aims. This study examines the impact of implementing MDT approach in managing

HNC patients. It assesses the effects of MDT on clinical quality indicators (CQI), time quality indicators (TQI), and patient outcomes, based on the researchers' clinical experience.

Methods. A retrospective analysis was conducted on a cohort of patients treated for HNC at our hospital between 2015 and 2022. The study cohort was divided into two groups: pre-MDT (before the establishment of MDT) and post-MDT (after the implementation of MDT). CQIs and TQIs were assessed to determine adherence to recommended guidelines. TQIs were calculated in days elapsed from delivery of histological diagnosis to medical evaluation or PET/CT.

Results. In the pre-MDT, TQI of radiotherapy (RT) and oncology assessment were 7 and 10 days, respectively; in the post-MDT, both evaluations were performed at the time of delivery of the histological diagnosis (0 days). Dental assessments saw a remarkable increase in adherence in post-MDT (87% *vs* 15%); TQI was five days post-MDT and 14 days pre-MDT. Nutritional assessments also showed significant improvement (69% *vs* 20%); TQI was of 7 days in post-MDT and 25 days pre-MDT. PET staging demonstrated substantial improvement in the post-MDT(69% *vs* 22%); TQI was 15 days post-MDT and 35 days pre-MDT. Furthermore, the utilization rates of chemo-RT (CRT) for locally advanced disease (49% *vs* 21%) and adjuvant CRT for high-risk disease (51% *vs* 35%) saw substantial increases in the post-MDT.

Post-MDT also experienced a shorter interval between surgery and RT (47 days *vs* 62 days), contributing to more timely treatment initiation. Additionally, patients in post-MDT experienced a reduced mean hospitalization length, indicating improved care delivery efficiency.

Conclusions. Our study demonstrates that implementing a HNC MDT in our clinical practice has significantly improved adherence to CQI, TQI and patient care. MDT approach has led to enhanced dental and nutritional assessments, increased utilization of PET staging, and improved utilization rates of CRT in locally advanced and high-risk diseases. Furthermore, integration of MDT has reduced therapeutic delays, which is reflected in the shorter time interval between the communication of the diagnosis and the subsequent specialist evaluations and PET staging, between surgery and RT, together with a lower length of stay.

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CASE REPORT: HEAD AND NECK POSITIONING AND MONITORING USING A SURFACE-GUIDED RADIATION THERAPY (SGRT)

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Aims. SGRT is an emerging technology that enables three-dimensional surfaces image guidance for RT. The technology is commonly employed in the setup for breast cancer patients (pts); however, it would be challenging for head and neck cancer pts. We present a case report of a pt, treated for nasopharyngeal carcinoma, aligned and monitored using SGRT.

Methods. In February 2023 a 61 year old pt with diagnosis of nasopharyngeal carcinoma (stage cT4N2) was treated with induction chemotherapy (CT) prior to exclusive CT-RT. Due to claustrophobia, pt did not tolerate the conventional thermoplastic mask or mask with mid face opening. Therefore we decided to perform the planning CT using the OPTEK system™ and a VAC-LOK™ cushion. The isocentre has been defined both through vacuum

lock cushion marks and tattoos on the skin. The patient's surface contour generated from the CT dataset was imported into the SGRT system (AlignRT®) and we drew the target region of interest (ROI) on it. Pt underwent Volumetric Modulated Arc Therapy (VMAT) technique, with a total dose of 66 Gy/33 fractions (fr) to the tumor, 60 Gy/30 fr to positive lymphnodes and 50Gy/25 fr to negative lymphnodes. On the day of treatment, pt was first set up to VAC-LOK™ cushion marks and tattoos on the skin and subsequently with optical image guidance to the reference parameters. The positional errors for translational and rotational shifts were acquired by aligning the daily IGRT ConeBeam CT (CBCT) with the treatment planning kVCT images. During the delivery the pt was monitored with SGRT system.

Results. The mean positional errors in the vertical, longitudinal and lateral directions were as follows: 0.0±0.2, 0.0±0.3, and 0.0±0.3 mm. The mean rotational shifts pitch, roll and yaw were as follows: -0.9±1.1, 1.4±1.2, and 1.4±1.6 °. The distribution of translational and rotational shifts was described in boxplot (Figure 1). Median magnitude (MAG) of translational offsets reported via SGRT during the delivery was below 1 mm, while the rotational offsets was below 1°.

Conclusions. In our case, SGRT positioning and monitoring allowed to perform a treatment with curative intent. Larger rotational corrections needed were due to shoulder positioning; they were accepted because the treatment planning involved an avoidance sector, requiring no dose be delivered through this anatomical region.

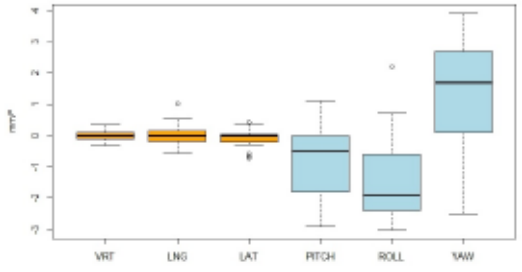

Figure 1.

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HOW RADIOMIC FEATURES AND CLINICAL DATA CORRELATIONS CAN BE DEPLOYED IN CLINICAL ENVIRORMENT IN A POPULATION OF HEAD AND NECK CANCER PATIENTS

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Aims. Many studies highlighted the utility of features signature in managing Head and Neck Squamous Cell Carcinoma (HN-SCC) patients but the complexity of the process made difficult to deploy this strategy in clinical routine. The aim of this work is to develop a clinical workflow to easily handle these data to achieve an outcome prediction. A commercial software, Elekta ProKnow (PK) has been customized to simply visualize aggregate clinical and radiomic parameters, in order to choose the most appropriate clinical approach for each specific patient.

Methods. Consecutive HN-SCC patients with radiologically detectable primary tumor treated between 2014 and 2022 with curative IMRT-VMAT, were included. A set of 32 retrospective HN-SCC patients, who met the inclusion criteria, has been collected in PK as a cohort, consisting of pre and post treatment PET/CT images, simulation CT images, RT plan, RT structure, RT dose files. Custom metrics have been implemented in PK to host patient specific data as tumour histology, P16+, lesion site and staging. Semi-automatic segmentation on pre-treatment PET/CT has been performed and utilized to extract radiomic features. The selected features have been uploaded into PK and correlated with clinical and radiotherapy parameters.

Results. The developed method has been focusing on the extraction of some PET related relevant features (Pre and Post treatment) for both primary tumors and positive lymph-nodes. All those features and their statistic values can now be visualized as histograms or box-wiskers plots in an interactive fashion and grouped by classes of Site, Subsite, Outcome, Staging, P16 Status and Outcome.

Conclusions. This work is going to be improved by inserting the non-response prediction model based on the selected features into the software.

The dynamic and easy real time visualization of clinical, radiotherapy and radiomic parameters can help in customizing clinical treatment strategy decision, such as dose de-escalation or chemotherapy duration.

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EFFICACY AND SAFETY OUTCOMES OF CHEMO-IMMUNOTHERAPY IN PATIENTS WITH RECURRENT/METASTATIC HNSCC: A RETROSPECTIVE ANALYSIS

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Aims. KEYNOTE 048 added PDL1 CPS score to the other factors considered by oncologists in the choice of a

personalized therapeutic approach for patients with squamous cell carcinoma of the head and neck (HNSCC) not eligible for curative treatment. This report aims to analyze data on efficacy and safety outcomes in a cohort of patients treated in our center with first line systemic therapy (FLST) from 2021.

Methods. Data about stadiation, prognostic factors and treatment were retrospective collected from patients with recurrent/metastatic HNSCC treated in our center with FLST according to CPS. The primary endpoints were overall survival (OS) (time from the start of FLST to death or last date of follow-up) and progression-free survival (PFS) (time from the start of FLST until death or progressive disease). Toxicity data were reported according to CTCAE v4.0.

Table 1. Patients, disease and treatment characteristics.

SEX				
Male		21 (53.8%)		
Female		18 (46.2%)		
AGE (years)		Median age 62.8y (22-85)		
<70		24 (61.6%)		
≥70		15 (38.4%)		
PS ECOG				
0		24 (61.6%)		
1		11 (28.2%)		
2		4 (10.2%)		
SMOKING				
Never smoker		11 (28.2%)		
1-20 py		7 (18%)		
≥20 py		21 (53.8%)		
PRIMITIVE SITE				
Oral Cavity		22 (56.4%)		
Oropharynx		11 (28.2%)		
Larynx		4 (10.2%)		
Nasal cavity and paranasal sinuses		1 (2.6%)		
Hypopharynx		1 (2.6%)		
HPV STATUS (OPC n=11)				
HPV+		7 (63.6%)		
HPV-		4 (36.4%)		
CPS STATUS (PDL1)				
CPS negative		8 (20.5%)		
CPS 1-20		9 (39.1%)		
CPS > 20		22 (56.4%)		
SITE OF DISEASE AT FIRST LINE ST				
Local (T)		30 (76.9%)		
Regional (N)		29 (74.4%)		
Distant (M)		16 (41%)		
CPS SCORE	TREATMENT CHOICE			
0 (n=8)	Platinum+5FU+Cetuximab	5 (62.5%)		
	Platinum+Cetuximab	3 (37.5%)		
>1 (n=31)	Platinum+5FU+Pembrolizumab	17 (54.9%)		
	Platinum+Pembrolizumab	3 (9.7%)		
	Pembrolizumab	11 (35.5%)		
TOXICITIES (≥G3+)		EXTREME	PF-PEMBRO	PEMBROLIZUMAB
Skin toxicity		3 (0)	0	1 (1)
Nausea and Vomiting		1 (1)	2 (1)	0
Neutropenia		1 (1)	4 (3)	0
Hypothyroidism		0	2 (0)	2 (1)
Mucositis		1 (0)	4 (4)	0
Anaemia		2 (0)	4 (2)	0
Thrombocytopenia		1 (0)	2 (0)	0
Liver toxicity		0	0	1 (1)

Results. 39 patients who underwent FLST in our center between Jan 2021 and May 2023 were included in this retrospective study, with a median follow-up of 9 months [95%CI 1.2-16.8]. Patient and treatment characteristics are reported in Table1. Median age was 62.8 years and PS ECOG mostly 0-1 (90%); CPS resulted negative in 8 patients (21%), >1 in 9 (23%) and >20 in 22 (56%). 16 patients (41%) had distant metastases, the others locoregional disease not eligible for radical treatment. EXTREME schedule (3 without 5FU) was chosen in the 8 CPS-negative patients; 20 in the CPS-positive cohort received Platinum+5FU+Pembrolizumab (PFP) (3 without 5FU) and 11 Pembrolizumab alone. Considering all patients, median OS was 9 months [95%CI 3.1-14.8], 1-year OS was 46%, 2-year OS 20%; median PFS was 5 months [95%CI 3.4-6.5]; 1-year PFS 21%. In the CPS positive cohort, pembrolizumab group had median OS of 9 months [95%CI 3.5-14.5] and 1-year OS of 38%; PFP group had median OS of 10 months [95%CI 0-23.9], 1-year OS 45% and 2-year OS 30%. At univariate analysis, younger age was associated with longer survival with a median OS of 17 months [95%CI 4.2-29.7] and 5 months [95%CI 1.7-8.3] for patients aged <70y and >70y respectively (p=0.01). Regarding toxicity, we reported 15 events ≥ G3; the most frequent were mucositis (4) and neutropenia (4) in chemotherapy groups; only 3 occurred with Pembrolizumab alone.

Conclusions. In our cohort, patients with recurrent/metastatic HNSCC had efficacy and safety outcomes in line with published chemo-immunotherapy data (KN048). Younger age was significantly associated with longer survival.

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MAPPING THE RESEARCH LANDSCAPE OF HPV-POSITIVE OROPHARYNGEAL CANCER: A BIBLIOMETRIC ANALYSIS

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Aims. HPV-positive (HPV+) Oropharyngeal Squamous Cell Carcinoma (OPSCC) is a specific OPSCC subset whose incidence is rising in developed countries. It is characterized by a specific epidemiological and molecular profile and, more importantly, by a better prognosis in terms of overall survival and locoregional control. Our study aims to evaluate the interest, the collaboration patterns and the emerging trends regarding HPV+ OPSCC.

Methods. Cross-sectional bibliometric analysis of articles about HPV+ OPSCC retrieved in Scopus database through the search of "oropharynx", "cancer", and "HPV" in title, abstract, and/or keywords. The search was conducted on February 8th, 2023 all documents published until December 31th, 2022 were eligible for analysis.

Outcomes included the exploration of key characteristics (number of manuscripts published per year, growth rate, top productive countries, most highly cited papers, and the most well-represented journals), collaboration parameters (international collaboration ratio and networks, co-occurrence networks), keywords analysis (trend topics, factorial analysis).

Results. A total of 5200 documents was found, published from March, 1987 to December, 2022. The number of publications increased annually with an average growth rate of 19.94%, reaching a peak of 680 documents published in 2021. The 10 most cited documents were published from 2000 to 2012, likely due to a longer citation time period, with more than 1000 citations (range 1105-4645). The factorial analysis of the keywords revealed two main clusters: one on epidemiology, diagnosis, prevention and association with other HPV tumors; the other one about the therapeutic options, including chemotherapy, radiotherapy and surgery. According to the frequency of keywords, new items are emerging in the last three years regarding the application of AI (machine learning and radiomics) and the diagnostic biomarkers (circulating tumor DNA).

Conclusions. This bibliometric analysis highlights the importance of research efforts in prevention, diagnostics, and treatment strategies for this disease. Given the urgency of optimizing treatment and improving clinical outcomes, further clinical trials are needed to bridge unaddressed gaps in the management of HPV+ OPSCC patients.

Figure 1.

P121

OVERALL AND CANCER SPECIFIC SURVIVAL IN OROPHARYNGEAL CANCERS ACCORDING TO P16 STATUS

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Aims. To evaluate overall survival (OS) and cancer specific survival (CSS) in patients (pts) with oropharyngeal squamous cell cancer (OSCC) treated with radical radio-chemotherapy according to p16 status.

Methods. From September 2013 to May 2023, we retrospectively analyzed 95 pts with OSCC, stage III according to TNM 8th edition. The immunohistochemical expression of p16 has been examined in all pts. All pts underwent clinical and radiological evaluation every 6 months for the first 5 years and then every year. The clinical evaluation consisted in clinical examination and fiberscopy performed by the otolaryngologists. The radiological evaluation included Whole Body PET-TC and head and neck MRI. The median age was of 62.2 (range 42 - 77) years. The median follow-up was 38 months. 74 pts were males, 21 females (77.9% *vs* 22.1 %). Strong smokers were 37 (38.9 %). 71 pts (74.7 %) were p16 positive, another cancer was present in 12 (17%) of p16 positive pts and in 5 (20%) of p16 negative pts. For all pts the treatment was completed without interruptions with the exception of 3 pts who stopped radiotherapy at 38, 44 and 46 Gy because of declining conditions. All pts were treated using volumetric modulated arch therapy (VMAT), IGRT was performed with daily kV-CBCT checks and from 2016 an adaptive radiotherapy approach was introduced with a second TC simulation at 5th week. The dose prescription was 70 Gy in 2 Gy/fraction (5 fr/w) to high risk volume, 60 Gy and 50-54 Gy to intermediate and low risk volumes respectively, according to AIRO guidelines. Concomitant chemotherapy with CDDP-CBDCA/w was prescribed in 70/95 pts, 45 pts performed ≥ 5 cycles, 25 pts < 5 cycles. CT with CDDP/3w in 25/95 pts (3 pts performed 1 cycle, 14 pts 2 cycles and 8 pts 3 cycles). The Kaplan Meier method was used for survival analysis and log-rank test for the inference to p16 status and other independent variables.

Results. Crude median OS was 86.5 months; 86.5 in p16 positive and 31.7 in p16 negative pts; the 5 year survival was 69,2% and 38,3% respectively (p=0.03). The CSS never reaches the median in either P16 positive or P16 negative group, nevertheless there is a great difference, 82,2% and 52,7 % respectively (p=0.0073).

Conclusions. HPV/p16 status is one of the strongest predicting factor both for overall and cancer specific survival, much more than associated pathology such as pre-

vious or synchronous other cancers (p=0.24). Whether this behavior requires different therapeutic approaches is a source of debate.

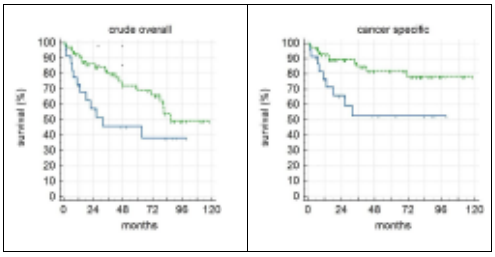

Figure 1.

P122

NUTRITIONAL EVALUATION IN PATIENTS WITH HEAD AND NECK CANCER (HNC) TREATED WITH RADIOTHERAPY +/- CHEMOTHERAPY (CT-RT): OUR EXPERIENCE

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Aims. Malnutrition and weight loss significantly contribute to the loss of adherence to CT-RT treatment in patients with HNC, and increased acute toxicity and reduced quality of life are observed. It is estimated that up to 10–20% of cancer patients die from the consequences of malnutrition rather than the cancer itself. The Dietetics Service (DS), in collaboration with the Department of Clinical Oncology section of Radiation Oncology and Nuclear Medicine, focuses on providing nutritional treatment to reverse or at least halt the malnutrition process before it progresses to cachexia. This study aims to evaluate the effectiveness of nutritional intervention through nutritional counseling in HNC patients under CT-RT. The objective is to provide nutritional guidance to restore or maintain good nutritional status during the CT-RT sessions cycle, addressing the patient's needs.

Methods. Nutritional status assessment is conducted during the medical visit and includes an initial validated screening test (MUST). The screening test measures anthropometric parameters (weight, height, usual weight, Body Mass Index or BMI). The patient's weight trend and current diet are also assessed during the medical examination. The patient is referred to the DS for a comprehensive nutritional assessment, including dietary habits, nutritional diagnosis, and nutritional counseling provided by the dietitian. The data collected, including screening test results, nutritional status, intervention outcomes, and weight maintenance or recovery, are analyzed. Occasionally, oral nutritional support may be provided to ensure effective nutritional assistance during radiotherapy sessions.

Results. From 10/01/2022 to 05/31/2023, 42 patients were admitted to the DS on an outpatient basis for nutritional status assessment and followed up for 5-6 months. BMI medium was normoweight (23,90-24,12 kg/m^2). There was stability of weight

during the treatment. The collected data revealed improved adherence to radiotherapy sessions, allowing many patients to complete the planned therapy cycle.

Conclusions. The collaboration between the DS and the Radiotherapy UOC is essential for improving the nutritional status of HNC patients undergoing CT-RT and enhancing therapeutic adherence. It is important to encourage patients to access the DS for specific nutritional assessments, considering the significant impact of these pathologies on their quality of life. The obtained results enable adjustments in service offerings to meet user needs.

P123

EFFICACY AND FEASIBILITY OF EXCLUSIVE STEREOTACTIC RADIOTHERAPY IN UNRESECTABLE PARAGANGLIOMA

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Aims. Paraganglioma(PG) are rare highly vascularized, with slow-growing and usually sporadic tumors of neuroendocrine origin. Head and neck PG generally arise from parasympathetic paraganglia and are non-functioning. To date, common treatment options are surgical resection (SR),with or without radiation therapy (RT),and a wait-and-wait policy.The aim of our study is to evaluate local control and effectiveness of exclusive fractionated stereotactic RT (FSRT) treatment in unresectable PG(uPG).

Methods. We retrospectively evaluated patients with uPG (medically inoperable or refuse SR)treated with FSRT with a CyberKnife System (Accuray Incorporated, Sunnyvale, California). A combination of contrast-enhanced computed tomography (CT) scanning, magnetic resonance imaging (MRI), and angiography were required for diagnosis and localization of the tumors. The Glasscock-Jackson (G-J) and Fisch classification were used.Toxicity and initial efficacy were evaluated.

Results. From May 2009 to January 2023,6 patients with median age of 68years (range 20-84)were treated with FSRT.The median delivered dose was 21Gy(range 20-30Gy) at a median isodose line 75.5% (range 70-76 %) in 4 fractions(range 3-5fx).The median volume was 13,6 cc(range 12,4-65,24 cc).The median cumulative BED(a/b 4,5)and EQD2 were 70Gy and 21Gy respectively. Sites of origin involved were timpanojugular glomus (4/6),temporal bone and were type 1(2/6), type 2(2/6) and one type 3 (G-J classification). According to Fish classification, two patients showed grade B, one grade C1 and two grade C2. One patients had cervical spine PG. In 2/6 patients follow up were insufficient; 4/6 showed a 5y-OS and 5y- PFS of 100%.We observed negligible toxicities during and after RT. The majority of patients showed stable symptoms during follow-up. Only one patient, with driver mutation, developed spine metastases 12 years after FSRT.

Conclusions. With the limitation of a small series of patients, our results suggest that FSRT could be an effective and safe alternative to SR.

P124

NEUROENDOCRINE CARCINOMAS OF THE HEAD AND NECK: A MULTICENTRIC EXPERIENCE AND REVIEW OF THE LITERATURE, FOCUSING ON THE ROLE OF RADIATION THERAPY

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Aims. Neuroendocrine carcinoma of the head and neck (HN-NEC) is an exceedingly rare and aggressive malignancy. Despite combining surgery, chemotherapy and radiotherapy is recommended, there is no consensus on optimal management. Herein, we reviewed the literature describing the management and conducted a retrospective analysis of HN-NEC patients treated at four different institutions over a period of twenty years.

Methods. Articles published in Pubmed/Scholar/Web of science databases were selected using specific search criteria. Eligibility criteria included reports published in English reporting data on the management of HN-NEC. Reports describing olfactory neuroblastomas and merkel cell carcinoma were excluded. Thirteen patients with pathologically proven HN-NEC and treated at our oncology department were selected.

Results. A total of 195 clinical cases of HN-NEC, 97 non-sinonasal, 98 sinonasal have been identified from the literature and 13 patients treated at our department. Many combinations of SX, CHT and RT are described, with different SX-based or non-SX-based approaches used, mainly chosen according to site and stage of disease. Our experience confirms the key role of SX in non-sinonasal and proposes the sequential use of RT and CHT or CHT and RT and concurrent CHT (CCRT) in sinonasal patients, most frequently in poor condition.

Conclusions. HN-NEC are characterized by an extreme variability in clinical presentation that determine major challenges in treatment planning. Consideration of the disease site, stage and clinical conditions is vital to tailor therapeutic intervention.

P125

CONCOMITANT SIB-IMRT/VMAT COMBINED WITH SISTEMIC THERAPY FOR LA-HNSCC IN REAL LIFE DAILY CLINICAL PRACTICE: MONOINSTITUTIONAL EXPERIENCE

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Aims. To evaluate, in daily practice, clinical outcome, feasibility and acute toxicities in locally advanced squamous cell head and neck cancer (LA-HNSCC) received Simultaneous Integrated Boost (SIB) with IMRT or VMAT technique and sistemic therapy.

Methods. We retrospectively analized 64 patients (pts), stage III-IVa of LA-HNSCC, who received mentioned above combined radical treatments in our Radiotherapy Unit from 2017 to 2023. 56 pts had concomitant chemotherapy (9 high dose cisplatinum, 34 weekly cisplatinum, 11 carboplatinum-5Fluorouracil) and 8 pts, unfit for platinum delivery, were treated with cetuximab For planning, according national and European guidelines, we identified differents treatment volumes reflecting different risks of holding disease and consequently that required different treatment doses: High-Risk (HR) volume (primary tumor GTV-CTV and positive neck nodes GTV-CTV), Intermediate-Risk (IR) volume (optional) and Low risk volume (elective nodal drainages). The median radiation dose was 69.96 Gy (66,03–69,96) in 33 fractions to the HR volume. Acute toxicities assessed according RTOG scale.

Results. The main toxicities recorded were skin toxicity/mucositis, hematological toxicity and dysphagia. No one experienced G4 toxicity. 42 pts recorded G2 skin toxicity/mucositis and 12 pts G3 (3 of them treated with cetuximab). 9 pts had G2 haematological toxicity and 8 pts G3 (resolved with leukocyte growth factors). 57 pts recorded dysphagia > G1 (5 pts G3). It was necessary to recur to artificial nutrition (PEG or TNP) for limited period of time in order to complete the treatment. Patients with baseline dysphagia or with a 5% reduction in body weight were immediately referred for a nutritional visit. All patients completed the treatment except one, who died of other causes. Complete response was observed in 52 pts (81%) of the patients, a partial response in 6 pts, while 5 pts had a disease progression in the following 3-6 months.

Conclusions. Concomitant SIB-IMRT/VMAT-chemotherapy/cetuximab is an effective and safe treatment for patients with LA-HNSCC and can be used in real-life daily clinical practice. In our experience, a timely nutritional assessment of patients has been found to be essential in order to complete the combined treatment.

Table 1.

64 patients	17 female	26.5%
	47 male	73.5%
Median age	61 (19-78) years old	
Primary tumor site	Oro-hypopharynx 45 pts	70.3%
	Nasopharynx 12 pts	19%
	Larynx 6 pts	9.3%
	Squamous cervical nodal metastases from occult primary tumor 1 pts	1.5%
Stage III	23 pts	35.9%
Stage IVa	41 pts	64.1%

P126

TOXICITY IN RADIATION THERAPY FOR HEAD AND NECK CANCER WITH USE OF HEXAPOD

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Introduction. the HexaPOD has been developed to correct for errors in six degrees of freedom (6DOF) to improve treatment set up accuracy. This is critical in head and neck radiation therapy plans wich have highly conformal dose distribution and close proximity of critical normal structures.

Methods. we evalueted 46 patients with head and neck cancer treated with hexapod from april 2021 And may 2023. Of these patients 38 underwent concomitant systemic treatment and 8 only radiotherapy. All the patients underwent a clinical check one week after the end of the treatment to evaluate its toxicity

Results. among all examined patients there were no acute or late grade 4 or 5 toxicities. Acute grade 2 and 3 toxicity was seen in 30 and 9 patients respectively while 7 patients did not show any toxicity. None of the patients needed to interrupt treatment due to severe toxicity.

Conclusions. treatement with Hexapod in patients with head and neck cancer it has proved to be effective and well tolerated for both acute and late toxicity.

P127

COMPUTED TOMOGRAPHY RADIOMIC FEATURES OF THE LUNG PARENCHYMA AND BASELINE RESPIRATORY FUNCTION IN PATIENTS TREATED WITH STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR LUNG LESIONS: PRELIMINARY CLINICAL RESULTS FROM A SINGLE-CENTER DATASET

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Aims. The interest in radiomics has been growing exponentially in the last years Aim of the present study is to test radiomics potentials in the prediction of radiation-induced modifications of the lung parenchyma following stereotactic body radiotherapy (SBRT), and to verify whether radiomic features are associated with either baseline and/or post-SBRT pulmonary function as assessed by spirometry. Here we present preliminary results from the clinical dataset

Methods. Retrospective data collection of patients who had received SBRT for intra-parenchymal lung lesions, per the following inclusion criteria: 1) treatment performed at European Institute of Oncology IRCCS (IEO)between 2013 and 2022, 2) lung disease of either primary origin or oligometastatic lung disease from any site 3) availability of 4D-simulation computed tomography (CT) scans, 4) availability of baseline spirometry, with diffusing capacity of the lungs for carbon monoxide (DLCO) values; post SBRT DLCO value were recorded whenever present, as well and 5) availability of written informed consent. As a further step, radiomic features

extraction will be performed with the IBSI (Imaging Biomarker Standardization Initiative) compliant software Pyradiomics.

Results. Overall, 123 patients and a total number of 156 nodules were eligible for the preliminary analyses. Median age was 68 (20-90) years, while the median Charlson Comorbidity Index (CCI) was 6 (1-11). Considering pulmonary function, median DLCO before and after radiation was 74 (4.2-160.0) and 69.0 (27.0-87.0), respectively. Forty-five patients had a primary lung cancer, while the remaining cases were treated for oligometastatic disease from the following sites of origin: 14pts from urological primary(11.4%), 21 pts from gastrointestinal primary (17.1%), 15 pts from gynaecological primary (12.1%), 7p ts from a primary breast cancer (5.7%), 11pts from Head and Neck primary (8.9%) and 10 pts from a primary sarcoma or melanoma (8.1%).

The median prescribed total dose was 45(range: 25-60) Gy, with a median number of fractions of 3 (range: 3-5). Please see the attached table.

Conclusions. Incorporation of ongoing radiomic analyses will provide complete insights on applicability of features as surrogates of spirometry, and on treatment-related modifications of the lung parenchyma.

Table 1.

	Number of patients N=123
Age Years (median range)	68 (20-90)
CCI (median range)	6 (1-11)
DLCO (median range)	Before SBRT 74 (4.20-160) After SBRT 69 (27.0-87.0)
Primary Lung Cancer	N=45
Sites of origin for oligometastatic lung disease	Urological primary N=14 (11.38%) Gastrointestinal primary N= 21 (17.07%) Gynaecological primary N=15 (12.1%) Mammary primary N=7 (5.69%) Head and neck primary N=11 (8.94%) Sarcoma/Melanoma N=10 (8.13%)
	Number of nodules N=156
Dose Gy (median range)	45(25-60)
Number of fractions	3 (3-5)

P128

MONOCENTRIC RETROSPECTIVE STUDY OF THE ROLE OF INTRATHORACIC CONSOLIDATIVE RADIOTHERAPY IN PATIENTS WITH ADVANCED NSCLC UNDERGOING FIRST LINE (CHEMO)-IMMUNOTHERAPY: A PRELIMINARY ANALYSIS

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Aims. Currently, first line (chemo)immunotherapy represents the standard of care in patients with advanced NSCLC. However, loco-regional progression of primary tumor is often a clinical problem. This study aims to evaluate the role of consolidative thoracic radiotherapy (TRT) in patients with stage IV NSCLC experiencing oligoprogression during first line (chemo)-immunotherapy in terms of safety and clinical outcome.

Methods. In this retrospective monocentric study, patients with stage IV NSCLC were included. Inclusion criteria were: no prior RT, intrathoracic progression during first line (chemo)immunotherapy treated with RT, no ongoing oncogene driven therapy, PS 0-2. The crude rate of acute and late toxicities was reported. Freedom from progression (FFP) and overall survival (OS) were calculated using the Kaplan-Meier method.

Results. Fifteen patients were retrospectively analyzed, from January 2018 to March 2023. All patients had stage IV NSCLC. Three patients had squamous carcinoma, 12 adenocarcinoma. Median age was 70 years(range 48-76). Three patients were smokers, 8 former smokers. Six patients underwent first line platinum-based (chemo)immunotherapy, 9 patients were treated with immunotherapy (IO) alone. All patients received consolidative TRT: 11 patients received 30-45 Gy in 10 to 15fractions, 1 patient received 25 Gy/5; 3 patients received 45 to 55Gy in 9-11 fractions and 1 one patient received 60 Gy/8 fractions. Regarding RT-related side effects, 2 patients had lung toxicities (1 G2 and 1 G3) and 4 patients experienced oesophagitis (all G1). Only one patient did not complete the RT course for G3 cardiac toxicity (pericarditis). After TRT, 11 patients interrupted IO and median IO duration of all patiens was 14 months (range1-34 months). Five patients suspended IO for toxicities, 4 patients for disease progression and 2 for other reasons. Estimated mean FFP and OS were 20.8 and 29.2 months (range1-51months). One year FFP and OS were 33.3±SE13.6% and 74.1±SE12.9%, respectively. Three patients (20%) underwent a second course of salvage RT using SBRT without changing first line systemic therapy.

Conclusions. Our study showed that advanced NSCLC patients with intrathoracic oligoprogression seem to clinical benefit from TRT as the switch to second-line systemic therapies can be postponed. No toxicity concerns emerged. Further data from prospective, preferably randomized, studies are needed to better clarify the role of local treatment in the setting of advanced NSCLC.

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ABSTRACT NOT PUBLISHABLE

P130

STEREOTACTIC ABLATIVE RADIOTHERAPY IN LOCALLY-ADVANCED NON-SMALL CELL LUNG CANCER PATIENTS: LITTLE PALLIATION OR BIG CURE? SUB-ANALYSIS OF START-NEW-ERA PHASE II TRIAL

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Purpose. Early analysis (1) of a single arm phase 2 trial (Clinical trials.gov NCT05291780) assessed local control (LC) and safety of stereotactic ablative radiotherapy (SAbR) unresectable locally advanced non-small cell lung cancer (LA-NSCLC) patients unfit for concurrent chemo-radiotherapy (ChT-RT). Here we report clinical outcomes of LA-NSCLC patients submitted to exclusive SAbR.

Methods and Materials. Between December 31, 2015 and June 30, 2022 71 LA-NSCLC patients were enrolled. 40 (56%) and 31 (44%) received neoadjuvant ChT+SAbR and exclusive SAbR, respectively. The tumor volume included primary tumor (T) and any regionally positive node/s (N). The co-primary study endpoints were LC and safety.

Results. The median age was 80 years (range, 45-88). Twenty (64%) and eleven (36%) patients had PS 0-1 and 2, respectively. Histology was adenocarcinoma (ADC) and squamous cell carcinoma (SCC) in 71% and 29%, respectively. 27 (87%) patients had ultra-central tumor. Median prescribed dose was 45 Gy (range, 35-55) and 40 Gy (35-45) in 5 daily fractions to T and N, respectively. After a median follow-up of 27 months (range, 6-92), 9 (29%) patients had experienced local recurrence (LR) at a median time of 13 months (range, 7-34). The median LR-free survival (FS) was not reached (95% CI, 28 to not reached). The 1-, 2- and 4- year LR-FS rates were 81±7%, 66±9% and 66±9%, respectively. At last follow-up, 23 (74%) patients were alive. Median overall survival (OS) was not reached. The 1, 2, and 4-year OS rates were 97±3%, 74±8% and 70±9%, respectively. Eight (26%) patients developed distant progression (dP). The median dP-FS was not reached (95% CI, 26 to not reached). The 1, 2, and 4-year dP-FS rates were 82±7%, 72±9% and 66±10%, respectively. The compliance to treatment was 100% and no patients developed grade (G) ≥ 3 toxicity. ADC (HR, 3.61;95% CI, 1.15-11.35) resulted significant predictor of better LC, while OS was significantly conditioned by smaller PTVs (HR, 1.004;95% CI, 1.001-1.010) and TNM stage (HR, 4.8;95% CI, 1.34-17).

Conclusions. LA-NSCLC patients treated with exclusive SAbR had optimal local control and promising overall survival with excellent treatment compliance and absence of ≥G3 toxicity. Our preliminary prospective clinical outcomes provide an attraction to evaluate this approach in patients unfit to ChT, to obtain a "big" cure beyond "little" palliation.

Reference

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P131

EXPLORATORY ANALYSIS OF CIRT-INDUCED CHANGES IN CARDIAC BIOMARKERS IN PATIENTS WITH PARA/INTRA-CARDIAC TUMORS

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Aims. Late cardiotoxicity is one of the worst side effects of thoracic Radiation Therapy (RT) and represents a significant risk factor for premature death. This exploratory study aims to assess the effect of thoracic Carbon Ion RT (CIRT) on serum levels of NT-proBNP, C-Reactive Protein (CRP) and Troponin I (TnI).

Methods. A retrospective analysis of clinical, laboratoristic and dosimetric data from 15 consecutive patients (pts) treated with CIRT for a para/intra-cardiac tumour was conducted. Data were collected before, during, at the end of CIRT and 3, 6 and 12 months of follow-up (FU). Wilcoxon signed-rank test was applied to evaluate changes during (from baseline to CIRT-end) and after treatment (from CIRT-end to 6m-FU). Spearman correlation test and point biserial correlation index were used to determine any relationship between dosimetric/clinical data and cardiac enzyme variations over time. The significance level was set to 0.05.

Results. Population features are shown in Table 1. Median FU was 6 months(m) [range: 0-12 m]. At baseline, diabetes (p=0,035) and hypercholesterolemia (p=0,023) were associated with higher CRP values, hypercholesterolemia (p=0,045) with higher TnI values, and thyroid disease (p<0.001) with higher NT-ProBNP values. Laboratoristic changes due to CIRT were unrelated to cardiovascular comorbidities, disease history, age, or gender. TnI and CRP values, both within the normal range, were unchanged while we found an increased

value of NT-ProBNP during CIRT (56.3 to 100 pg/mL, p=0.045) and a decreasing trend after (from 100 to 64 pg/mL, p=0.064). Reduction of NT-ProBNP was associated with minimum dose (Dmin) to the left atrium (p=0.013, r=0.69), maximum dose (Dmax) to the left main coronary artery (p=0.012, r=0.7) and Dmax to the circumflex artery (p=0.01, r=0.71). Other dosimetric parameters were not significantly correlated with NT-ProBNP variations.

Conclusions. TnI and CRP levels (during and at 6m) were not affected by CIRT delivered to para and intra-cardiac tumours. We observed a significant change in NT-proBNP (increase and then reduction). After the initial increase, the rate of NT-ProBNP reduction was positively associated with some dosimetric parameters. Whether these biomarker changes increase the risk of long-term cardiovascular morbidity or mortality will be addressed in the follow-up of our pts and with a larger prospective series.

Table 1.

Tabella1. Paziente	1	2	3	4	5	6	7	8	9	10	11
ETA	70	72	61	53	56	60	72	31	73	85	53
SESSO	F	M	F	M	M	M	M	F	F	F	M
ISTOLOGIA	B2/B1	B1	B2	B1	B2	B1	B1	B1	B1/B2	B1	B1
MASAOKA	IVA	III	IVA	IVB	IIIA	III	III	IIB	IVA	IVB	III
NEOADJ CT	1	0	1	1	1	0	1	1	1	0	1
CHIRURGIA	1	1	1	1	1	1	1	1	1	1	1
ADJ RT	/	50/25	54/27	50,4/28	50/25	25/5	54/27	54/27	50/25	54/30	50/25
TERAPIE CT O CHIR PER PRECEDENTI RECIDIVE	1	1	1	0	1	1	0	0	1	0	1

P132

ESOPHAGEAL TOXICITY IN RADICAL RADIOTHERAPY TREATMENT OF MALIGNANT PLEURAL MESOTHELIOMA: A MONOCENTRIC EXPERIENCE

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Aims. Aim of this study is to evaluate the incidence of acute esophageal toxicity during and just after radical radiation theraphy on the entire emithorax (RHR) in patients affected by pleural mesothelioma (MPM) and relate it to dosimetric parameters.

This is the most frequent toxicity, it worsens the quality of life during radiation treatment and, for rarely serious cases, can lead to the interruption of the treatment.

Materials and Methods. Between January 2010 and December 2018, 117 patients with diagnosis of malignant pleural mesothelioma received RHR with helical Tomotherapy in our center. The total dose was 50 Gy in 25 fractions with a concomitant boost of 60 Gy on residual disease. The mean age of our population was 68 years (33-83). Histologically, 105 of the patients had epithelioid MPM. In 69 cases the disease affected the right side. 64 patients were treated with pleurectomy / decortication surgery and all patients received neoadjuvant or adjuvant chemotherapy. Esophageal toxicity was registered with the "Common Terminology Criteria for Adverse Events (CTCAE) Ed.4.0.

Results. At the end of the radiation treatment we recorded 50 patients without esophagitis, 29 cases of G1 esophagitis, 34 cases of G2 and 4 cases of G3 no grade 4 to 5 toxicity were observed. At the six-month follow-up we recorded the persistence of 2 cases of G1 dysphagia, one case of G2 and one case of G3. After six months, only one G1 esophageal toxicity was recorded. No correlation was observed between esophageal toxicity and demographic data or previous therapy. A statistically significant relation (p=0.002) was observed comparing G0 *vs* G2-G3 if the esophageal circumference was covered by the dose of 47,5 Gy (95%). A statistically significant difference was observed comparing V30 (p<0.001), V50 (p<0.001) e D0.1 (p=0.005), Dmean (p<0.001) in G0 *vs* G2-G3. Even when comparing G0 and G1, statistically significant differences were observed for the same parameters. Using a parsimonious stepwise multivariate statistical approach only V30 (p=0.023) and V50 (p=0.009) resulted independent risk factors for esophageal toxicity (G0 *vs* G1-G3).

Conclusion. No treatment was discontinued due to esophageal toxicities and no patient needed hospitalization during treatment. The development of dysphagia is an acute event which resolves in almost all cases within 6 months. Among the dosimetric parameters V30 and V50 were the best predictors of esophageal toxicity.

P133

LUNG RE-IRRADIATION WITH SBRT: OUTCOMES IN THE RECURRENT SETTING

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Aims. Patients (pts) with primary or secondary lung lesions previously irradiated can experience a locoregional failure or the appearance of new lung lesions, thus requiring a thoracic re-irradiation. Aim of this monoinstitutional retrospective study is to evaluate outcomes in pts retreated on lung with Stereotactic Body Radiation Therapy (SBRT).

Methods. From April 2011 to October 2021, 42 pts (29 males, 13 females) received re-irradiation of lung lesions by SBRT. Median time between the two treatment was 24.6 months (range: 3-92). Median age was 73 years (range: 47-88). All pts had an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0–2. Of the 56 total lesions, primary cancer was lung in 57%, colon-rectal in 16%, not-typable in 11%, breast in 9%, endometrial and oropharyngeal in 3.5% respectively. Thirty-four lesions were treated in the same lobe, 12 in the ipsilateral lobe, 10 in the contralateral lung. Fifty-four lesions were peripherally located and 2 had a central location. Medium volume of clinical target volume (CTV) was 32.75 cc (range: 0.89-260.77). Medium BED10 of re-irradiation was 97.8 Gy (range: 37.5-151.2) and medium EQD210 was 82.18 Gy (range: 31.25-126). Thirteen lesions were re-irradiated with a single fraction, 43 with multiple fractions (range: 3-10). The most represented schedules in all subsequent courses of SBRT were 30 Gy in 1 fraction, 45 Gy in 3 fractions and 54 Gy in 3 fractions.

Results. After a median follow-up of 24.8 months (range: 3.2-141.7), Local Control (LC) was 53.2% at 1-year, 50.6% at 2-years and 35.5% at 3-years, Progression Free Survival (PFS) was 37.8% at 1- year, 28.1% at 2-years and 10.5% at 3-years, Disease Specific Survival (DSS) was 76.6 % at 1-year, 47.4% at 2-years and 36.9% at 3-years, Overall Survival (OS) was 78.3% at 1-year, 49.5% at 2-years and 40.1% at 3-years. On univariate analysis, CTV volume ≤ 33cc was statistically significantly related to LC (p=0.0157) and PFS (p=0.0106). Total number of treatments on lungs had a statistically significant correlation to PFS (p=0.0188), DSS (p=0.0007) and OS (p=0.0017). Number of re-irradiations was significantly related to PFS (p=0.0300) and DSS (p=0.0011).

Conclusions. Our experience showed favorable long-term outcomes in pts retreated on lung with SBRT. Data on role of SBRT in the recurrent setting are limited and further studies are necessary to confirm feasibility and safety of this approach.

Table 1.

	Volume CTV ≥ 33cc	Total number of treatments on lungs	Number of re-irradiations
LC	p=0.0157		
PFS	p=0.0106	p=0.0188	p=0.0300
DSS		p=0.0007	p=0.0011
OS		p=0.0017	

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LOCALLY ADVANCED LUNG CANCER TREATED WITH LATTICE RADIOTHERAPY: OUR EXPERIENCE

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Aims. To evaluate toxicities, overall survival (OS) and clinical response in locally advanced lung cancer treated with Lattice technique.

Patients and Methods. We enrolled locally-advanced/metastatic lung cancer patients with intrathoracic bulky-disease within Lattice_01 protocol. They were treated with a high radiation dose delivered using lattice technique. The primary endpoint was to evaluate clinical response and OS. Toxicities and Quality of life (QoL) were also evaluated during follow-up.

Results. From July 2021 to April 2023 6 patients (3 male and 3 female) were treated. The mean age was 77 years (range 66-86). The Karnofsky Performance status (KPS) before treatment was between 40 - 80. We delivered a vertex dose of 15 Gy in 1 fraction followed by 20-33 Gy in 4/10 fractions to clinical target volume (CTV). All patients ended irradiation with negligible toxicities. With a 3 months minimum-follow up, 5 patients are alive; 1 patient died without thoracic symptoms 8 months after the end of irradiation. A complete clinical response was observed in 2 cases; a partial response was observed in 4 patients. KPS at the end of treatment ameliorates in 5/6 patients, with a range that becomes 60-80. An improvement of QoL was reported in 67%. Pain disappeared in 2/2 patients with this symptom at the time of accrual.

Conclusions. LRT seems to be a safe and feasible technique for bulky tumors, with minimal toxicities to OAR'S. Our study confirms its validity in symptomatic treatment of locally advanced lung cancer, with a significant improvement of QoL.

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DOSIMETRIC PARAMETERS PREDICTING RADIATION-INDUCED LUNG TOXICITY AFTER STEREOTACTIC BODY RADIOTHERAPY: A SYSTEMATIC REVIEW FOR THE CLINICIANS

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Introduction. Lungs Stereotactic Body Radiotherapy (SBRT) represents a major therapeutic apAPproach in the management of primary and metastatic lung lesions.

Radiation. Induced Lung Toxicity (RILT) is considered a dose-limiting factor to be taken in account for SBRT. Patient-related features like age and site of tumour, as well as treatment-related features have been significantly correlated to the risk of RILT. The aim of this study was to provide a review of current evidence in the pathway of SBRT and RILI correlation, also providing dosimetric tools to be used in daily practice.

Methods. A Pubmed/MEDLINE and Embase systematic review was conducted. The search strategy was "Lung AND Radiotherapy AND dosimetric parameters" and only original articles referred to RILT and lung SBRT in the English language were considered.

Results. A total of 2896 studies were obtained using the mentioned search strategy on Pubmed and Embase. After the complete selection process, a total of 18 papers were considered eligible for the analysis of the results.

Discussion. Following the analysis, the dosimetric values suggested for lung SBRT can be resumed in Lungs V20 Gy < 10-15%, Dmean < 6-8 Gy, V10<19% and V12.5<9.5%. Data from prospective studies on the development of AI and omics-based tools for RILT prediction are needed to validate current evidence.

P136

STEREOTACTIC BODY RADIATION THERAPY FOR OLIGORECURRENT THYMOMA: UPDATE OF A MONOCENTRIC EXPERIENCE

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Aims. Limited data are available in the literature on what is the best treatment for recurrent thymoma. Despite radical surgery, recurrence rates range between 10% and 30%. The most common metastatic sites of thymoma are the pleura and lungs. The development of stereotactic body radiation therapy (SBRT) allows to perform radiation treatments with radical intent in selected types of patients. Our centre had already conducted a study in which patients with oligorecurrent thymoma were treated with SBRT with good local disease control (LC) and limited acute and late toxicities. This poster is an update of that study. We have since then increased the number of enrolled patients and extended the follow-up.

Materials and Methods. From November 2018 to May 2023, 11 patients for a total of 25 thymoma metastases have been treated in our centre using a Varian TrueBeam with FFF-RapidArc and daily kV-CBCT. All the patients underwent surgery for the primary tumor with or without neoadjuvant chemotherapy, followed by adjuvant RT except in one case. The approach for all the recurrences was discussed at our multidisciplinary board.

Table 1. Patient.

Tabella1. Paziente	1	2	3	4	5	6	7	8	9	10	11
ETA	70	72	61	53	56	60	72	31	73	85	53
SESSO	F	M	F	M	M	M	M	F	F	F	M
ISTOLOGIA	B2/B1	B1	B2	B1	B2	B1	B1	B1	B1/B2	B1	B1
MASAOKA	IVA	III	IVA	IVB	IIIA	III	III	IIIB	IVA	IVB	III
NEOADJ CT	1	0	1	1	1	0	1	1	1	0	1
CHIRURGIA	1	1	1	1	1	1	1	1	1	1	1
ADJ RT	/	50/25	54/27	50,4/28	50/25	25/5	54/27	54/27	50/25	54/30	50/25
TERAPIE CT O CHIR PER PRECEDENTI RECIDIVE	1	1	1	0	1	1	0	0	1	0	1

Results. The majority of the lesions were located in the pleura (12), the remaining in the lungs (4) and extrathoracic sites (3). The SBRT treatment was delivered in 5 fractions in all cases; the mean dose was 33.75 Gy (range 30 Gy-40 Gy), and mean BED10Gy was 58.5 Gy (range 48 Gy-72 Gy). The mean PTV volume was 48.4cm³ (5,5 cm³ – 121,7cm³). No relapse in the RT field was recorded. The treatments were well tolerated, there was only one case of acute esophageal toxicity G1. Median follow-up (FUP) is 15 months (3-24). During the FUP, one patient died of a different cancer histology (Breast cancer). Four patients experienced a second relapse, two a third relapse and one patient a fourth relapse. All the new lesions were treated with SBRT. At 3 months follow-up 50% of the patients achieved a partial response (PR) , 40% a complete response (CR) and 10% a systemic disease progression. At 6 months PR was

obtained in 57,1% of the patients and CR in 42,9%. In the 5 patients who reached the 2 years FUP, RP was maintained in 100% of cases.

Conclusions. Based on our updated data, due to its intrinsic radiosensitivity, SBRT is a valid approach for recurrent thymoma for its overall safety, excellent local disease control and viability of treating multiple lesions simultaneously.

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DOSIMETRIC AND RADIOBIOLOGICAL ANALYSIS OF ROBUST PENCIL BEAM SCANNING PROTON THERAPY OVER ROBUST X-RAY VMAT IN THE TREATMENT OF STAGE III NSCLC IN THE IMMUNOTHERAPY ERA

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Aims. Chemoradiation (CRT) followed by immunotherapy (IT) is the standard of care for PD-L1+, unresectable Stage III non-small lung cancer (NSCLC) patients (pts). In RTOG trial 0617 secondary analyses higher doses to the immune cells (EDIC) and to the left anterior descending (LAD) coronary artery significantly reduced overall survival. Proton therapy (PT) is an advanced, complex and costly type of RT with limited availability. It is crucial to define where PT could provide a clinical benefit over x-ray RT. This study aims to examine the dosimetric robustness and NTCP advantages of PT over VMAT in this setting

Methods. 10 Stage III NSCLC pts treated with CRT were re-planned with two methods for both VMAT and pencil-beam-scanning PT (PBSPT): 1) ITV-based robust optimization (RO) with 0.5 cm setup uncertainties and (for PT only) 3.5% range uncertainties on free-breathing CT 2) CTV-based RO including all 4DCTs anatomies. Nominal target coverage (NTC), organs at risk dose and TC robustness (TCR), set at V95%, were compared. The NTCP risk was evaluated for RT pneumonitis (RP), 24-month mortality (24MM) and G2+ acute esophageal toxicity (ET) using Appelt 2014, Defraene 2020 and Belderbos 2005, respectively. The LAD V15<10% was scored. The mean dose to the thoracic vertebral bodies (MDTVB) was recorded. EDIC was scored using Jin 2021. Wilcoxon test was used for statistics

Results. Both PT methods improved NTC with p=0.002 for CTV-based plans. TCR was significantly improved with both PT methods (p=0.001/0.006 for ITV/CTV-based plans, respectively). The mean lung dose (p=0.002 for both methods), lung V20 (p=0.002 for both) and the risk of RP (p=0.002 for both) were significantly lower with PT, with a mean ΔNTCP=6%, range (R)=1-17%. Mean PT heart dose reduction was 8 Gy (p=0.001 for both). The risk of 24MM was significantly lower with PT (p=0.004 for both methods), with a mean ΔNTCP=4%, R=1-9%. The risk of acute ET was not reduced. PT significantly lowered median LAD V15 (p=0.004 for both methods); PT achieved V15<10% in 80% of cases where VMAT had failed. PT significantly reduced MDTVB (p=0.02 for both methods). PT significantly halved median EDIC (4.9/5.1 Gy for ITV/CTV-based VMAT *vs* 2.3 Gy for both ITV/CTV-based PT, p=0.002 for both)

Conclusions. PBSPT is a robust approach for NSCLC with significant dosimetric and NTCP advantages over VMAT. In the IT era, lung, heart as well as EDIC dose reduction could provide a significant clinical benefit for a subset of NSCLC pts

Table 1 Comparison of radiobiological indexes between: a) ITV based VMAT-PSBT plans and b) CTV-based VMAT-PSBT plans, see abstract text for abbreviations and details.

a

ITV-based plans Radiobiological indexes		VMAT	PBSPT	p
Edic (Jin 2021)	Median	5.1	2.3	0.002
	Min	2.8	1.3	
	Max	6	3.2	
Esophagus (Belderbos 2005)	Median	23.95	17.9	0.084
	Min	3.4	3.3	
	Max	55.30	60.9	
Heart (Defraene 2020)	Median	75.2	70.25	0.004
	Min	55.2	49.1	
	Max	81.5	78.1	
Lung (Appelt 2014)	Median	7.3	3.5	0.002
	Min	4.2	2	
	Max	33.4	16.4	

b

CTV-based plans Radiobiological indexes		VMAT	PBSPT	p
Edic (Jin 2021)	Median	4.9	2.3	0.002
	Min	2.6	1.3	
	Max	5.9	3.2	
Esophagus (Belderbos 2005)	Median	25.3	15.65	0.232
	Min	3.4	3.3	
	Max	47.7	59.8	
Heart (Defraene 2020)	Median	74.1	70.15	0.004
	Min	54.7	49	
	Max	81.9	78.1	
Lung (Appelt 2014)	Median	7.15	5.1	0.002
	Min	3.1	2	
	Max	35.6	15.9	

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RETROSPECTIVE EVALUATION ON LOCALLY ADVANCED LUNG PATIENTS , UNDERGOING CHEMO-RADIOTHERAPY, AND THE ROLE OF ACE-INHIBITORS IN RADIO-RELATED TOXICITY

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Aims. To study the radioprotective function of ACE inhibitors in patients with locally advanced lung cancer and evaluation of related toxicities during concomitant treatment.

Methods. From our database we retrospectively evaluated locally advanced NSCLC patients receiving concomitant radio-chemotherapy, irradiated with VMAT technique (total doses: 60-66 Gy) and platinum-based chemotherapy. The inclusion criteria for the analysis were: tests of respiratory function within the limits, absence of previous major cardiovascular diseases such as myocardial infarction and heart failure, absence of diabetes. Patient-reported outcome (PRO) questionnaires were also administered.

Results. A total of 39 patients with the previous characteristics and the similar volume disease (studied on PET imaging) were selected from our database, 21 of whom had been taking ACE inhibitors for at least five years, the remaining 18 had never taken antihypertensives, all smokers or former smokers with an average age of approximately 65 years. Of these, approximately 12% (3 patients) developed grade > 2 actinic pneumonia (all in the no ACE group), upon evaluation of the PRO questionnaires, all patients ACE inhibitors group report a lower incidence of dyspnoea, fatigue, inappetence or steroidal dose increasing. In both groups there was evidence of worsening cough.

Conclusions. Although underpowered due to low patient numbers, the reported results suggest solid safety in the use of ACE inhibitors in this patient setting, with a possible advantage in terms of protection from actinic pneumonia (0% of cases in the ACE-i group *vs* 12% in no-ACE group) and radio-related side effects, as well as the evaluation of the PROs shows fewer clinical disturbances in the ACE-i group. Further randomized studies with greater statistical power will be useful to verify their efficacy in the prevention of radio-related toxicities.

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PATTERN OF LOCAL RECURRENCE OF STEREOTACTIC ABLATIVE RADIOTHERAPY IN UNRESECTABLE LA-NSCLC PATIENTS UNFIT FOR CONCURRENT RADIO-CHEMOTHERAPY: ANALYSIS OF START-NEW-ERA PHASE II TRIAL

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Aim. local control (LC) continues to be a major challenge in LA-NSCLC. In Pacific trial, Durvalumab reduced both intrathoracic and distant relapse risks, however, the first progression frequently occurred in the thoracic compartment. Early analysis (1) of a single arm phase 2 trial (Clinical trials.gov NCT05291780) investigating stereotactic ablative radiotherapy (SAbR) in unresectable locally advanced non-small cell lung cancer (LA-NSCLC) patients unfit for concurrent chemo-radiotherapy (ChT-RT) was published. Here, we aimed to assess pattern of local recurrence (LR).

Methods and Materials. Between December 31, 2015 and January 31, 2023 77 LA-NSCLC patients were enrolled. 43 (56%) and 34 (44%) received neoadjuvant ChT+SAbR and exclusive SAbR, respectively. The tumor volume included primary tumor (T) and any regionally positive node/s (N). 24 (31%) developed local recurrence.

Results. The median age was 73 years (range, 45-88). 17 (71%) and 7 (29%) were male and female, 19 (79%) and 5 (21%) PS 0-1 and 2; 18 (75%) and 5 (25%) squamous cell carcinoma (SCC) and adenocarcinoma ADC), 66% had stage IIIA/IIIB with multiple lymph nodes (58%). 15 (63%) received neoadjuvant ChT and 4 (16%) with PD-L1 ≥1% Durvalumab. The median dose for primary tumor and regional node/s was 40 Gy (range, 35-50) and 40 Gy (range, 35-45) in 5 fractions. 14 (58%) had isolated LR, while in other patients regional recurrence and distant progression was reported in addition to LR. 7 (29%) patients with isolated LR were submitted to second course of SAbR, 71% received systemic treatment alone.

Conclusions. In a cohort of unresectable LA-NSCLC patients treated with SAbR one third of patients develop local failure, half of these have isolated local recurrence. The strongest predictor of LR was SCC histology; higher SAbR dose and synergy with immunotherapy may improve local control in intriguing ChT-free approach.

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IMPROVEMENT OF DOSIMETRIC PARAMETERS AFTER ADAPTIVE RADIOTHERAPY WITH VMAT IN PATIENTS WITH LOCALLY ADVANCED NSCLC UNDERGOING 4DCT

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Objective. To investigate dosimetric difference to organs at risk (OARs) and cardiac substructures in patients with locally advanced non-small cell lung cancer (NSCLC) between adaptive radiotherapy (ART) and non-ART group.

Methods. Thirty patients were treated with definitive radiotherapy +/- chemotherapy. Cardiac substructures including left anterior descending coronary artery (LAD) and large vessels were contoured. Eight patients had a tumor shrinkage and were replanned (ART). Cumulative plans after ART was compared to the original plans (not considering volume reduction) in terms of dosimetric parameters. The cumulative plans of the ART group (n=8) and the non-ART group (n=22) were compared in terms of the same dosimetric parameters.

Results. Within the ART group the following parameters were found to be significantly improved after re-planning: mean lung dose (MLD) (13.79Gy vs. 15.6Gy), V20Gy both lungs (17.88% vs. 27.38%), ipsilateral MLD (20.87Gy vs. 24.44Gy) and esophagus mean dose (20.79 Gy vs. 24.2Gy). No dosimetric difference was found for heart or cardiac substructures. Dosimetric parameters in particular for LAD were significantly worse in the ART group than in the non-ART group. Probably because this OAR was not taken into account in the plan optimization after re-planning since it is not routinely contoured as OAR.

Conclusions. Our analysis showed an improvement of dosimetric parameters in lung and esophagus in case of ART. This approach could lead to a possible reduction of toxicities. Contouring of cardiac substructures could lead to an optimization of their parameters and eventually reduce the risk of cardiac toxicities in these patients.

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PNEUMONITIS INCIDENCE IN A SINGLE-CENTRE SERIES OF PATIENTS TREATED WITH CHEMORADIOTHERAPY WITH OR WITHOUT DURVALUMAB FOR UNRESECTABLE STAGE III NSCLC

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Aims. Pneumonitis is the most common clinical and radiological adverse effect in patients (pts) receiving chemoradiotherapy (CRT) with or without durvalumab as maintenance for unresectable locally advanced NSCLC. Several risk factors related to the patient, tumour, and treatment could influence the severity of lung injuries. The aim of this study is to investigate the rate of pneumonitis and related factors within a single-centre retrospective series.

Methods. Clinical, therapeutic and dosimetric data of 85 pts were collected from October 2018 to July 2022. Both radiation and immune-related pneumonitis were registered when occurred after CRT and recorded according to CTCAE version 5.0. Chi-square test and T-test were used to relate the different factors to pneumonitis grouped in G0-G1 and G2-G5, for continuous and categorical variables, respectively. A p-value <0.05 was considered statistically significant.

Results. Eighty-five pts were retrospectively included in this series, and all received 60 Gy on the thoracic disease combined with platinum-based chemotherapy (concurrent in 87,1% of cases). Pulmonary functional test (PFT) was performed for all pts before treatment. Fifty-two cases (63%) received maintenance immunotherapy with Durvalumab for at least 1 cycle. Median age was 68 years and 29,4% of pts was female, PS ECOG was 0-1 for all pts. Median pack/year resulted 45 and COPD was recorded in 52,9% of cases. The median volume of PTV was 439 cc (range 169-1171 cc). The median follow up was 20 months. Twenty-one pts experienced pneumonitis, with 7, 11, 1, 1, and 1 cases being grade 1, 2, 3, 4, and 5, respectively. Pulmonary dosimetric variables alone (V5, V20 and mean dose) resulted significantly related to the higher incidence of G2-G5 pneumonitis. Notably, neither the addition of durvalumab nor the PFT results significantly affected the rate of pneumonitis.

Conclusions. The results of this large single-center series indicate that pulmonary toxicities after CRT plus or minus Durvalumab is a common but typically low-grade side effect. Many factors are potentially involved in the onset of pneumonitis. However, it seems that dosimetric

parameters play a central role in this regard. The crucial point of treatment of these pts remains the planning optimization, but clinical and functional features have also to be carefully considered.

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MONO-INSTITUTIONAL EVALUATION OF RESPONSE AND OF CLINICAL OUTCOMES IN LUNG OLIGOMETASTATIC CANCER PATIENTS TREATED WITH STEREOTACTIC RADIOTHERAPY

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Aims. The benefit of local ablative therapy in lung metastases has been investigated and integrated into the treatment framework. In recent decades, Stereotactic Body Radiation Therapy (SBRT) has been increasingly used to ablate metastasis for high rate of local control. We retrospectively investigated the efficacy of SBRT for lung metastases analyzing the characteristics of the patients and their survival outcome.

Materials and Methods. We retrospectively reviewed 41 patients treated with SBRT for lung metastases between 2016 and 2022. The histological type of the primary lesion, the presence of comorbidities, the smoke factor and the number of lung metastases and their localization have been evaluated. Overall survival (OS) and local control (LC) were reported. The response was divided in complete (CR) and in partial (PR) response and analyzed with LC. Treatment outcomes were evaluated using Kaplan–Meier analysis. A P-value less than 0.05 was considered statistically significant.

Results. The median age was 71 years old. Male/Female ratio was 70%/30%. Non–small cell lung cancer (51%) and rectal cancer (18%) represented the most common primary tumors. 78% of patients had no smoking habit. Cardiovascular diseases were the most frequent comorbidities (51%) followed by the endocrine diseases (30%). 90% of the metastases was detected by PET-CT. The superior lobe of left lung and of the right lung were the two most frequent localization in our setting: 27% and 24% respectively. The most used RT schedule was 50 Gy (10 Gy/day) followed by 40 Gy (8 Gy/day). The median follow-up was 12 months. 73% of patients achieved a lesion response of which 57%, a complete response. Figure 1 shows the Kaplan–Meier analysis both for OS and for LC. The median OS was 13 months. The 1-year and 2-year OS rates were 81%, and 70%, respectively. The 1-year and 2-year LC rates were both 87%. CR patients had a greatly better and longer LC compared to PR patients (99% *vs* 50%, p<0,001). No treatment-related death occurred after SBRT; 37% of patients in response had a progression/recurrence in lungs in a median time of 9 months (range: 1-30).

Conclusions. SBRT for lung metastases showed excellent local control and promising survival rates, with an optimal correlation between response size and local control.

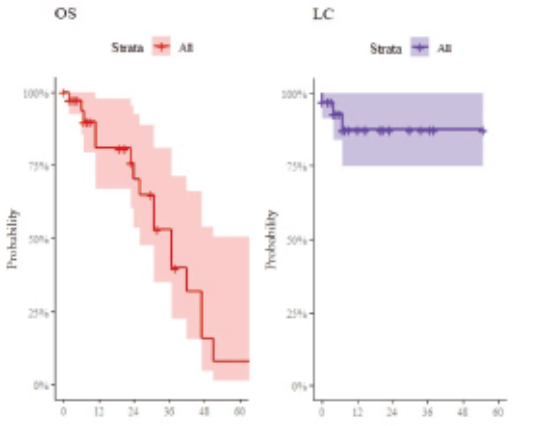

Figure 1.

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IS REBIOPSY AN OPTION IN STAGE III NSCLC PATIENTS WHO ARE PD-L1 NEGATIVE? A MONOCENTRIC EXPERIENCE

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Aim. To prove the efficacy and feasibility of rebiopsy before the start of radical chemo-radiotherapy in PD-L1 negative stage III NSCLC patients.

Methods. The 5 years updated results of the Pacific study published in 2022 have once again proven that concomitant chemo-radiotherapy followed by Durvalumb is superior to chemo-radiotherapy alone in patients with Stage III non small cell lung cancer (NSCLC). The overall survival of patients treated with immunotherapy or placebo was respectively 42.9% (38.2 to 47.4) versus 33.4% (27.3 to 39.6) whilst the progression free survival was 33.1% (28.0 to 38.2) versus 19.0% (13.6 to 25.2). In order to use this treatment schedule, European patients need to have a PD-L1 expression of at least 1%. If PD-L1 is not expressed patients are treated with chemotherapy and radiation therapy and referred to follow up only. In

our center the use of consolidation Durvalumab has become the standard of care for the majority of the patients but there is still a small percentage of patients who are PD-L1 negative and therefore are excluded from this treatment. In these occurrences we discuss the patients at our Thoracic multidisciplinary board to decide whether a new biopsy can be performed or not.

Results. In the last 6 months 4 patients (all males) with a negative PD-L1 expression at diagnosis were discussed and got a rebiopsy before the first day of chemotherapy. In Table 1 are summarized their characteristics.

Two of them got a new biopsy of the mediastinal nodes and two of the primary tumor.

The biopsies were taken only a few days prior to the start of the concomitant chemo-radiotherapy treatment and the results were available during treatment. None of these patients experienced a delay of the start of the therapy due to the biopsies which were well tolerated and performed without complications.

The results came back positive for PD-L1 and 3 out of 4 patients received consolidation immunotherapy with Durvalumab, whilst one is still completing the chemo-radiotherapy treatment.

Conclusions. The experience in our center has proven that the procedure of re-biopsy is a feasible and safe option for PD-L1 negative stage III NSCLC patients that can benefit from consolidative immunotherapy without compromising the time to the first cycle of chemotherapy. It is worthwhile to mention that this approach could lead to better oncological outcomes in this subgroup of patients.

Table 1.

Patient	Histology	Staging	date of 1st biopsy	date of 2nd biopsy	PDL1 status at second biopsy	start of chemo-radiotherapy
1	adenocarcinoma	cT4 cN3	26/1/2023	25/02/2023	2%	28/02/2023
2	squamous cell carcinoma	cT4 cN2	16/03/2023	05/04/2023	5%	10/04/2023
3	squamous cell carcinoma	cT1c cN2	02/04/2023	26/04/2023	40%	03/05/2023
4	carcinoma non otherwise specified (NOS)	cT2a cN3	04/04/2023	27/04/2023	60%	28/04/2023

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INTEGRATED ONCOLOGIC AMBULATORY INTO THE MULDISCIPLINAR MANAGEMENT OF STAGE III LUNG CANCER: A MONOCENTRIC EXPERIENCE

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Aims. There has been a growing emphasis on using integrated care plans to deliver cancer care. Based on substantial evidence demonstrating that combined care improves patient outcomes, we have developed a new healthcare model called "integrated oncologic ambulatory", where a medical oncologist and a radiation oncologist make a joint evaluation of stage III lung cancer patients.

Methods. All consecutive patients with stage III non small cell lung cancer (NSCLC) discussed in multidisciplinary team meetings (MDTMs) were reviewed. Then, patients performed a first medical examination by the integrated oncologic ambulatory team, which consisted of two medical oncologists and one radiation oncologist. Patients were jointly evaluated weekly during treatment and every three months during the follow-up. Endpoints were time from diagnosis to treatment initiation (TTI); time from diagnosis to the end of the treatment (TTE), meant as concurrent or sequential chemo-radiotherapy.

Results. Between September 2019 and February 2023, a total of 80 patients were evaluated. Fifty-three percent of evaluations resulted in an indication for concurrent treatment, 47 percent for sequential one. In both cases, RT delivered 60 Gy in 30 fractions to gross tumor volume and involved nodes. Median TTI was 18 days (4-46); median TTE was 93 (54-265) days. At a median follow-up of 13 months (2-50), no patient has been lost to follow-up and 37 presented disease progression.

Conclusions. Implementation of a lung cancer integrated care pathway reduces all treatment intervals and ameliorates oncological outcomes. An optimal compliance was observed, with no patient lost at follow-up. These data promote integrated clinical approaches in oncological patients.

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PATTERNS OF CT LUNG INJURY AFTER SABR FOR PRIMARY OR SECONDARY LUNG LESIONS

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Aims. Radiological lung density changes are commonly observed in the majority of patients undergoing stereotactic ablative radiotherapy (SABR). In this study we analyzed the acute and long-term radiation-induced

lung changes in terms of radiological findings observed at CT.

Methods. We retrospectively analyzed the pre-treatment and follow up CT scans of patients treated with SABR in the lung between 2016 and 2022 at a single Institution. Eligible patients with primary or secondary lung lesions were treated on a Linac platform with a VMAT technique to median dose of 50 Gy (range 45-60 Gy), corresponding to a BED10≥100 Gy. After SABR, follow-up CT scans were performed at 3 months, 6 months and annually, and double-checked by 3 experienced radiation oncologists. Radiation-induced lung injuries were evaluated according to Ikezoe (within 6 months) and Koening (> 6 months) classification, respectively.

Results. Between December 2016 and August 2022 98 patients with a total of 114 lung lesions (87 peripheric and 27 central) were treated. Median age was 74 years (range 51-90) and 37 patients were females. Median follow up was 12 months (range 3-40). Median PTV was 14.33 cc (range 3.47-83.02). Smoking history was available for 61 patients, and 18 presented a history of Chronic Obstructive Pulmonary Disease (COPD). Among the 110 lesions available for the earlier assessment, the following findings were obtained: no evidence of increased density in 45, diffuse consolidation in 19, patchy consolidation in 18, diffuse ground glass opacities in 16, patchy ground glass in 10, progressive disease in 1 and complete tumor regression in 1. Koening classification for 92 examined lesions revealed: mass like pattern in 24, modified conventional pattern in 23, scar-like pattern in 31 and progressive disease in 14.

Conclusions. Lung injuries represented common radiological findings after SABR, irrespective of clinical symptoms. A correlation between radiological appearance and clinical and dosimetric parameters at different time points is underway to identify predictive factors for lung radiological toxicity.

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RESPIRATORY MONITORING SYSTEM FOR 4D TREATMENT UNDER FREE BREATHING FOR THORACIC OR ABDOMINAL CANCER PATIENTS

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Aims. Radiotherapy of thoracic and abdominal cancer implicates treatment uncertainties due to respiratory-induced tumor motion and breathing motion variations. Surface Guided Radiation Therapy offers near real-time patient motion monitoring in RT workflow. Breath-hold, abdominal compression and 4D imaging techniques represent clinical strategies for motion management. Respiratory-gated radiotherapy (RGRT) is delivered only at a certain phases of the respiratory cycle and different gating windows can be used for radiation treatment. In this paper we evaluate the clinical applicability of the C-RAD Sentinel/Catalyst system (C-RAD AB, Uppsala, Sweden) in combination with the 4D CT mode of a Brilliance Big Bore Philips CT scanner and we determined the optimal gating windows for RGRT of thoracic or abdominal cancer patients.

Methods. Planning 4DCT images (10 phases) of five patients have been acquired by using a Big Bore Brilliance Philiphs CT. SGRT C-RAD optical system (Sentinel) has been used to identify patient's breath rate based on the position of a reference point placed on the thoracic skin surface. Moreover, all patients received a training period before CT scan. A pulmonary protocol was obtained with different pitch values depending on breath rate for minute. Respiratory signals were acquired and analyzed. Raystation v11B TPS 4DCT functionalities combined with Python scripting have been used to automatically create the ITV contour for each breathing phase.

Results. Four of the five patients breathed quite regularly so the absolute peak-to-peak amplitudes of the Sentinel system range between 4 to 8 mm. One patient had an extreme shallow respiration and the absolute signal from the Sentinel system ranges only between 0.5 to 1 mm. With a rotation of a 0.44 second rotation-time, the pitch value ranged from 0.09 for breath rate of 14 to 0.065 for breath rate of 10. All patients successfully succeeded to maintain treatment position with a regular breathing. Phases of 30–60% and 30–70% retrieved the lowest respiration variability among patients.

Conclusions. The combination of a Big Bore Brilliance Philiphs CT and C-RAD Sentinel/Catalyst system provide a feasible and effective method for 4D respiratory-gated radiotherapy of thoracic and abdominal cancer patients under free breathing showing a comfortable and reproducible position for patients. The optimal gating window should be accurately defined in order to obtain effective radiation treatment and shorter time of therapy.

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SAFETY AND EFFICACY OF ABLATIVE STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR EARLY STAGE LUNG CANCER IN ELDERLY PATIENTS: A MONO-ISTITUTIONAL EXPERIENCE

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Aims. to evaluate outcomes and safety rates after ablative Stereotactic Body Radiation Therapy (SBRT) of inoperable lung cancer in the very elderly.

Methods. patients with early lung cancer treated with definitive SBRT were included in this retrospective analysis. Inclusion criteria were: patients with histologically confirmed lung cancers or patients with clinically suspected NSCLC with medical comorbidities that increase biopsy risks, early stage (I-II), FDG-PET avid lesions, no surgical indications due to comorbidities or refusal of the patient to undergo surgery treatment, age ≥ 80 years, patients with an expected survival > 3 months, and Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 3. All lesions were contoured on 3 mm CT-scan using free breathing. A FDG-PET/CT-scan fusion was used. Radiotherapy was delivered with fractionated SBRT using VMAT technique. A median total dose of 44.5 Gy (range: 37.5 - 50.0) in a median of 5 daily fractions (range; 3-9). Instrumental revaluation (CT-scan and/or FDG-PET/CT) were performed every 2-6 months after the treatment. CTCAE v.5 scales were prospectively recorded during follow-up and utilized for toxicity assessments.

Results. from January 2019 to March 2023 a total of 19 patients were consecutively treated [M/F=14/5; median age: 85 years (range: 80-89 years); median ECOG performance status was 1 (range: 0-2). With a median follow-up time of 8 months (range: 2-32 months), 63.1% of patients showed a radiological overall response (36.8% CR, 26.3% PR), 36.8% of patients presented a PD. No patients showed ≥ G1 acute toxicity (mild cough), late toxicities occurred in 2 patients (2 patients with asymptomatic radiation pneumonitis G1).

Conclusions. ablative SBRT showed favorable and promising results in terms of local efficacy and safety for early lung cancer also in very elderly patients. Further studies are needed to obtain more uniform results using a BED10 ≥100Gy.

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HYPOFRACTIONATED CONCURRENT CHEMORADIOTHERAPY IN SUPERIOR VENA CAVA SYNDROME IN NSCLC: EARLY REPORT OF CLINICAL RESULTS

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Introduction. Superior Vena Cava Syndrome (SVCS) represents an oncological emergency that is difficult to manage. Although the prognosis is often poor, integrated radio-chemotherapy (RCT) remains a fundamental therapeutic approach to improve symptoms and quality of life. In order to investigate the early clinical benefits of this combined treatment, we performed a retrospective analysis on 6 patients treated at our institution with induction chemotherapy followed by concurrent hypofractionated radio-chemotherapy.

Materials and Methods. Between March 2022 and March 2023, 6 patients with SVCS were treated at our institution. The age of the patients ranged from 62 to 78 years with a median age of 70 years. The primary malignancy was non-small cell lung cancer, with five patients with stage III and one patient with stage IV tumor. All patients received RCT with hypofractionated radiotherapy (HFRT) with (3 patients) or without induction chemotherapy (3 patients). HFRT was administered in daily fractions of 3 Gy to a median total dose of 45 Gy (tanging from 42 to 50 Gy) by 3D-CRT or IMRT. To evaluate early clinical benefits, all patients were examined weekly during the entire course of treatment and quarterly after its conclusion. Toxicities were collected according to CTCAE 5.0. Moreover, at the end of the treatment, all patients underwent diagnostic examinations (PET/CT) to evaluate radiological response, according to RECIST criteria.

Results. During the RCT treatment, all patients rapidly showed early clinical benefits with reduction of collateral circulation (particularly in extension), jugular turgor, dyspnoea, cough and nasal congestion. About toxicities, only one patient showed G1 anemia while one patient referred G1 esophagitis and radiation dermatitis. One month after the end of the radiotherapy treatment, all patients underwent PET/TC restaging with partial response. In particular, 2 patients had partial response of 30%, 3 patients of 50% and one patient of 70%.

Conclusions. Basing on our result, even if SVCS is characterized by poor prognosis, integrated treatment

with RCT has been demonstrated to be effective in terms of early clinical benefits and feasible with only G1 toxicities. No patients showed hemathological toxicities of any grade.

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EVALUATION OF RESPONSE AFTER STEREOTACTIC TREATMENT OF PULMONARY NODULES: PRELIMINARY RESULTS OF A SINGLE-CENTRE STUDY

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Aims. Stereotactic body radiotherapy (SBRT) represents a modern technique to achieve good local control and improve survival in pulmonary metastases or primary lung nodules. The timing and modalities for assessing response to radiotherapy are not yet clearly defined. The aim of this study is to present the results of a group of patients treated in our centre.

Methods. Patients treated for lung metastasis or primary lesions between 2019 and 2022 were included. Data related to patients' characteristics and radiotherapy dose fractionations were collected. The response rate at different time points after SBRT was assessed at 3-month intervals after the end of treatment (0-3 months, 4-6 months, 7-9 months, 10-12 months, > 12 months) and evaluated both by size using RECIST criteria and by metabolic response considering SUV reduction.

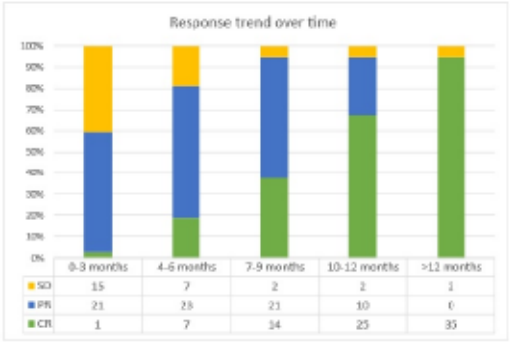
The CR (complete response), PR (partial response), and SD (stable disease) of these lesions were assessed. We considered a CR if we observed stability of the lesion in at least 2 consecutive radiological examinations.

Results. Fifty-seven lesions were evaluated, thirty-seven had at least 2 radiological examinations within 1 year (with the first occurring at least 3 months after SBRT), so they were included in the response rate analysis.

The SBRT dose ranged from 40.0 to 60.0 Gy (median 48.0 Gy) and was delivered in a median of 5 fractions (range 5-8). All patients underwent 4D-CT and breath tracking with RPM system (VARIAN). ITV was delineated in all lesions. Almost all treatments were performed in free breathing after 4D CBCT imaging; 11% of lesions were treated with the deep inspiration technique after breath-hold CBCT. The median follow-up time was 12 months (range, 6-26 months).

Within 3 months after the end of treatment, radiological CR was observed in only 3% of cases, PR in 57%, and SD in 41%. Between 7 and 9 months after treatment, 38% of lesions had CR, 57% had PR and 5% had SD. After more than 12 months, 95% of lesions had CR. The graph shows the trend of response over time (Figure 1).

Conclusions. In our study with limited follow-up (median 12 months), the majority of SD or PR turned into CR even up to 12 months after the end of SBRT. This leads us to consider that in cases of initial SD or PR, it may be necessary to wait a longer time to assess the correct response before considering the beginning of systemic treatment. In the next future, we plan to review the radiological examinations of the patients studied to find radiological signals predictive of a major response.



Percentage overall response rate over time

	0-3 months	4-6 months	7-9 months	10-12 months	>12 months
SD	41%	19%	5%	5%	5%
PR	57%	62%	57%	27%	0%
CR	3%	19%	38%	68%	95%

Figure 1.

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IT'S NOT NECESSARILY GOD: IMMUNE LANDSCAPE ANALYSIS TO ASSESS SPONTANEOUS REGRESSION (SR) IN A PATIENT WITH ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC)

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Aims. SR of cancer is defined as an extremely rare phenomenon characterized by a complete or partial, temporary, or permanent disappearance of tumour in the absence of specific therapy. Among the histologic proven lung cancer SR cases, recent evidence suggested a role of the immune system as key player in disease outcome.

Here, we studied the immune landscape of a patient with advanced, poorly differentiated stage IV NSCLC that remitted spontaneously.

Case presentation. A 64-year old current smoker man presented haemoptysis and was diagnosed a stage IV right lower-lobe lung cancer. Clinical stage was T3N2M1 for right adrenal metastasis. Diagnosis was performed with CT, PET/CT, brain MRI and biopsy through mediastinoscopy of sub-carinal lymph-node that confirmed a poorly differentiated lung adenocarcinoma, highly expressing PD-L1 (>90%). After biopsy we repeated CT and PET-CT with a complete regression of the adrenal metastasis and a reduction of the primary tumour and mediastinal lymph nodes, thus we re-staged disease as T3N2M0. It was debated whether treat patient with IT alone considering first stage or to treat him with concurrent chemo-radiotherapy (cChT+RT) and Durvalumab according to re-staging. After multidisciplinary discussion, he received cCT+RT (20x 2.75Gy) and started Durvalumab 15 days upon. PET/TC 3 and 6 months after cCT-RT revealed a metabolic complete response of cancer. No treatment related toxicity has been registered. In the effort to characterize the patient immune landscape we performed a third-generation flow cytometry analysis of both innate and adaptive immune cells including activation/exhaustion markers before any therapy but upon surgical biopsy of a mediastinal lymph node. Interestingly, among the several cell subsets identified, we observed a dramatic reduction of the circulating CD8 T cells as compared with CD4 counterpart. Moreover, the immunohistochemistry analysis of the metastatic lymph nodes showed an enrichment of tumour infiltrating CD8 T cells thus suggesting a cytotoxic T cell response at tumour site probably triggered by surgical biopsy related inflammation.

Conclusions. Altogether our observations suggest a role of CD8 T cells as key players of SR in this case study thus highlighting the importance of personalized medicine to elucidate the pathogenesis of cancer as well as to identify new circulating biomarkers.

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NSCLC III STAGE IN "ERA PACIFIC TRIAL": THE ABHIT OF TOBACCO SMOKING CAN WORSE THE COMPLIANCE TO ICIS AFTER RADIOCHEMOTHERAPY?

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Aims. The aim of this retrospective study is to evaluate how tobacco smoking could impact on compliance treatment in pts with stage III NSCLC, after concurrent radiochemotherapy CDDP-based, during administration of anti-PD1 ICIs.

Methods. We selected retrospectively pts smokers with diagnosis of NSCLC in stage III- PD1 >1% from February 2021 to March 2023, treated according to PACIFIC schedule. At the time of enrollment, all pts had diagnosis of Chronic Obstructive Pulmonary Disease (COPD) of mild or moderate degree on spirometry, no COPD-Acute Events recorded in previous month to recruitment. Therapeutic program included: Radiationtherapy on tumor site and mediastinal nodes with VMAT technique for total dose 60 Gy/2 Gy concurrent to CDDP, administrated weekly to dose 40 mg/m^2, then durvalumab (10 mg/kg q.2 w) for 12 months. All patients (n.14 pts) completed RT-CTx CDDP-based and durvalumab was administred until to progression disease. The doses at OARs were respected according to QUANTEC constraints. During follow-up we performed outpatient clinical evaluation 30-40 days after the end RT-CTx to evaluate the acute toxicity, then we administered COPD Assessment Test, simple and reliable instrument that with small question covers a broad range of COPD on pts'health, during the ICIs.

Result. After a median follow-up of 14 months we recorded 3 interruptions to ICI-s due to progression disease: 2 pts in recurrence local failure after 2 cycles of durvalumab, 1 distant progression disease after 10 administrations of durvalumab, with brain metastasis. The remaining pts (n.11) were alive in durvalumab therapy maintenance. No hospitalization COPD-Acute Events treatment related was recorded. Through COPD assessment test (CAT) we detected worsening of cough in 2 pts, "phlegm in my chest" in 3 pts, dyspnoea in 2 pts, and 4 pts had "lower energy level". No pts had to interrupt treatment due to these symptoms.

Discussion. The smoking addition had bad impact on the toxicities treatment-related and then on the quality of life of our pts during RT-CTx, but contrary to our expectation no worsening of compliance treatment-related was shown in smoker pts during immunotherapy with no increase of interruption of administration of durvalumab. Several study are necessary to determine the real role of smoking cigarettes on compliance treatment-related.

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SAFETY AND EFFICACY OF A TWO TIME RADIOTHERAPY TREATMENT IN PATIENTS WITH ADVANCED SCLC AND IPSILATERAL PLEURAL EFFUSION

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Aims. Safety and efficacy of a two time radiotherapy treatment (8 Gy x 2 frz then consolidation of 3 Gy x 10 frz) interspersed by 4 cycles of chemo-immunotherapy in patients with advanced sclc and ipsilateral pleural effusion.

Methods. We retrospectively evaluated 12 patients affected by advanced stage SCLC with ipsilateral pleural effusion. All patients were initially irradiated with a dose of 8 Gy x 2 (3D Conformal technique) followed by 4 cycles of chemo-immunotherapy. At the disease iconographic re-evaluation, patients in response and without PS deterioration were treated with consolidation treatment (3 Gy x 10 frz) by VMAT technique.

Results. Four patients (30%) progressed at iconographic disease re-evaluation, one of the eight patients who responded suffered a worsening of PS. The seven remaining patients started the second cycle of radiotherapy preceded by spirometry. All remaining pts completed the 10 sessions with G1-G2 toxicity (according to CTCAE). Median survival was 16,5 months.

Conclusions. The results, albeit limited by the low statistical power of the sample, demonstrate how the aforementioned radiotherapy sequence (8 Gy x 2 frc —> CT-Immuno —> 3 Gy x 10 frc) is safe and effective in this patients setting. Further studies are needed to investigate and evaluate the best therapeutic combination and the highest adoptable radiotherapy dose.

P153

INCIDENTAL DOSE TO INTERNAL MAMMARY NODES IN BREAST CANCER PATIENTS: A MONO-INSTITUTIONAL RETROSPECTIVE ANALYSIS.

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Aims: Post-operative radiotherapy (RT) to the internal mammary nodes (IMNs) in breast cancer (BC) patients (pts) is a controversial issue. The Danish trial[1] showed that IMN irradiation improved overall survival in ≥pN2 pts. Since IMNs could be exposed to incidental irradiation due to its proximity to the breast and the chest wall, we decided to evaluate the incidental dose delivered to the IMNs in a series of BC pts treated with adjuvant RT, where IMNs were not treatment target.

Methods. Data of 95 ≥pN2+ pts treated between 2015 and 2022 were retrospectively analyzed (pts' characteristics in Table 1). Pts received adjuvant RT (50Gy/25fr or 40.05Gy/15fr) to the breast/chest wall and nodal levels III-IV after breast conserving surgery (BCS) or mastectomy. Treatment volumes were defined according to the AIRO guidelines[2] (GL). No neoadjuvant therapy was administered. On the basis of the results of the Danish trial, the IMNs were delineated following the ESTRO GL[3] and were divided into 4 sub-regions based on the first 3 intercostal spaces (ICS): IMNupper, ICS1, ICS2, ICS3. The mean dose (D_{mean}) to the targets was correlated to tumor side and location, type of surgery and reconstruction, RT technique and boost. Statistical analysis (Mann-Whitney and Kruskal-Wallis test) was performed using the IBM-SPSS program v.16.

Tables 1 and 2.

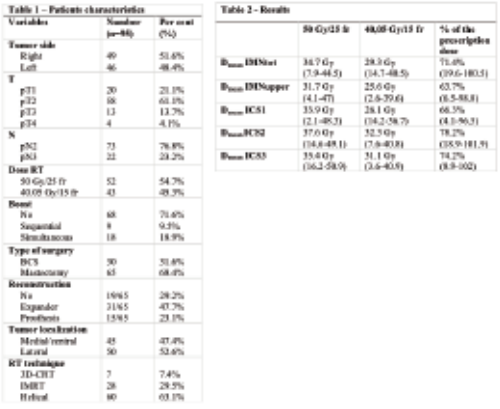

Table 1 – Patients characteristics		
Variables	Number (n=94)	Per cent (%)
Tumor side		
Right	49	51.6%
Left	46	48.4%
T		
pT1	20	21.1%
pT2	58	61.1%
pT3	13	13.7%
pT4	4	4.1%
N		
pN2	73	76.8%
pN3	22	23.2%
Dose RT		
50 Gy/25 fr	52	54.7%
40.05 Gy/15 fr	43	45.3%
Boost		
No	68	71.6%
Sequential	8	9.5%
Simultaneous	18	18.9%
Type of surgery		
BCS	30	31.6%
Mastectomy	65	68.4%
Reconstruction		
No	19/65	29.2%
Expander	31/65	47.7%
Prosthesis	15/65	23.1%
Tumor localization		
Medial/central	45	47.4%
Lateral	50	52.6%
RT technique		
3D-CRT	7	7.4%
IMRT	28	29.5%
Helical	60	63.1%

Table 2 - Results			
	50 Gy/25 fr	40,05 Gy/15 fr	% of the prescription dose
D_{mean} IMNint	34.7 Gy (7.9-44.5)	28.3 Gy (14.7-48.5)	71.4% (19.6-100.5)
D_{mean} IMNupper	31.7 Gy (4.1-47)	25.6 Gy (2.6-39.6)	63.7% (6.5-88.8)
D_{mean} ICS1	35.9 Gy (2.1-48.2)	28.1 Gy (14.2-58.7)	68.3% (4.1-96.3)
D_{mean} ICS2	37.6 Gy (14.6-49.1)	32.5 Gy (7.6-40.8)	78.2% (18.9-101.9)
D_{mean} ICS3	35.4 Gy (16.2-58.9)	31.1 Gy (3.6-40.8)	74.2% (8.9-102)

Results: Mean D_{mean} to IMNs was 71.4% (range 19.6-100.5) of the prescription dose (complete results in Table 2). Considering each sub-region, D_{mean} was higher in the ICS2 and ICS3 segments rather than in the ICS1 and the upper one. Only the D_{mean} of 4 pts exceeded the 90% of the prescribed dose, 3 of these were treated with helical RT, and the other one with IMRT. The mean V95 and V90 were 15.4% and 26.2% respectively. In the univariate

analysis, mastectomy (p=0.002), helical RT (p=0.000) and simultaneous boost administration (p=0.004) were found to be significantly correlated with a higher IMNs D_{mean}. No significant correlation was found with side, tumor localization and type of reconstruction.

Conclusions. In our series, higher IMNs incidental dose was observed in mastectomized pts, in those treated with helical RT and who received a simultaneous boost. A more medial margin in the chest wall delineation compared to the breast and the helical RT dose distribution could explain our results. However, as most pts did not receive a therapeutic dose to IMNs, high-risk cases should be discussed to intentionally include the IMNs in the treatment target.

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P154

LARGER BREASTED PATIENTS ARE EXPOSED TO HIGHER HEART DOSES IN WHOLE BREAST VMAT PLANNING

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Background and aim. In breast cancer volumetric arc therapy (VMAT) planning, the rotation of the gantry around the target implies a greater lower dose spreading to the heart, compared to tangential fields standard treatment. This can be even greater in case of large breasted patients. The aim of this dosimetric study is to evaluate heart dosimetry in VMAT breast cancer treatment plans according to breast size.

Material and Methods. a consecutive cohort of 121 breast cancer patients treated with VMAT technique was investigated. All patients were treated at University Campus Bio-Medico of Rome, Italy from June 2022 to December 2022. The plan design consisted of 2 small tangential arcs (each partial arc consisted of four arcs spanning 40-60 degrees amplitude each) with 6MV photons. Prescription dose was 40.05 Gy delivered in 15 fractions. The following heart constraints were evaluated: Heart mean dose < 5 Gy (optimal < 3.5 Gy), Left Descending Artery (LDA) Dmax < 20 Gy for left sided and < 10 Gy for right sided, LDA Dmean < 10 Gy for left sided, <3 Gy for right sided patients. The patient cohort was stratified into 2 subgroups: group A, presenting with breast size < 1000 cm^3, and group B, presenting with breast size >1000 cm^3. Paired t-test was used to compare groups and a P-value <0.05 was considered significant. Separate analysis for right sided and left sided patients was carried out.

Results. VMAT treatment plans from 56 left breast cancer and 65 right breast cancer patients were analyzed. Mean age of the whole population was 65.20 ± 11.12 years. Breast size ranged from 256.79 cc to 1852.58 cc in right sided group and from 233.48 cc to 2189.57 cc in left sided group (p=NS). In the whole patients population (right sided and left sided) mean heart dose was higher in larger breasted patients compared to smaller breasted patients (mean heart dose: 2.1 Gy *vs* 1.7 Gy, p=0.05). In rights sided patients mean heart dose (1.53 Gy *vs* 1.28 Gy; p= 0.008) and mean LDA dose (1.36 *vs* 1.17 Gy; p= 0.038) were significantly increased in larger breasted patients. In left sided patients mean heart dose was 2.80 Gy *vs* 2.39 Gy and mean LDA dose was 5.55 Gy *vs* 6.13 Gy in larger breasted patients, but statistical significance was not reached.

Conclusions. Breast size increases heart dose in breast cancer patients when VMAT planning is used. This can be of particular relevance for right sided patients for which deep inspiration breath hold (DIBH) is not routinely used.

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VISUAL COACH TO IMPROVE THE USE OF DIBH FOR LEFT BREAST PATIENT RADIOTHERAPY

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Aims. Deep Inspiration Breath Hold (DIBH) is a technique used to deliver radiotherapy only while the patient holds her breath at the maximum inspiration. DIBH for radiotherapy of the left breast have been demonstrated to reduce the mean dose to the heart, and many centers currently use it. However, there is still limited evidence on intra-breath hold stability. In this study, we systematically evaluated the stability of breathing during DIBH and the impact of introducing a visual coach to the patient during delivery.

Methods. Since 2018, 1499 left breast patients were treated at our center in 15 fractions of 3.2-2.7 Gy/fr using volumetric modulated arc therapy (VMAT). The breathing cycle was monitored using RPM (Varian). Patients was instructed to breath hold using a human voice. A visual coach was introduced in January 2020. The intra-

breath hold stability of each session was categorized as "stable" or "unstable". The number of interruptions, and the upper/lower DIBH threshold were also considered.

Results. The percentage of patients treated with DIBH increased from 25% (2018 – before the introduction of the visual coach) to 43% (2022/23 – after a consolidated use of the visual coach). The percentage of "stable" intra-breath hold sessions increased from 40.3% to 56.2% thanks to the introduction of a visual coach (see figure 1). The number of interruptions were stable (3.0±1.1 vs. 3.0±1.3) while the mean threshold was reduced from 7.9±2.1 mm to 6.1±1.7 mm.

Conclusions. Our results suggest that introducing a visual coach can improve intra-breath hold stability and increase the percentage of patients treated with DIBH. This study provides evidence that a visual coach can be used as an effective tool for improving radiotherapy treatment quality in breast cancer patients.

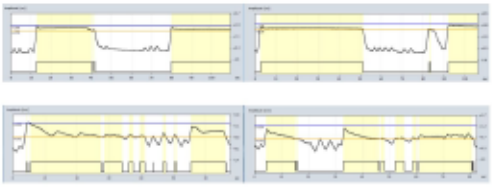

Figure 1: left: breathing curve with (up) and without (down) visual coach

Figure 1.

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DOSE TO HEART AND CARDIAC SUBSTRUCTURES IN HYPOFRACTIONATED LOCOREGIONAL RADIATION THERAPY INCLUDING INTERNAL MAMMARY CHAIN IN ADVANCED BREAST CANCER: ANALISYS OF A MONO-INSTITUTIONAL EXPERIENCE

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Aims. Radiation-induced heart disease is a serious late complication following radiotherapy(RT) mostly in patients(pts) also treated with cardiotoxic drugs. This study investigated outcomes and cardiotoxicity in advanced breast cancer pts who underwent hypofractionated adjuvant RT(HRT) including internal mammary chain(IMC).

Methods. We reviewed data of 20 pts treated between 3/2018 and 1/2023 at our Institute. Dosimetry of heart, left anterior descendent and right coronary arteries(LAD,RCA) was recorded. RCA was retrospectively delineated as OARs (it's not standardly outlined in our clinical practice). Median age at diagnosis was 49(30-70)years. TNM stages were III(80%) and IV(20%). All pts had IMC-positive imaging(TC, PET or MRI). IMC nodes size was ≥1cm in 30% of pts. Three pts(15%) had history of cardiovascular disease. Systemic treatments were: chemotherapy(CHT) 100%(100% taxane,60% anthracyclines,25% carboplatin,10% capecitabine); HER2-targeted therapy 65%; endocrine therapy with aromatase inhibitors 60%, LH-RH analogue 40%. RT was delivered with Tomotherapy(60%), VMAT(30%) and 3DCRT(10%) to a dose of 40.05 Gy in 15 fractions. Targets were: whole breast 45%(45% right,55% left), chest wall 55%(55% right,45% left), regional lymph nodes 100% and a simultaneous integrated boost to tumor bed 35%(57% right, 43% left). Cardiological examinations, pre and post-treatments ECG and cardiac ultrasounds were used to evaluate cardiac events. Overall survival(OS), local and distant relapse free survival(LRFS,DRFS) were evaluated.

Results. Heart, LAD and RCA median mean dose were 5.4(1.39-8.83)Gy, 6.88(1.48-28.57)Gy and 7.36(1.15-20)Gy, respectively; median heart V20 and V8 were 1(0-8.13)% and 14(0.8-44)%; median LAD and RCA V16 (for right breast) were 0(0-42%) and 15.53(0-66.5)%; median LAD and RCA V30 (for left breast) were 2.41(0-86.7)% and 0(0-1.2)%. With a median follow-up of 34.1(3.4-61.3) months(m), 4 pts(20%) had cardiac events (Table 2); all pts were alive and free from local and distant relapse. Median OS was 39.23(12.2-79.6)m, median LRFS and DRFS were 34.1(3.4-61.3)m respectively.

Conclusions. Locoregional HRT including IMC may increase risk of heart disease related both to cardiotoxic systemic treatments and RT. Cardiotoxic CHT with anthracyclines +/- trastuzumab is a confounding factor. Constraints to heart substructures could help to reduce this probability. Longer follow-up and a larger cohort of pts is needed to establish a dose-response relationship.

Table 1. Characteristics of pts with cardiac events and doses to heart, LAD and RCA (the exceeded dose constraints are highlighted in blue). Chest wall (CW), whole breast (WB), Simultaneous integrated boost (SIB).

No pts	Age	Right /Left	Target	SIB	Systemic treatments	Previous cardiovascular disease	Cardiac Event	Mean Dose Heart (Gy)	Mean Dose LAD (Gy)	Mean Dose RCA (Gy)	V20 Heart	V8 Heart	V16 LAD	V30 LAD	V16 RCA	V30 RCA
2	35	R	CW	no	Taxane+ anthracycline + platinum + HER2 targeted therapy	None	Mitral valve insufficiency	5,92	6,81	15	0,87%	20%	0%	/	46,8 dGy	/
3	49	R	WB	no	Taxane + HER2 targeted therapy	None	Septum interventricular aneurisma	3,5	3	5,79	0%	5,89%	0%	/	0%	/
14	57	L	WB	yes	Taxane+ anthracycline + platinum + HER2 targeted therapy + aromatase inhibitor	Hypertension	Left atrial dilation and arrhythmia	7,63	28,57	3,9	7%	25,90%	/	86,70%	/	0%
16	69	L	CW	no	Taxane+ anthracycline + aromatase inhibitor	Hypertension	Arrhythmia	4,73	8,13	6,97	1,24%	11,50%	/	0%	/	0%

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VOLUMETRIC MODULATED ARC THERAPY (VMAT) FOR SYNCHRONOUS BILATERAL BREAST CANCER (SBBC)

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Introduction. Volumetric Modulated Arc Therapy (VMAT) for synchronous bilateral breast cancer (SBBC) has been shown to provide adequate target volume coverage while sparing the organs at risk (OAR). Aim of the study was to assess safety of VMAT, analyzing early and late skin and cardioplulmonary toxicities showed by patients during treatments and follow-up, evaluating dose distribution to OAR.

Methods. Patients with SBBC with or without axillary nodes involvement undergoing radiotherapy using VMAT with a single isocenter, were retrospectively evaluated. A total dose (TD) of 50Gy in 25 fractions or 40.05Gy in 15 fractions was delivered to breast Planning Target Volume (PTV) and to supra-and-infra clavicular nodes when indicated. Boost was prescribed according to risk factors. Lungs, heart and anterior descending artery (LAD) were considered as organs at risk. Mean Lung Dose (MLD), V5 e V20 of each and both lungs, Mean Heart Dose (MHD) and LAD Dmax were recorded for each patient. Acute and/or late toxicity were monitored during treatment and follow-up visits, according to the NCI-CTCAE V5.0.

Results. 31 patients with SBBC were included. Supra and infraclavicular nodes were irradiated in 4 patients (12.9%). Bilateral tumor boost was delivered to 8 patients (25.8%), unilateral boost to 4 patients (12.9%) for a total dose of 10 Gy in 5 fractions. Mean Lungs Dose was 7.7 (range: 2.0-14.0), Mean Lung Dose left lung was 7.4 (range: 1.4-14.0) Mean Lung Dose right lung 7.7 (range: 2.4-14.1), V5 Lungs was 42.6 (range: 4.7-95.4), V20 Lungs was 10.1 (range:1.0-18.9), V5 Right lung was 42.5(range: 10.9-96), V20 Right lung was 10.5(range: 1.8- 21.1), V5 left lung was 43.1(range: 4.9-94.7.0), V20 left lung was 9 (range: 0-23.3), Mean Heart Dose was 3.8(range: 1.0-5.5) and LDA Dmax was 13.8 . We analysed cardiological and pulmonary history of all patients, and only one patient (3%) had cardiological problems (mild mitral insufficiency) before starting radiotherapy. None of the patients had pulmonary disease. Concerning acute toxicities, acute radiation-related toxicities were recorded every week during VMAT and at the end of the treatment. Only 8 patients (25.8 %) experienced grade 1 skin toxicity, recorded at the end of treatments. Late toxicities were recorded every 3 months after RT completion. Respiratory, cardiac and cutaneous toxicity were systematically evaluated. Only one patient (3.2%) showed pulmonary fibrosis during follow up and only one presented a decrease in cardiac ejection fraction at cardiology checkups.

Conclusions. In conclusion, for SBBC, the use of VMAT with a single isocenter provided excellent dosimetric results and resulted in limited toxicity.

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ACUTE AND EARLY-LATE TOXICITY IN BREAST CANCER PATIENTS TREATED WITH ADJUVANT RADIOTHERAPY PLUS TDM-1: A RETROSPECTIVE SINGLE INSTITUTIONAL REPORT

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Aims. The phase III KATHERINE study showed that adjuvant Trastuzumab Emtansine (TDM-1) reduced the risk of recurrence and death in patients (pts) with HER2-positive early breast cancer (BC) with residual invasive disease after primary systemic therapy. However, a recent subgroup analysis has raised concerns about increased toxicity when TDM-1 is administered concurrently with adjuvant radiotherapy (RT). The aim of this real-life single-institution report was to assess the acute and early-late toxicity of TDM-1 administered concurrently with adjuvant RT in pts with BC.

Methods. We retrospectively evaluated patients treated between January 2021 and December 2022 with concurrent adjuvant TDM-1 and RT. To evaluate cardiac toxicity, left ventricular ejection fraction (LVEF) was assessed at baseline, before and after RT. All toxicities were evaluated and scored using Common Terminology Criteria of Adverse Events (CTCAE) version 5.0.

Results. Thirteen patients were included in the analysis. The median age was 49 years (range 36 to 72). All patients received a total dose of 50 Gy to the breast/chest wall and regional lymph node. In the acute setting, grade 1-2 dermatitis was recorded in 11 patients, with two grade 3 events; no grade 4 was reported. One patient with G3 acute skin toxicity, had long-term dermatologic complaints, fibrosis and oedema G2 after 9 months of follow-up. The LVEF remained stable between TDM-1 start and the end of RT.

Conclusions. Our findings suggest that acute and early-late toxicity may occur in pts treated with TDM-1 and RT. Most pts experienced low-grade toxicity, but

high-grade dermatitis may occurs in few patients. The stable LVEF values suggest the feasibility of concurrent treatment regarding acute cardiac toxicity. These findings emphasize the importance of careful monitoring when TDM-1 is administered concurrently with adjuvant RT, and call for clinicians to remain vigilant of unexpected toxicities with newly approved therapies.

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DE-ESCALATION DELLA RADIOTERAPIA DOPO LA TERAPIA SISTEMICA PRIMARIA NEL CARCINOMA MAMMARIO NON METASTATICO: DATI DI REAL-WORLD SU OUTCOMES DI SOPRAVVIVENZA

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Aims. The risk of recurrence after primary systemic therapy (PST) for women with invasive breast cancer (BC) depends on multiple factors and the optimal postoperative treatment management remains unclear, mostly in the intermediate-risk group. This is a retrospective single-centre study aimed to provide real-world data on treatment patterns and survival outcomes.

Methods. We analysed data from patients treated in our centre between 2012 and 2017 with breast surgery after PST, and with a minimum follow-up of 5 years for alive patients. Clinical features, type of PST and surgery, pathological response, adjuvant systemic and local therapy were collected. Most patients (>75%) with pathological nodal complete response (ypN0) or 1-3 residual lymph nodes (ypN1) did not receive – per local policy – regional nodal irradiation (RNI). Locoregional recurrence (LRR), distant metastasis (DM) and overall survival (OS) were analysed.

Results. 146 patients were included: 60.9% stage II and 39.1% stage III, 67.1% had clinically nodes positive disease (cN+). Pathological complete response (pCR) was achieved in 29.3% cases, ypN0 in 56.8%, including 47 cN+ (48%). Among them, 12.8% received RNI. 36 cases resulted ypN1 (24.6%), 18.6% ypN2-3; 22.2% of ypN1 received RNI. At a median follow-up of 6.4 years (1.5-10.9), LRR was 7.7% (n=12), 11 events occurred in no-pCR patients. The DM and BC-specific mortally rates were 19.9% and 5.5%, respectively. Among cN+ patients achieving ypN0, LRR was 2.1%, DM and BC-specific mortality rates were 12.8% and 4.3%, respectively. Among ypN1 patients, LRR was 11.1%, DM and BC-specific mortality rates were 22.2% and 5.5%, respectively. At univariate analysis ypN0 was significantly associated with better OS and LRR (p=.008 and p=.003).

Conclusions. In study series, postoperative locoregional treatment was de-escalated in cN+/ypN0-1 patients after PST. Compared to historical data and RAPCHEM study, despite the small and retrospective series, our data suggests strong caution in de-escalation of postoperative RNI in ypN1 patients after PST. Existing guidelines should be strictly followed, large databases on real-world data are needed.

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DEEP INSPIRATION BREATH-HOLD OR FREE BREATHING? DEVELOPMENT OF A KNOWLEDGE-BASED MODEL FOR ORGANS AT RISK DOSE ESTIMATES IN LEFT-SIDED BREAST RADIOTHERAPY, AS A TOOL TO IDENTIFY THE MOST APPROPRIATE TREATMENT FOR EACH PATIENT

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Aims. For patients undergoing left-sided breast radiotherapy (LSB-RT), free breathing (FB) and Deep Inspiration Breath-Hold (DIBH) CTs are acquired and contoured by the Radiation Oncologist. Two treatment plans are optimized independently by the Medical Physicist (MP). The plans are compared in terms of Dose Volume Histograms (DVH) taking into account target coverage and Organs at Risk (OARs) doses. This process is time consuming and can be critical in a busy and understaffed department, with the risk of producing under-optimized plans that can bias the final plan choice. Aim of this work is to use knowledge-based planning as a tool to predict achievable organ doses supporting the choice on which plan to optimize.

Methods. RapidPlan(RP) is a commercially available software for knowledge-based planning. To generate an RP model, a database of patients was created and used to train the system. For each patient, both FB and DIBH planning CTs were fed to the system. The generated model was used to provide predicted DVH prior to the plan optimization, solely based on patient anatomy and chosen field geometry. Two models were created for

patients with or without Simultaneous Integrated Boost (SIB) (respectively no-SIB and SIB model). The generated models were analyzed and cleaned, by identifying geometric and dosimetric outliers and reoptimizing plans in which one or more organs received a dose higher than predicted. The models were used to generate predicted DVHs for the DIBH and FB datasets in order to compare achievable organ doses.

Results. A total of 48 and 35 LSB-RT patients (with or without supraclavicular lymph nodes) were selected for the no-SIB and for the SIB model respectively, representing a database population of 96 and 70 patients in terms of model statistics. Considered OARs were: left anterior descending artery (LAD), heart, ipsilateral lung, contralateral lung and contralateral breast. Interestingly, for both SIB and no-SIB models, no separated clusters were observed in the distribution of OAR doses, meaning that a single model can be used to represent both DIBH and FB conditions. The predicted DVH accuracy allowed to discriminate the need for DIBH treatment for each single patient.

Conclusions. RP proved to be a useful tool to identify organs that were under-optimized in the treatment planning. Predicted DVHs allowed to compare the FB and DIBH treatments prior to optimization, choosing the most appropriate one that will be optimized by the MP.

P161

OUTCOMES AND QUALITY OF LIFE IN PATIENTS UNDERGOING PRE-PECTORAL RECONSTRUCTION AND RADIOTHERAPY

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Aims. In patients (pts) with locally advanced breast cancer, mastectomy followed by reconstruction is indicated. Historically implants have been positioned under the pectoralis major muscle in a submuscular pocket. Recently, a new technique has been used in which prosthesis have been placed in the prepectoral plane. This innovative procedure emerged as a viable option for reducing surgical postoperative complications and improving esthetic outcomes. This study aimed to compare the impact of PMRT on surgical complications, oncological outcomes and pts quality of life after pre-pectoral ipsilateral breast reconstruction (PP – IPBR).

Methods. All the pts who underwent PP-IBRT were retrospectively included in the study. Inclusion criteria were breast cancer diagnosis, surgery with pre-pectoral reconstruction, availability of follow up data. Data collected were pts characteristics (age at diagnosis, comorbidity), tumor characteristics (immunophenotypes, stage, grading) and treatments characteristics (chemotherapy administered, surgery performed, radiotherapy administered, toxicities). Quality of life was analyzed by a home-made questionnaire (aesthetic results 1-5 points, arm impairment, preservation of sensitivity, post-surgery sports activity, sexual activity, local pain) Results are expressed as means with associated median and range. Statistical significance was set at $p < 0.050$. Chi-square test was used for comparison of categorical variables.

Results. From January 2018 to December 2021, 187 pts underwent PP – IPBR after mastectomy. In this group, 111 (59.35%) pts were not exposed to PMRT, whereas 76 (40.65%) pts underwent PMRT according to NCNN Breast guidelines. Among them, 16 pts underwent IMRT, while 60 pts underwent VMAT technique. Mean follow up was 18 months (11-48). Four pts presents a local relapse, all in not irradiated group ($p<0.0001$). PMRT did not correlate with aesthetic results (p 0.82), arm impairment (p 0,10), preservation of sensitivity (p 0,71), post-surgery sports activity (p 0,64), sexual activity (p 0.95). Analysis of pain showed a worst outcome in PMRT group (p 0.01).

Conclusions. Pre-pectoral reconstrution is an emerging recostructive optiont for breast cancer pts. PMRT in PP – IPBR showed a good outcomes in terms of early local control and quality of life. Further data are needed to extend these considerations also to long term follow-up.

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A RAPIDPLAN MODEL FOR BREAST IRRADIATION: OUR EXPERIENCE

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Aims. Treatment planning in radiotherapy requires time and resources. Different automation softwares are available to improve planning efficiency. Varian's solution is a software called RapidPlan (RP), that estimates a patient's DVHs based on an atlas of previously treated

patients. The aim of this study is the validation of single-center breast RP models and the evaluation of models' performance on both time reduction and outcome quality.

Methods. A database of 300 plans was assembled and revised by radiotherapy and radiology clinicians, according to the danish contouring guidelines. We considered breast IMRT and VMAT plans from patients treated between January 2020 and December 2022. We considered both left and right-sided breast treatments for whole-breast, SIB and supraclavicular lymph-nodes irradiation, and for different dose prescriptions (50Gy/25fr, 2.56Gy/16fr, 37.05Gy/13fr). For each irradiation technique three models were evaluated: a *unified* model with both right and left-sided breasts and two *divided* models with only right-sided or left-sided breasts. Some plans were not statistically comparable with the others so they were considered outliers and excluded from the models. The validation of the models was performed, for 60 patients both inside and outside the models. The validation procedure consisted in evaluating new plans using RP and comparing them to previously approved and erogated plans for the same patients. Finally, we tested the equivalence of *unified* and *divided* models. The comparisons were performed using a two-tailed Wilcoxon test on the clinical constraints used in our center.

Results. All constraints considered resulted in no significant differences ($p>0.05$) between RP and approved plans. The only exceptions were ipsilateral lung IMRT external validation ($p=0.03$) and heart VMAT validation ($p=0.04$). In both these significantly different constraints we observed a lower OAR mean dose for RP plans, indicating a benefit in using the automation algorithm. It should also be noted that, in comparison to conventional plan optimization, RP VMAT models determined a significant time reduction, while IMRT models did not. *Unified* and *divided* models showed no significant differences ($p>0.05$). The only exception was observed for LAD constraints, in which *divided* VMAT models resulted in higher OAR's doses.

Conclusions. The models were successfully validated and the analysis showed that RP plans were comparable or better than the approved plans.

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WEEKLY ULTRAHYPOFRACTIONATED (UHF) RADIOTHERAPY IN EARLY BREAST CANCER: UPDATE TO 36 MONTHS

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Aim. to reduce treatment time in patients (pt) with early stage breast cancer (EBC) undergoing breast conserving surgery (BCS) also after COVID-19 pandemic experience.

Methods. From June 2020 to February 2023, we recruited 98 women ≥60 years old, with EBC, undergoing BCS (pT1□2(≤3 cm) pN0), G1-2 and negative margins. The prescribed dose was 28.5 Gy in once weekly fractions over 5 weeks. The primary end-point was local tumor control, acute and chronic toxicity (tox) end esthetic outcomes. Secondary end points were impact on quality of life (QoL) and on waiting list. After a CT□scan, a whole breast irradiation 3D-planning was performed using opposite tangent with fields in fields, with 6 Mv photons, and subfields to improve dose homogeneity. Skin tox was assessed with the RTOG score. In order to evaluate esthetic outcomes, two photos were taken for each pt (antero-lateral and antero-medial), at the beginning, at the end of the treatment, and then at 3, 6, 12, 24, 36 months (mo) follow up.

Results. We enrolled 98 pt with mean age of 69 years (range 60-84). The median follow-up was 18 mo (range 3-36). The most common tox were acute erythema and edema and late breast fibrosis and shrinkage. With the limit of the short follow-up, no one developed recurrence and only three had significant esthetic changes with moderate fibrosis and breast shrinkage a 12, 24 e 36 mo. Acute tox evaluated was not greater than G2, with 85(86,7%), 90(91,8%) pt respectively G0-1 at end radiotherapy and 3 mo later. Similarly, chronic tox evaluated was not greater than G2 with 89(92,7%), 76(89,4%), 49(89%), 17(85%) pt respectively G0-1 at 6, 12, 24 and 36 mo. All patients showed a high level of satisfaction and among all patients who experienced tox, this impacted QoL only in 5 (5.2%) cases and with low entity. The UHF regimen reduces treatment sessions by 66.6% compared to the standard hypofractionated, with an obvious impact on waiting time list.

Conclusions. Once weekly UHF radiotherapy it has proven to be an advantageous treatment even in the post-covid era. It is well tolerated and particularly appreciated by pt, has a low acute and chronic tox and good cosmetic outcomes. For these reasons, it is a feasible alternative in the adjuvant management of EBC.

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MODERATE HYPOFRACTIONATION WITH SIMULTANEOUS INTEGRATED BOOST AFTER CONSERVATIVE SURGERY FOR BREAST CANCER

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Aim. Moderately hypofractionated radiotherapy (HRT) to whole breast(WB) is the standard treatment for breast cancer(BCa) after conservative surgery. Simultaneous integrated boost(SIB) to the tumor bed is delivered to high risk local recurrence(LR) patients(pts). We report toxicity and outcomes in BCa pts treated with WB+SIB HRT in our Institute.

Methods: From 12/2017-3/2023 260 BCa women were treated with WB+SIB HRT after conservative surgery (right 116, left 144). Median age was 60(29-88)y. Molecular subtypes were: Luminal A 37%, Luminal B Her2- 24.5%, Luminal B Her2+ 14%, HR negative Her2+ 4.5%, Triple negative(TN) 18%. The remaining 2% were in situ BCa. Chemotherapy(CHT) was prescribed to 132 pts(50.7%): neoadjuvant 14.2%, adjuvant 38%, concomitant 0.3%. Adjuvant endocrine therapy was prescribed for 186pts (71.5%)(Aromatase Inhibitors or Tamoxifen-/+LH-RH analogue), 48pts(18.5%) underwent HER2-targeted therapy. HRT was delivered with Tomotherapy (79.2%), VMAT(20%) or 3DCRT(0.8%), to a total dose of 40.05Gy to WB and 48Gy to the tumor bed, in 15fractions. Acute and late toxicity and cosmesis were registered according to RTOG, SOMA-LENT and Harvard breast cosmesis scale respectively.

Results: Median follow-up was 38.6(4.8 – 65.5)months(m). All pts were evaluable for acute toxicity. Late toxicity and cosmesis data were available for 251pts. Acute and late toxicity are summarized in Table 1. Only 3pts experienced ≥G3 acute toxicity and only 1≥G3 late toxicity. Cosmetic outcome according Harvard breast cosmesis scale was available for 241pts: excellent 41.5%, good 47.5%, fair 8%, poor 3%. Fourty pts (16%) had liponecrosis, evaluated by mammography, ultrasound or MRI. At the last follow-up cardiac events were diagnosed in 4pts (3 cases of Trastuzumab-induced pericarditis and 1 case of post-CHT heart failure) and lung fibrosis with symptomatic pneumonitis in 2 cases. Raw local control was 98.8%. Only 3pts(1.2%) had LR(1 TN, 1 Luminal B HER2+, 1 Luminal B HER2-) and 5pts(2%)(3 Luminal B HER2-, 1 TN, 1 Luminal A), had distant progression(4 bone metastasis, 1 axillar lymph node), at median TTP of 38.4(22.8-44.5)m. Four pts were dead at the last follow-up (2 old age, 1 comorbidity, 1 metastatic lung tumor diagnosed 21m after RT). Median OS was 44.5(8.9-73.9)m.

Conclusions. In our experience HRT+SIB was feasible with low acute and late toxicity profile, highly satisfying cosmetic outcome and excellent local control. A longer follow-up is necessary to confirm these results.

Table 1. Acute and late toxicity according to RTOG and SOMA-LENT scale respectively.

ACUTE TOXICITY				
	G0	G1	G2	G3
Breast erythema and/or edema	27 (10%)	194 (75%)	36 (14%)	3 (1%)
LATE TOXICITY				
	G0	G1	G2	G3
Hyperpigmentation	160 (64%)	89 (35.2%)	2 (0.8%)	0
Edema	204 (81%)	36 (14.5%)	10 (4%)	1 (0.5%)
Fibrosis	211 (84%)	38 (15%)	2 (1%)	0
Pain	230 (91.6%)	20 (8%)	1 (0.4%)	0
Telangiectasia	248 (98.8%)	3 (1.2%)	0	0

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ACUTE TOXICITY IN ULTRA-HYPOFRACTIONATED WHOLE-BREAST IRRADIATION IN PATIENTS WITH EARLY BREAST CANCER

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Aims. The purpose of this study is to evaluate acute toxicity rates in ultra-hypofractionated post-operative whole-breast irradiation (WBI) after breast-conserving surgery (BCS).

Methods. Between November 2020 to May 2023, the FAST Forward schedule (26 Gy/ 5 fr, 1 week) and FAST schedule (28.5 Gy/5 fr/5 weeks) was adopted in 125 and 39 patients, respectively (total number 164). Acute toxicity was evaluated at the end of WBI, 4 weeks and 6-8 months thereafter, according to the Common Terminology Criteria for Adverse Events (v.5.0).

Results. A total of 87/164 (84%) patients (median age 67 years, range 51-84) completed the assessments. In 69% of patients no side effects were reported. No one developed ≥Grade 3 toxicity. 12% showed brisk erythema or breast swelling (Grade 2), while 19% reported faint erythema (Grade 1) as the worst skin toxicity. Only two

patients required active medications. The highest prevalence of grade 2 toxicity occurred at week 1 after treatment, and decreased to 1% by week 4.

Conclusions. Implementation of ultrahypofractionated breast radiotherapy was feasible and acute toxicity rates are acceptable. Such short schedules might enhance treatment's compliance mostly in elderly patients. Longer follow up is needed to confirm these findings.

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ACUTE SKIN TOXICITY AND IMPACT OF BREAST VOLUME IN EARLY BREAST CANCER PATIENTS TREATED WITH THREE- DIMENSIONAL CONFORMAL RADIOTHERAPY (3D-CRT): A SINGLE-INSTITUTION RETROSPECTIVE ANALYSIS

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Aims. This study aimed to evaluate acute skin toxicity and the impact of breast volume in early breast cancer patients treated with hypofractionated or conventional radiotherapy (HF RT or CF RT) after breast conserving surgery (BCS).

Methods. This retrospective observational study included patients treated at our institution between June 2017 to December 2022. All patients with early breast cancer received BCS (pT1-2, pN0 R0 M0) and were treated with 3D hypofractionated RT (40 Gy in 15 fractions) or 3D conventional RT (50 Gy in 25 fractions). Acute skin toxicity was monitored at the end of RT and after 3 months according to the CTCAE scale. Many studies show that large breast volume seems to be a risk factor for acute adverse events independently of dose inhomogeneity and regardless of the conformal radiotherapy technique or fractionation schedule. Therefore the patients treated with hypofractionated radiotherapy, acute skin toxicity was observed in a subgroup with breast volume ≥ 1000cc.

Results. 602 patients were included in the study: 281 (46.7%) were treated with hypofractionated RT (HF) and 321 (53.3%) with conventional RT (CF). 36% of HF patients showed no toxicity vs. 16% of CF; Acute skin toxicity G1 57% HF vs. 63% CF; toxicity G2 6% HF *vs* 15% CF and toxicity G3 1% HF *vs* 6% CF. A significant statistical difference wasn't observed in both groups (P > 0.05). The percentage of patients with ≥ G2 toxicity was the highest in the subgroup of large breasted patients, (94 pz), 48% breast volume ≥ 1000cc *vs* 10% breast volume < 1000cc. (No statistical difference, P>0,05).

Conclusions. Acute skin toxicity is acceptable in both the examined groups. Toxicity levels G4 and G5 were not observed in any of the patients. Both treatments were well tolerated by patients, although lower rates and severity of toxicity G1, 2 and 3 were observed in the HF group. In addition, analyses of breast volumes indicate that there could be a connection, although still unclear, between a volume > 1000cc and a higher level of toxicity G2.

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H-VMAT AND VMAT FOR BREAST CANCER: COMPARING TECHNIQUES IN OUR CLINICAL PRACTICE

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Aims. Hybrid volumetric modulated arc therapy (H-MVAT) represents an innovative technique that combines the three-dimensional conformal technique (3D-CRT) with volumetric-modulated arc therapy (VMAT). This technique has been used in our centre since 2021, and so far, more than 50 breast cancer (BC) patients (pts) with different clinical situations have been treated. The aim of this paper is to present some examples of the dosimetric difference between VMAT and HVMAT plans in BC pts with complex clinical situations.

Methods. We selected five BC patients with different clinical situations and unfavourable anatomy in whom the two techniques were compared by clinical need with different treatment regimens: right whole breast irradiation (WB) RT 26 Gy/5 fractions (frs) (pt1), left WBRT (40.05/2.67 Gy) with simultaneous integrated boost (SIB) (48/3.2 Gy) in 15 frs in breath hold (BH) (pt2), right WBRT plus axilla (40.05/2.67 Gy) with SIB (48/3.2 Gy) in 15 frs (pt3), left chest wall with supra-infraclavicular and interpettoral (SC-IC-IP) lymph nodes (LN) in BH (pt4), right chest wall with prosthesis sparing with SC-IC-IP LN including internal mammary nodes (pt5). The two plans were compared to evaluate coverage and dose distribution at organs at risk (OARs). The data obtained were then entered in a table for better comparison.

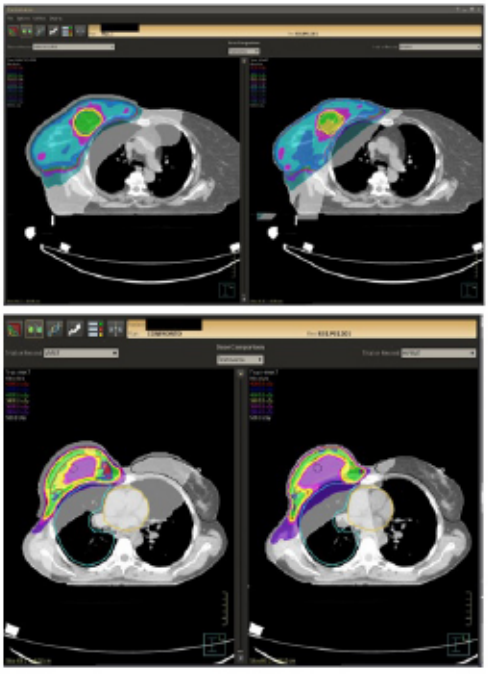
Results. Target coverage, hot spot, and dosimetric distribution data for the main OARs are provided in Table 1. The attached images illustrate the different dose distribution between the two techniques Figure 1 and Figure 2.

Conclusions. Dosimetric data show that the two techniques have overlapping target coverage. The H-VMAT technique reduces low doses and allows greater sparing of contralateral organs at risk, such as contralateral lung, controlateral breast and heart (in the case of the right breast), whereas VMAT reduces high doses to the

ipsilateral lung. The availability of different treatment techniques allows the best technique to be chosen depending on the clinical situation.

Table 1.

		Target Coverage	107 % (cc)	Dmean Hearth	Dmax LAD	Dmean controlaterale breast	Dmean controlaterale lung	Omolaterale lung
Pt 1	HVMAT	95 – 99%	0.04	0.66 Gy V1.5=1% V7=0% Dmax 1.8 Gy	0.95 Gy	1 Gy	0.56 Gy	V8=12%
	VMAT	95 – 95.8%	5.4	2 Gy V1.5=50 % V7=1%	4.8 Gy	3 Gy	2.25 Gy	V8=4.2%
Pt 2	HVMAT	95 – 98% Boost 99%	0	1.6 Gy	4.3 Gy	1.7 Gy	1.5 Gy V5=1.6%	V16=15% V8=27% V4=46%
	VMAT	95 – 96% Boost 92%	0	2.5 Gy	5 Gy	3.7 Gy	3 Gy V5=21%	V16=18% V8=31% V4=45.6%
Pt 3	HVMAT	95 – 98% Boost 95 – 99%	0	1.4 Gy		0.8 Gy	1 Gy V5=0%	V16=20% V8=28% V4=40%
	VMAT	95 – 95% Boost 95 – 100%	0	2.1 Gy		2.1 Gy	2.6 Gy V5=14%	V16=13% V8=29% V4=50%
Pt 4	HVMAT	95 – 95%	3.7	3.1 Gy	15.8 Gy	0.7 Gy	0.88 Gy V5=0%	V16=18% V8=25% V4=40%
	VMAT	95 – 95%	2.8	3.2 Gy	10.7 Gy	2.3 Gy	3.4 Gy V5=34%	V16=14% V8=27% V4=45%
Pt 5	HVMAT	95 – 95% Dmean protesi=5 7 Gy	10	3.4 Gy	2.8 Gy	1.9 Gy	1.8 Gy V5=5%	V16=34% V8=42% V4=57%
	VMAT	95 – 97% Dmean protesi=5 9 Gy	6	4 Gy	6 Gy	5.2 Gy	4.9 Gy V5=40%	V16=20% V8=38% V4=59%



Figures 1 and 2.

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BREAST CANCER RADIOTHERAPY AFTER NEOADJUVANT SYSTEMIC THERAPY: A RETROSPECTIVE EVALUATION.

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Aims. Neoadjuvant chemotherapy (NAC) is increasingly used in selected high-risk, locally advanced breast cancer (BC) patients in order to downstage the primary tumor in the breast and the metastatic axillary lymph node, often resulting in a small increase in breast conservation rates. The increasing use of NAC in BC has resulted in treatment issues for radiation oncologists, caused by few literature experiences in this setting of patients. Furthermore, the value of pathologic complete response (pCR) after NAC is not established. The aim of this study is to evaluate the pattern of care of patients undergoing NAC and adjuvant Radiotherapy (RT).

Methods. We retrospectively analyzed BC patients treated in our RT Unit. All patients underwent NAC followed by breast conserving surgery (BCS) or mastectomy. NAC was prescribed according to staging and tumor biology. Whole breast RT with or without supraclavicular lymph node RT was performed. Clinical outcomes, as loco-regional recurrence (LRR), disease-free survival (DFS) and overall survival (OS), were analyzed, measured from surgery until first event. RTOG scales were used for acute RT toxicity evaluation.

Results. Ninety locally advanced BC patients who underwent NAC and treated between 2015 and 2020 were retrospectively analyzed. The median age was 53 years (range=29-80). Patients, tumor and treatment characteristics are summarized in Table 1. A clinical response was obtained in 64% of patients. After NAC, 40% of patients underwent BCS, while 60% underwent mastectomy; axillary dissection was performed in 66% of patients. All patients underwent adjuvant RT: conventional fractionation was chosen in 31%, while in 69% a moderate hypofractionation was used (total dose 4005 or 4256 cGy); 73% of patients underwent supraclavicular lymph node RT. The median follow up was 41 months (range=24-98). Five-years OS, DFS, and LRR were 83%, 78% and 9% respectively. In patients achieving pCR (34%), OS, DFS and LRR were 84%, 84% and 2%. Hypofractionated treatment resulted in better clinical outcomes (+ 6%, +16%, -2% for OS, DFS and LRR). RT was

well tolerated: 12% of patients reported an acute toxicity ≥ 2.

Conclusions. NAC resulted a good tratment in order to downstage disease before performing local treatment: about one third of our patients achieved a pCR. In this setting of patients, an hypofractionated schedule resulted safe and well tolerated with good results in terms of clinical outcomes.

Table 1. Patients, tumor and treatment characteristics.

Patients	n (%)	Patients	n (%)
Age (years)range	53 (29-80)	Pathological Tumor Stage	
Clinical Tumor stage		Complete Response (pCR)	21 (23)
cT1	7 (8)	ypTis	10 (11)
cT2	42 (47)	ypT1a	8 (9)
cT3	21 (23)	ypT1b	6 (7)
cT4	20 (22)	ypT1c	16 (17)
Clinical Nodal stage		ypT2	21 (23)
cN0	22 (24)	ypT3	5 (6)
cN1	58 (64)	ypT4	3 (4)
cN2	3 (4)	Pathological Nodal Stage	
cN3	7 (8)	ypN0	46 (51)
Molecular subtypes		ypN1mic	3 (4)
Luminal A	7 (8)	ypN1a	19 (21)
Luminal B	22 (24)	ypN2	15 (16)
HER2+	35 (38)	ypN3	7 (8)
Triple negative	27 (30)	Hystological Type	
Neoadjuvant Therapy		Ductal	62 (70)
Hormone Therapy	4 (4)	Lobular	5 (6)
Chemotherapy	51 (57)	Other	2 (2)
Chemotherapy +Trastuzumab	35 (39)	Not evaluable (pCR)	21 (23)
Clinical Response		Grade	
Complete Response	8 (9)	1	2 (2)
Partial response	56 (62)	2	41 (46)
Progression Disease	2 (2)	3	26 (29)
Stable Disease	7 (8)	Not evaluable (pCR)	21(23)
Not available	17 (19)	Molecular subtypes	
Type of Surgery		Luminal A	16 (18)
BCS	36 (40)	Luminal B	20 (22)
Mastectomy	54 (60)	HER2+	15 (16)
Axillary Dissection		Triple negative	18 (17)
Yes	59 (66)	Not evaluable (pCR)	21(23)
No	31 (34)	Adjuvant Therapy	
BRCA 1-2		Hormone Therapy	23 (26)
Wilde Type	21 (23)	Chemotherapy	20 (22)
Mutate	4 (4)	Trastuzumab	34 (38)
Not available	65 (73)	None	13 (14)

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ADJUVANT RADIOTHERAPY IN CN+ PATIENTS SUBMITTED TO NEOADJUVANT CHEMOTHERAPY FOLLOWED BY SURGERY WITH PATHOLOGICAL NODAL RESPONSE WITH OR WITHOUT AXILLARY DISSECTION: A RETROSPECTIVE EVALUATION

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Aims. Neoadjuvant chemotherapy (NAC) is increasingly used in breast cancer (BC) patients with large primary tumors or involved lymph nodes. Axillary dissection (ALND) has been standard treatment for BC patients before the advent of the sentinel lymph node (SLN) procedure. However, clinical trial assessing the optimal treatment for cN+ BC patients in terms of surgery and radiotherapy (RT) are needed. The aim of our study is to report the clinical outcomes of cN+ patients undergoing NAC and surgery with pathological nodal response (pNR) with or without ALND followed by RT.

Methods. We retrospectively analyzed cN+ BC patients treated in our RT Unit. All patients were cN+ and underwent NAC followed by breast conserving surgery (BCS) or mastectomy with (Group 1) or without ALND (Group 2) with complete pNR. All patients underwent whole breast RT with or without supraclavicular (SC) RT; patients who underwent intentional axillary RT were excluded. To assess the incidental axillary dose, a retrospective dosimetric evaluation of axillary levels I (L1) and II (L2) was performed. Clinical outcomes, as locoregional recurrence (LRR), disease-free survival (DFS) and overall survival (OS), were analyzed, measured from surgery until first event.

Table 1. Patients, tumor and treatment characteristics.

Axillary Dissection		Sentinel Lymph Node Biopsy	
Patients = 12	n (%)	Patients = 21	n (%)
Age (years) range	51 (34-74)	Age (years) range	48 (29-67
Clinical Tumor Stage		Clinical Tumor Stage	
cT1	1 (8)	cT1	4 (19)
cT2	5 (42)	cT2	10 (48)
cT3	2 (17)	cT3	5 (24)
cT4	4 (33)	cT4	2 (9)
Clinical Nodal Stage		Clinical Nodal Stage	
cN1	10 (83)	cN1	18 (86)
cN2	0 (0)	cN2	1 (5)
cN3	2 (17)	cN3	2 (9)
Hystological Type		Hystological Type	
Ductal	12 (100)	Ductal	20 (95)
Lobular	0 (0)	Lobular	1 (5)
Other	0 (0)	Other	0 (0)
Molecular subtypes		Molecular subtypes	
Luminal A	0 (0)	Luminal A	0 (0)
Luminal B	2 (17)	Luminal B	3 (14)
HER2+	4 (33)	HER2+	11 (52)
Triple negative	6 (50)	Triple negative	7 (34)
Neoadjuvant Therapy		Neoadjuvant Therapy	
Chemotherapy	8 (67)	Chemotherapy	10 (48)
Chemotherapy +Trastuzumab	4 (33)	Chemotherapy +Trastuzumab	11 (52)
Type of Surgery		Type of Surgery	
BCS	5 (42)	BCS	15 (71)
Mastectomy	7 (58)	Mastectomy	6 (29)
Pathological Tumor Stage		Pathological Tumor Stage	
ypT0	3 (25)	ypT0	8 (38)
ypTis	4 (33)	ypTis	6 (29)
ypT1a	0 (0)	ypT1a	0 (0)
ypT1b	0 (0)	ypT1b	3 (14)
ypT1c	1 (8)	ypT1c	3 (14)
ypT2	4 (33)	ypT2	1 (5)
ypT3	0 (0)	ypT3	0 (0)
ypT4	0 (0)	ypT4	0 (0)
Grade		Grade	
1	0 (0)	1	2 (9)
2	7 (58)	2	7 (34)
3	2 (17)	3	3 (14)
Not Evaluable (pCR)	3 (25)	Not Evaluable (pCR)	9 (43)
Molecular subtypes		Molecular subtypes	
Luminal A	0 (0)	Luminal A	1 (5)
Luminal B	1 (8)	Luminal B	1 (5)
HER2+	2 (17)	HER2+	7 (34)
Triple negative	6 (50)	Triple negative	3 (14)
Not Evaluable (pCR)	3 (25)	Not Evaluable (pCR)	9 (42)

Results. aA total of 33 patients treated from 2015 to 2020 was retrospectively evaluated. The median age was 53 years (range=29-80). Patients, tumor and treatment characteristics are reported in table 1. ALND was performed in 36% of patients (Group 1), while SLNB in 64% (Group 2). In Group 1, 83% of patients received a moderate hypofractionation and 75% of patients performed SCRT. In Group 2, 86% of patients received a moderate hypofractionation and SCRT was performed in 67%. The median L1 and L2 volumes were 75.5 cc (range=19.6-106.2) and 10.2 cc (range= 4.8-18.8) respectively. The median D_{max} and D_{mean} were 41.3 Gy (range=37.7-42.6) and 24.3 Gy (range=3.85-37.5) for L1, 38.8 Gy (31.6-41.7) and 18 Gy (3.5-37.1) for L2. The median follow-up was 41 months (range=12-83). The 4-year OS, DFS and LRR were 75%, 75%, 8% and 95%, 95%, 5% for Group

1 and 2 respectively. One patient had axillary relapse in Group 1.

Conclusions. Although the small sample size, our study demonstrated good results in patients who underwent SLNB alone. However, patients submitted to ALND presented more risk factors respect to patients submitted to SLNB. Incidental dose to axillary levels resulted low and did not delivered a therapeutic dose to L1 and L2.

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CLINICAL IMPACT OF HER2 LOW EXPRESSION IN HORMONE RECEPTOR POSITIVE (HR+) BREAST CANCER PATIENTS TREATED WITH CYCLIN-DEPENDENT KINASE 4/6 INHIBITORS (CDK4/6I) PLUS ENDOCRINE THERAPY

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Aims. Cyclin-dependent kinase 4/6 inhibitors (CDK4/6i) currently represent the milestone for the treatment of patients with hormone receptors positive (HR+) HER2 negative (HER2-) metastatic breast cancer (BC). Recently, a new nomenclature has been proposed for cases with HER2 score at immunohistochemistry (IHC) of 1+ or 2+ with negative in situ hybridization (ISH), defined as HER2-low BC. Based on the observed benefit with new anti-HER2 compounds, HER2-low has been proposed as a biologically distinct subtype of BC. We conducted a retrospective study to explore whether HER2-low expression can affect the clinical efficacy of CDK4/6i in HR+ metastatic BC patients.

Methods. We retrospectively evaluated patients diagnosed with metastatic HR+ HER2- BC, who started treatment with CDK4/6i between January 2017 and June 2021. We collected clinical data related to the diagnosis of metastatic disease, treatment with CDK4/6i, toxicities, survival data and biological characteristics of both primary tumor and metastases, when available.

Results. Data of 138 consecutive patients treated with CDK4/6i at our institution were retrospectively evaluated. Median age was 59 years old (range 34-82). With a median follow up of 31 months, median overall survival (OS) was 31 months. No difference was found regarding PFS and OS between patients with HER2 0 and patients with HER2 low (p=0,5532 and p=0,5506, respectively), as shown in Figure 1. At the multivariate analysis, only endocrine resistance (p=0,0028) impact on OS. Considering the subgroup of endocrinoresistant patients (n=68), HER2 status did not impact neither on OS (p=0,2495) nor PFS (p=0,3236). CDK4/6i type (palbociclib, ribociclib, abemaciclib) did not affect both OS at univariate (p=0,1632) and multivariate analysis (p=0,3512) and PFS at univariate (p=0,1092) and multivariate analysis (p=0,5193).

Conclusions. Preliminary results from our retrospective study showed that HER2-low expression did not affect the clinical efficacy of CDK4/6i and suggest not to incorporate it into systemic therapy decisions in metastatic HR+ HER2- BC. Further evidence from larger series is needed to confirm these findings.

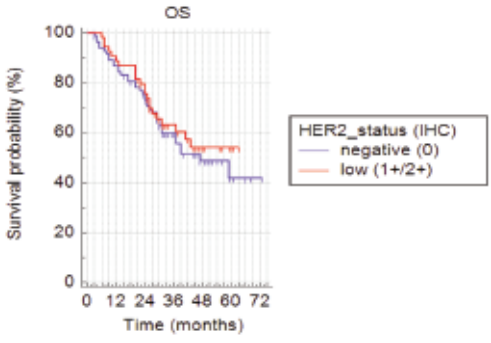

Figure 1.

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POSTMASTECTOMY RADIATION THERAPY FOR BREAST CANCER PATIENTS AFTER IMPLANT-BASED IMMEDIATE RECONSTRUCTION

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Aims. To evaluate feasibility postmastectomy radiation therapy for breast cancer patients (pts) after implant-based immediate reconstruction with saving prosthesis and pectoral muscle to reduce toxicity and extent of capsular contractures.

Methods. Between February 2021 to November 2022 twenty-six consecutive pts underwent postmastectomy radiation therapy after implant-based immediate reconstruction. All pts underwent irradiation of the chest wall and ipsilateral supra-infraclavicular and interpectoral lymph nodes (LN), in 2 pts the internal mammary LN were also included. Target volumes delineation were

defined following the ESTRO ACROP consensus guidelines for chest wall, differentiated according to the type of reconstruction and on the basis of prognostic factors. Contouring guidelines in the AIRO Breast Cancer Group Best Clinical Practice were used for LN delineation. Sixteen pts were treated with conventional fractionations (frs) of 50 Gy in 25 frs, 10 pts with moderate hypofractionated scheme of 40.05 Gy in 15 frs. Twenty-three pts underwent radiotherapy (RT) with volumetric modulated arc therapy techniques, 2 pts with Tomotherapy and 1 pt with hybrid volumetric modulated arc therapy. All pts with left breast cancer underwent a deep inspiration breath hold (Figure 1).

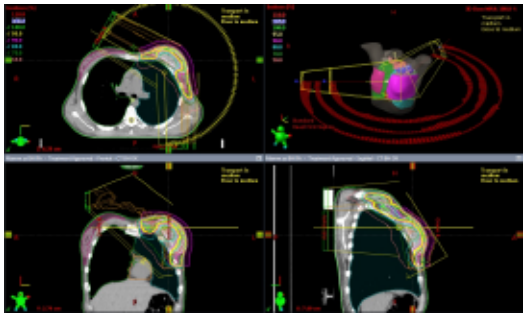

Figure 1.

Results. The median follow-up was 8 months. The average age of the pts was 48 years (range 34-73). Fifteen pts had a reconstruction with a pre-pectoral implant, 8 retro-pectoral and 3 prosthesis/expander. Ten pts underwent neoadjuvant chemotherapy and initial clinical stage was cT2-cT3 N+, two of these achieved a complete pathological response. For pts that underwent surgery as first treatment step the pathological stage was pT1-2 pN1a in 7 pts, pT1-2 pN2a in 7 pts and pT3 pN2a in 2 pts. Median V95% to chest wall CTV was 96% and median V95% to LN CTV was 98%. There were no hot spots on the prosthesis, mean dose was 47 Gy (range 43-50) for conventional fractionation and 38 Gy (range 36-39) for moderate hypofractionation. The treatment was well tolerated in all pts. Cosmetic outcomes were very good in most of the pts, only 7 pts presented capsular contracture according to Becker: 5 pts G1 (1.3%), 2 G2 (0.26%) and 1 pt G3 which required prosthetic replacement.

Conclusions. This technique ensure an excellent target coverage and sparing prosthesis and partially the pectoral muscle. Long-term follow-up data are needed to assess late toxicity and entity of prosthetic replacement for this subset of pts

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PRESCRIPTIVE APPROPRIATENESS IN EARLY BREAST CANCER STAGING EXAMS: PRELIMINARY INVESTIGATION ABOUT ADHERENCE TO THE GUIDELINES IN THE CLINICAL PRACTICE.

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Aims. The main national and international guidelines do not recommend staging exams for early breast cancer (BC) patients. Nevertheless, in the clinical practice, clinicians may decide, for different reasons, to not adhere to recommendations, prescribing laboratory biomarkers and instrumental exams for patients with early stage BC.

Methods. A retrospective analysis of clinical data of BC patients (type of surgery performed, pTNM disease staging, type and outcome of prescribed staging exams or laboratory markers, type of specialist who requested the investigations), along with the prescriptive appropriateness of these staging exams in relation to the reference guidelines, was performed in different Apulian Centers between September 2015 and December 2016.

Results. Data from 147 BC patients (85% stage I-II,15% stage IIIA-B) were collected. Only 4% of the staging exams was prescribed by the Multidisciplinary Tumor Board (MTB). 43% of patients underwent overuse of at least one laboratory biomarker. First level imaging was prescribed for 88,4% (chest X-ray) and 93% (abdomen ultrasound) of patients and for all (6/6) women with in situ BC. Regarding the second level staging exams, 57,4% and 40,6% of patients at early stage performed radionuclide bone scan (RBS) and total body computed tomography (CT), respectively. A positron emission tomography (PET) was inappropriately prescribed in 7/10 patients.

Conclusions. Our analysis showed that the adherence to the reference guidelines was still suboptimal during the years 2015-2016. Future studies will evaluate changes in clinical practice and adherence to guidelines in relation to the implementation of regional and local recommendations.

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ULTRA-HYPOFRACTIONATED ADJUVANT RADIOTHERAPY FOR EARLY BREAST CANCER: AN UPDATE

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Aims. Moderate hypofractionation is the standard of care for adjuvant whole-breast radiotherapy (WBRT) after conserving surgery for breast cancer (BC). Recently, 10-year results from the FAST and 5□year results from the FAST-Forward (FW) trial evaluating adjuvant WBRT in 5 fractions over 5 weeks or one week have been published. We evaluate acute and late Radiation Therapy (RT) toxicities in women treated with 26 Gy in 5 daily fractions in our institution from November 2020 to November 2022. Adverse skin reactions were assessed according to CTCAE v. 5.0 at the end of treatment. Clinical follow-up was performed at 1, 3,6, 12, 18 and 24 months to evaluate acute and subacute adverse effects.

Methods. 50 early BC patients (median age 72 years, 65-8) were treated with 26 Gy in 5 fractions in a week using VMAT (32/50 pts) and IMRT (18/50) and daily IGRT. Inclusion criteria were: pT1/pT2 invasive BC, no or limited axillary involvement (pN0/pN1), and age ≥ 65 years. 8 pts (16%) underwent deep-inspiration breath-hold (DIBH). Target volumes and organs at risk were defined, and plans were evaluated according to the Fast FW trial planning objectives. The main exclusion criteria are carcinoma in situ, mastectomy and chemotherapy. Pts underwent follow-up clinical visits documented with photographs at the end of RT and 1, 3,6,12, 18 and 24 months after RT-end.

Results. Lung and heart dose constraints were never exceeded. Most pts were T1 (87%), while the remaining were T2 (13%). 74% of the pts were axillary status negative; only 26% were pN1. 26 (57%) of the cases were right breast, and 24 (43%) were left breast. No patients interrupted radiotherapy. Median follow-up was 9 months (range 4-30). At the end of RT, 12 pts (24%) had G1 breast erythema which was resolved in the next 2 weeks. One month later, we found only 2 cases of self-resolved G1 breast fibrosis and one case of new-onset G1 breast hyperchromia, which persisted for two months. 3 months later, we found one benign mastitis. One patient experienced a keloid in the surgical area one year later. No G≥2 erythema (acute skin toxicity) was detected. No patients reported major cardiac events or acute pulmonary toxicities. Late Skin toxicities were collected six months post–RT (5 pts: G1 fibrosis), one year later (1 pts G1 fibrosis), and two years later (None G1). No early ipsilateral breast tumour recurrence was observed.

Conclusions. Our results confirmed the safety of the Fast FW protocol in terms of acute and late skin toxicities.

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COMPARATIVE DOSIMETRIC ANALYSIS BETWEEN FREE BREATHING AND DEEP INSPIRATION BREATH-HOLD TECHNIQUES IN THE ADJUVANT RADIOTHERAPY FOR LEFT-SIDED BREAST CANCER AND EVALUATION OF PREDICTOR PARAMETERS TO IDENTIFY PATIENTS WITH THE BEST POTENTIAL BENEFITS

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Aims. The purpose of this study is to evaluate the benefit of the Deep Inspiratory Breath-Hold (DIBH) technique performed with the Respiratory Gating for Scanners (RGSC; Varian Medical Systems, Palo Alto, CA, USA) system, as regards the left lung, heart and left anterior descending artery coronary (LADAC) sparing and to identify pre-treatment anatomical parameters as possible predictors for the most appropriate technique choice.

Methods. Thirty-four patients with left-sided breast cancer (LSBC) after breast conservative surgery treated in our institution with 40.5 Gy in 15 fractions (or 48 Gy with simultaneous integrated boost) were enrolled. All patients underwent two sequential CT simulations in supine position: the first in free breathing (FB) and the second in DIBH, using the RGSC system. A combined tangential and volumetric fields has been used for treatment plans for both CT scans. The Dose-Volume Histograms were generated for both plans. The deep inspiration amplitude in DIBH and the average respiratory excursion in FB were recorded. The cardiac contact distances in axial (CCDax) and parasagittal (CCDps) plans and the lateral heart-to-chest distance (HCD) in the FB and DIBH techniques were measured. Paired t-test and correlation analysis were performed to compare anatomical and dosimetric variables and to get predictor parameters for cardiac, LADAC and left lung sparing.

Results. A significant dose reduction (p-value<0.05) with DIBH compared to FB was recorded in all analysed parameters regarding heart (Dmean,Vmax,V5, V10,V20,V30), left lung (Dmean,V5,V10, V20) and LADCA (Dmean,Vmax,V5). In particular, reductions of 42%, 44% and 13% respectively for the mean heart dose (1.6 Gy *vs* 2.7 Gy, p<0.001), maximum LADAC dose (14.6 Gy *vs* 26.8 Gy, p<0.001) and mean ipsilateral lung

dose (5.5 Gy *vs* 6.3 Gy, p<0.001) were obtained with DIBH. A greater threshold amplitude of DIBH has not shown to an improvement of dosimetric parameters. The FB-CCDps distance, FB-HCD, and the FB-CCDps/FB-HCD ratio were weakly correlated with the FB mean cardiac dose and the DIBH mean cardiac dose reduction.

Conclusions. DIBH in postoperative hypofractionated radiotherapy for LSBC leads to significant dose reduction to heart, LADCA and left lung, without compromising target coverage, proving to be an important and effective therapeutic option. Further studies on the effectiveness of the predictive parameters are needed to identify patients who could benefit most from this technique.

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COMPARISON OF DIAGNOSTIC PERFORMANCE OF ULTRASOUND, MAMMOGRAPHY AND MAGNETIC RESONANCE FOR THE CLINICAL STAGING OF LOCALIZED BREAST MALIGNANCIES

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Aims. Locoregional clinical staging of breast cancer, given the more frequent use of preoperative systemic therapy (PST), became an important issue for the appropriate management of the disease for both, evaluation of indication to PST and indication to postoperative RT. The aim of our study was to assess which diagnostic investigation allows a clinical (c) measure of disease better corresponding to the pathological (p) finding.

Methods. 519 cases of breast cancer patients treated or discussed at the multidisciplinary meetings of our institution, not treated by neoadjuvant chemotherapy, were reviewed. Clinical tumor (T) size, related T stage, and clinical nodal (N) stage according to mammography (MMX), ultrasound (US) and magnetic resonance imaging (MRI) were compared to the pathological ones, according to the AJCC system. T size discrepancies were defined as pT minus cT (mm). Stage variations (T1a/b vs. T≥1c; T1 vs. T≥2; N+ vs. N-) were also considered for analysis. Chi squared or ANOVA test was employed, as appropriate.

Results. MMX, US and MRI were performed in 72%, 84% and 37% of cases, respectively. MMX didn't detect T in 13% of cases, while US and MRI only in 2% and 1%, respectively (p<.00005). No investigation was significantly better to perfect size T (9% by MMX, 11% by US, 9% by MRI). T size was underestimated of 6.5 (1-44) mm in 54% by US, 7.4 (1-45) mm in 43% by MMX, 5.2 (1-42) mm in 30% by MRI; overestimated of 5 (1-64) mm in 33% by US, 5 (1-34) mm in 35% by MMX, 7.6 (1-67) mm in 60% by MRI. Mean crude T size discrepancy values were similar: 5.1 (0-64) mm by US, 5.4 (0-45) mm by MMX, 6.2 (0-67) mm by MRI. Furthermore, T size discrepancies didn't cause differences in T stage in 78-80% of cases. However, considering, in details, detection of T ≥2, MRI trended to have the highest sensitivity (65%, p=.07), vs. MMX (50%) and, lastly, US (44%). The same trend was shown for T ≥1c detection (88%, 84% and 80% by MRI, MMX, US, respectively). No one showed an acceptable detection of positive N involvement (23% by MRI, 16% by US or MMX).

Conclusions. Clinical locoregional staging for breast cancer by MMX, US and MRI is not reliable as it should. Nodal involvement detection is not well performed by all diagnostic tools considered. MRI showed the highest sensitivity for T≥1c and T≥2 detection but wasn't routinely performed. MMX showed a significant lower ability to detect T than US and MRI; however, when T was detected, MMX discriminated better than US between T1 and T≥2 and between T1a/b and T≥1c.

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THE QLQ-C30 AND BR23 QUESTIONNAIRES (EORTC) IN BREAST CANCER PATIENTS SUBMITTED TO DIFFERENT SCHEMES OF HYPOFRACTIONATED RADIATION THERAPY

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Aims. Breast cancer is the most diagnosed malignancy in women. Adjuvant treatment after conservative surgery includes radiotherapy which shows a significative impact on local control and survival. We evaluate the health-related quality of life in breast cancer patients' treated with two hypofractionated schemes.

Patients and Methods. The QLQ-C30 and BR23 questionnaires (EORTC) were submitted to patients one month after the end of hypofractionated radiation therapy. The patients were stratified in two groups according to the radiotherapy schedules: Group A (START B - 40 Gy/15Fx) and Group B (Fast Forward - 26 Gy/5Fx).

Results. From December 2022 to April 2023 we evaluated 30 patients with breast cancer, with Karnofsky Performance Status (KPS) ≥60. Of them 15 patients were enrolled in Group A and 15 in Group B. The total mean value score of health and quality of life were respectively 88.3 for Group A and 85.8 for Group B. Particularly, the mean functional scale value were 82.25 in Group A and 85.25 in Group B; the mean symptoms scale value were 8.3 in Group A and 4.3 in Group B.

Conclusions. The higher values in functional scale are associated with a better perception of quality of life in term of physically and socially aspect while lower values in symptoms scale with minor toxicities rate. According to these results, hypofractionation with Fast Forward (26 Gy/5Fx) seems to have a better impact on health-related quality of life.

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APPLICATION OF DIBH TO VMAT TECHNIQUE FOR THE TREATMENT OF LOCALLY ADVANCED LEFT BREAST NEOPLASMS WITH IRRADIATION OF THE INTERNAL MAMMARY CHAIN

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Aims. In patients (pts) diagnosed with locally advanced breast cancer with lymph node involvement, locoregional radiotherapy is required in most clinical situations. New technologies can achieve a better dose homogeneity at the target, with also preservation of critical organs even on more complex irradiation volumes. Volumetric Modulated Arc Therapy (VMAT) and Deep Inspiration Breath Hold (DIBH) are among the most advantageous techniques for the treatment of breast cancer, especially for heart dose sparing and dose distribution, but are rarely used in combination. The aim of this study was to analyse the dosimetric benefits in terms of target dose coverage and organ at risk doses of VMAT treatments combined with DIBH compared with VMAT treatments in Free Breathing (FB) on the left breast, locoregional lymph nodes and internal mammary chain (IMC).

Methods. The retrospective analysis included all breast cancer pts undergoing radiotherapy on the breast or chest wall and locoregional lymph nodes including CMI and treated with VMAT-DIBH technique. Baseline FB CT scans were also contoured and a rival VMAT treatment plan was calculated. From each treatment plan, both the V95% and V105% of the target organs (PTV WB, PTV boost, PTV_claveo, PTV CMI, PTV RA (PTV sum excluding boost) and the dose of the organs at risk were extrapolated. For each dosimetric parameter, a 't-student test' was applied to assess statistical significance.

Results. Since 2018, 12 pts who met the inclusion criteria have been selected. Analyzing the means of V95% values of Whole Breast PTV in FB and DIBH, a small difference (p=0.065) emerges, probably due to the small number of patients. From the analysis of the average values of the V95% of the PTV CMI, the analysis shows that the VMAT DIBH technique results in a better coverage of the target (p=0.011). The analysis of the V95% values of the PTV_RA, shows better coverage in VMAT DIBH than VMAT FB, with statistical significance (p=0.011). Organ at risk dosimetric analysis showed a clear reduction to heart and LADCA. Differences in mean heart dose (p = 0.051), V20 heart (p=0.001) and Dmean LADCA (p = 0.029) were also statistically significant.

Conclusions. In the radiation treatment of left breast cancer with concomitant lymph node irradiation and IMC, the VMAT technique integrated with DIBH, is particularly effective in reducing doses to heart structures and in covering IMC lymph nodes, respect FB tecnique

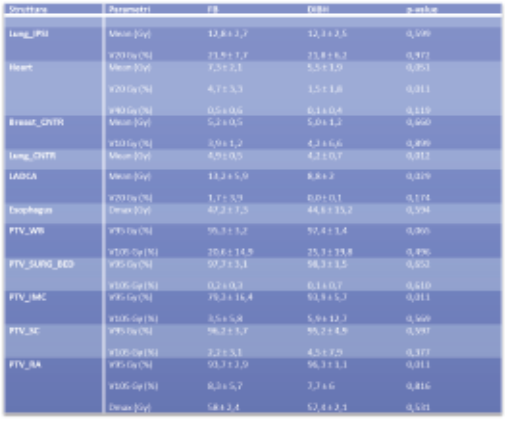

Figure 1.

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EVALUATION OF LIMBUS SOFTWARE FOR AUTOCONTOURING IN BREAST CANCER

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Background. Accurate delineation of structures in CT datasets is essential in radiotherapy treatment planning. Manual contouring is the current standard but can be time-consuming and subject to inter-observer variability. Autocontouring software, such as Limbus, has the potential to reduce workload and improve efficiency. This study aims to evaluate the performance of Limbus software in breast cancer by comparing its autocontours with two other datasets: contours generated by Limbus and further modified manually, and manual contours.

Methods. A total of 44 breast cancer patients who received adjuvant radiotherapy after breast-conserving surgery were included in the study. The organs at risk (OARs) were contoured using three different methods: (1) Limbus-generated autocontours, (2) Limbus-generated autocontours further modified manually, and (3) manual contours. The accuracy of OARs volumes was assessed using the Dice similarity coefficient (DSC). Time-saving effects were also evaluated.

Results. The DSC values were compared between the three contouring methods using the paired t-test. Statistical significance was set at $p<0.05$. The results demonstrated that Limbus-generated autocontours, even when further modified manually, showed comparable accuracy to manual contours in terms of OARs volumes (Table 1).

Table 1.

	DICE (mean ± dev std)		
OAR	Manual vs Limbus	Manual vs Limbus refined	Limbus vs Limbus refined
A_LAD	0,46 ± 0,17	0,51 ± 0,17	0,92 ± 0,17
Esophagus	0,76 ± 0,07	0,77 ± 0,07	0,97 ± 0,06
Lung L	0,97 ± 0,03	0,97 ± 0,03	1 ± 0
Heart	0,94 ± 0,02	0,94 ± 0,02	1 ± 0,01
Spinal Canal	0,85 ± 0,06	0,86 ± 0,06	1 ± 0
Lung R	0,94 ± 0,21	0,94 ± 0,21	1 ± 0
BrachialPlexR	0,75 ± 0,21	0,75 ± 0,21	0,99 ± 0,01
Breast R	0,85 ± 0,06	0,92 ± 0,04	0,91 ± 0,1
Breast L	0,85 ± 0,06	0,91 ± 0,04	0,91 ± 0,09
Humerus R	0,83 ± 0,18	0,86 ± 0,07	0,99 ± 0,04
Humerus L	0,82 ± 0,09	0,83 ± 0,1	0,98 ± 0,04
BrachialPlexL	0,71 ± 0,34	0,79 ± 0,21	0,99 ± 0,02
Gland_Thyroid	0,75 ± 0,09	0,79 ± 0,04	0,95 ± 0,14

The time-saving effect was observed in the contouring process modifying Limbus software contours (average time: 8min; range 2-29min) compared to manual contouring (average time: 20min; range 10-36min) .

Conclusions. Limbus software for autocontouring in breast cancer demonstrated promising results, providing accurate and time-efficient contours of target volumes and OARs. The software showed comparable performance to manual contouring, and its utilization can potentially reduce inter-observer variability and workload in the planning process. Further studies with larger sample sizes and multicenter validation are recommended to confirm these findings.

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ULTRAHYPOFRACTIONATED BREAST RADIOTHERAPY ACCORDING TO FAST FORWARD TRIAL: PRELIMINARY RESULTS ON ACUTE-SUBACUTE TOXICITY

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Aims. FAST FORWARD (FF) schedule is a new standard of care for adjuvant whole-breast radiotherapy after conservative surgery. This study retrospectively analysed acute and sub-acute toxicity in 55 patients treated using FF schedule (consecutive five-fraction).

Methods. A total of 55 patients were treated with WBRT from August to December 2022. A dose prescription of 26 Gy in 5 consecutive fractions was delivered. In nine patients a concomitant/simultaneous integreated boost of 4Gy was added. Radiotherapy was administered through volumetric modulated arc therapy (VMAT) or conformal 3D technique. Deep inspiration breath hold was used in 12 patients to limit the heart dose in left breast. Acute and subacute toxicity was evaluated according to the CTCAE v. 5.0 scale at the end of radiotherapy and at the first follow up.

Results. Median follow-up was 6 months. Mean age was 60 years (49-83). The totality of tumor biology was Luminal A (60%) or B (40%). Most patients received adjuvant hormonal therapy (72,7%), and adjuvant chemotherapy or cyclin inhibitors was given in only 1,8%. At the end of radiotherapy the maximum detected acute skin was G1 in 32.7% of patients or G2 in 1,8%. No G3-G4 toxicity were found. The most frequent toxicities were skin erythema (20%), pruritus (7,2%) and skin ulceration (3,6%). Two patients reported hyperaemia or hyperchromia of the irradiated breast and other two moderate pain. A small percentage of all patients 9.1% showed more than one side effect at the same time. Subacute toxicity in terms of fibrosis was G1 in 10.9% of

all patients and G2 in 5.4%. Hyperpigmentation G1 was reported in 14.5% and G2 in 1,8%. Grade 1 breast oedema or G1 pruritus was detected in 5.4%. At the first follow-up, at six months to the end of radiotherapy, most of the previously reported side effects had resolved and the totality of patients were satisfied about the aesthetic results. No cardiovascular and pulmonary acute-subacute toxicity was reported.

Conclusions. Our preliminary results showed that the FF adjuvant breast radiotherapy allow to limit hospital access, increase the tolerability of treatments and is well tolerated. The majority of treated patients do not report important acute and subacute side effects. A longer follow-up and a larger cohort of patients are needed to assess late toxicity and to confirm the results reported in this study.

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ULTRA-HYPOFRACTION RADIOTHERAPY AFTER CONSERVATIVE SURGERY FOR BREAST CANCER: EARLY REPORT ON SAFETY, TOXICITIES AND QUALITY OF LIFE (QOL)

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Aims. Ultra-Hypofractionated adjuvant radiotherapy according to Fast forward scheme, is a modern five-fraction schedule radiation therapy delivered in 1 week after primary conservative surgery for early breast cancer. This schedule proven to be non-inferior in terms of local cancer control and safety than international standard hypofractioned regimen. We report our experience on safety, toxicities and quality of life (QoL) of breast cancer patients treated in our Radiotherapy Unit.

Methods. Between March 2022 and March 2023 we enrolled 22 patients (age range: 45-65 years old). All patients underwent conservative surgery, with pT1-3 pN0-1 MO disease. Patients received ultra-hypofractionated radiotherapy to whole breast; total dose administred was 26 Gy in 5 fx over one week. At the end of radiation therapy, we submit a QoL questionnaires (EORTC QLQ-C30, version 3), regarding daily activities and possible limitations during the administration of radiation therapy. The possibility of response ranges from 1 to 4 (from best to worst result). Clinic visits were scheduled for all patients during radiation treatment. Normal tissue effects were assessed by clinicians using CTCAE scale. 10 patients with left breast cancer were evaluated in cardio-oncologic specialistic dedicated course.

Results. Median follow-up of 7 months. All patients completed the planned radiation treatment, underwent scheduled clinical visits and answered the questionnaire. No cardiac or pulmonary toxicities was found. Among skin toxicities, the most frequent were erythema (G1 for 8 patients, G2 for 2 patients) and edema (G1 for 6 patients). Evaluation of the questionnaires scores showed a good clinical compliance in all patients treated; median score 46 (range 42-51).

Conclusions. Ultra-hypofractionated radiation therapy result safe, with low evidence of acute toxicities and good impact on QoL. Despite the small number of patients, we found better compliance, minimal skin toxicity, better aesthetic results and less psychological impact. Further studies are needed to evaluate late toxicity and to standardize combination treatments in this population.

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ULTRA-HYPOFRACTIONED ADJUVANT RADIOTHERAPY IN PATIENTS UNDERGOING CONSERVATIVE SURGERY FOR EARLY BREAST CANCER MONO-INSTITUTIONAL EXPERIENCE IN OLDER PATIENTS

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Aims. The Fast-Forward (FF) trial showed that a five-fraction regimen of radiotherapy (RT) delivered in 1 week to the whole breast is non-inferior to the standard 3-week regimen. Based on the results of the FF trial, we have retrospectively evaluated patients (pts) treated with ultra-hypofractionated schedule of adjuvant whole breast radiotherapy (RT). We report acute and early- skin toxicity.

Methods. From August 2021 to February 2023, we treated 19 patients in our Radiation Oncology Unit. A total dose of 28.5 Gy in once weekly fractions over 5 weeks was prescribed for 10 pts and 26 Gy in 5 daily fractions was prescribed for 9 pts. The whole breast was contoured as CTV. A total dose of 28.5 Gy or 26 Gy in 5 daily fractions was prescribed to the PTV. All treatments were delivered with static IMRT technique. The median age is 82 years. 1 patient underwent to mastectomy and 18 breast pts to conserving surgery (pT1-2, pN0) with negative margins. The patients population includes invasive ductal or lobular carcinoma. Patients' details, and histological features are reported in the Table 1. Skin tox was assessed with the RTOG score.

Results. Among our patients, right breast was irradi-

ated for 13 cases. OARs constraints (Heart: V1.5<30%, V7<5%; ipsilateral lung: V8<15%) were obtained in all plans. No RT-related cutaneous toxicity (RTOG score 0) was observed during treatment in pts undergoing 26 Gy in 5 daily fractions. RTOG grade 1 was observed during treatment in pts undergoing 28.5 Gy in once weekly fractions over 5weeks. Mean follow-up was 11 months. Late skin toxicity was not observed.

Conclusion. Our preliminary clinical experience confirms the tolerability and safety of the ultra hypofractionated radiotherapy. In selected cases (*e.g.* elderly patients with comorbidities limiting the adherence to standard therapies), this approach could be safe considered as alternative to standard hypofractionation in clinical practice. As additional benefits, the reduction of treatment duration with 1-week regimen improves patient's compliance and satisfaction, as well as treatment costs, as compared to the 3-week or 5-week regimens.

Table 1. Patients, tumor and treatment characteristics.

1 fx/week		5 fx/week	
Patients = 10	n (%)	**Patients = 9**	n (%)
Age (years) range	81 (72-87)	**Age (years) range**	83 (79-91)
Type of Surgery		**Type of Surgery**	
BCS	9 (90)	BCS	9 (100)
Mastectomy	1 (10)	Mastectomy	0 (0)
Hystological Type		**Hystological Type**	
Ductal	10 (100)	Ductal	8(89)
Lobular	0 (0)	Lobular	0 (0)
Other	0 (0)	Other	1 (11)
Pathological Tumor Stage		**Pathological Tumor Stage**	
pTis	0 (0)	pTis	1 (11)
pT1a	0 (0)	pT1a	0 (0)
pT1b	2 (20)	pT1b	1 (11)
pT1c	7 (70)	pT1c	3 (33)
pT2	1 (10)	pT2	4 (45)
Pathological Nodal Stage		**Pathological Nodal Stage**	
pNx	0 (0)	pNx	2 (22)
pN0	7 (70)	pN0	6 (67)
pN1	3 (30)	pN1	1 (11)
pN2	0 (0)	pN2	0 (0)
Grade		**Grade**	
1	1 (10)	1	1 (11)
2	7 (70)	2	6 (67)
3	2 (20)	3	2 (22)
Molecular subtypes		**Molecular subtypes**	
Luminal A	7 (70)	Luminal A	5 (55)
Luminal B	1 (10)	Luminal B	4 (45)
HER2+	1 (10)	HER2+	0 (0)
Triple negative	1 (10)	Triple negative	0 (0)
Adjuvant Therapy		**Adjuvant Therapy**	
Hormone Therapy	8 (80)	Hormone Therapy	7 (78)
Chemotherapy	2 (20)	Chemotherapy	2 (22)
Skin AcuteToxicity (RTOG scales)		**Skin Acute Toxicity (RTOG scales)**	
G0	6 (60)	G0	9 (100)
G1	4 (40)	G1	0 (0)
G2	0 (0)	G2	0 (0)
G3	0 (0)	G3	0 (0)

1 fx/week

8 (80%) pz mammella sx constraints cuore: V1.5 Gy<1 = 1 (13%) ; <5 = 3 (38%); <10= 2 (25%); <15= 1 (13%). V7Gy <1= 5 (63), < 2= 1 (13%); <5= 1 (13%).

Constraints polmone (tutte=10pz) : V8 Gy<10= 6 (60%); <13=1 (10%); <6= 1 (10%); <5= 1 (10%); <2= 1 (10%)

5 fx/week

5 (55%) pz mammella sx constraints cuore: V1.5 Gy<5=2 (22%); <6=1 (11%); <102 (22%). V7Gy <1= 3 (33%); <5=1 (11%); <7=1 (11%).

Constraints polmone (tutte=9pz): V8 Gy< 2= 11 (11%); <5=3 (33%); <6=1 (11%); <8=1 (11%); <10=3 (33%).

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ADJUVANT BREAST CANCER RADIOTHERAPY IN A PATIENT WITH DBS (DEEP BRAIN STIMULATION) DEVICE FOR PARKINSON DISEASE: CASE REPORT

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Aims. To evaluate the management of a patient with DBS (Deep Brain Stimulation) device for Parkinson disease treated with adjuvant radiotherapy (RT) after conserving surgery for breast cancer.

Methods. A 69 years old woman with a DBS (Deep Brain Stimulation) device for Parkinson disease presented to our department for adjuvant RT after left lumpectomy. The device was placed in the upper outer quadrant of the residual left breast. The planned treatment was delivered with conventional technique with 6 MV photons reaching the total dose of 5000 cGy to the left breast in 25 daily fractions. All radiation beams avoided the device's pump and leads. The device was turned off during the dose delivery of each RT fraction. A dedicated engineer from the device manufacturing company evaluated the correct functionality of the device once a week throughout the radiation treatment and a report of its functionality was elaborated with particular attention to battery level.

Results. From 11th October 2022 to 15th November 2022 the patient was treated with adjuvant RT to the left breast with the planned dose without any interruptions and showing only mild skin toxicity (G1). The device received a maximum dose of 5000 cGy. The device was evaluated weekly as protocol without showing mechanical or electromagnetic alterations.

Conclusions. Our experience confirms the feasibility and security of an adjuvant RT after breast conserving surgery in patient with Parkinson device sited inside the treatment field without the need to relocate it. Our results are based on one case and further study is encouraged.

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EVALUATION OF SKIN ACUTE TOXICITY OF VOLUMETRIC MODULATED ARC THERAPY USING SIMULTANEUS INTEGRATED BOOST IN THE ADJUVANT TREATMENT OF BREAST CANCER. OUR EXPERIENCE

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INI S. p. a.

Aims. We aimed to evaluate the acute dermatological adverse effects using volumetric modulated arc therapy using simultaneous integrated boost (SIB-VMAT) for early breast cancer patients (pts). We compare acute toxicity between these pts and others treated with 3D conformal radiotherapy followed by sequential boost (3DCRT-SB).

Materisls and Methods. Clinical records from 81 consecutive pts (Table 1) with breast cancer treated in our department with adjuvant radiotherapy from January 2020 to January 2023 were retrospectively analyzed. 41 pts were treated with volumetric modulated arc therapy with simultaneous integrated boost, while 40 pts were treated with conformal radiotherapy followed by boost. In the SIB-VMAT group 33 pts were treated with 50 Gy to the whole breast (WB) with additional daily concomitant boost of 0.30 Gy to the surgical cavity (2.30 Gy/25 fractions) while 8 pts were treated with 42.5 Gy (2.66 Gy/16 fractions) to the whole breast and 51.2 Gy (3.2 Gy/16 fractions) on the tumor bed using simultaneous integrated boost. In the 3DCRT-SB group 24 pts were treated with 50 Gy to the WB (2.0 Gy/25 fractions) followed by a boost dose of 10 Gy in 5 days delivered on the tumoral bed, while 16 were treated with 42.5 Gy (2.66 Gy/16 fractions) followed by a boost dose of 10 Gy (2.5 Gy/4 fractions) on the surgical cavity. Acute skin toxicity was assessed by physical inspection during and at the end of radiotherapy and was described and graded according to the RTOG scale.

Results. 31 pts had grade 1 radiation dermatitis while 12 pts had grade 2, only 3 pts had grade 3. 44% of all 41 pts in SIB group had grade 1 dermatitis (16 treated with conventional radiotherapy, 2 with Hypofractionated schedule), while 33% of all 40 pts in non-SIB group had grade 1 dermatitis (6 with standard dose, 7 with Hypofractionated regimen) (p=0,31). 17% in SIB-VMAT group had grade 2 dermatitis (5 treated with conventional RT, 2 with Hypo fractionated RT), while 12.5% in 3DCRT-SB, all treated with standard dose. (p=0,57). In SIB group there was no patient with grade 3 toxicity while 3 pts in non-SIB group had grade 3 dermatitis, all treated with standard dose (5%, p=0.14).

Conclusions. Our findings suggest that no significative difference in acute toxicity was found between the two groups. Grade 3 skin acute toxicity did not occur in the SIB-VMAT group . However longer follow-up and more pts are needed to evaluate late toxicity.

Table 1. Patient's characteristic.

		VMAT-SIB		3D CRT-SB	
		Standard	Hypo	Standard	Hypo
Age (median)		61 aa		61 aa	
Histology					
	Duttal	37		32	
	Lobular	3		3	
	Other	1		5	
Tumor Stage					
	pTis	3		6	
	pT1N0	25		22	
	pT1 N+	6		4	
	pT2N0	7		8	
Surgery					
	Lumpectomy	2		0	
	Quadrantectomy	3		7	
	Quadrantectomy+BLS	33		28	
	Quadrantectomy+Lymphadenectomy	3		5	
Chemotherapy					
	Yes	9		10	
	No	32		30	
Radiation dermatitis (End of treatment)					
	G0	12	4	10	9
	G1	16	2	6	7
	G2	5	2	5	0
	G3	0	0	3	

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ROLE OF PROBIOTICS IN THE PREVENTION OF GASTROINTESTINAL AND GENITOURINARY TOXICITIES IN PATIENTS UNDERGOING PELVIC RADIOTHERAPY

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Aims. A significant proportion of patients undergoing pelvic radiotherapy will develop gastro-intestinal (GI) and urinary (GU) disorders during treatment. Probiotics such as Lactobacillus Rhamnosus GG have been shown to reduce the frequency and severity of side effects as well as to improve response to cancer treatment and patients' quality of life. The primary aim of this study is to evaluate the effect of probiotics on treatment-induced GI and GU toxicities during pelvic irradiation on 64 patients who performed radiotherapy at the Radiation Oncology Unit of Univeristy of Catania in 2022.

Methods. For this study we enrolled 64 patients (PS ECOOG 0-1) with gynecological (17 patients), rectal (19 patients) or prostate cancers (28 patients), who performed conventionally fractionated radiotherapy to a total dose to the pelvis between 45-54 Gy and an average dose of 50 Gy, with or without chemotherapy. Chemotherapy schemes included cisplatinum or fluoropyrimidine (5-FU

or capecitabine). Out of 64 patients, 29 received supportive therapy with Lactobacillus Rhamnosus GG, 2 cp per day, while 35 did not receive supportive therapy. Patients were educated to record their symptoms in standardized diaries on daily basis. Then, we evaluated side effects such as diarrhea, abdominal pain, constipation, weight loss, dysuria and non-infective cystitis, according to CTCAE 5.0, during the treatment course and 60 days after completion.

Results. During treatment course, the intervention group showed significant reduction in frequency and severity of side effects compared to the control group (8% *vs* 22,2%); 60 days after completion, the proportion of patients with grade 2 and 3 GI (diarrhea, constipation, abdominal pain) and GU (dysuria and cystitis) toxicities was highly reduced in the intervention group (5,3% *vs* 25,5%). These results suggest that probiotics may have an important role in the prevention of genitourinary and gastrointestinal toxicities associated with radiotherapy in cancer patients.

Conclusions. The results of this study suggest that the intake of probiotics, in particular Lactobacillus Rhamnosus GG, during pelvic radiotherapy can reduce the frequency and severity of GI symptoms, improving patients' quality of life, furthermore it can also improve response to cancer treatment thanks to its ability to modulate the microbiota.

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POST MASTECTOMY RADIATION THERAPY AFTER ADM-PREPECTORAL IMPLANT POSITIONING: A SINGLE CENTER'S PRELIMINARY EXPERIENCE

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Aims. Recently, among advancements in oncoplastic breast surgery, the use of acellular dermal matrix (ADM), allows more easy placement of breast pre-pectoral implants. ADM-pre-pectoral implants (ADM-ppi) have better aesthetics results and less postoperative pain. It follows that ADM-ppi is becoming more common. In this setting, it is useful to collect toxicities data in patients with ADM-ppi undergoing to Post Mastectomy Radiation Therapy (PMRT).

Materials and Methods. From November 2021 to March 2023, at our Center, every breast cancer patients (pts) treated with mastectomy, immediately reconstructed with ADM-ppi and receiving PMRT on chestwall +/- RNI were considered for the analysis. CTVs and Organs At Risk definition were based on ESTRO/ACROP guidelines for PMRT. RT was delivered with 3DCRT (1/5 pts) or VMAT. Capsular contracture grading of the breast implant were collected according to the Baker classification. Toxicity was registered according to CTCAE v 5.0.

Results. 5 pts with ADM-ppi underwent to conventional RT on chestwall. Median age was 52 years old (46-62). 3 pts received a total dose of 50 Gy in 25 fractions (according to literature data in this setting). Due to focal margin involvement, 2 pts continued RT with a sequential boost of 16 Gy/8frs on surgical bed. 2 pts had been treated with chemo pre-PMRT, 1 pt in neoadjuvant setting and the other in adjuvant set. All pts were treated with adjuvant endocrine-therapy. Median follow-up was 8 months (1-15). No RT interruption were reported. A capsula contracture G III according to Baker classification was recorded 6 months after PMRT-3DCRT plan in a pt that wasn't previously treated with chemo; the pt showed erithema, chestwall's skin oedema, clinically irregular surface and chronic pain (G3 CTCAE toxicity). She has to undergo to implant substitution. In another case we reported a CTCAE G2 toxicity 3 moths after PMRT-VMAT plan, this pt had post-surgical oedema and mastitis; in all other pts no toxicity greater than G1 was reported.

Conclusions. Although the short-term follow up did not allowed any conclusion, our preliminary data show that PMRT in pts with ADM-ppi is feasible with an higher acute e sub-acute toxicities (40% G2-G3), without relation to RT-tecnique and boost administration. According to literature data PMRT seemed not to be the only risk factor for unsatisfactory postoperative outcomes in ADM-ppi but more clinical data is needed.

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3DCRT IN FAST FORWARD PROTOCOL

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Aims. To evaluate toxicities and clinical outcomes in early breast cancer patients treated with Fast Forward adjuvant radiotherapy using 3DCRT technique.

Methods. we analized early breast cancer patients treated with adjuvant RT following conservative surgery. Toxicities and clinical outcomes were prospectively collected at baseline, during RT (acute), ≤4 weeks after RT (subacute). Clinical outcomes evaluated symptoms domains and skin alterations. Toxicities were scored according to RTOG scale. Besides we evaluated, the association from neoadjuvant/adjuvant chemotherapy, sup-

portive care, RT and skin alterations using 3D conformal RT (3DCRT).

Results. From December 2022 to April 2023 30 patients were treated, according to Fast Forward scheme, using 3DCRT techniques; Median Age was 64 years (range 51-85); 80% (24/30) of patients had histological diagnosis of N.S.T., 6,67% (2/30) Papillar, 10% (3/30) with Neuroendocrine component and 3,34 (1/30) Mucinos. Only 33,34% (10/30) patients did chemotherapy (4 adjuvant and 1 neoadjuvant). 90% (27/30) of patients had hormonaltherapy. Patients were treated with 26 Gy in 5 fractions. Only 6,67% (2/30) of patients had mastodynia, 6,67% (2/30) of patients had scar pain, 3,34% (1/30) of patients had dimpled skin, 33,34% (10/30) of patients had erithema ≤G2, 1 patient lost of sight.

Conclusions. Fast Forward scheme is feasible using 3DCRT with minimal toxicities.

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CLINICAL AND COSMETICS OUTCOMES IN PATIENTS TREATED WITH FAST-FORWARD SCHEDULE: OUR EXPERIENCE

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Aims. The aim of this study is to evaluate toxicity rates and cosmetic outcomes in early stage breast cancer patients treated at our institution with conservative surgery followed by whole breast ultra-hypofractionated radiotherapy.

Patients and Methods. From December 2022 to May 2023, we enrolled 35 patients with early-stage breast cancer, with ages ranging from 50 to 80 years (median age 64 years). 82.3% of patients had Invasive Ductal carcinoma, 8.7% had Papillary carcinoma, 4,3% had Mucinous carcinoma and 4.3% had Neuroendocrine component. 82.6% of patients were LUMINAL A, 4.4% were LUMINAL B and 13% of patients were HER2 positive. 4.3% of patients were treated with neoadjuvant chemotherapy and 13% with adjuvant chemotherapy. All patients received 26 Gy in 5 daily fractions, 5.2 Gy per fraction. During treatment, the patients underwent support therapy with hyaluronic acid-based cream, applied twice a day for the entire period. Out of the total of patients, 91.3% were treated with 3D-cRT technique and the rest with VMAT technique. The primary endpoints were clinical and cosmetic outcomes during and after treatment. We performed outpatient clinical evaluation at baseline, the day of the end of radiotherapy and at follow-up (30 days post-RT). Toxicities were evaluated according to the RTOG criteria for skin and subcutaneous tissues.

Results. In our population study, at baseline evaluation, no patients had erythema or signs of skin inflammation. At the end of the treatment, only one patient showed mild signs of skin toxicity (slight erythema).

During follow-up outpatient clinical evaluation (30 days post-RT) we observed erythema G1 in 26% of patients, 8,7% had pain G1 (such as scar or breast pain) and 13% showed one of the following G1 toxicities: nipple retraction, dimpled skin or scar fibrosis. Only one patient was lost in follow-up.

Conclusions. At 30 days after RT no patient manifested toxicities greater than G1, supporting the safety of ultra-hypofractionation in terms of clinical and cosmetic outcomes. Our results are consistent with the literature. Based on these data, we are hopeful that longer follow-up will confirm the cosmetic outcomes of this schedule.

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ULTRA-HYPOFRACTIONED WHOLE BREAST RADIOTHERAPY: A MONOINSTITUTIONAL EXPERIENCE IN A RETROSPECTIVE SERIES OF 17 PATIENTS

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Aims. To evaluate CTV coverage and respect of dose constraints in adjuvant ultra-hypofractioned whole breast radiotherapy after primary surgery for early breast cancer in a retrospective series of 17 consecutive patients (pts).

Methods. Between December 2021 and May 2023, 17 consecutive pts, median age 79 yrs, Inter Quartile Range (IQR) 76-84 yrs, received adjuvant ultra-hypofractioned whole breast radiotherapy after primary surgery for early breast cancer with the "Fast Forward" schedule 26 Gy in 5 fr at 5,2 Gy/fr +/- tumor bed boost of 10 Gy in 5 fr at 2 Gy/fr. Patient characteristics are reported in Table 1. All pts were treated with 3D-CRT including the outline of breast/chest wall to define clinical target volume with planning target volume (PTV) encompassed by medial and lateral tangential beams. The beam energy was 6 MV Photon. Prescribed dose was 26 Gy in 5 fr at 5,2 Gy/fr to whole breast +/- tumor bed boost up to 10 Gy in 5 fr at 2 Gy/fr in 1 patient. The treatment plan was optimised to ensure >95% PTV receiving 95% of dose, <5% PTV receiving >=105%, <2% PTV receiving>=107% and a Dmax <110% of prescribed dose. CTV to PTV margins

were 6 mm; median CTV volume was 670.9 cc (IQR: 554-916 cc) and median PTV volume was 936.1 cc (IQR:784-1100 cc). Daily Portal Imaging was taken in all pts. Assessment of toxicity was evaluated (CTCAE V 4.0) during and at the end of treatment.

Results. CTV Coverage was: V95 median= 97.7% (IQR 96.5-98.6 %); median maximum dose was 110.3%. All dose constraints (Fast Forward Study Protocol) to organs at risk were respected. For all left breast treatments heart dose constraint was V7 <5%, median for all pts: 3.5% (IQR 2.5-5.3%); V1.5 <30%, median for all pts: 13.5 %(IQR 9-18.7%); mean dose IQR 0.97-1.81 Gy. For all treatment ipsilateral lung dose constraint was V8 <15%, median for all pts: 15.4 %(IQR 9.9-16.4%); mean dose 3.94 Gy. All pts completed treatment with excellent compliance. Median follow-up was 4 months (IQR 1.7-4.5) range: 1-16 months. A very low toxicity profile was observed (CTCAE V 4.0): there were no ≥ G2 acute/late reactions.

Conclusions. The ultra-hypofractioned regime used in our series showed excellent coverage of the CTV with respect of the dose constraints also in left breast treatments. Moreover, this schedule allows to obtain excellent compliance with a low toxicity profile. A larger series of patients is needed to confirm these preliminary data.

Table 1.

AGE (years)	
median (IQR)	79
range	65-86
60-69	1
70-79	8
>80	8
tumour grade	
1	5
2	7
3	4
risk group	
low (G1-2)	12
high (G3)	4
primary surgery	
breast conservation with oncoplastic tecl	17
sex	
female	17
male	0
side primary tumour	
left	11
right	6
maximal extent axillary s	
sentinel node biopsy guided	15
unknown	1
other	1
pathlogical	
positive	1
negative	15
unknown	1
hystological type	
infiltrating ductal	3
lobular	2
mixed	1
other	11
pathological tumour size	
median (IQR)	11
pathological T stage	
T1mi	0
T1a	3
T1b	4
T1c	7
T2	3
T3	0

ER and HER2 status	
ER positive HER2 pos:	3
ER positive HER2 nega	10
ER negative HER2 pos:	0
ER negative HER2 nega	4
progesterone receptor sta	
positive	12
negative	5
Lymphovascular invasion	
present	4
absent	9
uncertain	4
neoadjuvant chemotherapy	
yes	0
no	17
adjuvant therapy received	
chemotherapy	0
endocrine therapy	8
trastuzumab	0
boost given	
yes	1
no	16
boost dose	
10 Gy	1
16 Gy	0

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LONG-TERM RESULTS OF THE TARGIT A-IORT IN OUR CENTER

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Aims. During the last decade, partial breast irradiation (PBI) has gained traction as a relevant treatment option for patients with early-stage low-risk breast cancer after breast-conserving surgery. The TARGIT-A prospective randomized trial compared a "risk-adapted" intraoperative radiotherapy (IORT) approach with 50-kv X-rays (INTRABEAM®) as the PBI followed by optional whole-breast irradiation (WBI) and conventional adjuvant WBI in terms of observed 5-year in-breast recurrence rates.

Methods. In our company, the first IORT treatment on the breast was performed in October 2015, since then during these years, the IORT has increasingly established itself as a breast treatment modality thanks also Breast Unit.

Results. The Histogram defines year by year from 2015 to today the amount of treatments (IORT), approach with 50-kv X-rays (INTRABEAM), performed in our Center. The local recurrence rate was around 2 %, and is within the non-inferiority rate of PBI TARGIT-IORT compared to WBRT.

Conclusions. Taking into account all of the criticism on the TARGIT-A trial, also our experience confirms that PBI with TARGIT-IORT is a valid alternative to WBRT, if TARGIT-IORT is performed in a well-selected series of patients, including low-risk early Breast Cancer.

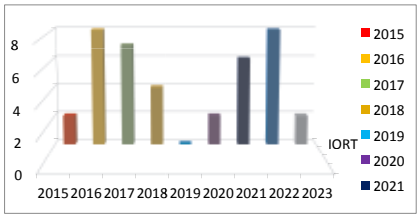

Figure 1.

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FIVE-FRACTION RADIOTHERAPY FOR RECURRENT BREAST CANCER: A CASE OF SATISFYING LOCAL CONTROL OF DISEASE

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Aims. Breast cancer (BC) is the most frequently diagnosed in women nowadays. When BC is linked to BRCA-1 gene mutations, it is associated with a worse prognosis due to its aggressiveness. We present the case of a 45 years-old BRCA1 mutated-patient, diagnosed with a triple negative BC localized in the right breast in September 2018.

Methods. The patient underwent neoadjuvant chemotherapy and then radical mastectomy with prophylactic mastectomy on the left side, with initial complete pathological remission at histological report (May 2019). No adjuvant treatments were performed. At the end of 2022, a 23 mm - node appeared at the upper-inner quadrant of the right chest wall. A biopsy led to the diagnosis of recurrence of the triple negative BC, with PD-L1 positivity. A CT-scan confirmed a pathological exophytic nodular lesion in the soft tissue, just medial to the right breast implant, with diffuse skin thickening and small subcutaneous extension. An internal mammary lymph node seemed to be involved, without other nodal or distant metastases. A nodular appearance was appreciable (Figure 1), and reported as painful, with erythematous halo.

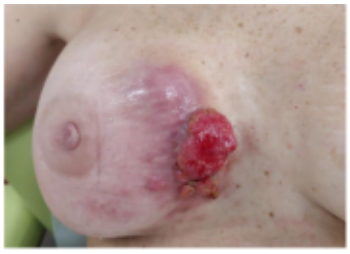

Figure 1. January, 2023, the exofitic lesion in its initial appearance.

The patient was considered unsuitable for surgery, so a Nab-Paclitaxel + Atezolizumab chemotherapy was started in January 2023 and the lesion started to blood. At that time, we discussed the case with the Multidisciplinary team and we were asked to perform a palliative external beam radiation treatment (EBRT). We considered local extension and external appearance of the lesion, the need for a local control in addition to systemic therapy and the aim of a shortest duration of the treatment: a total dose of 26 Gy in 5 fractions to the whole chest wall and a simultaneous boost at 30 Gy were then administered, with daily image guidance, completed on 03/02/2023. EBRT was performed through volumetric modulated arc therapy technique.

Results. The patient continued to be medicated at our Department: after a month, the exophytic lesion was no longer appreciable, but only a flat, non-oedematous one (Figures 2-5).

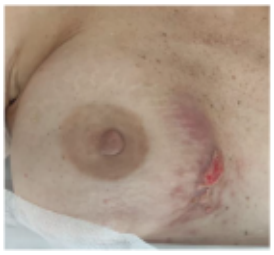

Figure 2. The lesion two weeks after EBRT was concluded.

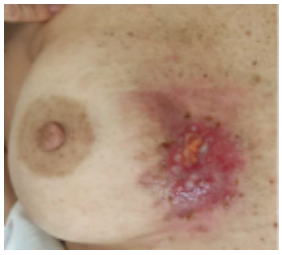

Figure 3. March, 2023. A month after EBRT was concluded

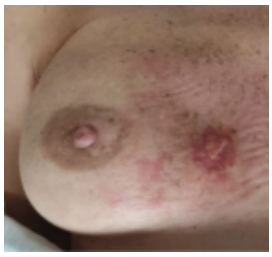

Figure 4. April, 2023.

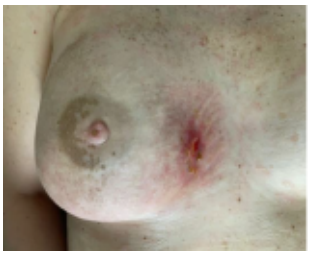

Figure 5. May, 2023.

A CT-scan was performed in March 2023, compared to the previous one: the nodular lesion and skin thickening, were no longer evident, only a residual thickening of

the adipose and skin layers, without clear nodular aspects was reported. (Figure 6)

Conclusions. Our case confirms the importance of locoregional treatment, integrated with systemic one, with the aim of both disease control and symptoms relief.

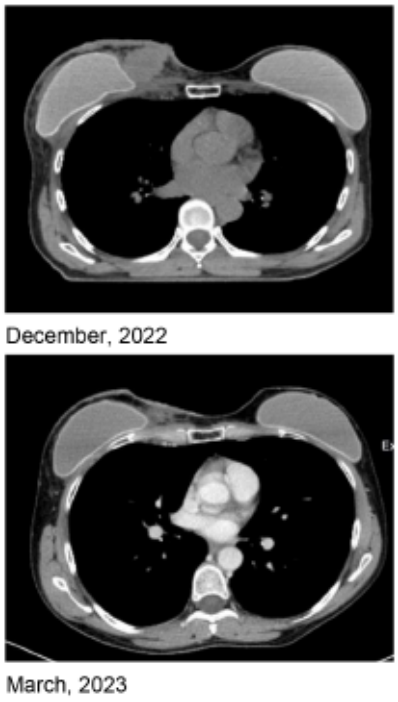

Figure 6. CT-scan appearance of the lesion before and after EBRT.

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DEEP INSPIRATION BREATH HOLD RADIOTHERAPY VS FREE BREATHING RADIATION THERAPY: IS IT BENEFICIAL TO HEART AND IPSILATERAL LUNG?

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Aims. To evaluate the feasibility of deep inspiration breath hold (DIBH) versus free breathing (FB) and their impact on radiation dose to the heart and to the ipsilateral lung in patients with left side breast cancer undergoing to adjuvant Radiotherapy.

Methods. Ten consecutively patients with left breast carcinoma were enrolled from 18/01/2023 to 22/02/2023. During the simulation we performed a CT scan in FB and a study of respiratory motion with a DIBH CT for all patients. During DIBH CT it was used Real Time Position Management (RPM; Varian Medical System, Palo Alto, CA) to have a reference surface. Gating window was initially defined as 5 mm and then personalized on respiratory study. During DIBH treatment it was used portal imaging to evaluate target position. Tangential fields were used with field in field technique to optimize the dose distribution. We used both conventional and hypofractionated schedule (consisting in 20 fractions), converting these last one in biologically effective dose. The constraints analyzed in this study are: mean dose, V25, V10, V5 of heart and V20, V10, V5 of ipsilateral lung.

Results. All 10 patients were treated with DIBH with good compliance and no interruption of the treatment. The mean heart dose was 2.97 in FB *vs* 1.54 Gy in DIBH with an average reduction of 50%. The mean ipsilateral lung dose was 6.7 in FB *vs* 5.5 Gy in DIBH with an average reduction of 18%. Analyzing DVHs the mean values of V5, V20 and V25 at the heart and the lung were decreased with the DIBH *vs* FB.

Conclusions. DIBH is a well-tolerated technique and can lower dose to the heart and ipsilateral lung without penalizing the coverage of the target.

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S.MA.RT OBSERVATIONAL STUDY: "MATRIXIN GEL EFFICACY, SAFETY AND TOLERABILITY EVALUATION IN RADIOTHERAPY": OUR EXPERIENCE

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Aims. To assess efficacy, safety, acceptability and tolerability of Matrixin gel: skin toxicity from radiation/pharmacological treatment

Methods. We collect data from 25 patients with breast cancer undergoing adjuvant radiotherapy. This is a prospective open-label study on the evaluation of efficacy, safety, acceptability and tolerability of MatriXin Gel in dermatological conditions with various degrees of radiodermatitis. The enrolled patients underwent a simulation CT scan on the day of the visit (T0), and then to adjuvant radiotherapy (RT). The patients used the product two times a day. During the RT period we visited the patients every week to evaluate skin alterations, and we collected data after 3 weeks (T1), after 5 weeks (T2) and at the end of the course (V4) using the Radiation Therapy Oncology Group (RTOG) score. The evaluation of treatment tolerability was evaluated through the Investigator Tolerability Assessment (ITA) score, according to this

scheme: 0 (very poor tolerability, necessary interruption of the application), 1 (fair tolerability, reported some disturbances during the application), 2 (good tolerability, reported only a few mild and transient disturbances), and 3 (Excellent tolerability, no disturbances).

Results. The data show that the use of MatriXin gel protects against the onset of grade 3 or higher radiodermatitis. At about halfway through treatment (T1), only one patient showed grade 2 erythema. At T1, five of the remaining patients had G1 toxicity, while the others did not show any notable side effects. At the end of treatment (T2), 10 patients had no side effects, 12 had grade 1 erythema and epitheliolysis, and only three patients had grade 2 toxicity. One week after the end of treatment, 10 patients had G1 toxicity, five showed G2 erythema and epitheliolysis and the rest of patients showed no side effects. The degree of tolerance to the use of Matrixin gel was good (ITA 2).

Conclusions. MatriXin Gel has demonstrated good efficacy in the prevention of grade 3 or greater radiodermatitis, without treatment interruption. Further studies are needed for more consistent data.

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WHOLE BREAST IRRADIATION WITH SIMULTANEOUS INTEGRATED BOOST (SIB) USING VOLUMETRIC MODULATED ARC THERAPY (VMAT): OUR EXPERIENCE

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Aims. We retrospectively evaluated the cosmetic outcome in breast cancer patients treated with simultaneous integrated boost (SIB) using Volumetric Modulated Arc Therapy (VMAT) at our facility.

Methods. Twenty Breast cancer patients (11 left, 9 right sided), treated between April 2021 and November 2022, were selected for this study. Sixteen patients had invasive ductal and four invasive lobular histology of early stage breast cancer. Three patients received neoadjuvant chemotherapy, five adjuvant chemotherapy and twelve patients received hormone therapy (five of whom after adjuvant chemotherapy). All patients underwent VMAT-SIB to irradiate the whole breast with concomitant boost irradiation of the tumor bed. Doses to whole breast and surgical bed were 50 Gy and 60 Gy respectively, delivered in 25 fractions. Plans were optimized with a maximum of four partial arcs, spanning up to 210 degrees. The organs at risk such as ipsilateral and contralateral lungs, heart, left anterior descending artery (LAD) and contralateral breast were spared as much as possible. Each patient underwent clinical examination every week during the Radiotherapy (RT) treatment. Follow up was performed every three months during the first year, then every six months. Acute and late toxicity were evaluated according to the RTOG grading scale and cosmetic outcome using Harvard NSAPB-RTOG scoring scale by visual scale.

Results. All women concluded their treatment without interruptions. Acute skin G0, G1 and G2 toxicity was in 17, 2 and 1 patients, respectively. None of patients presented acute skin G3 toxicity. During follow-up, no late side effects were registered. All patients had minimal difference in the size and shape of the treated breast with respect to the untreated breast. Only two over 20 patients had fluid accumulation within the breast without changing the appearance.

Conclusions. Our clinical results support the use of SIB-VMAT as a safe and effective RT option in patients with early breast cancer after conservative surgery with a good cosmetic result and excellent satisfaction for all patients.

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SUPPORTIVE TOPIC THERAPY IN PATIENTS TREATED WITH ADJUVANT THORACIC RADIATION THERAPY

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Aims. To evaluate clinical outcomes in breast cancer (BC) patients (pts) underwent adjuvant radiotherapy (RT) and treated with AVEC MOUSSE and AVEC ÉMULSION to prevent radiation dermatitis (RID).

Material and Methods. An Observational study was conducted in pts with histologically confirmed BC diagnosis scheduled to receive adjuvant breast RT. Patient's age was from 18-80 and the Karnofsky index (KPS) was in the range 100-80. Pts with known psychiatric pathology and/or cognitive deficits, hypersensitivity to the used excipient, and pregnant women were excluded. The primary aim is to evaluate the efficacy of AVEC MOUSSE and AVEC EMULSION to treat and avoid the onset of RID. Secondary aim is to evaluate side effects and quality of life. Pts were divided in two heterogeneous cohorts:

Group A, treated with Corticosteroid topical therapy and neutral pH cleaner and Group B treated with Avec Mousse and Avec Emulsion twice a day. Skin toxicities were evaluated after half scheme, at the end and 15 days post RT by clinical evaluation, using RTOG scale and imaging report.

Results. From December 2021 to October 2022 we enrolled 100 pts underwent adjuvant RT at our department. 99 of them were female and 1 male. Mean Age in Group A was 56.5 years (range 33-80), Group B was 52,5 years (range 25-80). Mean KPS was 90 (range 100-80). 30 pts in Group A and 31 in Group B received Hypofractionated RT (4005 cGy/267cGy die), the remaining pts underwent 5000 cGy/200 cGy die. In group A, 32 pts had G1 RID, and 8 G2 at mid treatment visit. At the end of RT, G3 skin toxicity was in 6 pts, G2 in 25 and G1 in 18. During the follow up visit no G3 skin toxicity was registered. 23 and 17 pts reported G1 and G2 skin toxicities respectively. In Group B acute RID G1 after half scheme of RT arose in 20 cases and G2 in 6. At the end of treatment, toxicities were G3, G2, G1 in 4, 22 and 21 pts respectively. 15 days post RT, 19 pts reported G1 toxicities and G2 in 6 cases.

Conclusions. Supportive AVEC therapies seems to be well tolerated for BC pts without onset of side effects. It promotes reparative processes ensuring the balance and repair of skin tissues. Further study could be useful to evaluate the effect in BC treated with new hypofractionated schemes.

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HYPOFRACTIONATED ADJUVANT RADIOTHERAPY(RT) ACCORDING TO FAST PROTOCOL IN ELDERLY PATIENTS (PTS) UNDERWENT CONSERVATIVE SURGERY FOR BREAST CANCER

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Aims. evaluate FAST protocol feasibility and toxicity in elderly breast cancer pts.

Methods. from January '22 to March '23 ten elderly breast cancer pts, (median age 77 years), were submitted to adjuvant radiotherapy, according to FAST protocol. All of them underwent conservative surgery, 8 with sentinel node sampling and 2 with axillary nodal dissection. Nine of them received aromatase inhibitors as hormonal adjuvant therapy and 1 no therapy for comorbidity contraindication. None underwent chemotherapy. Median Karnofsky performance status was 90. Pts characteristics are reported on Table1. Median time from surgery to RT was 11 weeks. Total dose of 28.5 Gy was erogated with 3D field in field technique in 5 weekly fractions. This thecnique has been chosen with the aim of minimizig dose hot spots and better respect protocol contraints, especially for heart and lung, in consideration of possible comorbidity. Check film preceded each fraction. Topic prophylactic treatment was prescribe to all pts, from the beginning of RT, avoiding skin toxicity, wich has been valued, according to RTOG scale, at treatment end and after 1 and 6 months.

Results. all pts well tolerated RT and no treatment interruption occurred. No G3 toxicity has been detected. At RT completation 2 pts reported G0 toxicity, 5 G1 and 3 G2. After 1 month only G0 toxicity was detectable for all of them and the same after 6 months for the 4 patients for whom this evaluation was avalilable.

Conclusions. in elderly breast cancer pts hypofractionated FAST RT demonstrated to be feasible and well tolerated, improving quality of life of pts who considerably appreciate weeky fractions.

Table 1.

Age	pT	pN	G	ER	PgR	KI67	Her2	Histology	Margins
78	1c	0	2	>90%	>90%	30%	Negative	Ductal	Negative
74	1c	0	2	>90%	>90%	25%	Negative	Ductal	Negative
86	2	0	2	>90%	Negative	40%	Negative	Ductal	Negative
83	1c	0	2	>90%	>90%	30%	Negative	Ductal	Negative
77	1c	0	2	>90%	15%	30%	Negative	Ductal	Negative
72	1a	0	2	100%	80%	10%	Negative	Ductal	Negative
76	1c	1a 1/7	3	Negative	Negative	60%	Negative	Ductal	Negative
76	1a	0	1	100%	Negative	20%	Negative	Ductal	Negative
87	1c	0	3	>90%	20%	35%	2	Ductal	Negative
86	2	0	3	>90%	Negative	10%	Negative	Lobular	Negative

P196

MULTICENTER RETROSPECTIVE STUDY OF PATIENTS WITH LOCALLY ADVANCED RECTAL CANCER UNDERGOING NEOADJUVANT RADIOCHEMOTHERAPY WITH OR WITHOUT RADIATION DOSE INTENSIFICATION: PRELIMINARY RESULTS

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Introduction. Preoperative radiochemotherapy (RCHT) is the standard treatment for locally advanced rectal cancer (LARC). The evidence that pCR is a favorable independent prognostic factor for overall survival (OS) propted to investigate the role of RCHT intensification of. Other than intensifying systemic treatments, it is possible to enhance preoperative treatments by escalating radiation dose. However, currently there are no robust data directly comparing different radiotherapy (RT) dose levels in terms of downstaging and pCR. The present multicenter retrospective study aims to compare different levels of intensification of the RT dose in LARC patients.

Material and Methods. The present multicenter retrospective study involves 11 Centers. The primary objective is to evaluate whether the increase of RT dose is associated with an increase in the rate of pCR. The secondary objectives are to compare downstaging, acute and late RT-related toxicity, perioperative toxicity, local and distant recurrence, and OS between the 2 regimens.

Results. the results of 649 patients are herein reported. Patients were treated with concomitant RCHT with (329) or without (320) a RT boost. Dose boost range was 53.8-56 Gy. Patients were operated on after a median time of 9.7 weeks (IQ range 5-16). The median follow-up was 50 months. The overall pCR rate was 23.6% (153 patients). In the subgroup analysis pCR was 29.8% (98) and 17.2% (55) in the boost and no-boost group, respectively (p=0.00). The pCR rate stratified by interval to surgery (≤7, 8-10, 11-12, ≥13) was: 10%, 24%, 27.2%, 35%. In the subgroup analysis, the pCR stratified by interval to surgery was: 10.5%, 27.6%, 29.6%, 41.4%, and 10%, 20.8%, 22.7%, 19.4% for boost and no-boost group, respectively (p=0.00). At the univariate analysis, patients treated with boost had a higher rate grade 3+ acute gastrointestinal toxicity (6.4% versus 2.2%; p=0.08). Globally, Local relapse occurred in 62 patients (9.6%) and the 5-year local relapse-free survival rate was 88.1%. In the overall population, the median OS was 12.8 years, and the 5-year OS was 79.6%.

Conclusions. preliminary results of the present study suggest that RT dose-intensified regimens in LARC might significantly increase pCR rate, even if at the cost of higher GI toxicity. While pCR seems only partially improved by prolonged time to surgery in the no-boost group, a progressive and significant pCR improvement in patients treated with boost over time was observed.

P197

RETRY: RADIOTHERAPY & TOTAL NEOADJUVANT THERAPY FOR RECURRENT RECTAL CANCER IN PREVIOUSLY IRRADIATED PATIENTS, AN AIRO-GI PLATFORM: A MULTICENTER PROSPECTIVE OBSERVATIONAL STUDY

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Aims. Local recurrence of previously irradiated rectal cancer (LRRC) is a clinical entity with a poor prognosis. Historically, the integration of radiotherapy (RT) with surgery has led to an increase in R0 resections and thus improved survival, but unfortunately many recurrences are not amenable to surgery. The integration of chemotherapy (CHT) with advanced RT modalities and techniques, such as proton and carbon ion RT (CIRT) and stereotactic body radiation therapy (SBRT), has also opened up new therapeutic perspectives. Therefore, better therapeutic stratification of LRRC patients is needed. The aim of the RETRY trial is to assess whether CHT combined with RT in all its modalities can increase local control (LC) in LRRC patients and thus improve survival.

Methods. The core group of experts from Italian centres specialising in the management of rectal cancer and LRRC, collaborating within the AIRO group for gastrointestinal malignancies, shared their expertise during several meetings to design a prospective multicentre observational study. All adult patients with LRRC who have previously undergone pelvic RT, according to the inclusion and exclusion criteria, and who belong to the Italian centres involved in the study, will be enrolled. Patients must meet specific criteria if they are referred to CIRT.

Results. Figure 1 shows the study design. The total number of patients to be enrolled is 88 over 3 years. The primary objective is the 3-year LC rate. Secondarily, the other outcomes of survival, quality of life and resectability rates in patients undergoing surgery will be evaluated. If chemoradiotherapy (CRT) is chosen, a dose of at least

40 Gy is prescribed in conventional fractionation with fluoropyrimidine- and/or oxaliplatin-based CHT. If SBRT is chosen, the dose will vary from 35 to 40 Gy in 5 fractions, depending on clinical judgement. The latter two approaches would be evaluated with both protons and photons. The patient will then be assessed for surgery if operability is achieved. In inoperable cases CIRT 40-60 Gy relative biological effectiveness (RBE) will be prescribed in a daily fraction with dose/fraction between 3 and 4.8 Gy RBE. Subsequent CHT intensification will be evaluated at the discretion of the individual centre.

Conclusions. The RETRY trial investigates the combined effects of RT and CHT, possibly with surgery, to assess whether this combined approach can lead to a benefit in terms of survival and quality of life in patients with LRRC.

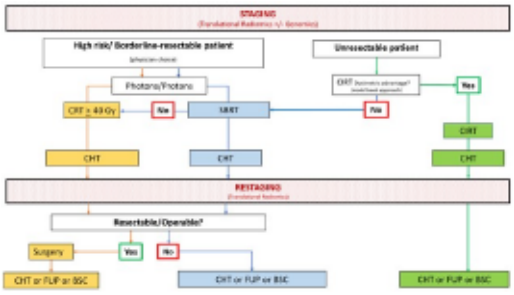

Figure 1.

P198

PRELIMINARY RESULTS OF AUTO-CONTOURING BASED ON A DEEP-LEARNIG TOOL: A MULTICENTER FEASIBILITY STUDY FROM THE AIRO-ERM GROUP

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Aim. Despite the availability of contouring guidelines for Organs at Risk (OaRs) delineation, significant inter/intra-user variability has been reported, mainly correlated with prior knowledge and expertise of radiation oncologists (ROs). The aim of this multicenter analysis was to assess the impact of a deep-learning (DL)-tool for OaRs delineation in terms of ROs satisfaction and time required for manual correction of automated contouring.

Methods. Seven Italian centers enrolled patients treated for abdominal cancers (January 2022 - March 2023). Patients were simulated with or without contrast medium (CM). Both oral and intravenous CM administration was admitted. Contours of bowel bag, large and small bowel were manually delineated using the available clinical treatment planning systems. After full anonymized simulation, CT images were exported to the DL-tool for auto-segmentation of small bowel, large bowel, and bowel bag. The level of ROs satisfaction for OaRs delineation was scored with a scale ranging from 1 to 5 (1: complete recontouring; 2 major editing; 3: some editing; 4: minor editing; 5: no editing) while manual correction time was analyzed using a semi-automatic tool. Differences between groups were assessed using the Wilcoxon test.

Results. Of 78 included patients, i.v. CM alone or plus oral CM was used in 12 (15.4%) and 4 (5.1%) patients, respectively. The time for manual correction was significantly higher for images without CM for all investigated OARs: bowel bag ($p< .001$), large bowel ($p=.004$), and small bowel ($p=.007$), respectively. Even the satisfaction score was significantly lower without i.v. CM: bowel bag ($p<.001$), large bowel ($p=.033$), and small bowel ($p=.027$). The satisfaction grade was 4 or 5 in 74%, 59%, and 42% of cases for bowel bag, and large and small bowel, respectively. Higher satisfaction grades (4-5) were statistically correlated with correction time ($p<.001$). The time required for the manual correction of automatic contours was 1 minute (range 0-11), 3 minutes (range 0-18), and 3 minutes (range 0-18) for bowel bag, and large and small bowel, respectively.

Conclusions. The application of a DL-tool can significantly improve ROs clinical practice in delineating OaRs, considering the positive judgment expressed by the ROs in most cases, and the very short time required for the manual correction of automatic contours.

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INTENSIFYING TREATMENT FOR IMPROVED OUTCOMES IN LOCALLY ADVANCED PANCREATIC DUCTAL ADENOCARCINOMA: A PROSPECTIVE PHASE II STUDY OF FOLFIRINOX AND CHEMORADIATION

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Aims. To evaluate the margin-negative (R0) resection rate in borderline resectable and locally advanced unresectable pancreatic ductal adenocarcinoma (PDAC) after induction FOLFIRINOX followed by chemoradiation (CRT).

Methods. In this single-arm, phase 2 clinical trial, patients with locally advanced PDAC underwent CT scan, 18FDG PET-CT scan and a staging laparoscopy to detect occult metastasis before the treatment. Patients received four cycles of FOLFIRINOX scheme. Those without disease progression, as detected by restaging exams, proceeded to long-course CRT with concurrent gemcitabine (600 mg/m² weekly). Four weeks after the completion of CRT, CT scan and PET-CT scan were performed. Surgery was considered for patients with technically resectable tumors. The primary objective was R0 resection rate with an alternate hypothesis of 55%. Secondary objectives included progression-free survival (PFS), overall survival (OS), local progression-free survival (LPFS), metastases free-survival (MFS), and safety.Adverse events were recorded using the NCICTC scale. The trial is registered under NCT05399394.

Results. Twenty patients (37%) were excluded due to evidence of metastatic disease, leaving a total of 34 enrolled patients. Among them, 14 patients (41%) had locally advanced unresectable tumors, while 20 patients (59%) had borderline resectable disease. Five patients (14.7%) experienced disease progression after induction chemotherapy. Surgical exploration was performed in 18 patients, of whom 16 (55%) underwent radical resection.Two patients are currently awaiting surgical evaluation. R0 resection was achieved in all 16 of the 29 eligible patients (55%). The median follow-up was 17 months (range, 6 to 63). Median OS and median PFS in patients who completed CRT were 17 months (95% CI, 13 to 22) and 12 months (95% CI, 9.8 to 16.1), respectively. OS, PFS, LPFS and MFS at one-year were 88%, 53%, 80% and 65%, respectively. Resected patients demonstrated significantly longer median OS compared to non-resected patients (22.4 months vs. 13.2 months, p=0.03). The median PFS for resected patients was 14.5 months compared to 8.7 months for non-resected patients (p<0.001). Treatment-related grade 3 to 4 toxicities included neutropenia (20%), nausea and vomiting (7%), and diarrhea (4%).

Conclusions. FOLFIRINOX followed by long-course CRT in borderline resectable and locally advanced unresectable PDAC resulted in high rates of R0 resection and prolonged median PFS and median OS.

Figure 1.

P200

IS SURGERY THE ONLY CHANCE FOR PROLONGED SURVIVAL IN PATIENTS WITH PANCREATIC CANCER? SECONDARY ANALYSIS OF A MULTICENTER OBSERVATIONAL STUDY (PAULA-1)

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Aims. Radical surgery with tumor-free margins is considered the only treatment with the potential to achieve long-term survival in pancreatic cancer. Unresectable locally advanced pancreatic cancer (LAPC) is known to have an extremely poor prognosis. Although rare, there are some patients who have unexpected long-term survival, but the reason is not yet clear. We performed a secondary analysis of a multicenter observational study (PAULA-1) including only long-survivors LAPC.

Methods. LAPC patients without distant metastases and treated with chemotherapy (CHT) or stereotactic body radiotherapy (SBRT), or concurrent chemoradiation (CRT), not previously or subsequently treated with surgical resection, were included from 15 institutions. We selected long survivor LAPC (overall survival > 60 months).

Results. Overall, 419 patients were included in this analysis, and 7 patients survived > 60 months (Table 1). Four patients were treated with CRT with a total dose of 50.4 Gy in 1.8 Gy/fraction; two with CRT with a total dose of 50.4 Gy in 1.8 Gy/fraction and a sequential boost of 20 Gy in 5 fractions, and one patient with SBRT (20 Gy in 5 fraction). CRT regimens were based on gemcitabine (2 patients), gemcitabine + oxaliplatin (1 patient), folfirinox (1 patient), and capecitabine (3 patients). Median tumor diameter was 3.0 cm (range:1.8-10.0 cm) of patients with OS > 60, only one died of LAPC 79 months after treatment.

Conclusions. In our large cohort of LAPC the rate of long-term survivors was 1.6%. All patients surviving > 60 months were treated CRT and/or SBRT while the highest rate of long-term survivors was in the group of patients treated with CRT plus SBRT boost.

Table 1.

Patients		Treatment: Chemotherapy	Chemoradiation	SBRT	Chemoradiation + SBRT boost
All patients	419	65	297	48	8
Long term survivors (> 5 years)	7 (1.6%)	0 (0%)	4 (1.3%)	1 (2.0%)	2 (25%)

P201

ABSTRACT NOT PUBLISHABLE

P202

IMPACT OF NEOADJUVANT RADIOCHEMOTHERAPY TREATMENT WITH DOSE INTENSIFICATION FOR LOCALLY ADVANCED RECTAL CANCER (LARC): A MONO INSTITUTIONAL EXPERIENCE

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Aims. Aiming to improve clinical outcomes, a single-institution experience is reported in order to evaluate the impact of Mandard Tumor Regression Grade (TRG) on overall survival (OS) and the locoregional control (LC) of LARC patients treated with dose intensification and concomitant Capecitabine in neoadjuvant Radio Chemotherapy schedule.

Methods. From 2012 to 2022, patients with LARC were retrospectively analyzed. Radiotherapy was performed with a total dose of 45 Gy, 1,80 Gy/day, to the pelvic nodes and a simultaneous integrated boost (total dose 55 Gy, 2,20 Gy/day) to mesorectum. Capecitabine was administered concomitantly twice a day for 5 days/week. Toxicities were recorded by the RTOG/EORTC scale. pCR was evaluated according to Mandard tumor regression grade (TRG) and the population was divided in 2 groups: TRG1-2 and TRG3-4-5. The Kaplan-Meier method was used to estimate OS and LC both for overall patients and for the 2 groups. A P-value less than 0.05 was considered statistically significant.

Results. 178 patients were analyzed in this study, with a median follow-up of 42 months. The median patient age was 68 years. Most patients (86%) had cT3 tumors. Lower gastrointestinal toxicity was the most fre-

quent acute side-effect: 120 patients had grade 1-2 toxicity, whereas only 2 patients experienced severe toxicity. Grade-1-2 skin toxicity was reported in 45 patients and grade-3 in 2 patients. There were reported no other severe toxicities. 168 patients underwent surgery and anterior resection was performed in 106 patients (59%), followed by Transanal Endoscopic Microsurgery in 20 (12%). Among late toxicities, bowel dysfunction (G3 toxicity) was reported in 6 patients (3%). No other severe late toxicities were recorded. The 5-year OS, and LC rates were 88%, and 98%, respectively. Long-term results at 10 years showed OS and LC rates of 82% and 98%, respectively. Figure 1 shows the 5- and 10-year OS and LC for patients with TRG1-2 and with TRG3-5. Patients with TRG1-2 had better OS, with 5- and 10-year rates of 89% and 89% compared with 86% and 67%, for patients with TRG3-5, respectively. The 5- and 10-year LC rates for patients with TRG1-2 were 89% and 89% versus 86% and 67%, respectively, for patients with TRG3-5.

Conclusion. Neoadjuvant chemoradiotherapy with dose intensification in LARC patients resulted in favorable long-term oncological outcomes specially with a high pCR rate, an optimal impact of TRG on LC and OS and with an acceptable toxicity.

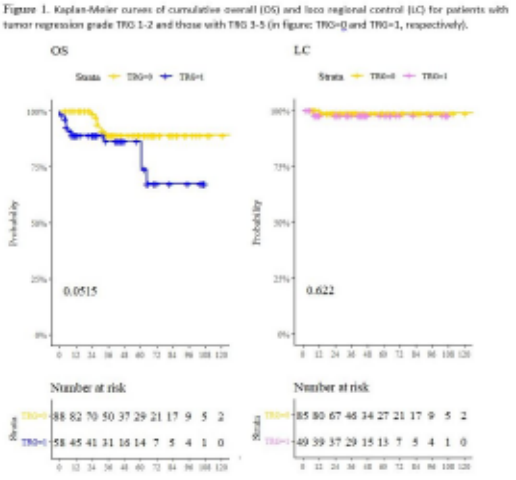

Figure 1.

P203

IMPACT OF COMBINED THERAPIES ON RESECTION RATE AND SURVIVAL OUTCOMES IN BORDERLINE RESECTABLE AND UNRESECTABLE PANCREATIC DUCTAL ADENOCARCINOMA

G.M. Petrianni[1], M. Fiore[1,2], P. Trecca[1], G. D'Ercole[2], M. Benincasa[2], E. Ippolito[1], D. Caputo,[3,4], R. Coppola[3,4], S. Ramella[1,2]

[1]Operative Research Unit of Radiation Oncology, Fondazione Policlinico Universitario Campus Bio-Medico; [2]Research Unit of Radiation Oncology, Department of Medicine and Surgery, Università Campus Bio-Medico; [3]Operative Research Unit of General Surgery, Fondazione Policlinico Universitario Campus Bio-Medico; [4]Research Unit of General Surgery, Department of Medicine and Surgery, Università Campus Bio-Medico, Italy

Aims. This study aimed to investigate the resection rate following the combined therapies and assess its influence on patient survival.

Methods. From 2008 to 2022, 3 prospective studies were conducted on borderline resectable or unresectable pancreatic ductal adenocarcinoma (PDAC) patients. They underwent chemoradiotherapy (CRT) with or without induction chemotherapy (IC). Pre-treatment staging involved CT scans, FDG-PET/CT scans, and laparoscopy with peritoneal washing. Re-evaluation using CT scans and FDG-PET/CT scans was performed after IC and 4 weeks after completing CRT to assess tumor response and resectability. The primary objective was the resection rate, and secondary objectives included progression-free survival (PFS), overall survival (OS), local progression-free survival (LPFS), and metastases-free survival (MFS).

Results. A total of 129 eligible patients (69 men, 60 women) with a median age of 64 years (range: 36–75) were included. Based on the pre-treatment workup, 39 patients (30.2%) with metastatic disease were excluded. 68 patients received IC (Gem-Ox or FOLFIRINOX). The dropout of patients is illustrated in Figure 1. Overall, 77 patients (59.7%) received concomitant CRT and were evaluated. Median follow-up was 21 months (range: 5 to 132). 38 patients (60%) underwent surgical resection, with R0 resection achieved in 97.4% of cases (37/38). Among the 77 patients undergoing CRT, median PFS was 13 months. One-year, 2-year, and 3-year PFS rates were 56%, 32%, and 22%, respectively. One-year, 2-year and 3-year LPFS rates were 83%, 68% and 60%, respectively. One-year, 2-year, and 3-year MFS rates were 65%, 40%, and 30%, respectively. Median OS was 17.5 months, with one-year, 2-year, and 3-year OS rates of 80%, 37%, and 29%, respectively. Resected patients had significantly longer median OS compared to non-resected patients (37.6 months *vs* 13 months, p<0.001). Median PFS for

resected patients was 22.5 months compared to 9.5 months for non-resected patients ($p<0.001$). Patients treated with upfront CRT had median OS and PFS of 14.6 and 9.9 months, respectively, compared to 19.2 and 17.8 months for patients treated with IC followed by CRT ($p<0.05$).

Conclusions. The resection rate was high, patients who underwent surgical radical resection had significantly longer median overall survival compared to those who did not. These findings emphasize the importance of accurate pre-treatment staging and patient selection to improve outcomes for PDAC patients.

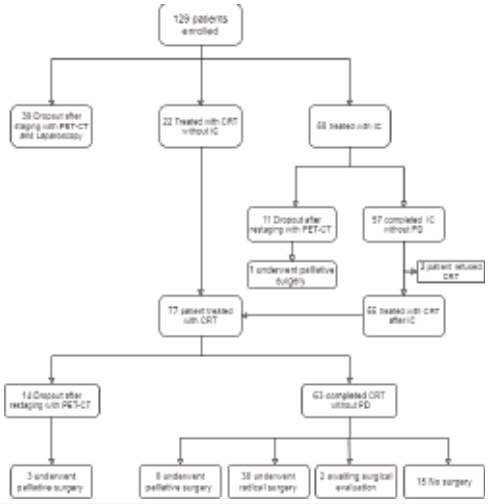

Figure 1.

P204

PRELIMINARY RESULTS OF MONO-INSTITUTIONAL EXPERIENCE IN PATIENTS WITH LIVER METASTASES TREATED WITH STEREOTACTIC ABLATIVE RADIOTHERAPY

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Aims. To report our results in patients (pts) with liver metastases treated with Stereotactic Ablative Radiotherapy (SABR).

Materials and Methods. All pts treated from 04/2016-04/2023 in our institution with SABR for liver metastases were retrospectively analyzed. Radiotherapy was delivered with Helical Tomotherapy (HT) or CyberKnife (CK). All pts underwent contrast-enhanced (ce) CT scan for simulation. A median number of 4 (3-8) fiducials were implanted before simulation for pts treated with CK. Overall survival (OS) and Local Relapse Free Survival (LRFS) were estimated with Kaplan-Meyer method. Toxicity was registered with CTCAE v5.0.

Results. Forty-four pts with 67 lesions were treated with SABR. Median age of pts was 44 years (29-83). Primary tumor was: 1 anal cancer, 6 gynecological cancer, 2 biliary tract cancer, 6 colorectal cancer, 1 melanoma, 4 esophageal and gastric cancer, 5 breast cancer, 8 pancreatic cancer, 7 lung cancer, 1 prostate cancer, 1 thymus, 2 bladder cancer. Twelve pts were previously treated: 6 with surgery, 3 RF, and 3 with SABR. Thirty-one pts received chemotherapy (ChT): 15 pts 1 line, 10 pts 2 lines, 6 pts 3 or more lines. Seventeen pts continued systemic treatment during SABR (most of them with hormonal therapies). Twenty-eight lesions were treated with CK, the remaining 39 with HT. Median number of liver metastases/pt was 4 (1-6). Median GTV 43.78 cc (0.8 – 190.5) for CK and 41.99 cc (0.3 – 631.7) for HT. Median dose prescribed was 45 Gy (35-60) in 5 fractions (3-6), Median BED calculated with tumor specific a/b coefficient was 100 (59.5-378) Gy. Acute toxicities were G1 gastrointestinal. No cases of radiation-induced liver disease (RILD) were registered. Two pts treated in the liver dome had late lung fibrosis. At a median follow of 14 months (0.5-81.5), 1 case of LR with CK and 11 cases with HT were observed. Six and 12-months Local Relapse Free Survival (LRFS) was 100% and 93.7% with CK, and 72.2%, and 69% with HT, respectively (P=0.03). No statistically significant difference was observed in OS between pts treated with HT and CK; it was 76.7%, 53.3%, and 41.1% at 6-, 12-, and 24-months, respectively.

Conclusions. SABR for liver metastases is effective and well tolerated. A better local control was obtained due to the higher precision of CK *vs* HT, without an impact on OS because of distant metastases. Larger cohorts and longer follow up are needed to confirm these results.

P205

INTENSIFICAZIONE DELLA DOSE NEL TUMORE DEL PANCREAS LOCALMENTE AVANZATO UTILIZZANDO LA RADIOTERAPIA STEREOTASSICA ROBOTICA

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Aims. SBRT has been proposed, in locally advanced pancreatic cancer (LAPC), as a consolidative local treatment after induction chemotherapy in stable disease, or as a primary treatment in patients unfit to either treatments. Although no formal dose schedule is mandated, in order to improve treatment outcome, Biologically Effective Dose (BED10, assuming α/β=10 Gy) of 100 Gy to the tumor is desirable. We reviewed the use of robotic SBRT with real-time tumor tracking to a target dose of 50 Gy in 5 fractions (BED10=100 Gy) in LAPC patients.

Methods. We reviewed a cohort of LAPC patients treated with robotic SBRT at our institution from May 2021 to Jan 2023. Planning aim was to cover ≥93% of the GTV with ≥95%(V47.5) of the target dose (50 Gy/5 fractions) and 95% of the PTV with 95%(V38) of the target dose (40 Gy/5 fractions). Dose constraints to Organs at Risk (OAR) were prioritized over target dose objectives. Mandatory constraint for dose-limiting OARs (duodenum, stomach, bowel) were V35≤0.5cc and V25≤10cc. Real-time tumor tracking was implemented with endoscopic ultrasound-guided fiducial marker placement. Toxicity was reported according to CTCAE v 5.1 scale.

Results. We included 11 patients (pts): 2 received exclusive irradiation, while 9 underwent SBRT as a local consolidation after obtaining stable disease/partial response following chemotherapy with different regimens: Nab-paclitaxel and Gemcitabine for 3 pts; Gemcitabine for 1 pts; FOLFIRINOX for 4 pts; FOLFOX for 1 pts. Median GTV was 45.0 (10.6-81.4) cc. The median number of implanted fiducials for each SBRT treatment was 2 (1-2). Planning aim was achieved in 7 cases. The median GTV (47.5Gy) and PTV(38Gy) coverage was 95.7% (79.9 – 100%) and 95,8% (92.1– 100%) respectively. Median V35 was 0.01 (0.0 – 0.49), 0.0 (0.0 – 0.5), and 0.19 (0.0 – 0.49) cc for duodenum, stomach and bowel respectively. Median V25 was 3.0 (0.0 – 7.97), 1.3 (0.0 – 7.78), and 5.6 (1.8 – 10.0) cc for duodenum, stomach and bowel respectively. [Figure 1].

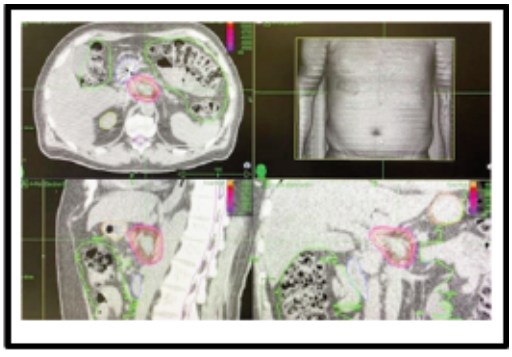

Fig. 1 Example of a patient plan with dose distribution. Axial, 3D, Coronal, Sagittal view (clock wise). Isodose lines 50 (red), 47.5 (magenta), 40 (purple), 38 (light violet), 35 (violet) Gy.

Figure 1.

At a median follow-up of 4 (3-12) months, median Progression Free Survival was 6.5 (95%CI 3.0-6.8)months. At the time of our analysis local-only, distant-only and local plus distant failure occurred in 0, 5 and 1 patient. No Grade ≥3 treatment-related toxicity was reported.

Conclusion. In patients with LAPC, robotic SBRT using a 50 Gy in 5 fractions schedule was feasible in the majority of patients, with no reported high-grade treatment-related toxicity.

P206

CLINICAL OUTCOME OF PATIENTS TREATED WITH HYPOFRACTIONATED EBRT BOOST FOLLOWING STANDARD CT-RT TREATMENT IN SQUAMOUS CELL CARCINOMA OF THE ANAL CANAL

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Aims. The aim of this study is to evaluate long term toxicity and efficacy of a hypofractionated External Beam Radiation Therapy (EBRT) boost technique, using a intra-anal probe for setup reproducibility after standard CT-RT treatment in Squamous Cell Carcinoma (SCC) of the anal canal.

Methods. We retrospectively reviewed a cohort of 26 consecutive patients (pts) between March 2008 and June 2017 (21 females, 5 males) with histologically proven invasive non-metastatic SCC of the anal canal (cT1–T3, cN0–N1, M0), all patients underwent EBRT + concurrent chemotherapy (5-FU/MMC or capecitabine/MMC) as standard Nigro regimen treatment followed by EBRT boost. First course of EBRT dose range was 45-50 Gy in 25 fractions (1.8–2 Gy/fraction) encompassing pelvis and locoregional nodes. The second course consisted of a EBRT boost delivered to the anal canal and/or the site of the initial disease, approximately 6 weeks after the first course in order to achieve a complete healing of acute local toxicity. The PTV of the boost was based on initial staging and on anoscopic examination conducted about 4 weeks after the first course of RT. An intra-anal probe was used in prone position prior to CT-simulation and during RT treatment sessions to ensure a reproducible setup. Boost dose ranged between 10 Gy in 2 fractions (4 pts)

and 15 Gy in 3 fractions (22 pts) and was delivered through Tomotherapy unit (Figure 1).

Results: After a median follow up of 82 months (range 36.3-115.3 months), no G4 acute toxicity was registered while the most common acute toxicity was perianal pain and skin toxicity. Acute gastrointestinal (GI) toxicity was recorded in 14 pts (G1 in 9 pts, G2 in 5), acute skin toxicity was G1 in 6 pts, G2 in 11 pts and 4 pts with G3, only 2 patients reported genitourinary (GI) acute G1 toxicity. With regard to late toxicity, only 2 patients had G3 late toxicity (vaginal stenosis, perianal pain), 3 pts had G2 toxicity while 21 pts had G1 or no late toxicity. To date 16 pts are NED (61.5%), local recurrence occurred in 4 pts (15.3%), 1 disease persistence occurred in a patient who initially rejected the boost and was treated with 3 months delay. Distant metastasis was reported in 6 pts, mainly to liver and lungs. Overall Survival (OS) at 5-year was 87.7% (95%CI: 66.5%-95.9%)

Conclusions. Our data suggests that hypofractionated EBRT boost using intra-anal probe seems to be feasible, safe and effective in SCC of the anal canal treatment.

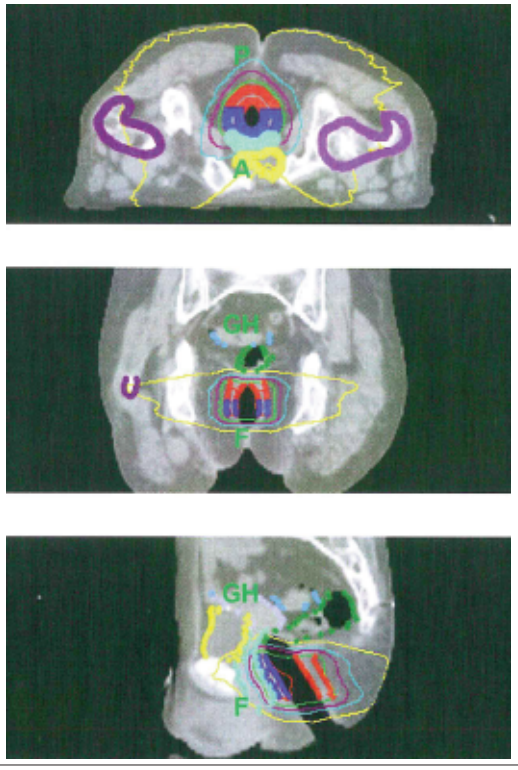

Figure 1.

P207

SURVIVAL RATES IN ANAL CANCER TREATED WITH INTENSIFIED SIB-IMRT AND CHEMOTHERAPY: RESULTS OF A SINGLE INSTITUTIONAL EXPERIENCE

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Aims. To investigate oncological outcomes of patients with anal cancer treated with a moderately accelerated radiotherapy schedule.

Methods. We retrospectively analyzed 142 patients treated consecutively from March 2009 to June 2022 at our Institution with IMRT and concurrent chemotherapy (CT). Radiotherapy (RT) was delivered with SIB technique by helical tomotherapy. We identified two clinical target volumes (CTV): CTV high risk (CTVHR) and CTV low risk (CTVLR). Doses were 2.2 - 2.0 Gy/Fx for CTVHR and 1,8 - 1,7 Gy/Fx for CTVLR, in 25 – 28 consecutive fractions, with total doses of 56-55 Gy for CTVHR and 47,6-45 Gy for CTVLR. Most of the patients received a CT regimen based on 5Fluorouracil or capecitabine and mytomicin. Primary endpoints were colostomy free survival (CFS), disease free survival (DFS) and overall survival (OS). Secondary endpoint was acute toxicity.

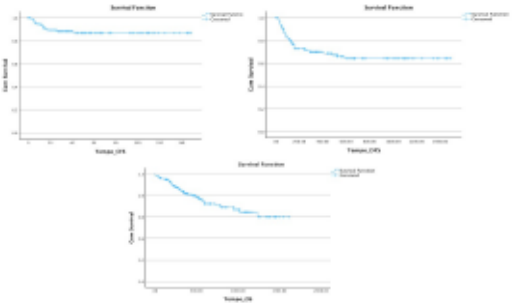

Figure 1.

Results. Median age was 67 years (range 32-97). Median follow-up was 48 months (range 0-161). HPV p16 expression status was positive in 62/105 (59%) patients. HIV infection tested positive in 8/142 (5,6%) patients. The stage of disease was: stage I in 17 (11,9%) patients, stage II in 38 (26,8%) patients and stage III in 87 (61,3%) patients. At 6 months after the end of treatment 136/142 patients were evaluable: 111/136 (81,6%) patients achieved a complete response (CR), while 25/136 (18,3%) patients developed disease progression (PD). During follow-up, among patients in RC 16

(14,4%) patients developed PD. The CFS and DFS were 88% and 74% at 2 years, respectively. The CFS, DFS and OS were 84%, 63% and 78% at 5 years, respectively (Figure 1). Acute grade III pain, skin and gastrointestinal toxicities were reported in 19 (13,3%), 43 (30%) and 4 (2,8%) patients, respectively.

Conclusions. in our experience moderate intensified SIB-IMRT with concurrent chemotherapy achieved excellent results in terms of local control and overall survival.

P208

NEOADJUVANT DOSE-ESCALATED CHEMORADIATION WITH SIMULTANEOUS INTEGRATED BOOST FOR LOCALLY ADVANCED RECTAL CANCER. SURVIVAL OUTCOMES AND RESPONSE RATE IN WHOLE POPULATION AND IN HIGH-RISK PATIENTS

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Background. Neoadjuvant chemoradiation with Capecitabine (CRT) is considered the standard of therapy in patients with locally advanced rectal cancer (LARC). Radiotherapy dose escalation represents a useful tool to improve tumor downstage and pathological complete response (pCR). We investigated the role of a volumetric modulated arc therapy with simultaneous integrated boost VMAT-SIB and its impact on survival outcomes, tumor regression grade (TRG) and pCR rate.

Methods. From January 2016 to december 2020 we retrospectively reviewed 50 patients with LARC underwent VMAT-SIB Radiotherapy in our center. Every patient received 50Gy/25fr of pelvic radiotherapy with 56Gy/25fr boost and 825mg/m2/bid of concomitant Capecitabine. We evaluated pCR and TRG according to Mandard classification. Overall Survival (OS), disease-free survival (DFS), 2-years disease free survival (2yDFS) and organ preservation rate were also evaluated. Toxicity was assessed according CTC-AE 4.0 scale. A subgroup analisys in high-risk patients, staged T4 or N2 or presenting infiltration of mesorectal fascia (MRF+) or extramural vascular invasion 3-4 according to RAPIDO criteria, was conducted.

Results. Median age at diagnosis was 64. Thirty-four patients underwent anterior resection (RAR), 11 abdomino-perineal resection (APR) and 5 transanal endoscopic microsurgery (TEM). At median follow-up of 41 months [6-64] OS was 88.6%, DFS was 83,3%. 2yDFS was also 83,3%. Organ preservation rate was 80%. The pCR rate, assessed as both ypT0 N0 and TRG1 was 38%. Nine patients received adjuvant chemotherapy. Treatments at relapse were chemotherapy in 3 cases, stereotactic body radiotherapy (SBRT) in 1 case and chemotherapy plus targeted therapy in 1 case. At univariate analysis, DFS correlated with higher stage at diagnosis and administration of adjuvant chemotherapy (p 0.03). DFS strongly correlated with OS (p<0.001). No acute or late radiation-induced toxicity ≥G3 was experimented. With regard to 20 patients in high-risk subgroup, at median follow-up of 42.5 months [26-64] OS was 77%, 2yDFS 75%. pCR was **30%**. TTS showed a significant correlation with major response (p 0.005).

Conclusions. In our experience, VMAT-SIB for LARC resulted effective and safe and led to high rate of pCR. In high-risk patients, pCR rate was higher when compared to findings from total neoadjuvant therapy studies.

P209

STEREOTACTIC BODY RADIATION THERAPY (SBRT) INOPERABLE PANCREATIC CANCER: A RETROSPECTIVE ANALISYS

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Aims. Evaluating safety and efficacy of SBRT in non-metastatic inoperable pancreatic cancer.

Methods. In this retrospective monocentric analysis, patients included in the evaluation had a histological diagnosis of pancreatic cancer, a multidisciplinary tumor board considered the lesion not eligible for surgery and they received SBRT. Stage IV pancreatic carcinomas, based on TNM, were excluded. Patients received SBRT to the lesion, with or without induction chemotherapy. Toxicity was scored according to CTCAE v4. Progression free survival (PFS), freedom from loco-regional progression (FFLRP), freedom from distant metastasis (FFDM) and overall survival (OS) were calculated using the Kaplan-Meier method.

Results. Between May 2014 and March 2023, 48 patients were treated with SBRT. Median age was 74 years (range 52-86 years). 45 pts had a performance status (PS) equal to 0 or 1 (ECOG scale) and only 3 pts had a PS of 2. Total SBRT dose was: 36 Gy/3 fx in 5 pts, 30 Gy/3 fx in 23 pts, 24 Gy/3 fx in 20 pts and 25 Gy/5 fx in 1 pt. Choice of dose was mainly driven by duodenum exposure. Eight patients had stage I disease, seventeen

stage II and twenty-three stage III, according to the TNM classification. Fifteen patients were alive at time of analysis, thirty-three were deceased, median follow-up of all patients was 10,8 months (range 1-84 months). Median FFLRP, FFDM, PFS and OS were 17, 11, 6.63, 18.2 months respectively. Estimated 1-year FFLRP, FFDM, PFS and OS rate were 68%, 43%, 25%, 82.4% respectively. After radiation therapy, 9 patients underwent surgery and their median OS was 17,8 months while it was 18,9 months for patients not undergoing surgery. 35 patients (73%) received neoadjuvant gemcitabine based chemotherapy. Median OS of patients who underwent NACT was 19,2 months and FFLRP was 17,8 months. For patients treated with SBRT alone, OS was 14,6 months and FFLRP was 18 month. Two patients developed a G2 gastric or duodenal ulcer, one patient had a fatal gastrointestinal haemorrhage and one patient experience a G2 gastric haemorrhage that was medically managed.

Conclusions. Stereotactic radiotherapy for patients with unresectable pancreatic cancer resulted in a low rate of side effects and showed excellent locoregional control. Neoadjuvant chemotherapy is crucial to improve systemic control and overall survival.

P210

NEOADJUVANT SHORT-COURSE RADIOTHERAPY AND ULTRA-DELAYED SURGERY IN RECTAL CANCER: A GOOD OPTION FOR ELDERLY PATIENTS UNFIT FOR COMBINED TREATMENTS

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Aims. Short-course radiotherapy (SCRT) was a neoadjuvant treatment in rectal cancer delivered in 5 fractions without chemotherapy (CHT). An interval of 6-8 weeks from the end of RT to surgery was recommended to obtain tumor downstaging before resection. This approach was particularly suitable for elderly patients (pts), unfit for CHT, without care-giver or who live far away from the RT unit. Aims of this report were to evaluate efficacy, quality of life (QoL) and tolerance of this treatment.

Methods. All pts were discussed in a multidisciplinary setting. All pts received 25 Gy in 5 fractions with VMAT or IMRT-technique. Surgery was performed after 10 median weeks (8-14 wks) from the end of RT. Customers questionaries for QoL assessment were collected during the last fraction and follow-up. Gastrointestinal (GI) and Genitourinary (GU) acute and late toxicities were assessed according to CTCAE vs5 first, at the end of treatment and then every four-six months.

Results. From June 2019 to December 2022, 28 pts received SCRT. Median age was 77 years (70-85 yrs). Anagraphic data showed that all these pts lived more than 50 kilometers far from our RT center. Almost of them were unfit for CHT. With a median follow-up di 28 months (range 6-44), 70% of patients experienced a tumor-downstaging. Tumor Regression Grading 1-2 according the Mandard Classification was assessed in 30% of cases and pCR in 18% of cases (5 pts). The treatment was well tolerated with no RT interruption. Excellent compliance by QoL questionaries was declared by 100% of pts. GI Grade 1 toxicities in 5 pts (18%) and G2 in 4 (14%) pts were recorded. GI grade I-II late toxicities in postoperative setting was assessed in 50% of pts. In 10% of pts (3 pts) GI/GU grade 3-4 late toxicities was complained. Moreover, the time to surgery over 8 weeks was related to the best pathological response.

Conclusions. This report shows that in selected cases, short-course radiotherapy with a delayed surgery over 8 weeks was a very-well tolerated treatment, with good results in terms of outcomes and toxicities. Moreover it was a best approach to offer in problematic logistic situations.

P211

PROGNOSTIC VALUE OF PRE-TREATMENT INFLAMMATORY MARKERS IN PATIENT WITH LOCAL ADVANCED RECTAL CANCER RECEIVING NEOADJUVANT RADIO-CHEMOTHERAPY: A MONOCENTRIC EXPERIENCE

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Aims. The aim of this study is to evaluate the prognostic impact of baseline inflammatory markers for predicting the pathological complete response (pCR) assessed by Tumor Regression Grade (TRG) according to Dworak's classification, as well as overall survival (OS) and progression-free survival (PFS) in patients with locally advanced rectal cancer (LARC) receiving neoadjuvant radiochemotherapy (NACRT).

Methods. The study included patients with newly diagnosed LARC who underwent NACRT between January 2015 and December 2021. All patients received capecitabine (825 mg/m^2, twice daily for 5 days/week) and concurrent long course radiotherapy (50.4 Gy/28

fractions). Surgery was performed 6-8 weeks after completing NACRT. Inflammatory markers were assessed using pre-treatment blood samples. The systemic inflammation index (SII) was calculated using the equation SII = P x N/L, where P, N, and L represent the peripheral blood platelet, neutrophil, and lymphocyte counts per liter, respectively. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were calculated as the ratios of neutrophil and platelet counts to lymphocyte count, respectively.

Results. A total of 121 patients were included in the analysis (median age of 64 years, M:F=75:46). Approximately 28.9% of patients achieved a pCR (TRG=4). The median PFS and median OS were 54 months (range: 3-92 months) and 57 months (range: 6-92 months), respectively. Survival analysis indicated that TRG=4 (complete response) was an independent prognostic factor for both PFS ($p<0.05$) and OS ($p<0.07$). None of the inflammatory markers showed a statistically significant impact on OS, PFS, or TRG in the survival/multivariate analyses.

Conclusions. Consistent with previous literature, a TRG score of 4 was found to be significantly associated with improved progression-free survival (PFS). However, none of the inflammatory markers evaluated in this study demonstrated significant prognostic value. It is possible that a larger database and more refined patient stratification could provide further insights into the influence of these inflammatory markers on pathological response, PFS, and OS in this context.

P212

SURVIVAL ANALYSIS AND PREDICTIVE FACTORS IN ESOPHAGEAL CANCER (EC) PATIENT POPULATION TREATED WITH PREOPERATIVE RADIOTHERAPY

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Aims. For locally advanced (LA) esophageal carcinoma neoadjuvant radiation followed by surgery is a cornerstone, both for squamous cell (SC) and adenocarcinoma (AC). The aim of our analysis was to assess survival outcomes and prognostic factors in EC patient population.

Methods. We retrospectively collected data of LA EC patients treated with up-front pre-operative radiotherapy (RT) with or without platinum-based chemotherapy (CT) between November 2004 and April 2023. Clinical and treatment related data were collected. Acute and late toxicities were assessed. Descriptive, univariate (UVA) and multivariate (MVA) survival analysis was performed to identify predictors of outcome.

Results. 72 patients (AC:n=29; SC:n=43) were included. Median age was 65 (42-85); ECOG-PS was 0 in 50 patients. Jejunostomy was performed in 29 patients. Nodal involvement was present in 35 cases. Patients received a CROSS schedule, Cisplatin-5Fluorouracil or exclusive radiation in 52, 13 and 7 cases, respectively. Planned surgery was not performed due to refusal (n=4) or in-treatment metastatic progression (n=14). Acute toxicity consisted mainly of grade (G) ≤2 esophagitis (n=29) or pneumonitis (n=4): one G3 and one G5 pneumonitis occurred, the latter in a patient with previously undiagnosed ILD. 6 patients developed tracheobronchial fistula after RT or surgery. In patients treated with concurrent CT, G3-4 hematologic toxicity occurred in 13 cases. After a median follow-up of 13 (3-192) months, 3-year overall survival (OS), local recurrence (LRFS) and distant metastases (DMFS) free survival was 46%, 83% and 44% (Figure 1A,B,C). ECOG PS0 ($p=0.015$), fistula ($p<0.0001$), surgery ($p<0.0001$) and chemotherapy ($p=0.029$) were correlated with OS at UVA, although only surgery, fistula and PS0 maintained their statistical significance ($p=0.0002$, $p=0.0003$ and 0.0013, respectively) at MVA (Figure 1D, E, F). At UVA, fistula ($p=0.0004$) and surgery ($p=0.0011$) were related to LRFS: only fistula was significantly correlated with LR ($p=0.0134$) at MVA. Concerning DMFS, nodal involvement ($p=0.013$), fistula ($p=0.004$) and surgery ($p<0.0001$) showed a significant correlation at UVA, although only surgery proved significant at MVA ($p=0.0001$).

Conclusions. Surgical management is strongly correlated with disease control and survival in candidates who are able to complete the planned preoperative strategy. Fistula impacts negatively on local control and survival.

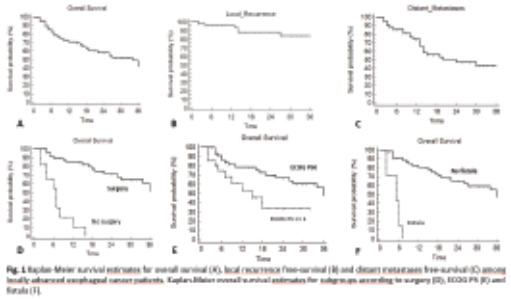

Figure 1.

P213

EXAMINING CLINICAL OUTCOMES AND TOXICITIES IN DEFINITIVE CHEMORADIATION FOR SQUAMOUS CELL CARCINOMA OF THE ANAL CANAL

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Introduction. Current standard treatment for locally advanced squamous cell carcinoma of the anal canal (SCCAC) is definitive chemoradiation (CRT), resulting in excellent oncological outcomes. Nevertheless, this particular treatment approach may be burdened by important side effects. In clinical practice there are many problems in balancing treatment toxicities and oncological outcomes . The purpose of this study was to evaluate the clinical outcomes and adverse events in real-world clinical practice in patients with SCCAC who undergo radiotherapy.

Methods. We analyzed a cohort of consecutive patients who received definitive radiotherapy with or without concurrent chemotherapy (CT) from 2013 to 2023. All patients underwent moderately hypofractionated radiotherapy (total dose of 55 Gy in 25 daily fractions schedule). We reviewed clinical and treatment related data. We calculated local control (LC), distant metastasis free survival (DMFS), overall survival (OS) and Grade≥ 3 (G≥3) toxicity rate according to CTCAE version 5.1 .

Results. A total of 104 patients, with a median age of 67 years, were enrolled in the study. All patients completed the prescribed treatment, and 77 received concurrent chemotherapy. Thirtyseven patients were Stage III or more and 47 patients had a node positive disease at diagnosis. After a median follow-up of 34 months, 18 patients experienced disease progression. The 3-year LC, DMFS and OS rates were 82%,88% and 85%, respectively. Stage III disease (p=0.0037) and omission of CT (p=0.0028) had an adverse impact on LC, while positive nodal staging was correlated with DMFS (p=0.042) at multivariate analysis. CT omission was also correlated with impaired OS (p=0.004). G≥3 diarrhea, dermatitis and hematologic toxicity were observed in 6, 15 and 10 patients, respectively.

Conclusions. Considering the favorable oncological outcomes seen in the analyzed patients and the occurrence of non-cancer-specific deaths, it is worth considering an evaluation of a de-escalation of treatment for patients diagnosed with stage II or lower disease. Initial strategies in de-escalation of treatment have been experienced in ACT4 trial reducing total dose erogated to tumor. Further experiences are needed to find the right strategy to achieve excellence tumor control reducing treatment toxicities.

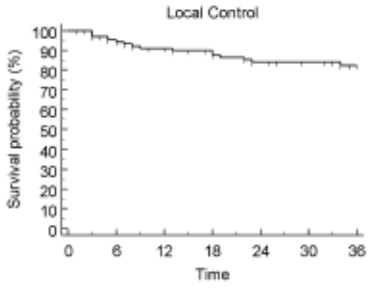

Figure 1.

P214

RUOLO DELLA POLI- CHEMIOTERAPIA E DEI REGIMI ABLATIVI NEL CARCINOMA PANCREATICO TRATTATO CON SBRT

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Aim. Pancreatic cancer (PC) is burdened by poor prognosis. The role of local radiotherapy in PC is unclear, although used with consolidative intent after induction chemotherapy, as primary treatment in unfit patients or in the palliative setting. Stereotactic body radiotherapy (SBRT) emerged as the preferred radiation treatment modality due to delivery ablative doses, benign toxicity profile, short duration of treatment that positively impact on compliance and integration with systemic therapy. In this retrospective study we analyzed patients (pts) treated with SBRT in our center for PC, with the aim to identify features correlated with overall survival (OS) and local control (LC).

Methods. We reviewed all pts with PC treated from Dec 2013 to Apr 2023, with available follow-up data. All patients were treated with SBRT delivered with Volumetric Modulated Arc Radiotherapy (VMAT) or Robotic Radiotherapy (Cyber Knife, CK). Clinical, treatment and outcome data were collected. Survival curves were calculated using the Kaplan-Meier method and compared with log-rank test. Toxicity was reported

according to CTCAE v 5.1 scale.

Results. We included 65 pts (34 male; 31 female), with median age 71 years (39-90). Almost 66%(43) had only unresectable local disease, while 15%(10) and 18%(12) had oligo and poly-metastatic disease respectively. Chemotherapy was delivered in 43 pts (66%) with to a median of 6 cycles (3-20). Most prescribed regimen was Folfirinox (16 pts), while other schedules were Gemcitabine ±Nab-paclitaxel or Capecitabine. SBRT was delivered for a median Total Dose of 30Gy (25-50 Gy) in 5 fractions, with CK (31 pts) and VMAT (34 pts). At a median follow up of 8.6 months(0.6 – 46), median LC was 9 months (95% CI 7-13), with LC rates of 70% and 37% at 6 and 12 months. Total SBRT dose >40 Gy showed higher median LC in non metastatic pts (11 *vs* 7 months), but with no statistic significance. Median OS was 9 months (95% CI 8-15), with 70% and 42% at 6 and 12 months, respectively. Only Folfirinox improved OS (21 *vs* 9 months, p=0,02). At the time of analysis, 55 pts showed disease progression (PD), with 8 local PD, 19 distant PD and 28 both. No toxicity >G2 was recorded.

Conclusions. In our analysis, Folfirinox in locally advanced/metastatic PC treated with SBRT improved OS, although selection bias of fitter patients may not be excluded. A total dose >40Gy in non metastatic pts may improve LC, although larger studies are needed. No severe toxicity was observed.

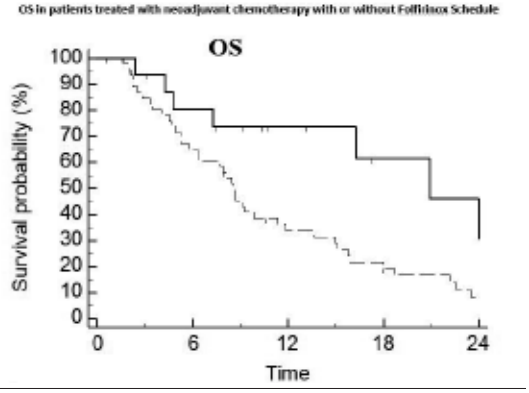

Figure 1.

P215

WHY INTENSIFY CHEMOTHERAPY IN RECTAL CANCER IN THE PREOPERATIVE SETTING?

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Aims. Despite optimal local control, chemoradiotherapy (CRT) overall and disease-free survival data are still equivocal. This meta-analysis aimed to estimate the pathological complete response (pCR), regression rate, disease-free survival and overall survival probabilities of rectal cancer patients treated with intensified chemotherapy.

Methods. Computerised bibliographic searches of MEDLINE and Cochrane Central Register of Controlled Trials databases (1970-2023) were supplemented with hand searches of reference lists. Studies were included if they were randomised controlled trials (RCTs) comparing intensified chemotherapy with CRT to preoperative CRT and if they had patients with resectable, histologically-proven, rectal adenocarcinoma without metastases. Eighteen RCTs (7695 patients) were analysed. Data on population, intervention, and outcomes were extracted from each RCT, following the intention-to-treat method, by three independent observers and combined using the DerSimonian and Laird methods.

Results. Intensified chemotherapy and CRT, compared to preoperative CRT, significantly increases the rate of pathological complete response (OR 1.37 (95% CI, 1.16-1.63) p=0.0003) and the regression rate (OR 1.57 (95% CI, 1.16-2.14) p<0.00001). Furthermore, it increases disease-free survival HR 0.87 (95% CI, 0.79 to 0.95) p=0.002 and overall survival HR 0.84 (95% CI, 0.74 to 0.95) p=0.007. Finally, the risk of therapy to severe adverse events (≥G3) is increased OR 1.96 (95% CI 1.35–2.85), p=0.0005.

Conclusions. In patients with resectable rectal cancer, intensified chemotherapy can reduce by 13% the hazard of disease progression and by 16% the hazard of death.

P216

INTESIFICATED NEOADJUVANT PROGRAM WITH CHEMOTHERAPY FOLLOWED BY CHEMORADIATION, WITH DOSE-ESCALATION IMRT-SIB, FOR LOCALLY ADVANCED GASTROESOPHAGEAL JUNCTION CANCER

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Surgery, CRO Aviano, Aviano Centro di Riferimento Oncologico di Aviano (CRO), IRCCS, Italy

Aims. Management of gastroesophageal junction (GEJ) cancer is challenging and no standard therapy has been established so far, in particular for Siewert type II adenocarcinoma. Because of its characteristic behaviour and the high risk of loco-regional failure combined modality therapy with Chemoradiotherapy (CRT) may represent a rational approach. Some series have reported a clear benefit in terms of both safety and efficacy from the integration of Chemotherapy (CT) and Radiotherapy (RT) but the optimal combination has not yet been established.

Methods. We retrospectively analyzed acute toxicity (according to CTCAE 4.0 scale), compliance, and response to treatment in a series of consecutive patients, treated at our Institution between 2019 and 2022, with neoadjuvant CT followed by intensificated CRT.

Results. Sixteen consecutive patients (pts) with locally advanced, HER2 negative, GEJ adenocarcinoma treated with curative intent were analyzed. Median age was 59 yrs, all pts were male. 62.5% of pts had Siewert I disease, 81.2% were cT3+ and cN+ at diagnosis. All pts received CT with fluoropyrimidine, oxaliplatin and docetaxel (FLOT or DOC regimens) and subsequent IMRT (45Gy/25fr plus simultaneous integrated boost of 52.5Gy) with concomitant capecitabine or carboplatin-paclitaxel. Disease assessment was performed with CT scan, endoscopy, and CT/PET, before and after CRT. FLOT was the iCT regimen in 56.3% of pts. Partial responses were 50% after iCT, 68.8% after CRT. 12 pts (75%) underwent surgery (Ivor-Lewis or McKeown) with a median of 9 [8.5.-11] weeks after CRT. 25% had a pathologic complete response (ypT0N0), 62.5% a Mandard tumour regression grade 1-2. 8 pts relapsed (2 locoregional recurrences); 3-year survival rate was 46%. Median event-free survival was 5months, median overall survival 34 months. Only 12.5% pts suffered G3+ iCT-related toxicities (diarrhoea in all cases). CRT was also well tolerated; G3+ toxicities were muco-cutaneous (mucositis 6.2%) and haematological (anaemia 6.2%). No significant delay in either iCT-CRT administration or surgery was observed.

Conclusions. Despite the limited number of pts, this intensificated neoadjuvant approach in pts with locally advanced GEJ cancer appears safe and feasible. IMRT–SIB dose intensification after induction CT did not add any substantial toxicity and the surgical program was not significantly delayed. Randomized clinical trials are ongoing to evaluate the clinical benefit of this approach.

P217

LONG-TERM RESULTS AND TOXICITY PROFILE OF RADIO-CHEMOTHERAPY TREATMENT IN PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE ANUS, RETROSPECTIVE ANALYSIS OF A SINGLE INSTITUTE

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Aims. To assess the treatment outcome and toxicity profile in patients (pts) with anal cancer with a particular emphasis on trends in elderly cases.

Methods. Medical records of 39 consecutive pts with squamous cell carcinoma of the anus, all stages, treated with curative intent between July 2013 and May 2022, and with follow-up until May 2023, were analysed. Radiotherapy was delivered using 3DCRT, IMRT, Tomotherapy, or VMAT. Five-year locoregional control (LRC), overall survival (OS), and colostomy-free survival (CFS) were calculated with Kaplan-Meier curves and log-rank test. We tested the association of outcome and age (>70 or < 70), PS-ECOG(0 or 1-2), and TNM stage. Acute and late Toxicities were assessed according to CTCAE 5.0 scale. Chi-squared test was used for differences in the toxicity rate of the categories above reported.

Table 1. Acute and late toxicity.

ACUTE Toxicity	G0-1 % (n pts)	G2+ % (n pts)
Diarrhea	83.4% (30/36)	16.6% (6/36)
Tenesmus	77.7% (28/36)	22.3% (8/36)
Skin	38.8% (14/36)	61.2% (22/36)
Bladder	88.9% (32/36)	11.1% (4/36)
Vagina	97.3% (35/36)	2.7% (1/36)
Anal pain	66.7% (24/36)	33.3% (12/36)
LATE Toxicity	**G0-1 % (n pts)**	**G2+ % (n pts)**
Pain	83.4% (30/36)	16.6% (6/36)
Bowel	88.9% (32/36)	11.1% (4/36)
Bladder	97.3% (35/36)	2.7% (1/36)

Results. Median age was 66 years (range 43–83). Most pts were female (90%). Thirteen pts were >70 years old. The TNM stages were I, IIA, IIB, IIIA, and IIIC in 7.5%, 10.5%, 2%, 23.5%, and 56.5% respectively; 20% of pts had N0 status. Concurrent mitomycin C and 5-fluorouracil-based chemotherapy (NIGRO) were given to all pts. Standard tumour and pathological lymph node median doses were 54 Gy (range 60–54 Gy) or 50.4 Gy (range 54–

50 Gy), respectively. Elective nodal regions were treated with 45 Gy (no deviations). The technique of choice was Tomotherapy for 74.4% (29/39), followed by VMAT, IMRT and 3DCRT for 15.4% (6/39), 5.1% (2/39), and 5.1% (2/39), respectively. Five-year OS, LRC, and CFS were 73.1% (CI 92.5-57.7 %), 85.5% (CI 100-72.7), and 87.9% (CI 99.9-77.3) for the whole group. Results in pts >70 years of age or ECOG >1 or TNM IIIC Stage were not statistically different from those in younger, ECOG 0, or TNM IIIA-II-I pts. Acute and late toxicities were reported in Table 1. No statistically significant differences were found in acute and late toxicities for older pts.

Conclusions. Real-word treatment outcomes per disease stage aligned with what is reported in the literature. Older pts have the same toxicity as the younger; for this reason, they should also be offered treatment with curative intent.

P218

CHEMOTHERAPY REGIMENS WITH DEFINITIVE RADIOTHERAPY IN SQUAMOUS CELL CARCINOMA OF THE ANAL CANAL

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Introduction. Mitomycin and 5-fluorouracil (5-FU) are used in combination with radiation therapy for definitive treatment of anal canal squamous cell carcinoma (ACSCC). However, duration of treatment and use of oral 5-FU prodrogues (capecitabine) are debated. In our study, we assessed efficacy and toxicity of different chemotherapy (CT) regimens concurrently with radiation therapy.

Methods. We reviewed data of consecutive patients treated with definitive chemoradiotherapy (RT) alongside concurrent chemotherapy (CT) between January 2013 and December 2022. Chemotherapy consisted of 1 (day 1) or 2 (day 1,29) cycles of Mitomycin (12 mg/m²) and either intravenous fluorouracil (5FU) at (1000 mg/m²/day, days 1–4 and 29–32) or capecitabine (825 mg/m² twice daily from day 1 to 5 every week). We evaluated local control (LC), distant metastasis-free survival (DMFS), overall survival (OS), and the rate of Grade≥ 2 (G≥2) toxicity, as per the CTCAE version 5.1 guidelines.

Results. Among 78 patients in the study 37 had Stage III or higher disease, while 47 patients were diagnosed with node-positive disease. Mitomycin was prescribed for 1 (n=21) or 2 cycles (n=57), while patients received either 5-FU or capecitabine in 25 and 53 cases respectively. Following a median follow-up of 34 months, 9 patients experienced disease progression. The 3-year rates of LC, DMFS and OS were 90%, 88%, and 81%, respectively. Stage III disease had a negative impact on LC (p=0.0046), while positive nodal staging (p=0.0336) and the use of 5FU (p=0.0291) were negatively correlated with DMFS. Among patients receiving 1 versus 2 Mitomycin cycles, Grade ≥2 neutropenia (45% *vs* 18, p=0.0143) and thrombocytopenia (27% *vs* 9%, p=0.0407) were significantly more frequent. Patients treated with capecitabine had higher rates of Grade≥2 thrombocytopenia (22% *vs* 0%, p=0.071) and proctitis (22.4% *vs* 3.6%, p=0.0291) compared to those treated with 5FU.

Conclusions. Duration of Mitomycin treatment or use of capecitabine versus 5FU did not result in impaired local control or survival. A higher rate of distant metastases was observed in patients treated with 5FU. A single course of mitomycin was associated with higher rate of G≥2 hematologic toxicity, suggesting individual sensitivity rather than impact of treatment duration affect tolerability. Capecitabin was associated with a higher rate of G≥2 toxicity.

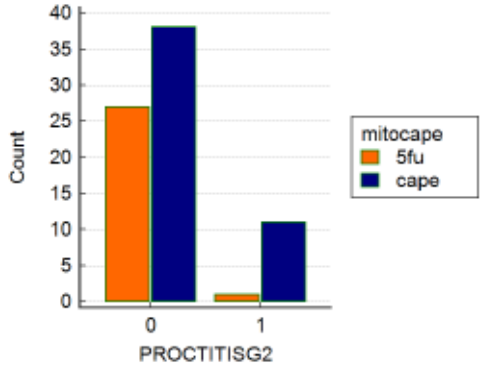

Figure 1.

P219

PREOPERATIVE SHORT-COURSE RADIOTHERAPY (SCRT) FOLLOWED BY NEOADJUVANT CHEMOTHERAPY (CHT) AND ROBOTIC SURGERY (RSURG) IN LOCALLY ADVANCED RECTAL CANCER (RC): A PROSPECTIVE MONOCENTRIC EXPERIENCE

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Aims. To evaluate efficacy (pathological complete response, pCR), feasibility and toxicities in locally advanced rectal cancer (LARC) of patients (pts) who underwent to total neoadjuvant therapy (TNT) which was short-course radiation (RT) therapy followed by up-front chemotherapy (CT) before planned surgery, according RAPIDO trial protocol.

Methods. From April 2021 to March 2023 we retrospectively analized patients with biopsy proven diagnosis of rectal adenocarcinoma staged with at least stage IIB (cT4 and/or N positive disease) as assessed by imaging and clinical examination. RT was delivered with Volumetric Modulated Arc Therapy (VMAT) technique with image guidance (IGRT). Myerson's consensus atlas was used to define elective nodal volumes. Pts received a total dose of 25 Gy to the pelvic PTV delivered in fractions of 5 Gy during 5 days with a maximum overall treatment time of 8 days. CT started 11-18 day after the end of RT with FOLFOX scheme for 9 cycles or CAPOX scheme for 6 cycles. Surgery was performed 2-4 weeks after the completion of CT and after restaging. Toxicities of RT and CT treatments were assessed according RTOG scale.

Results. 16 pts underwent to RAPIDO protocol, 7 male and 9 female. The median age was 67 yrs old (range 39-77 yrs). There were 2 pts with cT4 and 14 pts with cT3 disease; on the total, 15 pts (94%) had nodal involvment. All pts complete RT and sequentially CT, which was CAPOX schedule for 14 pts and FOLFOX schedule for 2 pts. The most common adverse events were leucopenia and thrombocytopenia during CT treatment, rectal mucositis and diarrhea during RT, but all toxicities were mild and there was no need to delay any therapy administration. No one experienced toxicity G3 or higher. Actually, 14 pts undervent surgery, which was rectum anterior resection for 11 pts and Miles surgery for 3 pts; the remaining 2 pts completed RT and CT but didn't underwent surgery yet. We observed an increased difficulty of the surgical time in performing an R0 resection. After surgery, 4 pts achived a pCR on T parameter, while 1 pts was ypT1, 5 pts were ypT2 and 4 pts were ypT3. We achieved a pCR on N paramter on 12 pts. We recorded a downstaging on the 80% of pts.

Conclusions. In our experience RAPIDO protocol delivered to LARC was well tolerated and also effective, but due to surgical concerns a more personalized, multidisciplinary approach for TNT are needed.

P220

ABDOMINAL COMPRESSION IMPACT IN SBRT FOR LIVER TUMORS

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Aims. Stereotactic body radiotherapy (SBRT) has emerged as a valuable therapeutic modality for primary and secondary liver tumor. However, the inherent motion of the liver, particularly due to respiratory motion, can compromise the precision and efficacy of radiation delivery. Abdominal compression (AC) has garnered attention as a potential solution to mitigate respiratory-induced motion and improve the outcomes of radiotherapy for hepatic metastases and primary liver tumors.This abstract aims to assess the impact of AC in SBRT in liver lesions.

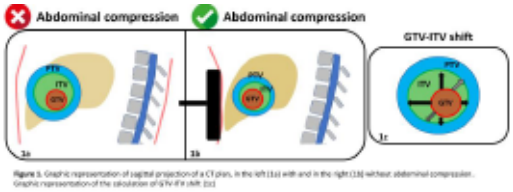

Figure 1.

Table 1.

lesion n.	Abdominal compression				NON-abdominal compression				Non-AC vs AC			
	PTV (cc)	shift CC (mm)	shift LL (mm)	shift AP (mm)	PTV (cc)	shift CC (mm)	shift LL (mm)	shift AP (mm)	ΔPTV (cc)	ΔCC (mm)	ΔLL (mm)	ΔAP (mm)
1	17,09	6	6,1	6,2	22,55	8,8	9	8	5,48	2,8	2,9	2,8
2	17,65	5,8	2,6	2,7	28,84	14,4	8,3	8,6	10,99	8,6	5,7	5,9
3	29,3	5,8	4,4	5,3	35,10	6,3	5	7,5	5,88	0,5	1,6	2,2
4	154,6 9	5,9	6,9	5,5	154,79	12	11,3	9,6	0,2	6,1	4,4	4,3
5	97,43	5,8	7,6	4,8	101,72	14,7	8,8	6,6	4,29	8,9	1,2	4
6	79,54	6	3,9	6,7	128,88	10,7	6,5	7,2	49,34	4,7	2,6	1,5
7	98,31	10	2,7	9	100,62	15,3	12,8	14,9	5,31	-2,7	9,9	5,9
median	79,54	5,9	4,4	5,3	100,62	12	8,8	8,6	5,48 (0,2-49,34)	4,7 (-2,7-8,9)	2,9 (1,2-9,9)	4 (1,5-5,9)

Table 1 Dosimetric and volumetric data with and without AC

Methods. We evaluate consecutive patients treated with SBRT to liver tumors. We included patients for whom both planning 4DCT with or without AC were available. For each tumor, GTV and ITV were manually delineated on both CTs, while PTV was obtained by a +5mm isotropic expansion. We extrapolated the difference between AC and non-AC contours for PTV and craniocaudal (CC), laterolateral (LL) and anteroposterior (AP) shift (respectively ΔPTV, ΔCC , ΔLL and ΔAP), see Figure 1. Wilcoxon test was performed on paired samples.

Results. We examined 7 hepatic lesions from 5 patients. Results are summarized in Table 1. Median ΔPTV, ΔCC, ΔLL and ΔAP were respectively 5.49 cc, 4.7 mm, 2.9 mm and 4 mm. At the Wilcoxon test, a significant difference ($p<0.05$) was observed between AC and non-AC for all the examined measures.

Conclusions. Use of AC for SBRT resulted in a significant reduction of volumes of treatment, mainly as a result of diminished shift in all directions, with potential dosimetric advantage. Larger cohorts are needed to identify treatment locations that may draw the higher benefit from AC.

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LONG-TERM OUTCOMES OF SHORT-COURSE RADIOTHERAPY IN RECTAL CANCER: A MONOCENTRIC RETROSPECTIVE STUDY

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Aims. To evaluate efficacy and tolerance of short-course radiotherapy (RT) prior to chemotherapy (CHT) and surgery unless contraindicated in 73 patients (pts) with locally advanced low lying rectal cancer, in terms of acute and early late toxicity, overall survival (OS) and local control (LC).

Methods. seventy-three pts affected by rectal tumor were treated from 2008 to 2023. At staging 2 pts had stage I (2.74%), 19 IIA (26.03%), 3 IIIA (4.11%), 31 IIIB (42.47%), 3 IIIC (4.11%) and 9 IV (12.33%). The pts underwent Volumetric Arc Radiotherapy (VMAT), with a total dose of 25 Gy in 5 fractions. Toxicity assessment has been considered in acute (from the end of RT to 6 months) and in early-late (after 6-12 months post RT completion) for gastrointestinal (GI), genitourinary (GU), cutaneous (CU) and hematological (HT) districts, according to Radiation Therapy Oncology Group (RTOG) scoring system. The Kaplan Meier method was used to assess OS and LC.

Results. Median follow-up was 37.43 months (ds 46.54; IQR: 10-81). Median actuarial follow-up was 52.23 (95CI 41.6-62.7) (range 2.1-149.7). Median OS was 63.5 (95CI:47.6-79.3) and 1- and 2-years OS were 91.1% and 74.5% respectively. Median LC was not reached and 1- and 2-years LC were 92.5% and 88.9% respectively. Acute GI toxicity G1 was registered in 4 pts (5.48%), G2 in 1 pts (1.37%), G3 1 (1.37%) pts respectively. Acute GU toxicity G1 was recorded in 1 pts (1.37%). No acute cases of CU and HT was reported. No early-late GI, GU, CU and HT toxicity was reported. Early late asthenia was recorded in 2 pts (2.74%).

Conclusions. Short course RT is an effective treatment in patients with rectal cancer and provides good outcomes in terms of OS and LC with very low rates of toxicity profile.

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RADIOTHERAPY TREATMENT OF GASTRIC LYMPHOMAS WITH DEEP-INSPIRATION BREATH HOLD TECHNIQUE

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Background. Radiotherapy (RT) is an important part in the treatment of gastric mucosa-associated lymphoid tissue Marginal Zone Lymphoma (MZL). The prognosis after radiotherapy shows an excellent local control with a good chance of long-term survival, therefore prevention of long-term adverse effects plays a key role for these patients. Intensity modulated techniques allow a good sparing of organs at risk, but cardiac toxicity remains of concern. We evaluated if deep inspiration breath-hold (DIBH) technique could reduce the dose to heart without compromising the dose to the target.

Methods. Two patients with gastric MZL were included; both patients underwent prior Helicobacter Pylori eradication therapy. CT scans were acquired with patients fasting for at least 4 hours: a 4DCT scan and a DIBH scan were obtained for each patient. Clinical target volume (CTV) was the whole stomach. An Internal Target Volume (ITV) was obtained from the 4DCT to take into account respiratory movement. Planning target volume (PTV) was obtained with 10 mm expansion of 4DCT-ITV and DIBH-CTV. RT plans were obtained using DIBH and 4DCT scans. Both patients were treated with a dose of 24 Gy in 12 fractions.

Results. DIBH allowed for a CTV/ITV volumes reduction from 315 cm^3 and 320 cm^3 with 4DCT scan to 247 cm^3 and 248 cm^3 for the two patients. Also the PTV volumes were reduced with DIBH technique from 919 cm^3 and 773 cm^3 to 707 cm^3 and 456 cm^3 respectively. Both plans showed excellent target coverage with a PTV V95 of 97,4% for both plans for patient 1, 97,7% and 99,7% for 4DCT and DIBH plans respectively for patient 2. For patient 1 DIBH plan allowed for a reduction of the mean heart dose from 3,9 Gy to 2,9 Gy; heart V20Gy was reduced from 5,5% to 2,5%, heart V15Gy from 8,5% to 4,8% and heart V10Gy from 11,8% to 7,9%. Also the kidney V5Gy was reduced from 18,1% to 10,1%. Similarly for patient 2 the mean heart dose was reduced from 2,6 Gy to 2,2 Gy, heart V20Gy from 2,1% to 1,6%, heart V15Gy from 6,3% to 2,8%, heart V10Gy from 10,9% to

5,0%. The dose to the kidneys was very low with both plans (kidney V5Gy 2,7% for 4DCT plan and 1,7% for DIBH plan).

Conclusions. RT with DIBH for gastric lymphomas allowed for a reduction of treatment volumes and of heart exposure without compromising PTV coverage. In one patient also the dose to the kidneys was reduced.

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INCIDENCE AND PREDICTIVE FACTORS OF FECAL INCONTINENCE IN ANAL CANCER RADIOTHERAPY: COMPARISON OF TWO TREATMENT SCHEDULES

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Aims. to examine the incidence and predictive factors of fecal incontinence (FI) in patients with anal cancer treated with simultaneous integrated boost (SIB) versus sequential boost (SeqB) radiotherapy (RT) with concomitant chemotherapy (CHT).

Methods. anal cancer survivors from a mono-institutional cohort, with minimum 2 years follow-up, were included in this cross-sectional analysis. Sixty-six pts were treated from 2007 to 2021. Thirty patients underwent SeqB and 37 received SIB, both with concurrent CHT. Because three-dimensional conformal radiation therapy (3DCRT) was the most commonly used treatment modality in the 2000s, the first cohort of pts primarily received 3DCRT. The second cohort of pts received Intensity-modulated radiation therapy (IMRT) treatment and volumetric modulated arc therapy (VMAT). The Wexner scale, among summary scoring systems, has been used as a tool to measure FI. The actuarial rates of FI were calculated using the Kaplan-Meier method. The incidence was measured from the date of the end of RT. Univariate logistic regression analysis were fit to evaluate predictive factors associated with FI. Covariates with P<0.20 in univariate analysis were used for stepwise backward selection on multivariate analysis. P values were 2-tailed and were considered significant if <.05. Odds ratios (ORs) were calculated with associated 95% confidence intervals (Cis).

Results. Median follow-up was 61.5 months (IQR:27.1-121.7). Thirty pts (45.4%) were treated with SeqB (years 2007–2012) and 36 pts (54.5%) with SIB (years 2012–2021). Pts from both treatment groups were of similar age, with a similar distribution of gender, T stage, and TNM stage. The median time from the end of RT to surgery was 9.23 months (IQR: 4.2–10.2). Twelve pts (18.1%) developed FI: 8 (22%) in the SIB group and 4 (13.3%) in the SeqB group. Most of pts developed FI after 2 years from the end of RT. Cumulative incidence of FI from date of the end of RT with 1-year, 2-year, and 5-year rates at 2.2%, 7% and 25.6% respectively. Incidence of FI was not significantly different between pts in SeqB group and pts in SIB group (p.value 0.240 (CI95% 116.05-149.25). In univariate analysis, no predictive factors were associated with the development of FI (Table). After the backwards elimination process, the selected factors were not statistically significant in multivariate analysis.

Conclusions. clinically detectable FI involves a minority of pts after RT (up to ≈20%). There were no differences between SeqB and SIB group.

Table 1.

Variable	Classification	N patients	p-value	OR	95% CI
Age	≥60 <60	7 5	0.861	1.12	0.31-3.91
Gender	Male Female	2 10	0.432	1.92	0.37-9.81
ECOG-PS	≥1 <1	1 11	0.116	0.182	0.02-1.51
Stage	III-IV I-II	2 10	0.268	0.400	0.07-2.01
Site	Anal canal anal verge	7 5	0.346	0.355	0.04-3.01
Group	SeqB SIB	4 8	0.356	0.538	0.14-2.01
RT duration (days)	Continuous		0.312	0.967	0.96-1.03
	≥37 <37	4 8	0.112	0.344	0.09-1.28
Technique	3DCRT IMRT VMAT	5 8 0	0.151	0.397	0.11-1.40
PTV HR (cc)	Continuous		0.115	0.995	0.98-1.00
	≥230 <230	4 8	0.252	0.464	0.12-1.72
PTV LR (cc)	Continuous		0.469	1.00	0.98-1.12
	≥1800 <1800	6 6	0.908	0.929	0.26-3.24
Dose RT (Gy)	Continuous		0.089	0.99	0.99-1.00
	≥59.4 <59.4	4 8	0.140	0.371	0.10-1.38
Salvge Surgery	Yes No	1 11	0.560	0.523	0.05-4.62

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VMAT FOR NEOADJUVANT RADIOTHERAPY IN LOCALLY ADVANCED RECTAL CANCER IN A DOSE-ESCALATION PROTOCOL AND SIMULTANEOUS INTEGRATED BOOST (SIB) APPROACH: THE EXPERIENCE OF OUR INSTITUTION

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Aims. To report the feasibility of volumetric modulated arc therapy (VMAT) for neoadjuvant radiotherapy in locally advanced rectal cancer in a dose-escalation protocol and simultaneous integrated boost (SIB) approach. Moreover, the VMAT technique was compared with three-dimensional conformal radiotherapy (3D-CRT) and fixed-field intensity modulated radiotherapy (IMRT), in terms of target coverage and irradiation of organs at risk.

Methods. Eighteen patients with locally advanced rectal cancer were treated with the SIB-VMAT technique. The VMAT plans were compared with 3D-CRT and IMRT techniques in terms of several clinically dosimetric parameters. The number of monitor units and the delivery time were analysed to score the treatment efficiency. All plans were verified in a dedicated solid water phantom using a two-dimensional array of ionisation chambers.

Results. All techniques meet the prescription goal for planning target volume coverage, with VMAT showing the highest level of conformality. VMAT is associated with 40, 53 and 58% reduction in the percentage of volume of small bowel irradiated to 30, 40 and 50 Gy, compared with 3D-CRT. No significant differences were found with respect to SIB-IMRT. VMAT plans showed a significant reduction of monitor units by nearly 20% with respect to IMRT and reduced treatment time from 14 to 5 min for a single fraction.

Conclusions. SIB-VMAT plans can be planned and carried out with high quality and efficiency for rectal cancer, providing similar sparing of organs at risk to SIB-IMRT and resulting in the most efficient treatment option. SIB-VMAT is currently our standard approach for radiotherapy of locally advanced rectal cancer.

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2012-2022: A TEN YEAR MONOINSTITUTIONAL EXPERIENCE IN THE TREATMENT OF ANAL SQUAMOUS CELL CARCINOMA (SCC)

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Purpose. To retrospectively analyse the therapeutic strategy adopted for patients with SCC focusing on clinical and radiological responses to treatment, local disease control, overall patient survival and late toxicity after radio-chemotherapy treatment.

Methods. We considered patients affected by SCC with the following eligibility criteria: age over 18 years, locally advanced disease (Stage II-III), concomitant radio-chemotherapy treatment, follow-up of at least 12 months. The primary endpoints were treatment efficacy in terms of radiological response and recurrence-free survival (RFS). Secondary endpoints were overall survival (OS) and late toxicity.

Results. 110 patients affected by SCC have completed the treatment from 2012 to 2022. At the first re-evaluation after treatment, 96 patients obtained a complete radiological response (87%), 8 patients a partial response (7%), 3 patients a stable disease (3%) and 3 patients progressed. The median ten-year follow-up was 47 months (range 6-172) with a median Relapse Free Survivor of 44 months (range 2-176) and a median Overall Survivor of 50.5 months (range 7-176). The most frequently observed late toxicities were faecal incontinence (26%) and dyspareunia (13% of women).

Conclusions. The data that we have analysed are in line with what is described in literature, confirming that to date radio-chemotherapy represents the standard of treatment for patients with SCC. The retrospective analysis of these data using artificial intelligence could improve the clinical-radiological descriptions of patients,

with the objective to personalize treatments for patients with SCC and hopefully reduce late toxicity.

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NEOADJUVANT CHEMOTHERAPY AND RADIOTHERPY FOR LOCALLY ADVANCED RECTAL CANCER. OUR EXPERIENCE

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Aims. To evaluate feasibility, tolerance and impact on local control in neoadjuvant chemotherapy and radiotherapy for locally advanced rectal cancer.

Methods. From January 2011 to December 2022, 300 Patients (pts) affected by locally advanced rectal cancer were treated with Neoadjuvant Chemotherapy (capecitabine) followed by radical surgery in our center. All patients had rectal adenocarcinomas, 175 G2 and 125 G3 at pretreatment biopsy. All patients had endoscopy and RM. The majority of patients had also an Endoscopic Ultrasound. At staging 74 patients had T3N0, 95 T3N1, 75 T3N2 and 56 T4aN1. All patients received 50.4 Gy in 28 fraction on whole pelvis, 1,8 GY for fraction, All patients had radical surgery after a median of 55 days (range 50– 60 days). 241 patients had radical anterior rectal resection, 59 pts a "Miles" surgery.

Results. After neoadjuvant treatment 222 pts had G0-1 rectal toxicity, 76 pts G2. In 2 cases treatment was interrupted. In one case per G3 local toxicity in a frail patient, In one case we founded lung progression during treatment. No genitourinary toxicity was recorded. At surgery 85 pts had a T0N0 (30%), 100 T1N0 (32%) 75 T2N0 (26%), 40 patient T2N1 (12%). 284/300 (94%) patients had a complete response on nodal site initially N+. During follow up one patient ad a gastric cancer (primary, total gastrectomy, NED after a total of 16 month). Four patients T3N1 had a T1N0 at surgery but a local recurrence after a median 14 month. The patient with lung progression during treatment had also liver metastasis 6 month after initial treatment, and died after 17 month. No patients had post treatment permanent toxicity.

Conclusions. Our data suggests the feasibility of the treatment, because it results in a nonaggressive management, with good results in desease local control.

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A DELPHI CONSENSUS STUDY ON SBRT FOR OLIGOMETASTATIC RENAL CELL CARCINOMA (RCC) AN ESTRO ACROP STUDY

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Aims. Currently, there are no guidelines on the management of oligometastatic RCC with SBRT. The purpose of this ESTRO ACROP project is to explore the expert opinion on the management of oligometastatic RCC patients using SBRT on extracranial metastases, with the aim of developing consensus recommendations to help with management decisions for treatment, improve patient selection, prescription doses and management alongside systemic therapy.

Materials and Methods. A questionnaire on SBRT in oligometastatic RCC was prepared by a core group and reviewed by a panel of 10 prominent experts in the field. The final version of the questionnaire included 58 questions dealing with controversial issues related to oligometastatic RCC and SBRT. It was implemented online via Google Forms and sent to clinicians identified as key opinion leaders. The Delphi consensus methodology was applied and involved sending three rounds of questionnaires to the experts. After the conclusion of each round, a fully anonymised summary of their and others' responses was provided to the participants, in order to drive the panellists towards the consensus. The agreement threshold was set at 80%.

Results. Among the 43 contacted professionals, a total of 25 experts (58%) agreed to participate. Responders, characteristics are reported in Table 1a. At the end of the third round, participants were able to find consensus on 9 out of 52 clinical questions. Specifically, SBRT was indicated as the elective treatment choice for RCC bone metastases (80%) and for adrenal lesions (88%) independently from site and from age. The upper threshold of three lesions was indicated for an SBRT treatment in the oligoprogressive setting by the 83% of the responders. Small bowel, duodenum, and stomach were the major dose limiting organs for both pancreatic and adrenal lesions, with the addition of kidney for the latter. A summary of the main areas of agreement and disagreement is reported in Table 1b.

Conclusions. The present ESTRO ACROP study represents one of the first efforts to achieve consensus on some critical aspects in SBRT in oligometastatic RCC, which is currently a controversial topic. This ESTRO ACROP consensus may serve as practical guidance for

the use of SBRT in oligometastatic RCC, and indicate the main areas where disagreement still persists, possibly guiding future efforts in filling knowledge gaps.

Table 1.

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OLIGOPROGRESSIVE RENAL CELL CARCINOMA TREATED WITH STEREOTACTIC BODY RADIATION THERAPY VERSUS SWITCHING OF SYSTEMIC THERAPY

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Aims. The excellent results in terms of high local disease control and little toxicity of stereotactic body radiation therapy (SBRT) as metastasis-directed therapy for oligometastatic renal cell carcinoma (mRCC) has laid the basis to evaluate its effects in the oligoprogressive setting. This refers to the clinical scenario where there is progression of one or a few metastases, while the majority of other lesions are stable or responding to a given systemic therapy (ST). Aim of our study was to evaluate if SBRT at sites of oligoprogression without switching of ST modified survival outcomes.

Methods. We conducted a single center retrospective study. Patients affected by mRCC on ST, who progressed with a maximum of 5 extracranial metastases were included in the study. We divided them in two cohorts: patients treated with SBRT to every oligoprogressive sites continuing the on-going ST (group A); patients who received a change in the systemic therapy at the time of oligoprogression (group B). The endpoints were progression free survival (PFS) and overall survival (OS) in both cohorts.

Results. A total of 68 patients (group A: 32; group B: 36) treated from 2012 to 2022 were included. Most patients were female (49, 72.1%) with an ECOG Performance Status of 0 (56, 82.4%) and a median age of 66.5 years (29.8 - 88.6). Majority of patients were treated with SBRT on single (31, 45.6%) or two metastases (20, 29.4%). Sunitinib (35, 51.5%) and pazopanib (16, 23.5%) were the most common concomitant systemic treatments. At a median follow-up of 23.6 months, median PFS was 11 months in group A and 10.7 months in group B (p=0.748). The 3-years PFS was 24.1% (95%CI 9.1 – 43.0) in group A and 24.0% (95%CI 10.6 – 40.3) in group B. Median OS was 49.3 months in group A versus 30.5 months in group B (p=0.056). The 3-years OS rate was 70.8% (95%CI 48.4 – 84.9) in group A versus 48.8% (95% CI 30.3 – 65.1) in group B.

Conclusions. Our study suggests that SBRT to oligoprogression without switching systemic therapy may be a viable option for selected oligoprogressive mRCC. No detrimental effect was observed on PFS and there was a trend towards improved OS in the SBRT group. Further investigation is warranted to establish the optimal role of SBRT in this setting, especially in the era of immunotherapy-combined first-line treatment.

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DIFFUSION-WEIGHTED MRI ASSESSMENT AFTER SINGLE-DOSE ABLATIVE RADIOTHERAPY FOR UNFAVORABLE PROSTATE CANCER

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Aims. To investigate diffusion-weighted (DW) MRI changes in patients with organ-confined unfavorable Prostate Cancer (PCa) following Single-Dose Ablative Radiotherapy (SDART).

Methods. Twenty-five patients included in the prospective clinical trial "ABRUPT" (NCT04831983) were treated with a single fraction of 24 Gy to the whole prostate gland with urethra sparing in association with

Androgen Deprivation Therapy (ADT), as per standard of care. Volumetric Modulated Arc Therapy (VMAT) was delivered on linear accelerator and using a real-time prostate tracking system. Multiparametric MRI was performed before SDART (time 0), one-hour post-SDART (time 1), and 3-months after treatment (time 2). To assess MRI changes, Region-of-Interests (ROIs) were placed on the areas corresponding to the Dominant Intraprostatic Lesion (DIL), at the aforementioned time-points. All MRI examinations were obtained on a 3.0 T MRI and were performed following the recommendations of the European Society of Urogenital Radiology (ESUR) guidelines.

Results. Seventy-five MRI were analyzed. At time 0 most patients (64%) showed a PIRADS-5 lesion and 36% a PIRADS-4. The median maximum diameter of DIL decreased from 17 mm (range 5-35) at baseline to 8,5 mm (range 0-33) at 3 months. The median prostate volume was 36,8 cc (range 10-59) at time 0, remained unchanged at time 1, while decreased to 29 cc (range 8,5-48) at time 2. An increase of median ADC value of tumor lesion was measured after SDART by about 20% (range 3%-178%) and 38% (range 5%-164%) at time 1 and time 2, respectively. No significant changes in ADC values were found in the peripheral zone and in the central gland (healthy tissue) at different time-points. T2 values of DIL were found decreased by about 7% and 8% at time 1 and time 2, respectively. In the peripheral zone, T2 values remained unchanged at time 0, while a median reduction of about 40% was assessed at time 2. At time 2, all patients were found b-NED and showed a radiological response at MRI (24% complete response).

Conclusions. Our findings show a correlation between early changes in ADC values after SDART and later tumor response in patients with unfavorable PCa. Long-term results are needed to confirm whether DW-MRI can be used as an early biomarker of treatment outcome in this context.

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A DOSE-ESCALATION STUDY OF STEREOTACTIC BODY RADIATION THERAPY BASED ON VMAT-SIB TECHNIQUE TO DOMINANT INTRAPROSTATIC LESION (DIL) FOR LOW- AND INTERMEDIATE-RISK PROSTATE CANCER

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Aims. To evaluate the tolerability of escalating doses of stereotactic body radiation therapy in the treatment of localized prostate cancer using a Volumetric Modulated Arc Therapy (VMAT) technique with simultaneous integrated boost (SIB) on MRI-defined Dominant Intraprostatic Lesion (DIL).

Methods. Eligible patients included those with low and intermediate – risk prostate carcinoma (NCCN risk classes) and International Prostatic Symptoms Score (IPSS) ≤ 15. Pretreatment preparation required an enema and placement of intraprostatic gold fiducials. SBRT was delivered in five consecutive daily fractions. For the first three patients, the DIL radiation dose was set at 8 Gy per fraction up to a total dose of 40 Gy (PTV1), and was gradually increased in succeeding cohorts to total doses of 42.5 Gy, 45.0 Gy, 47.5 Gy, and finally 50.0 Gy, while keeping the prescription of 35 Gy/7 Gy per fraction to the entire prostate gland (Table 1). Dose-limiting toxicity (DLT) was defined as grade 3 or worse gastrointestinal (GI)/genitourinary (GU) toxicity occurring within 90 days of follow-up (Common Terminology Criteria of Adverse Events scale 4.0). Patients completed quality-of-life questionnaires at defined intervals.

Table 1.

No. planned patients	No. accrued patients	Dose Level	PTV2	PTV1
3	8	1	35 Gy/7 Gy (70 Gy*, 117 Gy#)	40 Gy/8 Gy (88 Gy*, 147 Gy#)
3	5	2	35 Gy/7 Gy (70 Gy*, 117 Gy#)	42.5 Gy/8.5 Gy (97.7 Gy*, 163 Gy#)
3	4	3	35 Gy/7 Gy (70 Gy*, 117 Gy#)	45 Gy/9 Gy (108 Gy*, 180 Gy#)
3	4	4	35 Gy/7 Gy (70 Gy*, 117 Gy#)	47.5 Gy/9.5 Gy (118.8 Gy*, 197.9 Gy#)
3	3	5	35 Gy/7 Gy (70 Gy*, 117 Gy#)	50 Gy/10 Gy (130 Gy*, 216.7 Gy#)

PTV: Planning target volume; * EQD2: equivalent dose in 2 Gy fractions for late effects (α/β ratio: 3); # BED: biological equivalent dose in 2 Gy fractions, α/β ratio: 3; PTV1: MRI enhancing lesion with 3-mm margin; PTV2: prostate (+ 1 cm of seminal vesicles if intermediate risk prostate cancer) plus 3-mm margin

Results. Twenty-four patients with a median age of 75 (range, 58-89) years were enrolled. Other 24 patients were excluded from the trial after failing the predefined organ-at-risk constraints. Median follow up was 26.3 months (8.9-84 months). The 66.7% of patients were classified as intermediate risk group, while the others as low-risk group, according the NCCN guidelines. Enrolled patients were treated as follows: 8 patients (40 Gy), 5 patients (42.5 Gy), 4 patients (45 Gy), 4 patients (47.5 Gy), 3 patients (50 Gy). No severe acute toxicities were observed. G1 and G2 acute GU toxicities occurred in 4 (16%) and 3 patients (12.5%), respectively. Two patients (8.3%) and 3 patients (12.5%) experienced G1 and G2 GI toxicities, respectively. Since no DLTs were observed, 50 Gy in five fractions was considered as the MTD. The median nadir PSA was 0.20 ng/mL. A slight improvement in QoL values was registered after the treatment.

Conclusions. Based on the data from this phase I study, 50 Gy/10 Gy to macroscopic tumor and 35 Gy/7 Gy to prostate may be considered feasible and safe in a

well-selected low and intermediate – risk prostate carcinoma population. A phase II study is ongoing to confirm this tolerability and to assess the efficacy

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SHOULD WE DELIVER PROPHYLACTIC NODAL IRRADIATION IN SALVAGE RADIOTHERAPY OF PROSTATE CANCER? SECONDARY ANALYSIS OF AN OBSERVATIONAL MULTICENTER STUDY ON 454 PATIENTS

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Aims. Salvage radiotherapy (SRT) is the standard treatment option for biochemical recurrence from prostate cancer (PCa) after radical prostatectomy. However, prophylactic nodal irradiation (PNI) is still controversial in this setting. Therefore, the aim of this study is to evaluate the prognostic impact of PNI in PCa patients treated with SRT based on a comprehensive analysis of tumor-, patient- and treatment-related parameters.

Methods. Endpoints of the study were biochemical relapse-free survival (bRFS), local control (LC), regional control (RC), metastasis-free survival (MFS), disease-free survival (DFS), and overall survival (OS). Patients undergoing SRT for PCa biochemical relapse were selected from the database of a multicenter observational study. Univariate (logrank) and multivariate (Cox) analyses were performed including parameters regarding the characteristics of patients (age and Charson's comorbidity index), tumors (PSA level before surgery and before SRT, ISUP, pT stage, pN stage), and therapy (delivery of PNI, seminal vesicles irradiation, previous TURP, ADT type and duration, SRT fractionation and technique, type of image-guidance system, CTV to PTV margin, and EQD2α/β=1.5 to the prostate bed and pelvic nodes).

Results. Four hundred and fifty-four patients were included in this analysis. A summary of the univariate analysis results is shown in Table 1. Five-year bRFS was 58.3% and 35.1% in patients treated with and without PNI, respectively (p<.001). The multivariate analysis confirmed the favorable impact of PNI on bRFS (HR: 0.44, 95%CI: 0.32-0.61, p<.001) and DFS (HR: 0.49, 95%CI: 0.33-0.72, p<.001). Furthermore, compared to patients with ISUP 1, bRFS was significantly lower in patients with ISUP 3 (HR: 2.37, 95%CI: 1.34-4.19), ISUP 4 (HR: 2.09, 95%CI: 1.16-3.79) and ISUP 5 (HR: 3.99, 95%CI: 2.28-7.01, p<.001) and, compared to pN0 patients, in subjects with pN1 stage (HR: 1.91, 95%CI: 1.29-2.83, p=.001). Additionally, 5-year bRFS was, in pN0 patients with *vs* without PNI, as follows based on ISUP: **1**: 81.3% *vs* 55.4%; **2**: 66.5% *vs* 50.2%; **3**: 60.9% *vs* 33.3%; **4**: 71.5% *vs* 35.4%; **5**: 43.0% *vs* 9.5%, respectively.

Conclusions. Our study showed a significant benefit in terms of bRFS and DFS, independent of patient-, tumor-, and treatment-related parameters, in PCa patients with biochemical relapse treated with SRT. Furthermore, the bRFS advantage was clear for all ISUP grade groups.

Table 1. Univariate analysis and 5-year outcomes.

Variable	Value	No of patients (%)	bRFS %	P	LC %	P	RC %	P	MFS %	P	DFS %	p	OS %	p
Nodal irradiation	No	184 (40.5)	35.1	**.000**	93.5	.273	76.3	**.000**	86.7	.902	55.2	.213	89.8	**.025**
	Yes	270 (59.5)	58.3		90.2		93.5		82.2		63.5		94.5	
Lymphadenectomy	No	178 (39.2)	52.6		91.5		85.0		85.0		59.7		91.8	
	< 15 nodes	137 (30.2)	51.4	.504	89.3	.999	92.6	.224	84.9	.797	64.5	.476	94.0	.443
	≥ 15 nodes	139 (30.5)	43.8		93.0		83.7		81.8		57.0		93.1	
Margin status	R0	212 (46.7)	55.2	.098	93.1	.175	85.7	.355	85.5	.298	61.5	.762	94.0	.122
	R1	242 (53.3)	44.7		90.1		87.7		82.5		59.3		91.9	
Previous abdominal-pelvic surgery	No	417 (91.9)	49.7	.177	91.1	.756	86.4	.684	83.5	.325	60.1	.302	91.9	.399
	Yes	37 (8.1)	42.8		93.5		88.4		87.5		60.5		100.0	
Previous cancer	No	430 (94.7)	49.3	.812	91.3	.387	86.5	.693	84.2	.501	60.0	.682	92.5	.763
	Yes	24 (5.3)	55.9		95.2		92.3		76.0		70.2		100.0	
Androgen deprivation therapy (ADT)	No	163 (35.9)	48.1	.333	96.1	.064	78.4	**.010**	93.7	**.001**	61.8	.660	96.1	.122
	Yes	291 (64.1)	50.1		88.8		91.9		78.4		59.4		91.0	
Type of ADT	not prescribed	163 (35.9)	48.1	.348	96.1	.132	78.4	**.020**	93.7	**.002**	61.8	.903	96.1	.286
	LHRH agonist	215 (47.4)	44.4		89.6		89.9		77.7		57.7		89.5	
	Bicalutamide	76 (16.7)	61.0		86.5		96.3		78.7		61.5		93.6	
Actual duration of ADT (months)	not prescribed	163 (35.9)	48.1	.114	96.1	.169	78.4	.145	93.7	**.010**	61.8	.255	96.1	.051
	≤ 6	60 (13.2)	29.8		90.9		91.1		64.0		43.9		89.7	
	< 12	33 (7.3)	51.5		90.5		100.0		90.2		62.7		95.0	
	12-24	138 (30.4)	54.3		89.1		89.8		78.0		65.2		88.6	
	25-36	34 (7.5)	59.0		80.1		85.8		90.2		62.9		96.2	
	> 36	26 (5.7)	52.0		90.1		100.0		76.5		54.6		94.1	

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EARLY SALVAGE RADIOTHERAPY IN BIOCHEMICAL RECURRENCES FROM PROSTATE CANCER: PRELIMINARY OUTCOMES (EASY-1: EARLY SALVAGE RADIOTHERAPY-1)

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Aims. A meta-analysis of three randomized trials comparing immediate adjuvant radiotherapy (aRT) and early salvage RT (sRT) showed equivalence in terms of outcome but significantly lower toxicity rates in prostate cancer (PCa) patients treated with sRT compared to aRT. The aim of this analysis was to evaluate the preliminary results in terms of outcome and toxicity in PCa patient enrolled in a prospective trial on early sRT and showing biochemical relapse during the follow-up.

Methods. Seven hundred and twenty-one patients underwent radical prostatectomy between March 2018 and December 2022 and were enrolled in a prospective trial (EASY-1: EArly Salvage radiotherapY-1). Inclusion criteria were: prostate cancer treated with surgery, pT2 with positive surgical margins or pT3a regardless of surgical margins status or pT3b with negative surgical margins, and PSA undetectable 40 days after surgery (<0.01). The surveillance protocol included PSA assessment every 2 months after surgery during the 1st year, every 3 months during the 2nd and 3rd year, every 4 months until the 5th year, and then every 6 months until the 10th year after surgery. sRT was delivered in case of biochemical relapse (2 consecutive values of PSA ≥ 0.2 ng/mL) after ^{68}Ga-PSMA PET/CT-based restaging. We analyzed 2-year event-free survival (EFS) in the subgroup of patients with biochemical relapse and toxicity after sRT.

Results. Out of 721 enrolled patients, 64 pts (8.9%) had biochemical relapse. Of them, 50 patients (78%) already completed re-staging and sRT. The median follow up was 31 months and the median PSA range at biochemical relapse was 0.23 ng/mL (range: 0.10-5.82). The ISUP grade was 1, 2, 3, 4, and 5 in 1.6%, 9.3%, 34.4%, 32.8%, and 21.9% of cases, respectively. Two-year EFS was 56.3 %. No grade ≥ 3 acute and late GI or GU toxicity was recorded.

Conclusions. Despite close PSA monitoring, 2-year EFS rate was unexpectedly low in patients with biochemical recurrence. Further analyses are needed to identify patients with low risk of biochemical recurrence (in whom to avoid aRT) and to define the optimal PSA threshold for planning sRT.

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LEVERAGING PROCESS MINING FOR CARE PATH ANALYSIS IN PROSTATE CANCER PATIENTS UNDERGOING SALVAGE RADIOTHERAPY: AN INVESTIGATION BY AIRO GROUP

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Aims. Process mining is a robust machine learning technique with significant potential for aiding clinicians in the meticulous analysis of empirical data, thereby facilitating precise and efficient workflow prototyping and visualization. The objective of this study is to conduct a process mining analysis utilizing data derived from the AIRO endorsed nationwide survey on salvage radiotherapy (SRT) for patients diagnosed with prostate cancer.

Methods. A customized script was developed to enhance and transform the available data into event log format. The eligible event categories considered for the analysis were as follows: surgery, biochemical relapse, imaging restaging at biochemical relapse, radiation therapy treatment, disease progression, development of castration resistance, death, and last follow-up. The event analysis utilized the First Order Markov Model. CareFlowMiner model was used to assess patients' care path. The was conducted using R version 4.2.2 and the pMineR version 0.46 library.

Results. This analysis involved a cohort of 1450 prostate cancer patients, sourced from 10 different Italian institutions. A total of 5779 events were recorded and analyzed, with a median follow-up time of 4.4 years. Starting from surgical prostatectomy as the initial point of the patients' care path, only 403 patients (28% of the total subsequent events) underwent restaging through radiological imaging at the time of biochemical relapse. The average time from surgery to salvage radiotherapy was 2.16 years. Out of the patients who received SRT, 39% experienced disease progression. No significant difference was observed in terms of the percentage among the Imaging-preSRT group. The development of castration

resistance was noted in 0.1% of the cases experiencing disease progression.

Conclusions. Our study unequivocally showcases the influence and potential of process mining methodology in analyzing patients' care paths, particularly when dealing with large volumes of records. Subsequent investigations will concentrate on constructing more intricate models to attain enhanced stratification and gain deeper insights into the utilization of salvage radiotherapy, while also elucidating the role of various variables in the progression of prostate cancer.

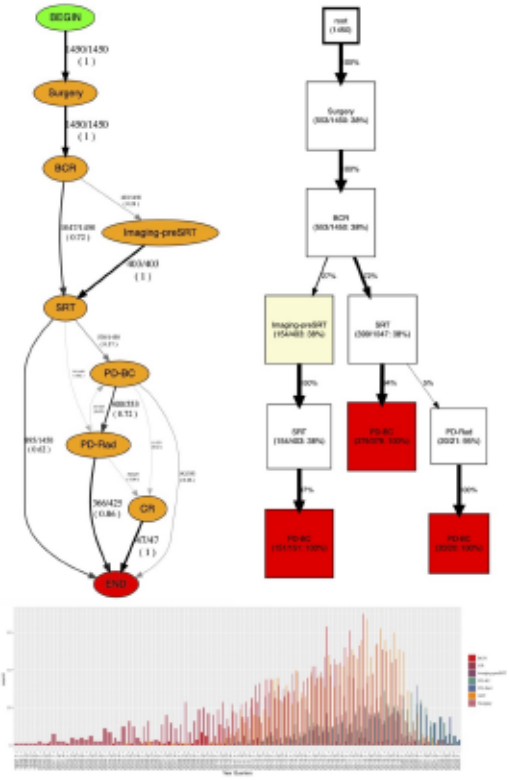

Figure 1.

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CORRELATION BETWEEN TREATMENT-RELATED PARAMETERS AND ACUTE TOXICITY IN SALVAGE RADIOTHERAPY OF PROSTATE CANCER: A MULTICENTER OBSERVATIONAL STUDY ON 454 PATIENTS

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Background. The aim of this study was to analyze the impact on acute toxicity, in prostate cancer (PCa) patients treated with salvage radiotherapy (SRT), of several treatment-related parameters.

Materials and Methods. For the purpose of this analysis, data from patients undergoing SRT were extracted from the database of a multicenter observational study. Endpoints of the analysis were Grade ≥ 2 and Grade ≥ 3 gastrointestinal (GI) and genitourinary (GU) acute toxicity. The following parameters were correlated with adverse events: prophylactic nodal irradiation (PNI; yes *vs* not), hypofractionation (yes *vs* not), lymphadenectomy (yes *vs* < 15 nodes *vs* ≥ 15 nodes), EQD2α/β10 to the prostate bed (< *vs* ≥ median value), EQD2α/β10 to the pelvic nodes (< *vs* ≥ median value), radiotherapy technique (3D-conformal *vs* IMRT/VMAT), image guidance (EPID *vs* cone-beam/CT), previous abdominal-pelvic surgery (yes *vs* not), adjuvant androgen deprivation therapy (ADT; yes *vs* not), and type of ADT (LH-RH agonists *vs* high dose bicalutamide). Acute toxicity was assessed by the RTOG scale.

Results. Four hundred fifty-four patients were enrolled in this analysis. Overall, the rate of grade ≥ 2 and ≥ 3 acute GI toxicity was 20.9% and 0.9%, respectively. In addition, the rate of grade ≥ 2 and ≥ 3 acute GU toxicity was 16.3% and 0.7%, respectively. Table 1 shows the results of the analysis. Briefly, patients undergoing adju-

vant ADT had higher rates of grade ≥ 2 GI toxicity (24.4% *vs* 17.2%, p=0.046), while no parameters correlated with grade ≥ 3 GI toxicity. Grade ≥ 2 GU toxicity rate was higher in patients undergoing PNI (20.0% *vs* 12.5%, p=0.024). Finally, also for GU toxicity, no parameter was found to be significantly related to grade ≥ 3 toxicity.

Conclusions. SRT was well tolerated. The correlation of intermediate-grade GU toxicity with PNI is likely related to the higher dose received by the bladder in these patients. However, the explanation for the higher GI toxicity rate in patients undergoing ADT is less clear. Therefore, the latter correlation, although sometimes previously reported, deserves future investigations.

Table 1.

Table 1: Acute gastrointestinal and genitourinary toxicity Grade ≥ 2 and Grade ≥ 3

		Gastrointestinal				Genitourinary			
		Gr ≥ 2 (%)	p	Gr ≥ 3 (%)	p	Gr ≥ 2 (%)	p	Gr ≥ 3 (%)	p
Nodal irradiation	No	34 (19.8)	.365	0 (0.0)	.124	23 (12.8)	.424	2 (1.1)	.814
	Yes	49 (24.1)		4 (1.8)		54 (23.0)		2 (0.7)	
Hypofractionation	No	34 (22.1)	.585	1 (0.6)	.592	25 (15.2)	.659	1 (0.6)	.842
	Yes	56 (21.7)		3 (1.2)		40 (15.3)		3 (1.2)	
Lymphadenectomy	No	40 (21.1)	.459	0 (0.0)	.223	27 (15.6)	.638	3 (1.7)	.201
	< 15 LNs	29 (21.2)		2 (1.5)		22 (16.1)		1 (0.7)	
	≥ 15 LNs	29 (30.9)		2 (1.4)		27 (19.4)		0 (0.0)	
EQD2 to the prostate bed α/β10	< 66.1 Gy	36 (19.0)	.221	1 (0.6)	.473	32 (17.6)	.424	2 (1.1)	.827
	≥ 66.1 Gy	53 (25.2)		3 (1.7)		45 (18.8)		2 (0.7)	
EQD2 to the LNs α/β10	≤ 44.1 Gy	45 (25.1)	.369	4 (2.2)	.191	42 (23.5)	.631	2 (1.1)	.410
	> 44.1 Gy	20 (22.0)		0 (0.0)		12 (15.2)		0 (0.0)	
Radiotherapy technique	3D-CRT	26 (21.3)	.455	1 (0.8)	.715	15 (12.8)	.659	1 (0.8)	.718
	IMRT/VMAT	74 (23.1)		5 (0.8)		62 (18.8)		3 (0.8)	
Image guidance	EPID	76 (21.3)	.325	4 (1.1)	.426	55 (15.0)	.160	4 (1.1)	.408
	Cone Beam	21 (34.2)		0 (0.0)		11 (12.8)		0 (0.0)	
Previous abdominal-pelvic surgery	No	84 (22.8)	.142	4 (1.2)	.711	79 (17.4)	.088	4 (1.2)	.711
	Yes	6 (13.6)		0 (0.0)		3 (6.7)		0 (0.0)	
Adjuvant ADT	No	26 (17.2)	.346	0 (0.0)	.150	23 (14.7)	.307	1 (0.6)	.847
	Yes	71 (24.4)		4 (1.4)		55 (19.2)		3 (1.0)	
Type of ADT	LHRH	49 (22.8)	.179	4 (1.8)	.295	41 (19.1)	.227	2 (0.9)	.868
	Bicalutamide	22 (40.7)		0 (0.0)		13 (16.9)		1 (1.3)	

Legend: ADT: androgen deprivation therapy; LNs: lymph nodes

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EARLY BIOCHEMICAL OUTCOMES FROM A PROSPECTIVE TRIAL TESTING STEREOTACTIC SALVAGE RADIOTHERAPY FOR MACROSCOPIC PROSTATE BED RELAPSE AFTER SURGERY - STARR (NCT05455736)

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Aims. Biochemical recurrences after radical prostatectomy (RP) can be managed with curative purpose through salvage radiation therapy (SRT). RT dose escalation, such as stereotactic RT (SSRT), may improve relapse-free survival in this setting.

Methods. STARR (NCT05455736) is a prospective multicenter study including patients treated with RP for localized prostate cancer and affected by macroscopic recurrence within the prostate bed. All patients with evidence of regional or distant metastatic disease were excluded from the trial. All patients underwent SSRT for a total dose of 35 Gy in 5 fractions. Treatment was administered with an every-other-day schedule. Concomitant Androgen Deprivation Therapy (ADT) was not allowed. Here we present early biochemical results after 3 months from treatment. Biochemical response (BR) was defined as PSA <50% if compared to baseline, and complete biochemical response (CBR) was defined as PSA < 0.2 ng/ml. Genitourinary (GU) and Gastrointestinal (GI) Toxicity were assessed according to CTCAE v 4.03.

Results. Forty six patients were enrolled, and data about BR and toxicity at three months after treatment were available for 27 cases. Overall, BR and CBR were detected after three months in 70.3% and 40. 7% of cases, respectively. Overall, only 3 G1-G2 GU adverse events were recorded; no G ≥ 3 or GI adverse events were detected.

Conclusion. SSRT appears feasible and safe. The STARR trial is one of the few prospective studies aimed at implementing this promising treatment strategy in this scenario.

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PSMA GUIDED APPROACH FOR BIOCHEMICAL RELAPSE AFTER PROSTATECTOMY-PSICHE TRIAL (NCT05022914)

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Aims. One of the fundamental approaches to treat biochemical relapse (BR) after radical prostatectomy (RP) is Salvage radiotherapy (SRT). A randomized controlled trial has indicated that next generation imaging (NGI) could influence the management of patients in this situation. However, further research is needed to deter-

mine the optimal management approach for oligometastatic patients identified through PSMA PET imaging. To address this, the PSICHE trial (NCT05022914) is a prospective multicentric study that aims to evaluate the effectiveness of a tailored strategy using [68Ga]Ga-PSMA-11 PET/CT imaging.

Methods. Patients who experienced biochemical relapse after radical prostatectomy (defined as PSA > 0.2 ng/ml, ≤1 ng/ml) underwent [68Ga]Ga-PSMA-11 PET/CT imaging. After staging, management was based on a predefined algorithm. Patients with negative PSMA results and prior postoperative radiotherapy were proposed observation and re-staging at further PSA progression. For patients with negative staging or positive imaging confined to the prostate bed, salvage radiotherapy to the prostate bed was recommended. In cases of pelvic nodal recurrence (nodal disease < 2 cm below the aortic bifurcation) or oligometastatic disease, stereotactic body radiotherapy (SBRT) was employed to treat all affected sites. Androgen deprivation therapy with or without an androgen receptor targeted agent was administered in case of widespread metastatic disease. This analysis focuses on the early biochemical response, specifically complete biochemical response (PSA levels ≤ 0.2 ng/ml) and biochemical response (PSA levels ≤ 50% if compared to baseline before treatment). Gastrointestinal (GI) and genitourinary (GU) toxicity were evaluated based on CTCAE v4.0 criteria.

Results. The current analysis involved a total of 110 patients. After 3 months from treatment, a complete biochemical response was observed in 45.4% of patients, while a biochemical response was seen in 53.6% of patients. Among the participants, seven patients experienced grade 1 gastrointestinal (GI) toxicity, while 30 patients reported genitourinary (GU) toxicity (27 with grade 1 and 3 with grade 2). No toxicity greater than grade 2 was reported in this study.

Conclusions. The prospective multicentric trial demonstrated promising results and favorable tolerability of a PET/CT PSMA based treatment strategy.

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TEN-YEAR RESULTS OF EXTENDED NODAL RADIOTHERAPY FOR PROSTATE CANCER RELAPSE, 11[C]-CHOLINE PET/CT GUIDED, IN PATIENTS OF A PHASE II PROSPECTIVE TRIAL

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Aims. To report 10-year outcomes of relapsed prostate cancer (PCa) patients, treated in a prospective single-arm study, approved by our institutional Ethics Committee, with extended–nodal radiotherapy (ENRT) and [11C]-choline positron emission tomography (PET)/computed tomography (CT)-guided simultaneous integrated boost (SIB) on positive lymph-nodes (LNs).

Methods. From 12/2009- 04/2015, 60 PCa patients with biochemical relapse and positive LNs only were treated in this study. Fifty-eight patients were previously operated on, and 34 of them treated with adjuvant/ salvage RT. ENRT at a median total dose (TD)=51.8 Gy/28 fr, and PET/CT-guided SIB on positive LNs to a median TD=65.5 Gy was prescribed. Median PSA at relapse was 2.3 (interquartile range, IQR:1.29-4.04) ng/ml, value at which PSMA and Choline PET/CT are equivalent (Fossati, J Urol 2020;204:296). Median number of positive LNs: 2 (range:1-18). Extra-pelvic lymph-nodes were present in 43.3% of patients. Androgen Deprivation Therapy (ADT) was prescribed for 48 patients, for a median of 30.71 (IQR: 18.46-43.07) months. Fifteen patients were castration resistant (CRPC).

Hormonal-naïve vs hormonal sensitive patients vs castration resistant patients; from post-hoc analysis emerged that OS for castration resistant patients was significantly different from that of either hormonal-naïve (p<0.0001, Bonferroni adjusted) and hormonal sensitive patients (p=0.0011, Bonferroni adjusted)

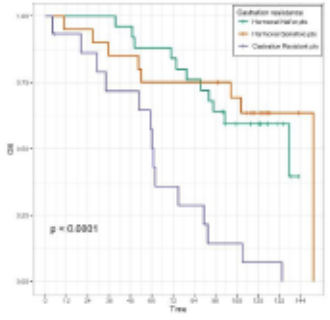

Figure 1.

Results. Median follow-up from the end of salvage treatment was 121.8 (IQR:116.10-130.94) months. Three, five, and 10-year Kaplan Meyer estimates of biochemical Relapse-Free Survival (bRFS) were: 45%, 36% and 24%; Clinical Recurrence-Free Survival (CRFS): 64.6%, 55.6% and 43.3%; Distant Metastases-Free Survival (DMFS): 67.9%, 59%, and 48.4%, and Overall Survival (OS): 88.2%, 76.3% and 47.9%, respectively. Castration resistance (HR=4.08;95%CI:1.77-9.37;p=0.0009) and ≥6 positive LN (HR=5.11;95%CI:1.87-14.01; p=0.0015) (see Figure 1) significantly influenced OS at multivariate analysis. Castration-resistance (HR=5.55;95%CI=2.24-13.74;p=0.0002) and para-aortic LN localization (HT=2.36; 95%CI=1.07-5.19;p=0.0327) influenced

CRFS at multivariate analysis. With ENRT+ SIB in-field relapses were only 8.3% in nearby lymph-nodes to the field *vs* 67% with SBRT (Decaestecker, Radiat Oncol 2014:9:135).

Conclusions. Good outcomes are registered in PCa relapsed patients treated with ENRT and PET/CT-guided SIB for positive LNs, with 43.3% without clinical relapse at 10 years. Castration resistance and presence of >5 positive LNs significantly influenced OS, while castration resistance and para-aortic LN localization influenced CRFS.

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CORRELATION BETWEEN TREATMENT-RELATED PARAMETERS AND LATE TOXICITY IN SALVAGE RADIOTHERAPY OF PROSTATE CANCER: A MULTICENTER OBSERVATIONAL STUDY ON 454 PATIENTS

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Aims. The aim of this study was to analyze the impact on late toxicity, in prostate cancer (PCa) patients treated with salvage radiotherapy (SRT), of several treatment-related parameters.

Methods. For the purpose of this analysis, data from PCa patients undergoing SRT were extracted from the database of a multicenter observational study. Endpoints of the analysis were 5-year grade ≥ 2 and ≥ 3 gastrointestinal (GI) and genitourinary (GU) late toxicity-free survival. The following parameters were correlated with adverse events: prophylactic nodal irradiation (PNI; yes *vs* not), hypofractionation (yes *vs* not), lymphadenectomy (no *vs* < 15 nodes *vs* ≥ 15 nodes), EQD2α/β3 to the prostate bed (< *vs* ≥ median value), EQD2α/β3 to the pelvic nodes (< *vs* ≥ median value), radiotherapy technique (3D-conformal RT *vs* IMRT/VMAT), image guidance (EPID *vs* cone-beam/CT), previous abdominal-pelvic surgery (yes *vs* not), adjuvant androgen deprivation therapy (ADT; yes *vs* not), and type of ADT (LH-RH agonists *vs* high dose bicalutamide). Late toxicity was scored using the RTOG/EORTC scale.

Results. Four hundred fifty-four PCa patients were enrolled in this analysis. Overall, 5-year grade ≥ 2 and ≥ 3 late GI toxicity-free survival was 91.5% and 97.7%, respectively. In addition, 5-year grade ≥ 2 and ≥ 3 late GU late toxicity-free survival was 81.6% and 95.8%, respectively. No grade 4-5 toxicities were recorded. Table 1 shows the results of the analysis. At univariate analysis, patients treated with hypofractionation (*vs* conventional fractionation) and those irradiated with modulated techniques (IMRT/VMAT *vs* 3D-CRT) showed a significant reduction in late GI toxicity grade ≥ 2 and grade ≥ 3. However, the multivariate analysis did not confirm these correlations. Furthermore, no parameter was significantly predictive of GU toxicity of any grade in univariate and multivariate analysis.

Conclusions. SRT of PCa was well tolerated regardless of treatment techniques. Considering the growing body of evidence on the efficacy of higher-than-standard (66-70 Gy) doses and PNI, at least in some patient subgroups, it is interesting to note that both of these parameters were not correlated to worse late toxicity.

Table 1. Five-year late gastrointestinal and genitourinary toxicity Grade ≥ 2 and Grade ≥ 3.

		Number of patients [%]	Gastrointestinal G ≥ 2 (%)	p	Gastrointestinal G ≥ 3 (%)	p	Genitourinary G ≥ 2 (%)	p	Genitourinary G ≥ 3 (%)	p
Nodal irradiation	No	154 (33.9)	93.8	.144	98.1	.428	79.7	.482	96.4	.565
	Yes	300 (66.1)	90.2		97.0		82.9		94.7	
Hypofractionation	No	154 (33.9)	86.9	**.035**	94.1	**.002**	82.5	.845	94.6	.196
	Yes	300 (66.1)	94.2		99.3		80.2		95.0	
Lymphadenectomy	No	178 (39.2)	90.1	.767	95.3	.124	85.2	.290	93.8	.511
	< 15 nodes	137 (30.2)	92.7		98.6		75.1		96.1	
	≥ 15 nodes	139 (30.5)	92.5		99.1		83.6		96.7	
$EQD2_{\alpha/\beta=3}$ to the prostate bed (Gy)	< 68.3	203 (44.7)	92.9	.956	98.0	.678	77.7	.256	91.3	.114
	≥ 68.3	251 (55.3)	90.8		97.0		84.3		98.0	
RT technique	3D-CRT	119 (26.2)	85.7	**.032**	93.6	**.004**	85.1	.645	94.4	.466
	IMRT/VMAT	335 (73.8)	94.2		99.0		79.4		95.2	
Image guidance	EPID	367 (80.8)	91.3	.083	97.0	.235	80.8	.220	94.7	.578
	Cone Beam	87 (19.2)	95.0		100.0		84.5		100.0	
Previous abdominal-pelvic surgery	No	212 (46.7)	92.1	.757	97.6	.764	80.8	.485	95.1	.823
	Yes	242 (53.3)	88.0		95.8		88.9		96.8	
Adjuvant ADT	No	163 (35.9)	93.7	.226	98.9	.154	82.5	.842	96.2	.903
	Yes	291 (64.1)	90.3		96.6		81.0		94.8	
$EQD2_{\alpha/\beta=3}$ to the lymph node (Gy)	No	184 (40.5)	93.8	.258	98.1	.501	79.7	.610	96.4	.369
	≤ 43.2	179 (39.4)	90.4		96.6		83.3		92.5	
	> 43.2	91 (20.0)	89.4		97.6		81.8		100.0	

Legend: ADT: androgen deprivation therapy; EQD2: equivalent dose in 2 Gy/fraction; EPID: electronic portal imaging device; G: grade; IMRT: intensity modulated therapy; RT: radiotherapy; VMAT: volumetric modulated arc therapy.

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STEREOTACTIC RADIOTHERAPY FOR OLIGOPROGRESSIVE METASTATIC CASTRATION-RESISTANT PROSTATE CANCER PATIENTS UNDERGOING ARTA THERAPY

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Aims. To retrospectively evaluate the role of Stereotactic Radiotherapy (SRT) as Metastasis-Directed Therapy (MDT) in patients (pts) with oligoprogressive metastatic Castration-Resistant Prostate Cancer (mCRPC), undergoing Androgen Receptor Target Agents (ARTA) therapy in our institution.

Methods. From August 2015 to January 2023 70 oligoprogressive lesions in 26 mCRPC patients undergoing ARTA therapy (Abiraterone Acetate or Enzalutamide) were treated with MTD. SRT was delivered using Cyberknife® (N= 41 lesions), TomoTherapy® (N= 28) or RapidArc™ (N=1). To delay time to NExt-line Systemic Therapy (NEST), 65.4% of pts received one course of SRT, 19.2% of pts two courses and 15.4% three courses, respectively. Median Target Volume was 11.52 (range 0.3-511.8) cc and median biologically equivalent dose (BED), considering $\alpha/\beta = 1.5$ for prostate cancer, was 151 Gy (range 73,33-383,3). Fifteen (58%) pts were treated with Abiraterone (ABI) and 11 (42%) with Enzalutamide (ENZA). Primary end-points were time to NEST) and Overall Survival (OS). Side-effects were assessed according to Common Terminology Criteria for Adverse Events v5.0.

Results. Median follow-up after RT was 21 months (range 4.8-57.4). Ten pts continued ARTA, while 16 (62%) pts switched to systemic therapy. One patient discontinued SRT and underwent laminectomy. All other pts completed SRT and no ≥G2 side effects were registered. Local recurrence was observed in two pts (lesions treated with BED1.5=108,3 Gy), while the other pts presented distant metastasis. Kaplan Meier estimate of median time to NEST was 13.6 months. Six-, 12 and 24-month NEST-free survival were 80.6%, 67%, and 26.8%, respectively, without a significant difference between pts treated with ABI *vs* ENZA (p=0.83) (Figure 1a). One-, 3- and 5-year OS from the end of SRT was 95.8%, 41.5% and 17.8%, respectively. Three and five-year OS from the diagnosis of mCRPC were 68.6%, and 28.6%, respectively, without difference between ABI *vs* ENZA (p=0.5) (Fig.1b). Five and 10-years OS from diagnosis were 92% and 69.3%, respectively.

Conclusions. SRT as MDT, in patients with oligoprogressive mCRPC, is well-tolerated and allows to postpone the transition to a subsequent line of treatment, which is not always effective, by more than one year, with good OS results from mCRPC diagnosis. Prospective trials are awaited to confirm these results.

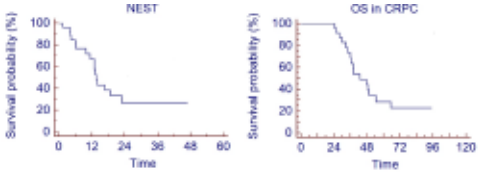

Figure 1. a) NExt-line Systemic Therapy-free survival from the end of salvage stereotactic radiotherapy for oligoprogressive disease during Androgen Receptor Target Agents (ARTA) therapy. b) Overall Survival for this cohort of patients from the diagnosis of metastatic castration resistant disease.

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IMPLEMENTATION OF SINGLE-DOSE ABLATIVE RADIATION THERAPY FOR PROSTATE CANCER WITH REAL-TIME TARGET MOTION MANAGEMENT

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Aims. To report the implementation of organ-confined linac-based prostate Single-Dose Ablative Radiation Therapy (SDART) using electromagnetic tracking as real-time intrafraction organ motion management.

Methods. Twenty-five patients with localized unfavorable intermediate or selected high-risk prostate tumor were enrolled (NCT04831983) to receive an ultra-high SDART of 24 Gy. Patients were simulated with empty rectum and bladder filled by a Foley catheter. Fused CT and MRI image sets were used to delineate the target and OARs. PTV included CTV with a 2 mm 3D-margin. A high-dose avoidance zone (HDAZ) was created by a 3 mm expansion of rectum, bladder, and urethra. Treatment planning aimed for minimum dose defined by OAR constraints, with dose escalation to 24 Gy in the target volume away from HDAZ using a 10MV FFF single arc. During the treatment delivery, CBCT matching ensured accurate patient setup and target localization. Real-time 3D prostate motion was tracked with an electromagnetic tracking device. Treatment

was interrupted and position was corrected when the signals exceeded a 2 mm threshold.

Results. All planning objectives were achieved. Median PTV volume was 70.9 cc [25.6-100.6]. Average MUs were 6785±569. All the treatment plans were quality assured using a 2D silicon diode array and fulfilled a 2%/2mm gamma passing rate >95% objective. Mean delivery time was 4.4±0.6 minutes, and mean overall treatment time was 15.2±7.5 minutes. Intrafraction tracking was successfully carried out in all sessions and beam interruptions due to target motion beyond limits were needed in 16 patients, with 2.1 [1-7] interruptions per patient on average. Mean target average deviation was -0.15±0.47 mm, 0.34±0.59 mm, and -0.32±0.64 mm in lateral, longitudinal, and vertical direction, respectively. Prostate displacement did not occur in a distinct direction. The prostate was found within 2 mm from its initial position in 82% of the treatment time, i.e. in 77% of the time during the setup phase and in 94% during the delivery phase (beam on + interruptions).

Conclusions. The volume of rectal mucosa receiving critical doses was limited by the use of an HDAZ. The accomplishment of urethra sparing via negative dose painting to minimize GU toxicity is feasible through appropriate imaging procedures and online tracking during treatment delivery. Our preliminary findings offer encouraging perspectives on the feasibility and safety of 24 Gy SDART in organ-confined prostate cancer.

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OLIGOMETASTATIC PROSTATE CANCER TREATED WITH STEREOTACTIC BODY RADIATION THERAPY: THE ROLE OF 3D TUMOR VOLUME ON PATIENTS' SURVIVAL

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Aims. The definition of oligometastatic prostate cancer (OPCa) is currently based on the maximum number of detectable metastases, as there are no validated biomarkers available. The objective of this study was to identify novel predictive factors for OPCa patients who underwent stereotactic body radiation therapy (SBRT).

Methods. This monocenter retrospective study included consecutive OPCa patients with a maximum of 5 metastases in up to 2 organs, detected with Choline- or PSMA- PET, who were treated with metastases-directed SBRT. Endpoints were overall survival (OS) and progression free survival (PFS), assessed with Kaplan-Meier analysis. Univariate and multivariable Cox regression was performed to evaluate the association between clinical factors and survival outcomes.

Results. Between 2009 and 2021, 163 patients and 320 metastases were treated with 226 SBRT courses. The median 3D metastatic tumor volume was 4.1 cc with a range from 0.01 to 233.4 cc. Eightyseven (53.4%), 21 (12.9%) and 55 (33.7%) patients were classified as cN1, cM1a and cM1b, respectively. The median follow-up was 28.5 months. The rates of OS at 1, 3 and 5-yr were 89.5% (95% CI 83.4-93.4), 74.9% (95% CI 66.1-81.7) and 57.2% (95% CI 45.8-67.1), respectively. Multivariable analysis showed that OS reduced with the increase of 3D total tumor volume (HR 1.93 95% CI 1.06-3.52; p=0.030) and confirmed a significant difference between cM1a-b *vs* cN1 disease (HR 1.81 95% CI 1.01-3.25; p=0.046). The cut-off value of total tumor volume correlated with highest risk of death was 20 cc (HR 2.37, 95% CI 1.34-4.18; p=0.003). The median PFS was 17.8 months with 1, 3 and 5-yr rates of 63.7% (95% CI 55.4-70.9), 31.5% (95% CI 22.8-40.6) and 24.7% (95% CI 16.0-34.3).

Conclusions. This study identified 3D total tumor volume and the site of oligometastases as significant predictors of survival in OPCa patients treated with metastases-directed SBRT. These parameters can be potentially used to personalized treatment and improve patient outcome.

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A NOVEL ANATOMICAL ROBUST OPTIMIZATION STRATEGY FOR PROSTATE CANCER: A RADIOSA TRIAL SPIN-OFF STUDY

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Purpose. CTV-to-PTV margins proposed in literature are based on assumptions no longer applicable, and classical optimization in SBRT considers uncertainties in patient-setup only. Aim of this retrospective study is to evaluate the dosimetric efficacy of robust optimization (RO) for lymphnodal lesions in oligometastatic prostate cancer (PCa) setting. Aim of the present study, side project of phase II randomized clinical trial RADIOSA (NCT03940235), is the development and testing of an anatomical robust optimization (aRO) method that can meet target coverage and dosimetric constraints despite variation in PTV position and bladder/rectal filling.

Methods. Twelve PCa patients treated at IEO and

with delivered plan isodose curve 50% intersecting bladder/rectum were selected. For each patient, two RT treatment plans were generated: (i) a PTVbased (PTVb) plan on the planning CT (pCT) using 5mm as CTV-to-PTV margin; (ii) a robust optimized (RO) plan on the pCT using 3mm as margin and including five additional CTs, four simulating shifts of PTV by 5 mm and one simulating an expansion of bladder and rectum by 0.24 and 0.27 mm, respectively. Both plans simulated 30Gy/3fractions VMAT. The two strategies were compared (i)on the pCT in terms of PTV-coverage and homogeneity index (HI), and constraints compliance; (ii)in terms of robustness, simulating eight error scenarios.

Results. Median value in the considered parameters on pCT and in the worst scenario (WS) across all pts can be seen in Table 1 for both strategies. Despite the smaller margin used, the proposed optimization method provided plans that can meet all constraints and clinical goals on the nominal scenario. RO plans provided target coverage comparable with PTVb plans, except D99% and PTV-HI which were significantly better ($p<.05$). Regarding robustness evaluation, considering the worst scenario (WS), target coverage and PTV-HI were significantly higher ($p<.05$) compared with PTVb plans, and variations between nominal and WS were significantly lower ($p<.05$) in all considered parameters, pointing the increased robustness of the novel optimization method.

Conclusion. Inclusion of CTs as additional scenarios in the optimization process provided plans more robust against changes in PTV position. RO, already used in PT, can be exploited in SBRT to reduce margins and increase confidence in treatment delivery.

Table 1.

Table 1 - Median values of considered parameters on the planning scenario (a) and worst scenario (b), and median percentage variations (c) across all patients for the two considered planning approaches. A p-value (from Wilcoxon signed-rank tests) < .05 was considered statistically significant.

	a) Planning CT			b) worst scenario			c) % variation (Worst scenario - planning CT)		
	PTVb	RO		PTVb	RO		PTVb	RO	
PTV									
D98%	92.91	93.48	p > .05	26.76	29.48	p < .05	-5.55	-5.98	p < .05
D99%	92.75	93.39	p < .05	25.26	29.28	p < .05	-6.18	-4.23	p < .05
D95%	93.55	93.58	p > .05	29.39	29.87	p < .05	-3.97	-2.55	p < .05
D50%	92.08	91.00	p > .05	30.95	30.96	p > .05	-0.58	-0.48	p < .05
D2%	91.47	91.22	p > .05	31.53	31.26	p > .05	0.35	0.21	p < .05
HI	0.95	0.97	p < .05	0.82	0.68	p < .05	-14.13	-9.79	p < .05
Bladder									
D2%	12.86	16.14	p > .05	15.91	17.42	p > .05	22.46	20.88	p > .05
Rectum									
D2%	18.93	21.38	p > .05	23.21	23.62	p > .05	16.23	16.83	p > .05

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YOUNGER AGE IS AN UNFAVORABLE PREDICTOR OF BIOCHEMICAL AND CLINICAL OUTCOMES IN POSTOPERATIVE RADIOTHERAPY OF PROSTATE CANCER. A SUBANALYSIS OF A MULTICENTER OBSERVATIONAL STUDY ON 381 PATIENTS

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Aims. Postoperative radiotherapy (PORT) is used in patients with prostate cancer (PCa) and high risk of recurrence or detectable PSA after radical prostatectomy (RP). The possibility of future optimization of the outcome in this setting requires the identification of prognostic factors to intensify the treatment in patients with a higher risk of PORT failure. Therefore, we analyzed patient-, tumor-, and treatment-related data in patients enrolled in an observational study and undergoing PORT.

Methods. From the database of a multicenter observational study we extracted the data of PCa patients undergoing PORT (<1 year after RP). Endpoints of the study were biochemical relapse-free survival (bRFS), local control (LC), regional control (RC), metastasis-free survival (MFS), disease-free survival (DFS), and overall survival (OS). Univariate (logrank) and multivariate (Cox's) analyses were performed including the characteristics of patients (age [1st *vs* 2nd-4th quartile] and Charlson's comorbidity index), tumors (pre- and post-RP PSA level, ISUP grade, pT stage, pN stage), and therapy (delivery of prophylactic nodal irradiation [PNI], ADT type and duration, PORT fractionation and technique,

type of image-guidance system, CTV to PTV margin, and $EQD2_{\alpha/\beta=1.5}$ to the prostate bed and pelvic nodes). Parameters with significance level p<0.2 at the univariate analysis were included in the multivariate analysis.

Results. Three hundred and eighty-one patients were included in this analysis whose results are shown in Table 1. The pT stage was 2, 3, and 4 in 18.9%, 79.5%, and 1.6% of cases, respectively. The pN stage was 0 and 1 in 85.3% and 14.7% of cases, respectively. Younger patients age (1st quartile: < 62 years) and pN1 were significantly and independently correlated with worse bRFS and DFS. Furthermore, bRFS was worse in patients with pN1 stage, higher postoperative PSA levels, and higher ISUP grade. In addition, the following significant correlations were recorded: worse LC in pN1 patients, better RC in patients undergoing PNI or with preoperative PSA <10 ng/dL, and better OS in patients with pN0 (vs pN1) and no prior cancer history (Table 1).

Table 1. Multivariable analysis (only statistically significant values are shown).

Variable	value	bRFS			DFS			LC			RC			OS		
		HR	95%CI	p	HR	95%CI	p	HR	95%CI	p	HR	95%CI	p	HR	95%CI	p
Age category (years)	<62	1.00 *(Ref)*			1.00 *(Ref)*											
	≥62	0.35	0.17-0.70	**.003**	0.42	0.19-0.91	**.029**									
pN stage	No	1.00 *(Ref)*			1.00 *(Ref)*			1.00 *(Ref)*						1.00 *(Ref)*		
	Yes	2.94	1.39-6.17	**.004**	2.78	1.16-6.69	**.022**	4.93	1.18-20.71	**.029**				11.81	2.82-49.51	**.001**
PSA postoperative	≤0.013	1.00 *(Ref)*		**.017**												
	0.114-0.039	11.14	2.44-50.82	**.002**												
	0.040-0.09	5.89	1.27-27.26	**.023**												
	> 0.09	6.27	1.36-28.93	**.019**												
ISUP grade	1	1.00 *(Ref)*		**.018**												
	2	1.07	0.23-4.89	.928												
	3	3.83	1.07-13.8	**.040**												
	4	0.90	0.21-3.91	.891												
	5	2.50	0.66-9.48	.176												
Previous history of cancer	No													1.00 *(Ref)*		
	Yes													12.63	2.11-75.66	**.005**
PNI	No										1.00 *(Ref)*					
	Yes										0.05	0.004-0.45	**.008**			
PSA preoperative	< 10										1.00 *(Ref)*		.068			
	10-20										15.23	1.53-151.77	**.020**			
	> 20										0.00	0.00-83.4	.994			

Legend: bRFS: biochemical relapse-free survival; CCI: Charlson's Comorbidity Index; DFS: Disease-free survival; ISUP: International Society of Urological Pathologists; LC: Local control; MFS: Metastasis-free survival; OS: Overall survival; PNI: prophylactic nodal irradiation; PSA: Prostate Specific Antigen; RC: Regional control.

Conclusions. Younger age is an unfavorable predictor of both biochemical and clinical recurrences in PCa patients undergoing PORT. Therefore, age should be considered in the design of predictive models in this setting.

P244

FIRST CLINICAL RECURRENCE AFTER RP: CHOLINE/PSMA-PET OR MPMRI GUIDED-SBRT ON DETECTABLE PROSTATE BED RECURRENCE

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Purpose or Objective. Biochemical recurrence (BR) on prostate bed occurred in about 30% of PCa patients (pts) after RP. Diagnostic imaging has made significant advances in recent years, enabling precise detection of disease recurrence. However, the most appropriate salvage RT for this clinical setting remains a matter of debate. The aim of the present study is to evaluate the efficacy and safety of SBRT on the detectable prostate bed recurrence.

Materials and Methods. Men who underwent SBRT to macroscopic bed recurrence after RP between December 2014 and June 2022 were retrospectively considered. All pts were staged with mpMRI and/or choline/PSMA PET. Toxicities were collected according to the RTOG scale.

Table 1. Summary of patients and treatment characteristics.

		n (%)
pT		
	2	39 (47)
	3	40 (49)
	4	1 (1)
	x	2 (3)
pN		
	0	69 (84)
	1	9 (11)
	x	4 (5)
Surgical margins		
	Negative	55 (67)
	Positive	25 (30)
	x	2 (3)
ISUP Grade		
	1	7 (8)
	2	27 (33)
	3	30 (37)
	4	7 (8)
	5	9 (11)
	missing	2 (3)
Perineural invasion		
	No	61 (74)
	Yes	19 (23)
	x	2 (3)
Type of imaging		
	PET + mpMRI	42 (51)
	PET only	11 (13)
	mpMRI only	29 (34)
PET tracer		
	Choline	26 (49)
	PSMA	27 (51)

Results. A total of 82 pts, with a median age at recurrence of 71 years, were included in the analysis. A summary of the pts characteristics is reported in Table 1. Median time to BR after RP was 46.2 months (IQR 21.9-91.9) with a median PSA at restaging of 1.1 ng/ml (IQR 0.4-1.83). All patients underwent SBRT on prostate of 30-35 Gy in 5 fx every other day with a dose/fx of 7 (n=76) or 6 (n=6) Gy. Twelve patients underwent concomitant ADT. Only one acute G2 GU toxicity was observed. No G≥3 GU/GI acute toxicities were noted and no toxicities were reported at last FU. After a median FU of 15.3 months (IQR 10.1-43.1), 27 (33%) pts experienced a BR with a median time to BR of 18.22 months (range 5.3-69.1) and a median PSA at recurrence of 1.27 (IQR 0.7-2.0). BR-free survival at 1- and 2-year was 74% and 41%, respectively. Eighteen out of 27 pts developed a clinical recurrence with 12 local, 6 oligo and 3 poli (≥ 5 lesions) relapses. Regarding local recurrences ten out of twelve (83%) were in the field of treatment. Interestingly all the six pts receiving 6 Gy/5 fx developed a local recurrence and five of them were in field. At last censored follow-up

(data available for 62 patients), 24 (39%) patients are alive with disease while 38 (61%) are alive with no evidence of disease. Median PSA at last FU is 0.16 (IQR 0.05-0.7).

Conclusions. These preliminary data showed that targeting macroscopic bed recurrence with SBRT resulted to be safe and effective. Dose escalation strategies should be considered in order to reduce the number of in field recurrences. Additional data and longer FU will provide a clearer indication on the most appropriate staging methodology and on the right way to treat these pts.

P245

ULTRA-HYPOFRACTIONATED RADIOTHERPY IN ELDERLY PROSTATE CANCER PATIENTS: RESULTS FROM A SINGLE CENTER EXPERIENCE

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Aim: Longer life expectancy has led to a significant increase in the number of elderly patients (pts) localized PCa candidates for curative RT. Pts aged ≥ 80 years often present a high prevalence of comorbidities and it is difficult to propose RT +/- ADT as recommended by NCCN guidelines. The aim of the present study (Ethical Committee approval UID 2684) is to evaluate the efficacy and safety of personalized ultra-hypofractionated RT (UHRT) +/- ADT in this setting of pts.

Methods. Elderly men aged ≥80 years with localized PCa who underwent UHRT on prostate between 2012 and 2022 were retrospectively included. Toxicities were collected according to RTOG scale.

Results. A total of 181 pts fulfilled inclusion criteria (Table 1). Median age at diagnosis was 82 years (Range 80-95) and median PSA at diagnosis was 7.625 ng/ml (range 0.72-220.4). The majority of pts (n = 116, %) had a Charlson Comorbidity Index (CCI) of six. A total of 63 (34.8%) and 33 (18.2%) were on regular anticoagulant and antiaggregant therapy, respectively. All pts underwent UHRT on prostate in 5 fx every other day with a dose/fx within 6.25 and 7.25 Gy. Of them, 59 pts received a SIB on dominant intraprostatic lesions of 7.5/8 Gy fx. The majority of pts (n = 100, 55.3%) underwent concomitant ADT with a median duration time of 12.0 months (IQR 6.1-12.7, available for 75 pts). Median follow-up (FU) was 24 months (IQR 13.1-34.8, FU available for 156 pts). Median PSA at last FU (available for 141 pts) was 0.5 ng/ml. A total of 17 pts (10.9%) experienced a biochemical recurrence, with a median time from the end of RT of 24.6 months (IQR 15.7-29.9). Among them, 9 developed a clinical progression (1 local relapse, two pelvic lymphnodal progression, and the others distant progression) of disease (respectively six, two, and one, in high, unfavorable intermediate and favourable intermediate risk classes). Considering pts with availability of maximum late toxicities data (n = 126, 70%), 31 and 8 pts had G1 and G>2 late GU toxicity, respectively. Three and five pts experienced G1 and G>2 late GI toxicities (Table 1).

Conclusions. Our data showed that, despite the high CCI scores, elderly and frail patients have excellent biochemical control and secure GI/GU toxicity profiles. Personalized UHRT +/- ADT course should be proposed as a treatment option in this setting of patients.

Table 1. General cohort characteristics and reported toxicities.

Table 1. General cohort characteristics and reported toxicities.

Pts characteristics	
	Median (IQR)
CTV Volume (cc)*	54.6 (42.4 – 73.1)
	n (%)
Risk class	
Low Lowing	18 (9.9)
Favourable intermediate	60 (33.1)
Unfavourable intermediate	40 (22.1)
High	62 (34.3)
Missing	1 (0.6)
HT = YES	100 (55.3)
Low risk	3 (16.7)
LHRHa	3 (100)
Favourable intermediate	19 (31.7)
Casodex	8 (44.4)
LHRHa	8 (44.4)
TAB	3 (15.8)
Unfavourable intermediate	19 (47.5)
Casodex	7 (36.8)
LHRHa	11 (57.9)
TAB	1 (5.3)
High	58 (93.6)
Casodex	15 (25.9)
LHRHa	38 (65.5)
TAB	5 (8.6)
CCI	
6	116 (64.1)
7	50 (27.6)
8	11 (6.1)
9	2 (1.1)
10	1 (0.6)
11	1 (0.6)
Follow-up data	
Acute maximum GU toxicity	
G0	116 (64.1)
G1	58 (32.0)
G2	6 (3.3)
G4	1 (0.6)
Acute maximum GI toxicity	
G0	169 (93.3)
G1	8 (4.4)
G2	2 (1.1)
G3	1 (0.6)
missing	1 (0.6)
Late maximum GU toxicity**	
G0	87 (69.0)
G1	31 (24.6)
G2	7 (5.6)
G≥3	1 (0.8)
Late maximum GI toxicity**	
G0	118 (93.7)
G1	3 (2.4)
G2	3 (2.4)
G3	2 (1.6)
Last follow-up status	
NED	142 (91)
AWD	11 (7.1)
DIED for other causes	3 (1.9)

*Data available for 154 patients

**Data available for 126 patients

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DCE-MRI-BASED ATLAS FOR PROSTATE BED RECURRENCE AFTER RADICAL PROSTATECTOMY: CONSISTENCY OF CTV DELINEATION WITH THE AVAILABLE CONTOURING GUIDELINES

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Aims. To create a magnetic resonance image (MRI)-based atlas of prostate bed recurrence for salvage radiotherapy (sRT) and to evaluate the consistency of contouring guidelines for the prostatic fossa clinical target volume (PF-CTV).

Methods. Patients with biochemical recurrence and prostate bed lesions at MRI were included. A reference patient was identified and the lesion(s) of each patient was mapped by a co-registration among T2 weighted images. The structure sets were combined to create a 3D recurrence incidence map, overlapped on T2w reference set, then transferred to the planning CT, and a 3D-recurrence incidence map was created. The volume and the location of the lesions were extracted. 5 PF-CTV contouring strategies were implemented: Radiation Therapy Oncology Group (RTOG); European Organization for Research and Treatment of Cancer (EORTC); Francophone Group of Urological Radiotherapy (GFRU); Faculty of Radiation Oncology Genito-urinary Group (FROGG) and Princess Margaret Hospital (PMH). Coverage was assessed after identifying the centroid of each lesion: if the centroid was included in the PF-CTV, fully covered (FC), otherwise uncovered (UC). The coverage was evaluated for each strategy and compared with the chi-squared test; the strength of the correlation was assessed with the phi coefficient.

Results. 112 patients with 124 recurrences were identified. The lesions were located at the vesicourethral anastomosis (VUA), around the bladder neck (BN) and beyond the bladder (RV) in 63, 36 and 25 cases. 81.9% of the lesions were FC. Coverage was higher for BN (95.6%) over RV (83.2%) and VUA (73.7%) lesions. FC/UC rates were 66.1%/33.9%, 83.9%/16.1%, 89.5%/10.5%, 83.1%/16.9%, 87.1%/12.9% for EORTC, FROGG, GFRU, RTOG and PMH, respectively. At pairwise comparison, the EORTC definition had lower coverage and was poorly correlated to the other strategies. After selecting VUA lesions, the probability of FC was 60.3%, 74.6%, 82.5%, 71.4% and 79.4% for EORTC, FROGG, GFRU, RTOG and PMH, respectively. The EORTC definition performed poorly than GFRU and PMH. When considering lesions above the VUA, the performance improved (FC: 72.1%, 93.4%, 96.7%, 95.1% and 95.1% for EORTC, FROGG, GFRU, RTOG and PMH, respectively) but the EORTC was significantly less covering and its correlation with others was ≤ 0.1.

Conclusions. According to the criterium of coverage our data do not support the use of the EORTC definition. Here we provide an MRI-based atlas of prostatic bed recurrence that can optimize sRT contours.

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1.5T MR-GUIDED RADIOTHERAPY VERSUS LINAC-BASED VOLUMETRIC-MODULATED ARC STEREOTACTIC BODY RADIOTHERAPY IN THE TREATMENT OF LOCALIZED PROSTATE CANCER: A TOXICITY COMPARATIVE STUDY

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Aims. To compare acute toxicity of prostate cancer (PCa) stereotactic body radiotherapy (SBRT) delivered by MR-guided radiotherapy (MRgRT) with 1.5T MR-linac or by volumetric modulated arc (VMAT) with conventional linac.

Methods. Patients with low-to- favorable intermediate risk class PCa were treated with exclusive SBRT (35 Gy in 5 fractions). Patients treated with MRgRT were enrolled in an Ethical Committee (EC) approved trial (Prot. n° 23748), while patients treated with conventional linac were enrolled in an EC approved phase II trial (n° SBRT PROG112CESC). The primary end-point was the acute toxicity. Patients were included in the analysis if they had at least 6 months of follow-up for the primary end-point evaluation. Toxicity assessment was performed according to CTCAE v5.0 scale. International Prostatic Symptoms Score (IPSS) was also performed.

Results. 135 patients were included in the analysis. 72 (53.3%) were treated with MR-linac, and 63 (46.7%) with conventional linac. The median initial PSA before RT was 6.1 ng/ml (range 0.49-19). Globally, acute G1, G2, and G3 toxicity occurred in 39 (28.8%) 20 (14.5%), and 5 (3.7%) patients. At the univariate analysis, acute G1 toxicity did not differs between MR-linac and conventional linac (26.4% versus 31.8%), as well as G2 toxicity (12.5% versus 17.5%; p=0.52). Acute G2 gastrointestinal (GI) toxicity occurred in 7% and 12.5% of cases in MR-linac and conventional linac group, respectively (p=0.06), while acute G2 genitourinary toxicity occurred in 11% and 12.8% in MR-linac and conventional linac, respectively (p=0.82). The median IPSS before and after SBRT was 3 (1-16) and 5 (1-18). Acute G3 toxicity occurred in 2 cases in the MR-linac and 3 cases in the conventional linac group (p=n.s.).

Conclusions. Prostate SBRT with 1.5T MR-linac is

feasible and safe. Compared to conventional linac, MRgRT might to potentially reduce the overall G1 acute toxicity at 6 months, and seems to show a trend towards a lower incidence of grade 2 GI toxicity. A longer follow-up is necessary to assess the late efficacy and toxicity.

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INCIDENCE AND PREDICTORS OF LOWER EXTREMITY LYMPHEDEMA AFTER POST-PROSTATECTOMY RADIOTHERAPY

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Aims. Rate and predictors of lower extremity lymphedema (LEL) after radiotherapy (RT) following radical prostatectomy (RP) + pelvic lymph node dissection (PLND) for prostate cancer.

Methods. This is a cross sectional study on patients (pts) treated with adjuvant or salvage RT after RP+PLND and with a minimum 2-year follow-up. LEL was defined as a volume difference of ≥10% between limbs determined using circumferential measurements. The onset of LEL was then retrospectively assessed. The following potential predictors of the endpoint were investigated at logistic regression: age; body mass index (BMI); exercise level according to the International Physical Activity Questionnaire; smoking; cigarette pack/year; hypertension; vascular comorbidity; diabetes; PLND; number of examined nodes; whole pelvis radiotherapy (WPRT); time between RP and RT; planning target volume (PTV); PTV/BMI. Statistical significance was claimed for p values <0.05.

Results. 101 pts accepted study enrollment. Median time from surgery to RT was 36.1 months (mths) (IQR: 15.0-68.3 mths) and median time from RT to the date of study examination was 51.1 months (IQR: 36.8-65.3 mths). All pts underwent RP & prostatic fossa RT, 70 pts (69.3%) underwent PLND with the removal of a median number of 12.5 nodes (IQR: 8-17.2) and 69 pts underwent WPRT (68.3%). 14 pts developed LEL (13.9%, 95%CI: 8.4-21.9%). Most of the pts (92.8%) developed unilateral LEL. Three pts dated the onset of LEL before RT while in the remaining pts LEL occurred after RT. The median time from RT to LEL was 4 mths (IQR: -0.5/17.3). The latest event was recorded 25.4 months after RT completion. At multivariable analysis (MVA) diabetes mellitus (OR=32.8, p=0.02), the time between surgery and RT (OR=0.966, p=0.039) and exercise (OR=0.03, p=0.002) were independently correlated to the risk of LEL. Smoking had a borderline effect (OR=4.8, p=0.052). The number of examined nodes was highly correlated to LEL at univariate analysis (OR=1.066, p=0.025) but disappeared at MVA (p=0.719). Interestingly, the distribution of examined nodes was statistically different between pts with low (median N=12) *vs* medium/high (N=5) exercise (p=0.034) suggesting exercise level being more a consequence of the extent of pelvic surgery rather than a cause of LEL.

Conclusions. LEL involves a minority of pts after RT (≈20%); diabetes and time between surgery and RT are a predisposing factor.

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GUIDING METASTASES-DIRECTED THERAPY WITH PROSTATE-SPECIFIC MEMBRANE ANTIGEN (PSMA) PET/CT IMPROVES THE ONCOLOGICAL OUTCOME OF OLIGOMETASTATIC PROSTATE CANCER PATIENTS

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Aims. To verify the impact of next-generation imaging compared to conventional imaging as a guide for metastases-directed therapy (MDT) in a real-world multicentric cohort of oligometastatic prostate cancer (PCa) patients.

Methods. We retrospectively recruited 256 de-novo oligometastatic or oligorecurrent PCa patients submitted to image-guided MDT in six tertiary-level cancer Centers. Inclusion criteria were: (i) histologically-confirmed diagnosis of PCa; (ii) imaging evidence of ≤5 pelvic or extra-regional nodal (M1a), or bone metastases (M1b); (iii) upfront MDT delivered through SBRT±systemic therapy guided by either bone scan+CT/MRI (conventional imaging), [18F]F-Fluorocholine, [68Ga]Ga-PSMA-11 or [18F]-PSMA-1007; (iv) availability of the subsequent clinical follow-up. Progression after MDT was defined as either biochemical recurrence (PSA raise ≥2 ng/dL and 25% above nadir), radiological or clinical progression, subsequent treatment changes, or death. Clinical, laboratory and imaging parameters were assessed as predictors of Progression-Free Survival (PFS, primary endpoint of the study).

Results. Clinical characteristics of patients enrolled at the time of MDT are shown in Table 1.

Table 1.

Table 1. Clinical characteristics of patients enrolled at the time of metastasis-directed therapy.

	Overall (n=256)	Conventional imaging-guided MDT (n=12)	[18F]F-Fluorocholine-guided MDT (n=162)	PSMA-guided MDT (n=80)	p-value
Pre-imaging clinical characteristics					
Age	73.38±8.99	72.58±8.17	71.38±7.09	72.89±8.64	0.800
Initial AJCC stage					
Stage I	12 (4.7%)	1 (7.7%)	9 (5.5%)	2 (2.5%)	<0.001
Stage II	57 (22.3%)	0 (0.0%)	37 (22.7%)	20 (25.0%)	
Stage III	142 (55.5%)	7 (53.8%)	91 (55.8%)	45 (56.0%)	
Stage IV	45 (17.5%)	5 (38.5%)	26 (16.0%)	10 (12.5%)	
ISUP grade					
ISUP 1	38 (14.8%)	1 (7.7%)	21 (15.9%)	12 (15.0%)	0.501
ISUP 2	89 (25.3%)	1 (7.7%)	38 (25.3%)	20 (25.0%)	
ISUP 3	62 (24.2%)	4 (30.7%)	33 (25.3%)	23 (28.8%)	
ISUP 4	41 (16.0%)	1 (7.7%)	29 (17.8%)	11 (13.7%)	
ISUP 5	36 (21.9%)	6 (46.2%)	36 (22.1%)	14 (17.5%)	
Systemic treatment					
Surgery	387 (75.0%)	3 (23.1%)	116 (71.2%)	68 (85.0%)	<0.001
Androgen-ogic (± cRT)	33 (12.7%)	3 (23.1%)	40 (24.5%)	10 (12.5%)	
Medical therapy	15 (5.2%)	7 (53.8%)	7 (4.2%)	2 (2.5%)	
CRPC at MDT	38 (22.7%)	9 (69.2%)	37 (22.7%)	12 (15.0%)	<0.001
Treatment at MDT	109 (42.6%)	12 (92.3%)	65 (39.9%)	32 (40.0%)	0.001
PSA, ng, MDT	1.76±6.12	9.18±15.30	3.98±6.39	3.81±6.72	0.001
Time of oligometastatic disease					
De novo	50 (19.5%)	8 (61.5%)	24 (14.7%)	18 (22.5%)	<0.001
Oligorecurrent disease	206 (80.5%)	5 (38.5%)	139 (85.3%)	62 (77.5%)	
Imaging findings					
Number of metastases					
1 lesion	174 (68.0%)	7 (53.8%)	111 (68.5%)	56 (70.0%)	0.034
2 lesions	56 (21.9%)	2 (15.4%)	40 (24.5%)	14 (17.5%)	
3 lesions	18 (7.0%)	2 (25.2%)	11 (6.7%)	4 (5.0%)	
4 lesions	6 (2.3%)	1 (7.7%)	1 (0.6%)	4 (5.0%)	
5 lesions	2 (0.8%)	0 (0.0%)	0 (0.0%)	2 (2.5%)	
Site of metastases					
Lymph node	175 (68.4%)	3 (23.1%)	119 (73.0%)	53 (66.3%)	0.001
Bone	81 (31.6%)	10 (76.9%)	44 (27.0%)	27 (33.7%)	
Oligoma			9.02±6.10	9.76±8.77	0.113
MTV			3.06±2.95	2.81±2.34	0.395
TLG			27.09±26.68	32.75±27.90	0.145
MDT parameters and clinical follow-up					
MDT total dose (per session)	35.35±4.29	30.54±2.46	35.36±3.78	35.88±4.62	0.028
MDT BED (per lesion)	121.72±28.39	101.67±17.04	127.38±31.76	118.38±23.31	0.037
Follow-up (months)	37.14±24.75	17.50±14.57	44.75±25.32	24.75±17.48	<0.001

MDT was guided by conventional imaging, choline PET/CT, or PSMA PET/CT in 5.1%, 63.7% and 31.2% of patients, respectively. After MDT, the PSA nadir was 2.58±8.97 ng/mL. The median follow-up was 30.8 months. At the univariate analysis, predictors of PFS were the castration resistance status at the time of MDT (p=0.013), the PSA pre-MDT value (p<0.001), oligorecurrent compared to *de novo* oligometastatic disease (p=0.030), the number of metastatic lesions (p=0.038), the presence of bone metastases (p=0.006), and the PSA nadir after MDT (p<0.001). Notably, the use of either conventional imaging or choline PET/CT compared to PSMA PET/CT significantly predicted PFS (p<0.001 for both). The multivariate analysis confirmed imaging modalities guiding MDT and the PSA nadir as the sole independent predictors of PFS (p<0.001 for both). Patients receiving MDT guided by conventional imaging, choline PET/CT, or PSMA PET/CT showed significantly different median PFS (5.8 vs. 13.1 vs. 34.5 months, respectively, p<0.001).

Conclusions. The use of next-generation imaging with PSMA PET/CT favorably impacts the oncological outcome of oligometastatic PCa patients treated with MDT.

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SBRT FOR CLINICALLY LOCALIZED PROSTATE CANCER: A PROPENSITY SCORES ANALYSIS BETWEEN TWO RT SCHEDULES

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Purpose. To report oncological outcomes and toxicities of a series of clinically localized prostate cancer (PCa) patients treated with SBRT using two RT schedules. Methods We analyzed a prospective database on clinically localized PCa patients treated with SBRT consisting of 42 Gy/7 fx or 36,25 Gy/5 fx from January 2013 and September 2020. The inclusion criteria were histologically verified adenocarcinoma, cT1c-T3bN0M0. No patients received any ADT. SBRT was delivered with volumetric-modulated arc therapy (V-MAT). Daily cone beam CT and fiducial markers image-guidance was used. Biochemical recurrence was defined according to Phoenix criteria (nadir +2 ng/mL). Survival analysis was performed using the Kaplan-Meier method and the log rank test was applied to compare the effect of the individual variables on different outcomes. Patients treated with 7 fx and 5fx were matched via propensity score. Acute and late genitourinary (GU) and gastrointestinal (GI) toxicities were graded using the Common Terminology Criteria for Adverse Events, version 5.0.

Results. Median follow-up was 50 months (IQR, 30,3-69,6). Twenty-five (16%), 48 (30,8%), 43 (27,6%), 31 (19,8%) 8 (5,1%) and 1 (0,7%) patient were classified as very low-risk (VLR), low-risk (LR), favourable-intermediate-risk (FIR), unfavourable intermediate-risk (UIR), high-risk (HR) and very high-risk group according to the NCCN risk classification. After PS matching 130 patients were identified (65 cases treated with 7 fx and 65 with 5 fx). The 5-year OS was 97,4%. Eight (13.5,1%)

patients developed biochemical recurrence after a median time of 34 months. 5- year bPFS was 97,3%. RT schedule did not influence bPFS before and after PS matching (p 0.34 and p 0.20). 5- year MFS was 98,6%. RT schedules were not related to LC and MFS before PS (p 0,97 and 0,66) and after (p 0,99 and 0,16). No acute nor late G ≥3 toxicities were reported. PTV>95cc (p 0,036, OR 2,25, 95% CI 1,05-4,81), PTV Dmedian%> 103,3% (p 0,006, OR 2,71, 95% CI 1,33-5,52), bladder D1ccEQD2>75,5 Gy (p 0,048, OR 2,05, 95% CI 1,0- 4,20) were related to G2 GU acute toxicities. Multivariate analysis confirmed PTVcc >95cc (p 0,045, OR 2,25, 95% CI 1,02-4,98) and PTV Dmedian > 103,3% (p 0,02, OR 2,47, 95% CI 1,15-5,23). SBRT schedule was not related to G2 acute GU toxicity (p 0,161).

Conclusion. SBRT delivered in 5-7 fx represents an effective and safe treatment for clinically localized PCa. No significant difference between 5 and 7 fx was observed.

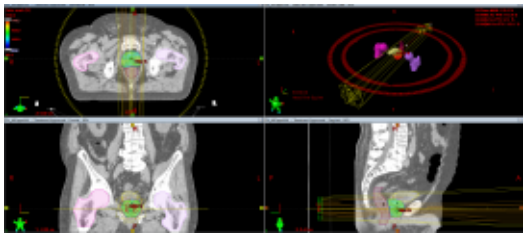

Figure 1.

P251

NUTRITIONAL AND INFLAMMATORY STATUS AS PREDICTIVE BIOMARKERS IN OLIGORECURRENT PCA (RADIOSA TRIAL) – AN UPDATE

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Aims. The biology task of the RADIOSA phase II trial (NCT03940235) entails the identification of predictive and prognostic biomarkers in the context of oligorecurrent PCa in order to distinguish polymetastatic from oligometastatic disease. This may lay the groundwork for personalized treatments for those pts who could really benefit from metastasis-directed therapies.

Methods. Oligorecurrent PCa pts with 3 or less bone or lymph nodal localizations where randomized 1:1 to receive SBRT alone (arm A) or SBRT + 6 months of ADT (arm B). Common serum-derived biomarkers were collected at baseline, and at 3 months after RT. The Nutrition Risk Index (NRI), and the controlling nutritional status (CONUT) score were calculated as nutritional status indicators. As inflammatory indicators, the hemoglobin, albumin, lymphocyte, and platelet (HALP) score, NLR and the NLR-albumin ratio (NLRAR) were assessed. Significant differences and the 3-months timepoint were assessed using the non-parametric Wilcoxon rank-sum test by grouping pts according to ADT administration (arm B *vs* A) and site of metastases (bone *vs* lymph node). Kaplan-Meier (KM) estimates were performed to investigate eventual correlations between baseline indexes and clinical recurrence (CR).

Results. The current analysis comprised 88 pts (45 arm A, 43 arm B). When pts were stratified by ADT administration (Fig1a), cholesterol values showed an increasing trend in the group receiving ADT ($p < .001$), and the change in albumin level was also different between the 2 groups ($p < .05$). When pts were stratified by site of metastases (52 lymph nodal, 29 bone localizations) (Fig1b), NLR value was found to be increased in pts with bone localizations ($p< .05$). No statistically significant correlation with CR was found at the KM estimates with CONUT (cut-off 2), NRI, HALP (median as cut-off) and NLR (cut-off 3).

Conclusions. The addition of ADT appears to have an impact on changes in cholesterol and albumin, two markers of a deteriorating quality of life. Additionally, the site of metastases is linked to the inflammatory status. As bone localizations are associated to a lower response rate, this is consistent with the fact that a higher inflammatory status results in a worse prognosis. These parameters seem to represent intriguing candidates for possible use in clinical decision-making to stratify oligorecurrent pts subclasses. Additional data and extended FU data are required to validate these potential biomarkers.

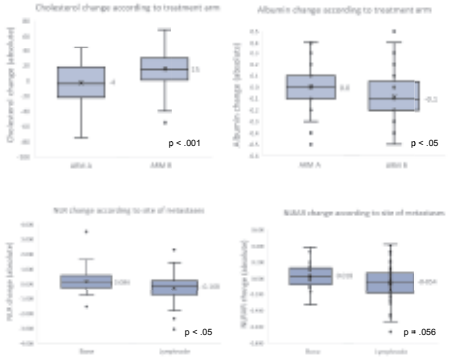

Figure 1. (a) Box plots showing cholesterol (left) and albumin (right) absolute change at 3 months in the cohort of pts stratified according to treatment arm and (b) Box plots showing NLR (left) and NLRAR (right) absolute change at 3 months in the cohort of pts stratified according to the site of metastases.

P252

ULTRA HYPOFRACTIONATED RADIOTHERAPY IN HIGH RISK PROSTATE CANCER PTS: RESULTS FROM A SINGLE CENTRE EXPERIENCE

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Aims. The aim of the present study is to evaluate the efficacy and safety of ultra hypofractionated RT (UHRT) in high and very high risk prostate cancer (PCa) pts.

Methods. Men with high and very high-risk localized PCa who underwent prostate UHRT+/-ADT between 2012 and 2022 were retrospectively included. Stratification of risk was performed according to NCCN guidelines. Toxicities were collected according to RTOG scale.

Results. A total of 143 pts with a median age at diagnosis of 76 (Range 51-88) years were included in the present analysis (Table 1). Median PSA at diagnosis was 7.25 ng/ml (range 0.7-220.4). Thirty-seven pts were included in high risk for iPSA, 36 for extension of tumour (T) and 101 for GS. A total of 118 pts had only 1 risk factor, 20 pts had 2 risk factors and only 5 of them had all of the 3 factors of risk. All pts underwent UHRT on prostate (44 pts prostate+SIB of 7.5/8 Gy fx on the dominant intraprostatic lesion) in 5 fx every other day with a dose/fx within 6.50 and 7.25 Gy. The majority of pts (n = 125, 87.4%) underwent concomitant ADT with a median duration time of 12.0 months (IQR 9–12; available for 95 pts). The remaining patients could not undergo ADT due to comorbidities, according to clinical evaluation. At a median FU of 24 months (data available for 112 pts – 78.3%) a total of 27 pts (18.75%) experienced a biochemical recurrence (BR), with a median time to BR of 23.3 months (IQR 16.38–31.58). Among them, 19 developed a clinical relapse (CR) (2 local, 7 pelvic lymph nodal, and 6 bone relapses) of disease; all of them underwent both UHRT+ADT as first treatment. Most of them (17 pts) had only one factor of risk at diagnosis, that in 14/17 pts was the GS; while the other two had respectively 2 and 3 risk factors. Considering maximum registered toxicities (data available for 83 pts - 58%), 24 G1, 5 G2 and one G3 GU toxicity were reported. Considering maximum GI toxicity, 4 G1, 3 G2 and only one G3 were registered (Table 1). Median PSA at last FU (data available for 109 pts – 75.6%) was 0.26 ng/ml.

Conclusions. These preliminary data suggest that UHRT +/- ADT course might be considered as a safe and effective treatment option in pts with high and very high-risk disease considering both the favorable toxicity profile and and low rate of local intraprostatic recurrences. Further studies are needed to understand if pts who have high GS deserve more aggressive treatments, including both systemic and regional (lymph node) approach.

Table 1. General cohort characteristics and reported toxicities.

Pts characteristics	
	Median (IQR)
CTV Volume (cc)*	60 (46.01– 78.26)
Risk class	
High	130 (91%)
Very high	13 (9%)
Factor of risk	
iPSA	38
T	36
tGS	101
Extension of T	
cT3a	20
cT3b	10
cT4	3
Number of risk factor	
1	118 (82.5%)
2	20 (14%)
3	5 (3.5%)
Staging exam	
Conventional staging:	
TC TAP	91 (63.6%)
Bone scan	101 (70.6%)
mpMRI	70 (49%)
Cho-PET	32 (22.4%)
WB MRI	4 (2.8%)
missing	2 (1.4%)
HT = YES	125 (87%)
CCI	
6	13 (9%)
7	7 (5%)
8	4 (3%)
9	2 (1.4%)
Follow-up data**	
Maximum GU toxicity	
G0	53 (37.5%)
G1	24 (16.7%)
G2	5 (3.4%)
G3	1 (0.7%)
G4	0 (0%)
missing	60 (41.7%)
Acute maximum GI toxicity	
G0	75 (52.8%)
G1	4 (2.8%)
G2	3 (2%)
G3	1 (0.7%)
missing	60 (41.7%)
Last follow-up status	
NED	85 (59%)
AWD	27 (18.75%)
missing	32 (22.25%)

*Data available for 116 pts
**Data referring to 83 pts with at least one-year FU and availability of toxicities data

P253

FEASIBILITY AND TOLERABILITY OF MR-GUIDED ADAPTIVE RT ON PROSTATIC BED: MONO-INSTITUTIONAL EXPERIENCE

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Aims. The prostate bed is a virtual region in the close

proximity to the rectum and the bladder. The volume of these organs can significantly change daily during the treatment. Thus, real time adaptive radiotherapy by means of 1.5T MR-Linac could be a promising choice in improving toxicity profile. Herein, we reported the evaluation of feasibility and acute toxicity related to postoperative moderately hypofractionated MR-guided adaptive radiotherapy on prostatic bed.

Methods. Fifty patients were treated on prostatic bed with daily adaptive radiotherapy by means of 1.5T MR-Linac inside an ethical committee approved protocol (MRI/LINAC n°23,748): 17 patients underwent adjuvant RT (total dose 66 Gy in 30 fractions) and 33 salvage RT (total dose 67.5 Gy in 30 fractions). Daily plan adaption was performed using one of the two workflows: adapt to shape (ATS, using contour adaptation and replanning) or adapt to position (ATP, rigid replanning onto the online anatomy with isocenter correction). Type of workflow, duration of treatments and acute toxicity were analyzed. Patient-reported outcomes were investigated by means of IPSS, ICIQ-SF, IIEF-5, EPIC-26, EORTC-QLQ-C30 and PR-25 questionnaires.

Results. A total of 1500 fractions were successfully delivered on the MR-linac. No interruption occurred during each procedure. Median patient age was 66 years (47-77). In total, ATP was chosen in 98 (6.5%) and ATS in 1402 (93.5%) of fractions. Median total duration of all fractions was 41 minutes (range 27-60). Acute toxicity (RTOG, CTCAEv5.0 and patient-reported outcomes) at the end of RT was mild with a tendency of recovery to baseline levels at 3 months post RT. No G3+ toxicity was scored. Concerning the PROMS, questionnaires showed only mild deterioration between the pre- and end-RT evaluations, but they fully recovered at first follow-up evaluations after 3 months.

Conclusions. In our experience daily adaptive postoperative RT on 1.5T MR-Linac appears well tolerated by the patients and achieved low rates of acute toxicity. Further studies are necessary in order to confirm a benefit in terms of long-term toxicity compared to conventional linac.

P254

IMPACT OF CHARLSON COMORBIDITY INDEX ON TOXICITIES IN PROSTATE CANCER (PCA) PATIENTS TREATED WITH RADICAL ULTRA-HYPOFRACTIONATED RADIOTHERAPY

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Aims. The aim of the present study (Ethical Committee approval UID 2684) is to evaluate the influence of pre-treatment CCI on acute and late RT-related side-effects in men with localized PCa.

Methods. Patients (pts) with localized PCa who underwent UHRT on prostate between 2012 and 2021 were retrospectively included. Risk groups were determined based on NCCN definitions. Overall CCI-score was calculated excluding Pca which is our key condition. Pts were stratified according to CCI into 5 groups and Chi square test was performed to test any association among CCI and reported toxicities collected according to RTOG scale.

Table 1a. General cohort characteristics and follow-up data.

Pts characteristics	
	Median (IQR)
CTV Volume (cc)*	60 (46.0 – 78.4)
	n (%)
Risk class	
Low Lowing	177 (21 5)
Favourable intermediate	353 (42.8)
Unfavourable intermediate	135 (16.4)
High	131 (15.9)
Very High	13 (1.6)
Missing	15 (1.8)
HT = YES	322 (39.1)
Low risk	32 (9.9)
Favourable intermediate	93 (28.9)
Unfavourable intermediate	67 (20.8)
High	113 (35.1)
Very High	12 (3.7)
CCI	
1	22 (2.7)
2	80 (9.7)
3	260 (31.6)
4	251 (30.5)
5	128 (15.5)
6	41 (5.0)
7	25 (3.0)
8	10 (1.2)
9	5 (0.6)
10	0 (0.0)
11	2 (0.2)
Follow-up data	
Acute maximum GU toxicity	
G0	481 (58.4)
G1	284 (34.5)
G2	50 (6.1)
G3	4 (0.5)
G4	2 (0.2)
missing	3 (0.4)
Acute maximum GI toxicity	
G0	741 (89.9)
G1	66 (8.0)
G2	13 (1.6)
missing	4 (0.5)
Late maximum GU toxicity	
G0	326 (64.0)
G1	137 (26.9)
G2	41 (8.1)
G3	5 (1.0)
Late maximum GI toxicity	
G0	450 (88.6)
G1	41 (8.1)
G2	13 (2.6)
G3	4 (0.8)
Last follow-up status	
NED	633
AWD	79
DIED for other causes	13

Results. A total of 824 pts were included; general cohort characteristics are reported in Table 1a. Median age at diagnosis was 76 years (IQR 71 - 80) and median PSA at diagnosis was 7.3 ng/ml (IQR 5.14 – 10.30). All pts underwent UHRT in 5 fx every other day with a

dose/fx within 6.25 and 7.25 Gy. Of them, 310 (37.6%) pts received a SIB on dominant intraprostatic lesions of 7.5/8 Gy fx. Concomitant ADT was received by 322 (39.1%) pts with a median duration time of 6 months (IQR 5 – 12, available for 237 pts). Median CCI score was 4 (range 1 – 11) and the most frequent comorbidities were diabetes mellitus (14.6%) and localized second malignancy (12.9%), followed by heart failure/myocardial infarction (7.0%) and cerebrovascular disease (6.7%). Median follow-up (FU), available for 709 (86%) pts, was 30 months (IQR 17 – 40). Median PSA at last FU (available for 642 pts) was 0.56 ng/ml. A total of 74 pts (10.4%) experienced a biochemical recurrence, with a median time of 27 months (IQR 18 - 41); respectively 9, 22, 15, 23 and 4 in low, favourable intermediate, unfavourable intermediate, high and very high risk classes. Clinical progression was observed in 63 pts (8.9%) with a median time from the end of RT of 26 months (IQR 18 – 41). Considering pts with the availability of maximum late toxicities data (n = 507), 46 and 17 pts experienced late G>2 GU and GI toxicities, respectively. Toxicities according to CCI-score are reported in Table 1b. No association was found for CCI and both maximum late GI and GU toxicities.

Conclusions. UHRT is a safe and effective treatment. Despite the high presence of comorbidities, these pts have excellent biochemical control and secure GI/GU toxicity profiles. Moreover, CCI score has shown no impact on reported toxicities, thus, UHRT should be proposed as a treatment option in this setting of pts.

Table 1b. Late maximum toxicities according to CCI group.

Late maximum GU Toxicitiy						
CCI group	Total	G0	G1	G2	G3	missing
1 - 2	102	44	20	4	0	34
3	260	104	43	18	3	92
4	251	103	36	10	1	101
5 - 6 - 7	194	68	36	8	1	81
8 - 9 - 10 - 11	17	7	2	1	0	7
Late maximum GI Toxicitiy						
CCI group	Total	G0	G1	G2	G3	missing
1 - 2	102	56	11	1	0	34
3	260	146	15	4	2	93
4	251	134	9	6	1	101
5 - 6 -7	194	104	6	3	1	81
8 - 9 - 10 - 11	17	10	0	0	0	7

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FURTHER EVIDENCE OF THE EQUIVALENCE OF LUTEINIZING HORMONE-RELEASING HORMONE (LHRH) AGONIST AND HIGH-DOSE BICALUTAMIDE IN COMBINATION WITH RADIOTHERAPY OF PROSTATE CANCER. RESULTS OF A MULTICENTER OBSERVATIONAL STUDY INCLUDING 800 PATIENTS.

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Aims. Luteinizing hormone-releasing hormone (LHRH) agonist-based adjuvant androgen deprivation therapy (ADT) has improved the outcomes in prostate cancer (PCa) treated with external beam radiotherapy (EBRT) in several randomized trials. However, LHRH agonists produce several side effects, significantly worsening patients QoL. Therefore, the use of high-dose bicalutamide (HDB; 150 mg/day) has been proposed as a substitute for LHRH-agonists in order to reduce the effects of pharmacological castration. However, randomized comparisons between LHRH-agonists and HDB are lacking. Therefore, the aim of this analysis is to compare the therapeutic outcomes in a large population of PCa patients undergoing EBRT and ADT.

Methods. Endpoints of the study were biochemical relapse-free survival (bRFS), local control (LC), regional control (RC), metastasis-free survival (MFS), disease-free survival (DFS), and overall survival (OS). Patients undergoing definitive EBRT for PCa were selected from the database of a multicenter observational study. Of these, 519 and 281 also underwent adjuvant ADT based

on LH-RH-agonist and HDB, respectively. An univariate (logrank) and multivariate (Cox) analysis was performed including parameters regarding patient characteristics (age and Charson's comorbidity index), tumors (PSA level, Gleason score, cT stage, cN stage), and of therapy (delivery of prophylactic lymph nodes irradiation, seminal vesicles irradiation, previous TURP, ADT [LH-RH-agonists or HDB] and duration, EBRT fractionation and technique, type of image-guidance systems, CTV to PTV margin, and EQD2α/β=1.5 to prostate, seminal vesicles, and pelvic nodes).

Results. The results of the univariate analysis (only therapy parameters shown) are summarized in Table 1. Regarding all the analyzed end-points, no statistically significant difference was recorded between LH-RH- agonists and HDB. Furthermore, multivariate analysis showed a significant impact of PSA level on bRFS (p: 0.003) and of Gleason score on bRFS (p<0.001), LC (p<0.001), MFS (p<0.001), and DFS (p<0.001).

Conclusions. The results of our study further confirm the efficacy of HDB-based ADT in combination with EBRT. Therefore, this treatment option could be offered to patients who want to avoid pharmacological castration.

Table 1. Univariate analysis (5-year outcomes).

Variable	Value	No. of patients [%]	bRFS [%]	P	LC [%]	P	RC [%]	P	MFS [%]	P	DFS [%]	p	OS [%]	p
Prophylactic nodal irradiation	No	562 [52.3]	88.0		91.3		96.1		94.9		87.6		91.3	
	Yes	513 [47.7]	85.7	NS	92.8	NS	99.1	.008	93.3	NS	86.4	NS	92.8	NS
SV irradiation	No	274 [25.5]	89.4		95.7		95.9		95.2		89.2		92.6	
	Yes	800 [74.5]	86.3	NS	94.5	NS	98.1	NS	93.8	NS	88.5	NS	91.9	NS
TURP	No	992 [92.4]	86.7		94.6		97.4		94.2		86.8		92.2	
	Yes	82 [7.6]	90.9	NS	96.7	NS	98.0	NS	92.8	NS	90.6	NS	89.3	NS
Adjuvant ADT	No	274 [25.5]	87.9		92.3		96.7		94.7		87.4		88.7	
	Yes	800 [74.5]	86.8	NS	95.6	.010	97.8	NS	94.0	NS	87.1	NS	93.2	.002
Type of ADT	LH-RH agonist	519 [48.3]	85.6		96.4		97.6		92.6		85.9		92.7	
	Bicalutamide	281 [26.2]	88.4	NS	94.6	NS	97.8	NS	95.7	NS	88.8	NS	93.9	NS
Actual duration of ADT (months)	not prescribed	255 [23.7]	89.2		93.8		96.9		95.7		89.6		90.2	
	≤ 6	236 [22.0]	94.3		96.9		97.8		98.1		95.8		95.4	
	6.1- 2	146 [13.6]	88.3	.001	93.9	NS	100	NS	95.4	.007	91.5	.002	97.9	NS
	13-24	360 [33.5]	81.0		94.7		96.7		88.6		85.4		89.1	
	25-36	61 [5.7]	89.5		93.4		97.9		100.0		93.4		93.6	
	> 36	16 [1.5]	70.7		100.0		100.0		100.0		100.0		83.6	

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IMPACT OF THE COVID-19 PANDEMIC ON RADIOTHERAPY OF PROSTATE CANCER. A SECONDARY ANALYSIS OF AN OBSERVATIONAL TRIAL

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Aims. Health care services across the world have been enormously affected by the onset of the coronavirus disease 2019 (COVID-19). In particular, cancer screening programs have been clearly interrupted since the onset of the COVID-19. This study examined changes in prostatic-specific antigen (PSA) testing, prostate biopsy testing, and radiotherapy (RT) regimens before, during, and after the COVID-19 pandemic in patients with localized prostate cancer (PCa).

Methods. From the database of an observational study, all patients who underwent definitive RT for PCa in a single center were extracted for each year from 2019 to 2022. The following data were collected for each patient: tumor and lymph node stage, PSA test value at diagnosis, ISUP grade at biopsy, radiotherapy regimen (conventional fractionation, moderate hypofractionation, ultra-hypofractionation). Then, the results recorded before and after the pandemic were compared using a chi-square test or T-test for categorical or continuous data, respectively.

Results. The results of the analysis are shown in Table 1. The comparison between PCa characteristics and the interval between PCa diagnosis and RT start between the period before and after the start of the pandemic did not show statistically significant differences. The rate of patients with cN1 stage increased from 9.7% (2019) to 21.1% (2020-2022) (p=.096). Furthermore, the rate of biopsies showing ISUP 4-5 increased from 39.7% before or in the early phase of the pandemic (2019, 2020) to 49.1% in the late phase of the pandemic (2021, 2022) (p=.054). Finally, the rate of patients undergoing ultra-hypofractionated RT increased from 13.6% (2019) to 35.3% (2020-2022) (p=.014).

Conclusions. A significant increase in PCa patients treated with ultra-hypofractionated RT was recorded in this single-center analysis. Furthermore, between the pre-pandemic or pre-pandemic/early phase of the pandemic period, there was a statistical trend towards an increase in patients with lymph node metastases and with unfavorable ISUP grade.

Table 1. Clinical-pathological and treatment-related features of patients with prostate cancer treated with radiotherapy.

		2019	2020	2021	2022	p:
Number of patients						
		75	51	55	51	NS
Tumor stage						
	1	6	5	6	3	
	2	56	39	40	39	NS
	3	8	5	9	9	
	4	0	1	0	0	
Nodal stage						
	0	62	40	46	42	NS
	1	6	9	9	9	
Median PSA (range)						
		6.89	7.01	7.82	7.42	NS
ISUP						
	1	8	1	1	2	
	2	22	20	14	17	
	3	15	10	14	6	NS
	4	23	15	17	19	
	5	7	5	9	7	
Median time interval between diagnosis and start of RT (range), months						
		8	7	6	7	NS
RT regimen						
Standard fractionation		0	0	0	0	
Hypofractionation		66	32	43	41	**.014**
Ultra-hypofractionation		9	19	12	10	

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KIDNEY SBRT FOR RENAL LESIONS: A MONO-INSTITUTIONAL ANALYSIS

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Aims. SBRT (Stereotactic Body Radiotherapy) has demonstrated high local control rate and low toxicity in retrospective and prospective trials for primary RCC. As SBRT has been successfully used in the treatment of intra- and extracranial RCC metastases showing high local control rates accompanied by low toxicity we tested the utilization of SBRT for the treatment of renal lesions localized in the contralateral/ipsilateral kidney in patients already treated with surgery (total or partial) on one kidney.

Methods. From 08/2019-10/2022 12 kidney lesions of 7 pts (5 male, 2 female) were treated with CyberKnife Accuray, Sunnyvale, CA, USA)(CK). Usage of the CK system requires the insertion of fiducial markers which are placed with ultrasounds guidance. Two pts were treated on 3 and 4 concomitant lesions (Figure 1). Median age at diagnosis was 65.6(54-81.2)years. Four pts had a prior contralateral nephrectomy, 1 prior ipsilateral partial nephrectomy and 1 prior ipsilateral cryotherapy ablation. No pts had pre-SBRT dialysis, but one patient had serious comorbidities (diabetes, resistant hypertension treated with bilateral renal denervation) and IIIB chronic renal failure. Pre-SBRT imaging was based on TC (7/7 pts) and TC plus RM in 4 pts. The metastasis histologies were: 5 clear cell kidney cancer, 1 papillary kidney and 1 metastasis from lung cancer. Median dimension was 1.95(0.9-3.5)cm. The lesions localization were: 1 hilum, 7 mesorenal, 3 inferior third, 1 superior third. Median SBRT prescription dose was 30(30-45)Gy in 5 fractions. The fiducial markers were placed in 10/12 lesions, because in pts with multiple lesions we have decided not to insert fiducials in each lesion. The median GTV was: 2.82(0.41-38.8)cc, while median PTV was 7.77(1.89-58.8)cc.

Results. No acute toxicities were registered. In some cases we have observed a slight transient increase in creatinine values (<20%) which returned to pre-SBRT values within four weeks. Only one patient, who had the largest GTV 38.8cc and serious comorbidities, had to start dialysis 21 months after SBRT. With a median follow-up of 14.3(5.1-39.2)months LRFS was 100% and only the patient who had renal metastasis from lung cancer died (for brain metastases).

Conclusions. SBRT is a promising non-invasive treatment in the management of renal lesions and appears to be a safe and tolerable therapy, with evolving clinical evidence demonstrating encouraging results with respect to local control and toxicity.

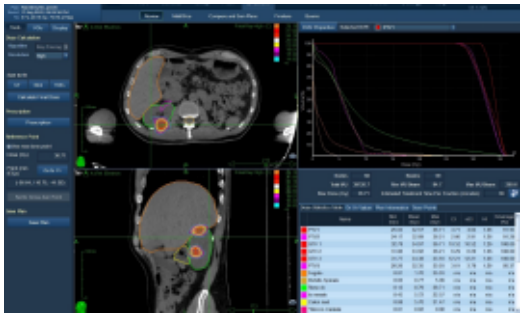

Figure 1. SBRT dose distribution of patient treated on 3 concomitant lesions.

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LONG TERM OUTCOMES FOLLOWING POSTOPERATIVE HYPOFRACTIONATED RADIOTHERAPY FOR PROSTATE CANCER

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Purpose/Objective. To retrospectively report long term outcomes following postoperative hypofractionated radiotherapy (PHRT) for prostate cancer, used in both the adjuvant and salvage setting.

Materials and Methods. Patients for whom adjuvant or salvage RT was indicated after prostatectomy were treated with a moderate course of hypofractionation consisting in the delivery of 62.5 Gy in 25 fractions (2.5 Gy per fraction) on the prostate bed in five consecutive weeks (EQD21.5 = 70 Gy) by means of 3D CRT. The CTV was delineated as per the RTOG Consensus Guideline and the PTV was obtained by adding 1 cm margins, except posteriorly where 5 mm was used. Androgen deprivation therapy (ADT) was allowed at physician's discretion. Patients were evaluated for urinary and rectal complications according to the RTOG/EORTC late effects score. Overall survival (OS), biochemical recurrence free survival (bRFS), and metastasis-free survival (MFS) were estimated using the Kaplan–Meier method.

Results. One hundred and ten men with a median age of 67 years (range 51-78) were enrolled. The majority of them (82%) had adverse pathologic features only, while 31 (28%) had early biochemical relapse. Median PSA level before prostatectomy was 8.6 ng/ml (range 0.3-47

ng/ml) and before RT was 0.12 ng/ml (range 0-9 ng/ml). The median PTV was 150 cc (range 62 – 364.8 cc). Twenty-eight patients (25.4%) also received ADT. At a median follow up of 103 months (range 19-138 months), late G3 (urethral stenosis) and G4 (fistula) GU side effects occurred in 9 (8%) and 1 patient (0.9%), respectively. The same features for late rectal toxicity were 0.9% (one instance of hematochezia) and 0.9% (one instance of fistula), respectively. Five and 10-years OS was 94.5% (95% C.I.: 96.1% - 92.4%) and 77.3% (95% C.I.: 82.1% - 72.5%), respectively. Five and 10-years b-RFS was 70.5% (95% C.I.: 74.9% - 66.1%) and 53.3% (95% C.I.: 59.9% - 47.6%), respectively. Five and 10-years MFS was 88.8% (95% C.I.: 91.8% - 85.8%) and 76.7% (95% C.I.: 81.2% - 72.2%), respectively.

Conclusions. Our findings show that PHRT either in the adjuvant or salvage setting resulted in acceptable rates late toxicity with optimal tumor control while reducing overall treatment time. This regimen can be an attractive strategy to reduce the burden of care without losing clinical effectiveness. Further improvements in image guidance and treatment delivery techniques may help improving long term GU toxicity profile.

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ONE IS BETTER THAN TWO: A COMPARATIVE STUDY OF SINGLE-ARC VERSUS DUAL-ARC VMAT PLANNING TECHNIQUES IN LINAC-BASED PROSTATE CANCER SBRT

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Aims. To investigate the dosimetric quality and the treatment efficiency of single-arc (SA) versus dual-arc (DA) volumetric modulated arc therapy (VMAT) plans in linac-based stereotactic body radiation therapy (SBRT) of localized prostate cancers.

Methods. Twenty low-risk prostate (36.25 Gy in 5 fractions) and twenty high-risk prostate (42.7 Gy in 7 fractions) SBRT plans treated during 2021 with dual-arc FFF-VMAT technique, were re-optimized. The same PTV margin expansion (5 mm isotropic except 3 mm posterior) was used. A single-arc approach was adopted and new optimization parameters based on the increased planning and clinical experience were incorporated. Dosimetric parameters of newly optimized SA plans were evaluated and compared with those from original DA plans. The analysis included target coverage, organ at risk (OAR) sparing, treatment delivery time and accuracy (perpendicular diode matrices, gamma analysis-passing ratio, PR).

Results. In all cases, the SA optimization technique resulted in a better treatment plan than the original one. The improvement was more influenced by OARs dose reduction than by target coverage. Mean PTV D95% was comparable between the two techniques (SA: 96.7 [90.0–99.0]; DA: 96.4% [88.0–99.0], P=0.058), while a significantly increased OAR sparing was observed in SA plans, especially in rectum and bladder mean dose (-3.5 Gy [-7.6– -0.6], P<0.001; -1.2 Gy [-0.4–0.4], P<0.001). The mean SA treatment delivery time was reduced by 22%, passing from 2.1 minutes [1.7 – 3.0] to 1.5 minutes [1.3 – 1.9] (P<0.001) on average. The mean monitor units rose from 1819±332 to 1967±301 (P<0.001) due to higher plan complexity. Despite the increased fluence modulation, dose measurements reported an optimal agreement with dose calculations with a PR greater than 95% for 2%(local)-2 mm criteria (SA: 98.7 [96.0–100.0]; DA 98.0% [94.5–100.0], P=0.004].

Conclusions. SA VMAT planning technique, with newly optimized parameters, achieved clinically equivalent target coverage while significantly reducing the dose to the rectum and bladder compared to DA plans. Moreover, the treatment delivery time was substantially reduced, lowering the probability of prostate motion beyond the margins. These findings indicate a potential decrease in treatment-related toxicity and an improvement in actual target coverage during prostate SBRT treatments. Further investigations are warranted to assess the long-term clinical outcomes associated with this planning technique.

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EFFICACY AND SAFETY OF SYNCHRONY IN SBRT FOR PROSTATE CANCER: MONOISTITUTIONAL EXPERIENCE

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Aims. To evaluate the potential offered by Synchrony®,a new tumor-tracking system available for Tomotherapy Radixact® compared to conventional Tomotherapy in the planning of SRT for prostate cancer.

Methods. From february 2022 to april 2023, 30 consecutive patients with localized prostate cancer (cT1-2, GS< 8, PSA<20 ng/ml) were randomized to Synchrony® procedure and to conventional Helical Tomotherapy. 16 patients (53%) were treated with Synchrony® and 14 (47%) with Tomo. In the first case intraprostatic gold fiducial markers were implanted under ultrasound guidance before CT scan. They allow you to view prostate position and motion before and during treatment. So Synchony® can correct them by adjusting the jaw and

MLC positions in real time. For all plans, 36.25 Gy in 7.25 Gy fractions (every other day) for a minimum coverage dose of 95% of planning target volume (PTV) (D95%) was prescribed. Dose to abdominal cavity, both femoral heads, bladder and rectum were constrained below each tissue tolerance. Acute and late GU and GI toxicity according to RTOG scales were recorded.

Results. Median age of the patients was 73 (range 48-83 years). At the end of the treatment, 10/14 (71%) patients in the Tomo group vs. 12/16 (75%) patients in the Syncrony group had not GI toxicity, while 4/14 (29%) patients in the Tomo group vs. 4/14 (25%) patients in the Synchrony group had G1-G2 grade of GI toxicity. 3/14 (21%) patients in the Tomo group vs. 6/16 (37%) patients in the Synchrony group had not GU toxicity, while 11/14 (79%) patients in the Tomo group vs. 10/16 (63%) patients in the Synchrony group had G1-G2 grade of GU toxicity. No G3-G4 grade of GI and GU toxicity was showed. After 3 months from the end of the RT, patients treated with Synchrony (n=11) reported the disappearance of urinary and intestinal disorders, while in Tomo group only some cases of G1 toxicity were found (1/14 GI Toxicity, 2/14 GU Toxicity). In both groups there was a significant reduction of the PSA.

Conclusions. Several trials have demonstrated safety and effectiveness of SBRT in prostate cancer. Synchrony® enables continuous delivery of radiation treatment to tumors while they are in motion by synchronizing the delivery beam position to the tumor location precisely, with sub-millimeter accuracy, and at all times during delivery of a treatment fraction. This approach allows tailor-made treatments, good toxicity profiles and short therapy sessions.

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DAILY ADAPTIVE RADIOTHERAPY IN POSTOPERATIVE HYPOFRACTIONATED SALVAGE RADIOTHERAPY FOR PROSTATE CANCER PATIENTS (DART-PHASER) (NCT05884632)

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Introduction. The role of hypofractionated radiotherapy in the postoperative salvage setting in prostate cancer (PCa) has been rarely investigated due to the risk of late complications. The recent introduction of daily-adaptive radiotherapy in the clinical practice might be a possible solution in this regard. While MR-guided technology might be limited in this specific setting by the average longer treatment duration related to MR procedures that might be not fit for patients with limited urinary continence, the use of CT-guided radiotherapy (CTgRT) systems with dedicated artificial intelligence for fast auto-contouring and plan calculation might overcome this problem, increasing the adherence and accuracy of treatment.

Methods. DART-PHASER (NCT05884632) (Ethical Committee approval: Prot. Negrar 2022-51) is a prospective interventional single-arm clinical trial that aims to evaluate safety and efficacy of CTgRT of an hypofractionated postoperative salvage treatment in patients affected by PCa with biochemical relapse. The primary objective of this study is to evaluate the acute gastrointestinal (GI) toxicity. The secondary objective of the study is to evaluate acute genitourinary toxicity, late tolerability, quality of life, and oncological outcome. Patients population consists of 184 patients to detect a 5% difference in grade 2 or higher GI toxicity compared to data from randomized clinical trials.

Results. starting from april 2023, the first two patients have completed the treatment. The recruitment period is 24 months. Patients are treated with postoperative hypofractionated salvage radiotherapy with a dose of 59 Gy in 20 fractions. Patients are treated on Ethos system (Varian Medical Systems, Palo Alto, USA). The treatment workflow consists of a pre-planning cone-beam CT, auto-contouring and verification phase, and a manual contour adaptation. Thereafter, an automated plan is calculated online by a dedicated artificial intelligence. If the pretreatment session last more than 15 minutes a verification cbCT will be performed before RT start.

Conclusions. the present is the first clinical trial of daily-adaptive postoperative hypofractionated radiotherapy using a CT-guided system. Clinical data are awaited to evaluate the safety of this new treatment modality.

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GENITO-URINARY TOXICITY AND OUTCOMES IN PATIENTS TREATED WITH PROSTATE TRANSURETHRAL RESECTION BEFORE RADIOTHERAPY

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Aims. To determine the genitourinary (GU) toxicity and outcomes in prostate cancer patients treated with radiotherapy who have undergone to transurethral resection.

Methods. In this single-center retrospective study, were collected data about prostate cancer patients, treated with moderately hypo-fractionated external-beam radiotherapy or with stereotactic treatment. All patients were screened by self-administered IPSS questionnaires and

underwent to uroflowmetry (UFM) before radiation treatment. UFM recorded the amount of urine emitted in the unit of time, the urination time, the maximum flow, and the average flow. Those patients with low UFM value and high IPSS score were evaluated for transurethral resection of the prostate (TURP). Data on acute and late toxicity along with progressive disease were analyzed and compared with other patients who underwent to radiation treatment without TURP at the same time. Acute and late GU toxicity were scored using Common Terminology for Common Adverse Events (CTCAE v 5.0).

Results. Between 2014 and 2023, 398 patients were treated at our institution. The median age was 74 years (range: 46-85 years), mean follow-up 33 months. Ninety patients (23%) underwent resection. Acute toxicity was recorded in 46% of patients who underwent resection and 54% of the other cohort. Grade 1 toxicity was predominant in both groups (88% *vs* 84%), G2 only in 10% *vs* 16% one's, while one patient for each group experienced a G3 toxicity (urinary retention). No Grade 4 urinary toxicities were observed in both groups. Dysuria (27% *vs* 38%) and increased urinary frequency (39% *vs* 42%) were the most reported symptoms. For late toxicity no significant differences was recorded between the two groups: Grade 1 (87% *vs* 88%) and Grade 2 (13% *vs* 12%). Progression free survival was 86% at 5 years and 83% at 8 years for both patients receiving or not resection. In multivariate analysis a statistically significant impact in PD was recorded for ADT use (0.24, 95%CI 0.08 to 0.72; p=0.011), Gleason score (1.8, 95% CI 1.193 to 2.865; p=0.006) and iPSA (2.17, 95% CI 1.296 to 3.653; p=0.003).

Conclusions. No significant difference was observed between the groups with or without resection, neither in terms of toxicity GU, acute and late, nor in terms of PD. This underlines the feasibility of TURP before RT without any harmful correlated event.

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CLINICAL IMPLEMENTATION OF ONLINE CT BASED ADAPTIVE WORKFLOW FOR THE TREATMENT OF LOCALIZED PROSTATE CANCER

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Aims. The introduction of Image-Guided Radiation Therapy (IGRT) has improved the quality of radiotherapy treatments and allowed a safe dose escalation to various anatomic districts including the prostate gland. The newest IGRT approach is the online adaptive radiotherapy (ART) that can deliver an adaptive plan taking into account the anatomical variations for every single fraction. We report a clinical online adaptive work-flow for prostate cancer patients.

Methods. We analyzed the first 8 patients treated in our center from February to April 2023 for localized prostate cancer with radical treatment using online ART with ETHOS (VARIAN Medical System). According to the Gleason score and ISUP grading group (GG) 5 patients had an intermediate favorable risk (GG II) and 3 a high risk disease (GG IV). For GG II the clinical target volume (CTV) was only the prostate, while for GG IV patients, seminal vesicles had also been included in the CTV. CTV to planning target volume (PTV) margins were 5 mm (isotropic). The dose prescription was 60 Gy in 20 fractions for all the patients (PTV D98%>95%), according to the current guidelines in which moderate hypofractionation is considered the standard of care. A 9 field IMRT plan was generated for each patient. We collected the data of all 160 fractions and reported our clinical work-flow with the overall treatment time, the plan's selection and the adaptive treatment time.

Results. The clinical work-flow is summarized in Figure 1. The median time for the adaptive process (from cone beam CT1 [CBCT1] to CBCT2) was 12'28'' minutes (7-26 min) while the median overall treatment time was 23'44'' minutes (15-39 min). We selected the adapted plan in the 98% of the scheduled fractions (156/160), mainly for the better PTV coverage compared to the scheduled plan although the CTV was always well covered by the prescription dose for both plans. IMRT fields were chosen in order to reduce the plan optimization time on the couch. In 7 out of 160 treatments we had to restart the entire process due to a significant change in the rectal filling between CBCT1 and CBCT2.

Conclusions. Implementation of the online adaptive process is feasible and could lead to a margin reduction to obtain a better sparing of the organs at risk without compromising the target coverage. A learning curve of the entire process is needed in order to reduce overall treatment time and consequently the chance of anatomical changes during the adaptation steps.

Figure 1.

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RADIORESISTANCE MECHANISMS IN PROSTATE CANCER CELL LINES SURVIVING ULTRA-HYPOFRACTIONATED EBRT:IMPLICATIONS AND POSSIBLE CLINICAL APPLICATIONS

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Aims. The use of a higher dose per fraction to overcome the high radioresistance of prostate cancer cells has been unsuccessfully proposed.

Methods. Herein, we present PC3 and DU-145, castration-resistant prostate cancer cell lines that survived a clinically used ultra-higher dose per fraction, namely, radioresistant PC3 and DU-145 cells (PC3RR and DU-145RR).

Results. Compared to PC3, PC3RR showed a higher level of aggressive behaviour, with enhanced clonogenic potential, DNA damage repair, migration ability and cancer stem cell features. Furthermore, compared to PC3, PC3RR more efficiently survived further radiation by increasing proliferation and down-regulating pro-apoptotic proteins. No significant changes of the above parameters were described in DU-145RR, suggesting that different prostate cancer cell lines that survive ultra-higher dose per fraction do not display the same grade of aggressive phenotype. Furthermore, both PC3RR and DU-145RR increased antioxidant enzymes and mesenchymal markers.

Conclusions. Our data suggest that different molecular mechanisms could be potential targets for future treatments plans based on sequential strategies and synergistic effects of different modalities, possibly in a patient-tailored fashion. Moreover, PC3RR cells displayed an increase in specific markers involved in bone remodeling, indicating that radiotherapy selects a PC3 population capable of migrating to secondary metastatic sites. Finally, PC3RR cells showed a better sensitivity to Docetaxel as compared to native PC3 cells. This suggests that a subset of patients with castration-resistant metastatic disease could benefit from upfront Docetaxel treatment after the failure of radiotherapy

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EBRT AFTER RADICAL PROSTATECTOMY: RECURRENCE, SURVIVAL OUTCOMES, PROGNOSTIC FACTORS AND TOXICITY OF 175 PATIENTS

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Aim/purpose. To evaluate clinical outcomes, toxicity and prognostic factors in patients (pt) with prostate cancer underwent surgery and adjuvant or salvage radiotherapy (RT).

Materials and Methods. From January 2016 to November 2022, 175 pt underwent adjuvant or salvage RT after radical prostatectomy according to international guidelines. Pt's median age at the time of RT was 69 (47-82) years old. 138 pt (79 %) received salvage RT and remaining 37 pt (21%) adjuvant RT. All pts were treated in our centre using Versa HD™ or Synergy linear accelerator of Elekta company (Stockholm- Sweden). The volume of RT treatment consisted on prostate bed (70-76 Gy/35-38 fraction based on risk factors; R1, clinical recurrences, PSA) and pelvic irradiation in case of N+ (46 Gy/23 fractions) in association with Androgen Deprivation Therapy (ADT).

Results. After prostatectomy, the majority of pt had R1 (70 %) and surgery sequelae (68 % erectile dysfunction; 59 % urinary disorders). The mean PSA before RT treatment was 0.9 ng/ml. In 88.6% of pt RT was prescribed only to prostate bed and in 11.4 % both to prostate bed and pelvis. After a median follow-up of 37 (3-83) months, overall survival (OS) and cancer specific survival (CSS) rates were 93 % and 99 %; the biochemical progression free survival (bPFS) and clinical progression free survival (cPFS) resulted 65 % and 78 %, respectively. We did not observe any recurrence at prostate tumor bed irradiated, only 1 pt died due to PD. At univariate analyses pT3a-pT4 stage, N1, GS ≥8, PSA nadir > 0,04 ng/ml after RT treatment resulted prognostic factors influencing negatively bPFS and cPFS, in addition, iPSA > 10 ng/ml and PSA pre-RT treatment > 0,7 ng/ml also negatively affect bPFS. At the multivariate analyses GS ≥8 and PSA nadir > 0,04 ng/ml after RT treatment were confirmed the main prognostic factors regarding bPFS and cPFS. Genitourinary (GU) and gastrointestinal (GI) acute toxicity was observed in 41 % of pt; of them, 15% had G2 and 2.8 % G3 (1 pt). Late GU and GI toxicity > G2 was 10,9 %; of them, only 5 pt reported G3 late toxicity (3,9 %).

Conclusions. In our study we found very good results in terms of bPFS, cPFS and excellent results regarding OS and CSS, with a considerable median follow up of 37 months. The main negative prognostic factors for PFS were GS and PSA nadir. Overall, the RT treatment was well tolerated with acceptable acute and late toxicity.

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PROTON *VS* PHOTONS IN PROSTATE CANCER, A META-ANALYSIS

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Aims. Aim of this study is to provide a systematic literature review to collect studies evaluating curative RT, with photons or protons, in prostate cancer, to evaluate the benefits in terms of oncological outcomes and treatment-related toxicities.

Methods. PubMed, Embase, and the Cochrane Library databases were systematically searched up to April 2022 and identified publications regarding prostate cancer irradiation. RCTs and observational studies were included if they met the following criteria: (1) population: patients with organ-confined or locally advanced prostate cancer, (2) intervention: photon therapy, (3) proton therapy as comparator; (4) oncological outcomes (e.g. overall survival, biochemical relapse free survival, relapse free survival) and gastrointestinal or genitourinary toxicities (early or late). Heterogeneity between study-specific estimates was assessed using Chi-square statistics and measured with the I2 index (heterogeneity measure across studies).

Results. A total of 248 studies were included in the present analysis (Figure 1). Main results for the investigated clinical outcomes and toxicities are reported in Table 1. More in details, no statistically significant difference was observed regarding 5-year OS, even if a trend towards proton therapy was present. With regards to the 5-year biochemical relapse-free survival a statistically significant advantage was found for proton therapy (0.96 *vs* 0.91, p=0.02). Regarding treatment-related toxicities, a lower rate of incidence ($p<0.05$) was observed for proton treatments for G>2 acute GU and GI, while no statistically significant difference was found for late G>2 toxicities. When considering different proton beam delivery techniques, Pencil Beam scanning (PBS) and intensity-modulated proton therapy (IMPT), a lower rate of incidence of acute GU toxicity was found for PBS, although not statistically significant.

Conclusions. Currently available evidence demonstrated that PT improved tumor outcome in terms of 5-year biochemical control and reduced acute GI and GU toxicity. These results, at the current stage of the knowledge, were not translated to overall survival benefit or reduction in late toxicity. Further well designed and more high-quality controlled studies are needed in the future to obtain more robust data.

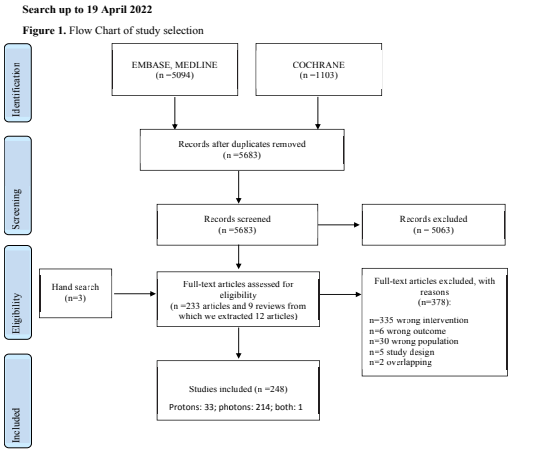

Figure 1.

Table 1.

		Included studies	Protons	Photons	p-value
OVERALL SURVIVAL (5 YEARS)		protons: 3 (1365 patients); photons: 28 (9414 patients)	0.95 (0.93-0.97)	0.93 (0.91-0.94)	**0.07**
RELAPSE FREE SURVIVAL (5 YEARS)		protons: 2 (565 patients); photons: 8 (3369 patients)	0.93 (0.77-0.98)	0.90 (0.82-0.95)	0.68
BIOCHEMICAL RELAPSE FREE SURVIVAL* (5 yrs)		protons: 2 (1443 patients); photons: 38 (10,862 patients).	0.96 (0.92-0.98)	0.91 (0.89-0.93)	**0.02**
Toxicities					
ACUTE GI grade ≥2		protons: 7 (1140 patients); photons: 84 (10,709 patients)	0.02 (0.02-0.04)	0.07 (0.05-0.08)	**<0.01**
Seminal vescicles irradiation	yes		0.02 (0.02-0.04)	0.07 (0.05-0.09)	
	no		0.03 (0.01-0.05)	0.07 (0.04-0.11)	
Pelvic irradiation	yes		0.02 (0.00-0.12)	0.10 (0.05-0.19)	
	no		0.03 (0.02-0.04)	0.06 (0.05-0.08)	
Rectal spacer	yes		-	0.03 (0.02-0.06)	
	no		0.02 (0.02-0.04)	0.07 (0.06-0.09)	
Protons	PBS		0.04 (0.03-0.06)	-	
	IMPT		0.02 (0.00-0.12)		
ACUTE GU grade ≥2		protons: 7 (1140 patients); photons: 88 (12,741 patients)	0.07 (0.03-0.16)	0.15 (0.12-0.19)	**<0.01**
Seminal vescicles irradiation	yes		0.05 (0.01-0.18)	0.18 (0.14-0.22)	
	no		0.15 (0.09-0.24)	0.09 (0.04-0.17)	
Pelvic irradiation	yes		0.35 (0.24-0.48)	0.18 (0.10-0.29)	
	no		0.06 (0.02-0.13)	0.15 (0.12-0.19)	
Rectal spacer	yes		-	0.09 (0.04-0.18)	
	no		0.07 (0.03-0.16)	0.16 (0.13-0.20)	
Protons	PBS		0.09 (0.07-0.11)	-	
	IMPT		0.35 (0.24-0.48)		
LATE GI, grade ≥2		protons: 6 (1758 patients); photons: 74 (14231 patients)	0.06 (0.03-0.13)	0.05 (0.04-0.06)	0.61
Seminal vescicles irradiation	yes		0.09 (0.05-0.16)	0.05 (0.04-0.07)	
	no		0.01 (0.00-0.03)	0.04 (0.02-0.07)	
Pelvic irradiation	yes		-	0.08 (0.04-0.13)	
	no		0.06 (0.03-0.13)	0.05 (0.04-0.06)	
Rectal spacer	yes		-	0.04 (0.03-0.05)	
	no		0.06 (0.03-0.13)	0.05 (0.04-0.07)	
Protons	PBS		0.10 (0.07-0.16)	-	
	IMPT		-		
LATE GU, grade ≥2		protons: 6 (1176 patients); photons: 75 (14379 patients).	0.05 (0.02-0.11)	0.08 (0.06-0.10)	0.30
Seminal vescicles irradiation	yes		0.04 (0.02-0.09)	0.09 (0.07-0.12)	
	no		0.14 (0.07-0.27)	0.05 (0.03-0.10)	
Pelvic irradiation	yes		-	0.09 (0.04-0.18)	
	no		0.05 (0.02-0.11)	0.08 (0.06-0.10)	
Rectal spacer	yes		-	0.09 (0.04-0.20)	
	no		0.05 (0.02-0.11)	0.08 (0.06-0.10)	
Protons	PBS		0.06 (0.04-0.09)	-	
	IMPT		-		

*Less than 3 studies considered

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TOWARDS PERSONALIZATION OF PLANNING TARGET VOLUME MARGINS FITTED TO THE ABDOMINAL ADIPOSITY IN LOCALIZED PROSTATE CANCER PATIENTS RECEIVING DEFINITIVE OR ADJUVANT/SALVAGE RADIOTHERAPY: SUGGESTIVE DATA FROM AN EXACTRAC *VS* CBCT COMPARISON

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Aims. This study aimed to assess whether the patient's abdominal adiposity affects the performance of the Exactrac imaging system compared to the Cone Beam Computed Tomography (CBCT)-based setup, which was taken as the reference positioning for the image-guided radiotherapy (IGRT) delivery to localized prostate cancer patients.

Methods. The daily positionings of localized prostate cancer patients undergoing definitive or adjuvant/salvage radiotherapy (RT) were analyzed. The abdominal fat areas and pelvic incidence angle were determined on the CT simulation for each patient. A couple of ExacTrac images and a CBCT were daily acquired to verify the patient setup. We recorded every daily set of the three residual translational errors detected on the CBCT after the ExacTrac-based setup. These sets were clustered within three different thresholds (0.1 mm, 0.2 mm, and 0.3 mm), for each of which the influence of adipose tissues on Exactrac accuracy was assessed as the percentage of sub-threshold displacements as the fat parameters varied. A full bladder and empty rectum preparation protocol was adopted as much as possible.

Results. From the assessment of 1770 daily positionings in 55 patients (38 definitive RT, 17 adjuvant/salvage RT), a good agreement between ExacTrac and CBCT can be inferred, which is quite robust against slight variations in the bladder and rectal filling, and the presence or not of the prostate. The percentages of above-threshold corrections increased with increasing abdominal fat, which therefore seemed to reduce the ExacTrac accuracy. This might be influenced by any intrafraction prostate displacement, likely induced by abdominal respiratory movements and more pronounced among overweight men.

Conclusions. Our results promote the CBCT use over ExacTrac for IGRT of overweight localized prostate cancer patients while calling for attention to the probable need for personalization of planning target volume margins depending on the patient's body habitus.

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ULTRA-HYPOFRACTIONATED STEREOTACTIC RADIOTHERAPY FOR PROSTATE TUMOR: OUR EXPERIENCE WITH THE 5 FRACTIONS

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Aims. The present is a retrospective evaluation of acute and late genito-urinary (GU) and gastro-intestinal (GI) toxicity, in addition to biochemical recurrence rate in 57 prostate cancer patients treated at our Institution with ultra-hypofractionated RT (UHRT) schedule.

Methods. From January 2021 to December 2022 we have treated 57 patients with prostate cancer, using an UHRT scheme of 5-fractions every other day for a total dose delivered of 36.25 Gy, according to the PACE-B trial treatment schedule. Most of our patients were intermediate risk (66.7%), while 19.3% were low risk and 14% were high risk (Table 1). Each treatment was performed by Accuray's TomoTherapy with daily IGRT. For these treatments, we didn't use devices such as fiducial markers or rectal spacers. Good urinary function, assessed by International Prostate Symptom Score (IPSS), were required. Patients were instructed to achieve appropriate bladder and rectum filling for adequate reproducibility during treatment sessions (comfortably full bladder and empty rectal ampulla). The evaluation of the set-up was very restrictive before daily treatment delivery. The simulation CT scans were acquired in supine position and fused with MRI for GTVs definition for every patient. An isometric expansion of 3-5 mm except for the posterior margin (1-3 mm) were added to the GTV to obtain PTV.

Results. According to RTOG toxicity scale, the acute GU toxicity recorded on the last day of treatment was G0 in 25 patients (43.9%), G1 in 31 (54.4%) and G3 in one patient (1,75%); in regards to GI toxicity, 55 patients showed G0 (96.5%), 2 patients showed G1 (3.5%). At 3 months from RT, GU toxicity was G0 for 30 patients (52.6%), G1 for 26 (45.6%) and G2 for one only (1.75%); rectal toxicity was G0 for 56 patients (98.25%) and G1 for one only (1.75%). The median follow-up (FU) was 9 months (2-24). In the following FU months, we observed progressively lower urinary and rectal toxicity, except for one patient who showed G2 GU toxicity at 12 months. All but one patient had a progressive PSA value decrease. For

this patient a PET/CT scan confirmed a recurrence located on the right seminal vesicle base, outside of the irradiation field.

Conclusions. In our experience, UHRT appears to be safe and well tolerated even without the use of rectal spacer devices. To date (median FU of 9 months) only one patient results in biochemical and radiological recurrence. A longer FU is necessary to evaluate disease control.

Table 1. Patients characteristics.

AGE (years)	Median	78
	Max	87
	Min	60
iPSA (ng/ml)	Median	6,87
	Max	16
	Min	1,1
ISUP grade group	I	11 (19,3%)
	II	27 (47,4%)
	III	11 (19.3%)
	IV	8 (14,0%)
	V	0
FUP (month)	Median	9
	Max	24
	Min	2

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THE ROLE OF METASTASES DIRECTED RADIATION THERAPY IN OLIGOMESTATIC PROSTATE CANCER

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Aims. The therapeutic approach to oligometastatic prostate cancer no longer recognizes the use of pharmacological therapy alone and, today, also provides for the possibility of using radiotherapy. Patients (pts) who, having already undergone curative treatment for prostate cancer, could experience biochemical progression during follow-up, with evidence of oligorecurrent or oligoprogressive disease and can be evaluated for radiotherapy treatment. In this setting, the use of stereotactic ablative radiotherapy (SABR) is increasingly frequent, allowing good local control of the disease with low rates of toxicity. The aim of this work is to evaluate the benefit of radiotherapy in terms of biochemical progression free survival (bPFS) in this population.

Methods. We reviewed data related to oligometastatic prostate cancer patients, defined as patients with a controlled primary malignancy and 1-3 metastatic lesions, who were treated with metastases directed radiation therapy. Patients were divided in oligorecurrent and oligoprogressive, depending on whether disease progression occurred more than 6 months after the end of the last active therapy or before this deadline, respectively. bPFS was calculated from the initiation of RT treatment to biochemical failure.

Results. A total of 55 pts were identified: 38 pts (69%) had oligorecurrent disease and 17 pts (31%) had metastatic castration resistant prostate cancer (mCRPC), of these 11 pts (64,7%) were oligoprogressive during androgen deprivation therapy (ADT) and 6 pts (35,3%) were oligoprogressive during ARSI. Among 38 pts with oligorecurrent disease, 27 (71%) treated all the metastases with radiotherapy alone with a median bPFS of 28 months. The other 11 pts (29%) were treated it with ADT plus radiation therapy on all sites of disease with a median PFS of 40 months. The 11 oligoprogressive pts during ADT had a bPFS of 20 months after treating all the metastases with RT, while the remaining 6 pts (11%) who oligoprogressed during ARSI gained with RT a bPFS of 17 months.

Conclusions. In our experience, the use of radiation therapy on all the metastases in patients with oligorecurrent or oligoprogressive prostate cancer has proved to be effective in postponing the use of subsequent line drugs so as to reserve them for any future needs.

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FOCAL BRACHYTHERAPY AS DEFINITIVE TREATMENT FOR LOCALIZED PROSTATE CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Aims. Focal therapy for prostate cancer has been proposed as an alternative to whole-gland therapy to reduce toxicity. In this systematic review and meta-analysis, we describe the oncologic and toxicity outcomes of definitive focal brachytherapy

Methods. An International Prospective Register of Systematic Reviews (PROSPERO) registered study (CRD42023410170) was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. PubMed, Embase

and The Cochrane Library were searched for studies between 2000 and 2022. Two authors independently performed the initial search. Biochemical recurrence-free survival (bRFS) and local recurrences were defined as endpoints. Generalized linear mixed-effects models were conducted to calculate effect size and quantify heterogeneity.

Results. Ten studies were identified and included 315 patients treated using focal brachytherapy as a definitive treatment. The mean (SD) age was 67.65 (7.9) years and the mean (SD) PSA was 7.15 (2.7) ng/mL. Most patients (n=236, 75%) underwent LDR Brachytherapy and 25% received HDR brachytherapy. Among the participants, 147 (46.5%) had a Gleason score ≤6, and 169 (53.5%) had a Gleason score ≥7. Only 11 (3.5%) patients received ADT. Overall, the bRFS rate at median follow-up 4 years (Range: 1- 6.42 years) was 91% (95% confidence interval [CI], 82%-95%) and the proportion of patients with local failure was 0.15 (CI 95%, 0.08-0.22). Acute grade ≤ 2 GU and GI toxicities were reported in 22 (7 %) and 11 (3.5%) patients, respectively. Late grade ≤ 2 GU and GI toxicity were reported in 6 (2%) and 14 (4.4%) patients, respectively. No acute or late grade 3 or higher GI or GU toxicity was reported.

Conclusions. Overall, definitive focal brachytherapy seems to have favorable oncological outcomes and low toxicity profile. However, the evidence is limited by the small number of studies with low patients' numbers, across study heterogeneity, and the possibility of publication bias. Results should be interpreted with caution and large prospective studies with long follow up are warranted.

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CLARITY 3D ULTRASOUND SYSTEM FOR PROSTATE LOCALIZATION: OUR EXPERIENCE

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Aims. To evaluate the accuracy of transabdominal ultrasound versus CBCT in image-guided radiotherapy for prostate cancer

Methods. From January 2021 to November 2022, prostate positioning was retrospectively evaluated in 150 prostate cancer patients using three-dimensional ultrasound (3DUS) and cone-beam CT (CBCT). All patients underwent definitive radiotherapy with a total dose of 76-78 Gy over 38-39 fractions and treated with a 6 MV linear accelerator with a volumetric modulated arc therapy (VMAT) plan. Each patients underwent CT simulation in supine position with empty rectum and full bladder and with a slice thickness of 3 mm. During the simulation session, we acquired 3-dimensional (3D) US prostate scan with the Clarity system installed in the CT-simulation room. The Clarity system has two mobile units,the first in the CT room, the second in the treatment room, and are connected to a workstation/server. . Reference images of CT scan and ultrasound images were sent to linear accelerator's treatment system. Both 3DUS and CBCT scans were repeated before each treatment. Setup errors detected by the different modalities were compared.

Results. In total 5850 ultrasound scans were performed trans-abdominally and compared to bone-matches in CBCT scans and no significant difference (<3 mm) were be detected in most patients.

Conclusions. 3DUS is feasible for image guidance for patients with prostate cancer and appears comparable to CBCTbased image guidance without additional radiation exposure but 3DUS guidance is more feasible in young patients with greater bladder volume control ability.

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MONO-INSTITUTIONAL SERIES OF 90 PROSTATE CANCER PATIENTS TREATED WITH RADIOTHERAPY WITH GOLD FIDUCIAL MARKERS IMPLANTATION

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Aims. The use of intraprostatic radiopaque fiducials in image-guided radiotherapy (IGRT) is an option for prostate cancer (PCa) daily positioning verification. The aim of this retrospective study was to determine the efficacy and safety of fiducial markers in PCa radiotherapy.

Methods. The study included patients who underwent radiotherapy for prostate cancer at our institution between October 2008 and June 2011. Patients who received hormone therapy were also included, while patients who received previus High Intensity Focused Ultrasound (HIFU) were excluded. Radiotherapy was delivered with image-guided radiation therapy (IGRT) using the Varian Clinac or the BrainLab VERO System. All patients underwent implantation of three-gold seed fiducial markers into the prostate gland before prostate radiotherapy. The prescribed dose was 70 Gy, with 2.5 Gy per fraction. IGRT was performed using kilovoltage (kV) orthogonal imaging with the On Board Imager system.

Results. 90 patients met the inclusion criteria and were included in the study. Patients characteristics are listed in Table 1. 78 (86.7%) patients resulted free from disease at last contact. Progression of disease (PD) was

observed in 12 out of 90 patients (13.3%) with 7 clinical and 5 biochemical progressions. Median Planned Target Volume (PTV) margin was 4mm (IQR: 4-4). Regarding acute toxicity outcomes, no genitourinary (GU) events higher than grade (G) 2 and no gastrointestinal (GI) events higher than G2 occurred. During follow-up, no patients but two experienced GU/GI events higher than 2. One patient experienced G3 GU maximum toxicity with positioning of urinary catheter. The other one experienced late G3 GE toxicity with radiation-induced proctitis conditioning anemia.

Conclusions. Gold fiducial markers implantation is a safe and effective technique for prostate cancer IGRT. Further studies are warranted to confirm these preliminary findings.

Table 1. Patients characteristics

Age at RT	*years, median (IQR)* 72 (69-76)
iPSA	*ng/ml, median (IQR)* 6.3 (5.0-8.9)
ISUP grade group	*Number of patients*
1	59
2	18
3	3
4	2
5	1
NA	7
Hormon Therapy	*Number of patients*
Yes	49
No	41

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RETROSPECTIVE ANALYSIS OF RADIOTHERAPY PLANS FOR PROSTATE CANCER AFTER REVISION OF MRI TARGET LESIONS DETECTED BY QUANTIB® PROSTATE

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Aims. The aim of this retrospective analysis is the coverage evaluation of RT plans after MRI revision of intraprostatic lesions detected by Quantib® Prostate system, version 2.1.1. (Quantib B.V. Rotterdam, The Netherlands).

Methods. We evaluated 5 patients treated with hypofractionated RT (70 Gy in 28 fractions) affected by intermediate-to-high risk prostate cancer (Table 1). All patients were staged with pre-RT MRI. The Quantib® Prostate artificial intelligence is an FDA and CE-approved MRI viewing and reporting platform based on deep learning, therefore it is able to help the Radiologist in identification of intraprostatic target lesions suspected as disease. This system was not available at our hospital at the time of diagnosis. It was decided to review these MRI with the Quantib® system, then to evaluate the coverage of these lesions on the previous treatment plan, through image fusion, and to assess PSA trend in the follow-up. Contouring was performed without MR fusion. The Radiologist carried out the analysis using Quantib® without consider the report previously produced to avoid bias.

Results. A total of 5 lesions were identified in 5 patients. In one case Quantib® failed to detect the lesions previously identified by Radiologist: these lesions had been identified as Pi-RADS 3 and Pi-RADS 4 and were located in the transitional zone, where Quantib® has the greatest difficulty in detecting. The remaining lesions detected by Quantib® are anatomically related to those previously identified on the MRI. The coverage of intraprostatic lesions was optimal (D95% between 67.9 Gy and 70.7 Gy and D98% between 65.4 Gy and 70.7 Gy). Moreover, evaluating the PSA value in the follow-up (between 3 and 9 months), a response to radiation treatment was detected with a drop of this value.

Conclusions. The analysis shows how the Quantib® system can help the identification of intraprostatic target lesions on MRI. The review of RT plans, after identification of Quantib® target images on MRI, confirms optimal coverage of target volumes and a subsequent biochemical response at minimum follow-up. These are preliminary results and a more detailed analysis is necessarily needed, particularly in case of simultaneous integrated boost.

Table 1. Patients characteristics.

	ISUP Grade	Number of lesion and Pi-RADS	Hormonal therapy	PSA value at diagnosis	PSA value at RT start post HT start	Medium PSA post RT	Lesions coverage	Notes
Patient 1	ISUP 4	One lesion Pi-RADS 4	Yes	5.25 ng/mL	5.62 ng/mL	0.05 ng/mL	D95% 68.3 Gy D98% 68 Gy	
Patient 2	ISUP 4	One lesion Pi-RADS 5	No	12.77 ng/mL		1.07 ng/mL	D95% 67.9 Gy D98% 65.4 Gy	
Patient 3	ISUP 5	One lesion Pi-RADS 5	Yes	8.58 ng/mL	1.44 ng/mL	0.41 ng/mL	D95% 69.5 Gy D98% 67.8 Gy	
Patient 4	ISUP 2	One lesion Pi-RADS 4 One lesion Pi-RADS 3	No	28.37 ng/mL				Quantib® not detected (transition zone)
Patient 5	ISUP 3	One lesion Pi-RADS 4 One lesion Pi-RADS 4	No	16.59 ng/mL		2.58 ng/mL	D95% 70.7 Gy D98% 70.7 Gy D95% 68.6 Gy D98% 69 Gy	

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CYBERKNIFE RADIOSURGERY FOR PROSTATE CANCER AFTER ABDOMINOPERINEAL RESECTION (CYRANO): THE COMBINED COMPUTED TOMOGRAPHY AND ELECTROMAGNETIC NAVIGATION GUIDED TRANSPERINEAL FIDUCIAL MARKERS IMPLANTATION TECHNIQUE

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Prostate cancer (PCa) is a common malignancy among males worldwide, and radiation therapy (RT) has become an established treatment for localized PCa. Recent advancements in imaging, treatment planning, and delivery systems have increased interest in hypofractionation, which involves delivering fewer large doses per fraction over a shorter treatment duration.

In this technical development report, we present the strategic placement of fiducial markers within the prostate under the guidance of computed tomography (CT) and electromagnetic navigation for the delivery of ultra-hypofractionated Cyberknife (CK) therapy in a patient with localized PCa who had previously undergone chemo-radiotherapy for rectal cancer and subsequent abdominoperineal resection due to local recurrence. The patient was positioned in a prone position with a pillow under the pelvis to facilitate access, and an electromagnetic fiducial marker was placed on the patient's skin to establish a stable position. CT scans were performed to plan the procedure, mark virtual points, and simulate the needle trajectory using the navigation system. Local anesthesia was administered, and a 21G needle was used to place the fiducial markers according to the navigation system information. A confirmatory CT scan was obtained to ensure proper positioning. The implantation procedure was safe, without any acute side effects such as pain, hematuria, dysuria, or hematospermia.

The clinical target volume of the dominant intraprostatic lesion (CTV-DIL) was delineated based on the multiparametric MRI sequences fused with the planning CT in the treatment planning system (TPS), and the planning target volume of the prostate (PTV-P) was created by expanding CTV-P by 5mm in all directions, except 3mm posteriorly. The PTV-P and the PTV-DIL received 36.25 Gy and 40 Gy in 7.25 Gy and 8 Gy fractions, respectively, over a total period of 11 days. The prescribed dose was normalized to the 85% isodose. Our technical development report highlights the capabilities of using electromagnetic navigation systems to virtually navigate within a pre-acquired imaging dataset in the interventional room, allowing for non-conventional approaches and potentially revolutionizing fiducial marker positioning, offering new perspectives for PCa treatment in selected cases.

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DOSIMETRIC EVALUATION OF TREATMENT PLANS WITH DIFFERENT BREATH CONTROL METHODS IN IRRADIATION OF ABDOMINAL RENAL CANCER RELAPSE

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Aims. The aim of this analysis is the dosimetric evaluation of treatment plans with different breathing control methods to determine the treatment plan with the best target coverage and spare of organs at risk in the irradiation of a renal neoplasm relapse not amenable to surgery.

Methods. The target volume was a renal cancer relapse previously treated with surgery. It was a single lesion in right renal cavity, measuring 52x37x48 mm. The lesion was inseparable from the dome and diaphragmatic pillar and was located posterior to the adrenal gland. Three simulation CT scans were acquired with 2 mm slices: breath hold, 4D gated CT and free breath (co-registered with the previous). The patient was positioned with a thoracic immobilization system and a personalized vacuum pillow. The breath control system was Varian Respiratory Gating RGSC. Breath hold CT and 4D gated CT scans were contoured and two different treatment plans were elaborated. The prescription dose was 49.5 Gy in 22 fractions, 2.25 Gy per fraction, in VMAT with daily IGRT-CBCT. The identified OARs were spinal cord, heart, liver, left kidney, bowel near target, bowel bag, stomach and duodenum. The expansion from GTV to CTV and from CTV to PTV was 2 mm for breath hold CT. For 4D gated CT the ITV was deduced from the different respiratory phases and then the expansion from ITV to PTV was 2 mm. The linac was a Varian Truebeam, 2.7 version.

Results. PTV coverage for breath hold plan was D95% 48.5 Gy, D98% 47.7 Gy, PTV coverage for 4D gated plan was D95% 47.9 Gy, D98% 46.7 Gy. For plan comparison the constraints were calculated in EQD2, using α/β 2 for spinal cord, bowel and bag bowel and using α/β 3 for other constraints (Table 1). Given the coverage values of the target and the sparing of organs at risk, it was chosen the breath hold treatment. The treatment was well tolerated. During therapy it was reported G1 fatigue and G1 nausea and the patient demonstrated good compliance. The follow up has shown stable disease 10 months after the end of RT.

Conclusions. An evaluation of several treatment plans with breath control is often necessary before evaluating the best treatment planning technique. In this specific case the breath hold plan was superior to the 4D gated CT plan, as often happens in abdominal tumors, according to literature. For this approach, however, patient compliance is required to best deliver the treatment plan.

Table 1.

	BH plan	4D gated plan
Heart	Dmean 0.3 Gy	Dmean 0.3 Gy
Left Kidney	V_{20} 0 % Dmean 0.7 Gy	V_{20} 0 % Dmean 0.9 Gy
Liver	Dmean 7.6 Gy V_{30} 3.4% V_{40} 1.9%	Dmean 7.7 Gy V_{30} 3.4% V_{40} 1.9%
Duodenum	Dmax 10.4 Gy	Dmax 16 Gy
Stomach	Dmax 10.5 Gy	Dmax 13.9 Gy
Bowel Bag	Dmax 45.3 Gy	Dmax 50.3 Gy
Bowel near target	V_{15} 2.4 cc	V_{15} 5.4 cc
Spinal cord	Dmax 6.7 Gy	Dmax 6.5 Gy

P276

SAFETY AND EFFECTIVENESS OF ALPHA-LYTHICS IN PREVENTING RADIO-RELATED GENITO-URINARY SIDE EFFECTS

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Aims. To evaluate the efficacy of alpha-blockers drugs alleviating urinary symptoms in patients with prostate cancer undergoing curative radiotherapy.

Methods. We retrospectively evaluated 30 patients with localized prostate cancer (GS: 3+3, 3+4, 4+3) with glandular volume, measured by ultrasound, greater than 30 cc and treated with radiotherapy plus hormonal therapy. All patients were on alpha-blockers for BPH (Benign prostatic hyperplasia) before starting radiotherapy. All treatments were delivered in VMAT technique with Total Dose: 70.2 Gy at 2.7 Gy per fraction after iconographic positional control by CBCT. Toxicity treatment was measured using modified LENT (Late Effects of Normal Tissues)/RTOG (Radiation Therapy Oncology Group). The results obtained in our evaluation were compared with the reference literature data.

Results. The overall incidences of grade 0, 1, 2 and 3 GU reactions in our patient group were 2.9%, 45%, 38% and 1% compared to the literature references respectively: 3.4%, 51.7%, 40.9% and 4.0%. Non differences in Gastrointestinal toxicities. No drug side effects were reported, except occasional episodes of vascular hypotension.

Conclusions. From our experience, limited by the small number of patients, it is highlighted that alpha-blockers are safe drugs, without important side effects, and above all useful in preventing and controlling radio-induced urological side effects. Further studies with larger series and longer follow-up are needed.

P277

HYPOFRACTIONATED VMAT RADIOTHERAPY FOR PROSTATE CANCER: A MONO-INSTITUTIONAL ANALYSIS OF ACUTE GENITOURINARY AND GASTROINTESTINAL TOXICITIES

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Aims. Reporting acute GU and GI toxicities of hypofractionated VMAT radiotherapy in curatively treated prostate cancer.

Methods. Patients were treated using Volumetric Modulated Arc Therapy (VMAT) Image-Guided Radiotherapy (IGRT), to a total dose of 60 Gy (3 Gy/fraction), with 6 MV energy photons. Cone beam Computed Tomography (CBCT) was daily performed. The CTV comprised the entire prostate with lower third of the seminal vescicle irradiation only in case of PSA higher than 10 ng/ml or Gleason score 4+3 and higher or T2b and higher. The CTV to PTV enlargement was 1 cm on every direction except posteriorly which was 0.5 cm. Toxicity was assessed using the Common Terminology Criteria for Adverse Events (CTCAE), V. 5.0. Clinical evaluation was performed during RT.

Results. From May 2022 to May 2023, a total of 26 patients were treated. Median age was 75 years (range 58-83). Clinical tumor stage (T) was: T1c (n=20); T2a (n=5); T3a (n=1). None had nodal involvement. Two patients had a single bone metastasis and were concurrently treated on both prostate and bone metastasis. Median maximum total PSA value was 8.57 ng/ml (range 1.15-131). Androgen deprivation therapy (ADT) was added in 20 patients (77%). No treatment-related interruptions occurred. All patients completed the planned treatment. Acute genitourinary toxicity included grade 1 (G1) e G2 urinary frequency [n=11 (42%) e n=1 (3.8%), respectively], G2 urinary incontinence (n=1; 3.8%), G1 urinary urgency (n=7; 27%), dysuria (n=4; 15%). Acute gastrointestinal toxicity included G1 constipation (n=1; 3.8%), G1 and G2 diarrhea [n=2 (7.7%) and n=2 (7.7%)], G1 proctitis (n=11; 42%), G2 fecal incontinence (n=1; 3.8%), G1 rectal hemorrhage (n=1; 3.8%). No G3 or higher acute toxicity was recorded. All patients were symptomatically treated.

Conclusions. Our experience supports the use of moderate hypofractionated (3 Gy x 20 fractions) radiotherapy for prostate cancer, with low toxicity and high

compliance. We continue to recruit and observe patients for both survival and late toxicity analysis.

P278

SWITCHING FROM AN LHRH ANTAGONIST TO AN LHRH AGONIST IN PATIENTS WITH PROSTATE CANCER: OUR EXPERIENCE

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Aims. Prostate cancer is the second most common cancer in men surpassed only by skin cancers and today's standard of care of advanced or high-risk hormone-sensitive prostate cancer includes hormonal therapy with luteinizing hormone-releasing hormone (LHRH) analogues. There are actually no clinical guidelines and few published data on switching from an LHRH antagonist to an LHRH agonist. The aim of our analysis was to evaluate characteristics and outcome of five patients with advanced prostate cancer who switched from an LHRH antagonist to an LHRH agonist.

Methods. Five patients with T3N0M0 hormone-sensitive prostate cancer were treated with external beam radiotherapy and neoadjuvant/concomitant hormonal therapy. All patients received the LH-RH antagonist monthly (Degarelix), with 240 mg as the first dose and 80 mg for subsequent doses subcutaneously and they were switched to the leuprorelin acetate/triptorelin pamoate after presenting adverse effects. PSA and testosterone levels were measured for all patients every three months during treatment to determine the PSA response. Castrated serum testosterone level was defined as <50 ng/dl. The Wilcoxon signed-rank test was used for comparisons of testosterone and PSA.

Results. Median age was 72 years (range between 65 and 79), Gleason Score ranged from 7 to 9. All patients experienced side effects with LHRH antagonist; four patients had pain/injection site reactions and one patient had an allergic reaction. After switching, prostate serum antigen levels were comparable or inferior from those measured prior to switching, showing the same efficacy. With leuprorelin acetate/triptorelin pamoate-treatment no patients reported injection site reactions, such as pain or swelling.

Conclusions. Our retrospective analysis shows that the switch from an LHRH antagonist to an agonist is safe and equally efficacious and it is suggested in case of reported side effects. Further prospective studies are necessary to better evaluate outcome of these prostate patients.

P279

RADIATION INDUCED EDEMA AND CORRELATION WITH RADIONECROSIS IN RE-IRRADIATION OF RECURRENT HIGH-GRADE GLIOMAS TREATED WITH PROTON THERAPY, FINAL ANALYSIS

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Purpose. During and after re-irradiation of recurrent high-grade gliomas (rHGG) variation of edema (ED) is frequent. The aim of study is to report a quantitative analysis of radiation induced ED analyzing the temporal changes before, during and after proton therapy re-irradiation (re-PT) and correlation with Radionecrosis (RN), as well as to evaluate use of prognostic factors with impact change ED values and correlation on survival (OS) and progression-free survival (PFS).

Methods. Fifty-three patients with rHGG were re-irradiated with active scanning PT at our institution and included in the study. ED was drowned on 212 MRI scans and was quantified as any T2w and FLAIR changes excluding the Gross Tumor Volume. Radiation induced imaging changes were defined as new areas of increased T2w and FLAIR signal surrounding the treated GTV on MRI imaging. We analyzed the temporal change of ED at baseline, mid, end and one month after re-PT and onset of RN as well as prognostic factors such: steroids, median time to re-PT, number of different lines of chemo before or concurrent chemo re-PT association, recurrence location disease site, histology and GTV re-PT volume with impact change ED values and correlation on OS and PFS.

Results. Pretreatment MRI mean ED value was associated with a statistically significant analysis and an increasing trend of mean values during and one month after the treatment. During follow up 9 patients (16,9%) experienced RN that was associated with a significant increase in ED on one month post treatment MRI. An increase in the re irradiation time interval between the first radiation treatment and re-PT was shown to be related with decrease ED values on planning MRI as well as a positive correlation between increase ED value at planning MRI with increasing GTV re- PT volume. The median OS was significantly higher in patient without onset of RN. The use of steroid before re-PT was associated with worse OS and PFS. No statistical impact in OS or PFS and increase of steroid dose during re- PT was seen, as well as between MRI edema values at baseline, mid-therapy, end and one month and increase of steroids.

Conclusions. The current study was conducted to analyse for the first time the variation of radiation induced ED before, during and after re-PT of rHGG

demonstrating that re-PT is a safe and effective treatment for rHGG and ED can be a predictive and prognostic factor for the onset of RN.

Table 1. Median values and interquartile range (IQR) of edema (in cm^3) at planning MRI, mid-treatment MRI, MRI at the end of treatment and on MRI, one month after the end of treatment. Comparison between modalities of variables through Wilcoxon and Kruskal-Wallis statistical tests (significant p≤0.05).

	Edema (cm^3) at planning MRI	Edema (cm^3) at mid-treatment MRI	Edema (cm^3) on MRI at the end of treatment	Edema (cm^3) on MRI, one month after the end of treatment
Radiation necrosis (Yes)	55.7 (45.5)	61.5 (58.2)	69.4 (41.8)	108.3 (92.8)
Radiation necrosis (No)	36.9 (36.5)	36.3 (48.3)	39.9 (49.1)	37.6 (53.7)
p-value	0.228	0.135	0.093	**0.024**
Pre PT surgeries (No)	35.7 (38.8)	34.6 (48.3)	39.0 (53.2)	45.3 (55.7)
Pre PT surgeries (Yes)	40.0 (41.8)	52.8 (64.1)	50.3 (62.5)	38.5 (87.7)
p-value	0.405	0.155	0.133	0.440
Pre PT chemotherapies (No)	36.9 (33.6)	36.7 (31.5)	39.1 (41.7)	45.4 (66.5)
Pre PT chemotherapies (Yes, 1 chemotherapy)	40.0 (43.4)	54.1 (62.7)	42.6 (60.0)	38.5 (36.1)
Pre PT chemotherapies (Yes, 2 chemotherapies)	32.3 (41.8)	43.1 (63.6)	61.5 (63.8)	69.5 (81.4)
p-value	0.861	0.895	0.835	0.733
Histology (AA)	27.2 (42.3)	32.2 (40.6)	38.9 (47.5)	38.5 (68.1)
Histology (GBM)	46.4 (37.0)	53.0 (60.1)	48.1 (59.3)	45.3 (84.6)
p-value	0.072	0.063	0.136	0.277
Steroid use before PT (Yes)	52.5 (56.6)	53.0 (71.2)	52.9 (80.8)	43.5 (81.3)
Steroid use before PT (No)	31.1 (28.7)	35.8 (34.4)	39.1 (45.6)	44.4 (68.1)
p-value	**0.022**	0.139	0.105	0.258
Increased use of steroids during PT (Yes)	56.4 (55.2)	79.2 (88.0)	98.7 (103.9)	115.1 (114.3)
Increased use of steroids during PT (No)	34.6 (41.3)	36.7 (37.9)	40.7 (40.1)	41.9 (36.1)
p-value	0.057	0.052	**0.026**	**0.006**

P280

HYPOFRACTIONATED RE-IRRADIATION FOR LOCOREGIONALLY RECURRENT HEAD AND NECK CANCER

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Purpose/Objective. Loco-regional recurrence (LRR) is the predominant pattern of failure in locally-advanced head and neck cancer (HNC), both squamous cell carcinoma (SCC) and non-squamous histologies. Despite the proven role of irradiation (RT) as primary treatment strategy, there is lack of high-quality evidence of the use of reirradiation (ReRT) in recurrent HNC (rHNC). Various regimens of hypofractionation are described in literature, without a clear consensus. The aim of our single-centre study is to evaluate the clinical outcome of unresectable rHNC patients treated with hypofractionated reRT.

Materials and Methods. All eligible patients had a recurrent, previously irradiated unresectable HNC. Each case was discussed multidisciplinary before treatment. Local control (LC) and overall survival (OS) were calculated using the Kaplan-Meier method and log rank test with time measured from the date of last day of reRT to date of progression or death.

Results. We retrospectively analysed data from 53 consecutive patients with rHNC who underwent reRT at our institute. First curatively-intended course of RT was delivered from 1997 to 2020, with or without chemotherapy. The majority of patients (40, 75%) had a diagnosis of SCC; 11 patients (21%) had other histologies than SCC and for 2 (4%), no histological confirmation was available. The median age was 60 years. The reRT, with a hypofractionated schedule, took place from 2012 to 2022. Details of reRT are shown in Table 1. After a median follow-up of 22 months (range 0-49), 24 out of 53 patients were alive. Causes of death were related to HNC in 14 patients (26%); 2 patients died for toxicities related to treatments (4%) and 13 for other causes (24%). The median LC and the 1-year LC rate were 9 months (95% CI 5,6-12,3 months) and 74.2%, respectively. The median OS after reRT and the 1-year OS rate were 11 months (95% CI 6.0-15.9) and 88,8% (Figure 1), respectively. At univariate analysis, a borderline negative association between time to ReRT ≤ 12 months and LC was shown (p 0.06). A significant dependence of outcome after ReRT from the hypofractionated schedule could not be demonstrated from our data (p 0.06). No statistically significant correlation was observed in respect with age ≤ or > 70 years (p 0.19) or gender (p 0.15).

Conclusions. From our analysis, hypofractionated ReRT schedules appear to be a well tolerated treatment option for rHNC with potential for prolonged local control in appropriately selected patients.

Table 1. Treatment characteristics.

Re-RT	
Technique	
-VMAT/IMRT	N=7
-Cyberknife	N=46
Schedules	
-40 Gy/16	N=5
-30 Gy/5	N=18
-30 Gy/3	N=2
-30 Gy/10	N=3
-25 Gy/5	N=25

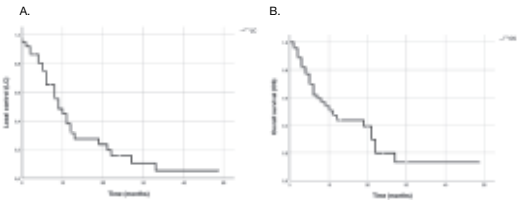

Figure 1. Kaplan Meier curves for (A.) local control (LC) and (B.) overall survival (OS).

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RE-IRRADIATION FOR DETECTABLE PROSTATE BED RECURRENCE: A MONOCENTRIC EXPERIENCE

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Aims. Aim of the present study is to evaluate the safety and effectiveness of re-irradiation for local relapse on patients who underwent prostatectomy followed by radiotherapy (RT), both adjuvant and salvage, as primary treatment for prostate cancer (PCa).

Methods. Patients who underwent prostatectomy and then adjuvant or salvage RT (external beam RT (EBRT) or brachytherapy) and with evidence of isolated relapse in prostatic bed at MRI or PET choline were retrospectively considered. GTV was contoured on the basis of the imaging available. Salvage re-EBRT was delivered with image-guided RT (RapidArc®, VERO® and CyberKnife®).

Results. A total of 38 patients, with a median age at salvage re-EBRT of 69 years, were included in the present analysis. A total of 12 patients received 25 Gy/5 fx, while 15 received 30/5fx and 11 received 35Gy.

Median GTV value was 5.4 cc. Median pre-salvage SBRT prostate-specific antigen (PSA) was 1.92 ng/ml. Hormone therapy was received by 11 (28.92%) of patients. Isolated relapse in the prostatic bed was assessed by MRI and PET choline in 34 (89.5%) and 26 patients (68.4%), respectively. At a median follow-up of 40.7 months, a total of 33 patients (86.8%) had biochemical progression with a median time to progression of 11.1 months. Biochemical recurrence-free survival rates at 1- and 2- year were 48.7% and 38.3%, respectively (Figure 1). Clinical progression was observed in 23 (60%) patients. Among them, 6 had both local relapse and distant metastasis, 7 developed only distant metastasis and 10 had only local relapse. Among the 13 patients who developed distant metastasis, four had only lymph nodal lesions, five had only bone lesions, three had both (1 missing). Among the 16 local relapses, 5, 8 and 3 were observed in the 25Gy, in the 30Gy and in the 35Gy groups, respectively. We registered no acute event worse than G1; considering maximum toxicity during the treatment, one G2 late GI event and two G3 and four G4 late GU events (two solved at last FU) were reported.

Conclusions. Salvage re-EBRT for isolated relapse of PCa in prostatic bed is an option as salvage treatment, especially in order to procrastinate systemic therapies as hormone therapy, however, correct doses and timing of re-EBRT should be furtherly investigated.

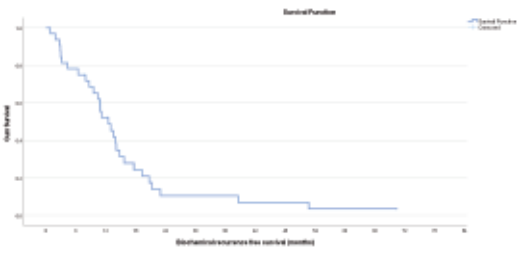

Figure 1.

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STEREOTACTIC BONE REIRRADIATION FOR RECURRENT METASTASES: A MONO-INSTITUTIONAL EXPERIENCE

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Aims. This retrospective study aims to evaluate the efficacy and safety of stereotactic bone re-irradiaton with CyberKnife™ (Accuray, Sunnyvale, CA, USA) (CK) in our institution.

Methods. From January 2018 to September 2022, 39 re-irradiations were performed in 36 patients (pts) with radiological diagnosis of bone metastasis. Median age was 72 (37-89) years at the time of the stereotactic bone re-irradiation. Primary tumor histology was: prostate cancer for 25 pts, lung cancer for 4 pts, endometrial cancer for 1 patient, renal cancer and breast cancer for 3 pts. Metastatic sites were as follows: 2cervical spine, 10 thoracic spine, 13 lumbar spine, 4 sacrum, 1hip, 1rib, 1skull, 1sternum and 6 pelvis. Twenty-nine of the previous treatments were delivered by conventional external beam radiation (cEBRT) and 10 with stereotactic body radiotherapy. Stereotactic bone re-irradiation was delivered with CyberKnife® (Accuray, Sunnyvale, CA, USA) real-time tracking radiation therapy. Median prescription dose was 20 (12-30) Gy in a median of 5 (1-5) fractions at a median isodose of 79% (69-82). Toxicity was assessed

with CTCAE version 5.0.

Results. Median follow-up was 40 (0.0 – 58.51) months. No grade (G) ≥ 3 acute toxicity was observed. Two pts experienced G1 back pain. Other two pts suffered from nausea: one G1 and the other G2. No late toxicity was observed. Nine pts were symptomatic before the treatment and after the SBRT a complete pain response was observed in all of them.

Kaplan Meier estimates of Overall Survival (OS) at 12-, 24- and 36- months was 84.2%, 64.5% and 58% respectively. Distant metastases free survival (DMFS) was 55.9% at 12 months, 45.6% at 24 months and 37.3% at 36 months. Local relapse free survival (LRFS), was 83.4% at 12 months and 24 months, and 74.2 % at 36 months (Figure 1).

Conclusions. In our experience, stereotactic re-irradiation in the management of recurrent bone metastases is feasible, with low toxicity. These findings suggest that stereotactic reirradiation is a viable therapeutic option for patients with recurrent bone metastases, improving quality of life and ensuring good local control for more than 3 years after re-irradiation. Prospective studies are warranted to validate these results.

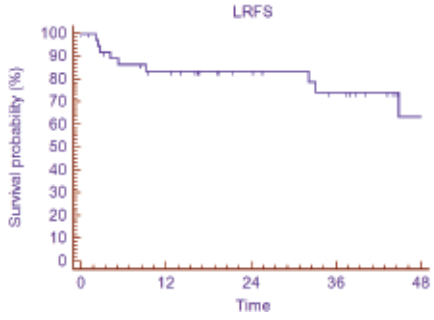

Figure 1.

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BRAIN METASTASES STEREOTACTIC RE-IRRADIATION FOR LOCAL RECURRENCE AFTER RADIOTHERAPY: SAFETY AND EFFICACY IN A MONOINSTITUTIONAL EXPERIENCE

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Aims. To present our results of salvage Stereotactic Radiotherapy(SRT)/Radiosurgery(RS) for recurrent BM after previous radiotherapy(RT).

Methods. From 01/2018- 07/2022, 134 BM in 32 cases were re-irradiated (ReRT). Two pts were treated 2 times for different relapses. Median ReRT BM per patient was 2(1-21). Site of primary was lung for 17 pts, breast for 11, melanoma for 2, colon for 1, and prostate for 1. Time interval between first BM RT and ReRT was 14(4.2-39.2)months. Previous RT on the same volume was performed as whole-brain(WB) radiotherapy in 14 pts(2 with simultaneous integrated boost), CyberKnife SRT(CK) in 7, Volumetric Modulated Arc Therapy SRT(VMAT) in 4, Gamma Knife RS(GK) in 3 pts, and in 1 as tumor bed RT. Median dose delivered was 30(12-50) Gy in 1-10 fractions. ReRT was performed with CK(23 pts), GK(8), and TomoTherapy(1). Median ReRT volume was 3.45(0.3-31.76)cc. Median delivered dose 30(16-37.5)Gy, in 5(1-5) fractions(fr), at the 77(48-95)% isodose. CTCAEv 5.0 was used to report toxicity.

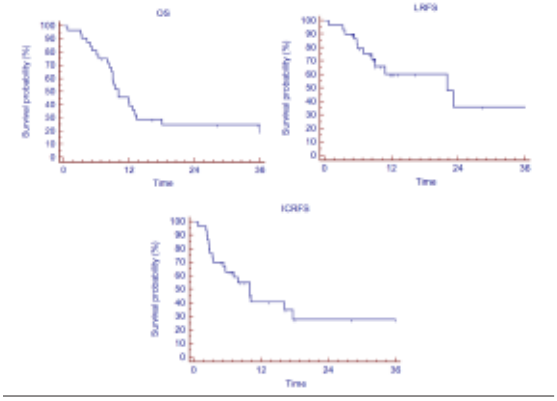

Figure 1. a) Overall survival (OS) of reirradiated locally relapsed brain metastases; b) Local relapse-free survival (LRFS) of reirradiated locally relapsed brain metastases; c) Intracranial relapse-free survival (ICRFS) of reirradiate locally relapsed brain metastases. Patients were censored at the event of interest or death.

Results. Median follow-up after ReRT was 9.7(0.7-54.4) months. Median age of pts at ReRT 56.1(40.9-70.7) years. Acute toxicity was low: 21/30(70.0%) evaluable pts did not present any toxicity, 7 pts(23.3%) G1 toxicity, and 2 pts (6.7%) G2 toxicity, and were more frequent in treatments performed in 1 fr (4/9, 44.4%), than in fractionated treatments (5/23, 21.7%). Six radionecrosis(RN) were registered, all in pts who survived ≥13 months, but only 5 were ReRT lesions. Local control, evaluable in 30 cases, was: complete response in 4 pts, partial response in 16, stable disease in 6, and progressive disease in 4 pts. Two pts underwent a second ReRT, and 1 patient a third ReRT. Two pts were operated on for RN (N=1), and relapse (N=1). Median overall survival(OS) was 10 months; 12, 24- and 36-month OS were 39.1%, 24.8%, and 18.6% respectively (Figure 1a). Median local

relapse-free survival was 22 months; 6-, 12-, 24- and 36-month LRFS were 79.8%, 60.1%, 36.1% and 36.1% (Figure 1b). Median intracranial relapse-free survival was 10 months; 6-, 12-, 24- and 36-month ICRFS were 63%, 40.8%, 28% and 28% respectively (Figure 1c). Initial WB did not reduce ICRFS at either the first or second event (p=0.14 and 0.13, respectively).

Conclusions. ReRT of recurrent BM is safe, with low toxicity, and effective with responses in 86.7% of pts. RN were recorded in ≤1% of ReRT lesions at a median of 13.5 months after ReRT. A prospective study is necessary to confirm these results.

P284

STEREOTACTIC BODY RADIOTHERAPY WITH CYBERKNIFE SYSTEM IN THE SCENARIO OF RE-IRRADIATION OF LUNG METASTASES: VOLUME OVERLAPS

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Aims. To evaluate feasibility and safety of SBRT with Cyberknife (CK) system in the scenario of geometrical overlap in re-irradiation (re-RT), as proposed by the recent ESTRO-EORTC consensus.

Methods. We reviewed retrospectively data of 86 consecutive patients (pts) who received multiple Stereotactic Body radiotherapy (SBRT) with CK system for lung metastases at IRCCS Pascale between 2014 and 2023 and then divided those pts according to the recent ESTRO-EORTC consensus on re-RT. We evaluated all treatment plans in order to extrapolate volume overlaps and categorize them as re-RT type 1 (volume overlaps). The remaining targets were divided within the other main categories, re-RT type 2 or organ re-irradiation (depending on whether targets were located in the ipsilateral lung with concern for toxicity from cumulative doses or not). We focused on clinical available data on pts belonging to re-RT type 1 group.

Results. Among a total of 230 lesions (118 right sided and 112 left sided) we found 10 lesions with volumes overlap -6 pts- (equally divided between right and left), 3 of which belong to a single patient and categorized those cases as re-RT type 1 group. Among this group, median re-RT dose was 50Gy (range 32.5-55) delivered in 5 fractions. Treatment was delivered every other day and prescribed at 80% isodose-line. Time interval between re-RT was at least 6 months with a maximum of almost 3 years. Primary was lower gastro-intestinal (GI) tumour in 3 pts, lung tumour in 2 pts and hepatocarcinoma (HCC) in one pt. Two re-irradiated targets were centrally located. All pts well tolerated SBRT with CK and none of them experienced severe toxicity (in particular no fatal bronchial bleeding and/or fistulae were recorded in central targets). One of the 2 pts with centrally located target reported onset of cough (grade 1) few weeks after re-RT.

Conclusions. SBRT with CK system seems to be safe and feasible in the setting of lung re-irradiation especially in the scenario of volumes overlap. It indeed allows a good compromise between high dose to the target and organ at risk sparing. However, due to the retrospective nature of our analysis as well as to the lack of clinical and radiobiological data, prospective trials are needed to build high-quality evidence.

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STEREOTACTIC RE-IRRADIATION IN RECURRENT BRAIN METASTASES FOLLOWING PREVIOUS WHOLE-BRAIN RADIOTHERAPY

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Aims. There are no clear treatment recommendation for recurrent brain metastasis. This report aims to assess the clinical outcomes, neurological functional changes and toxicity of stereotactic reirradiation as a salvage treatment after whole brain radiotherapy (WBRT) using a dedicated IGRT system.

Methods. Between June 2021 and November 2022, 15 patients with progressive brain metastasis from different histologies were treated with Stereotactic Radiotherapy (SRT). All patients had already received WBRT as initial treatment with 30 Gy in 10 fractions and hippocampal sparing technique in 5 of them. Median age was 53 years (34–75). All patients had extracranial metastasis, 60% of them had controlled extracranial disease. The median Karnofsky performance status (KPS) was 80 (70–100). The median interval time between the two courses of radiation was 12 months (4-29). The median metastases diameter was 39 mm (21-59) while the median total tumor treated volume was 2.3 cc (0.7–44). The median dose was 17 Gy (14-21) in 1 fraction or 26 Gy(24-27) in 3 fractions. All treatments were delivered with Brain-Lab® TPS (Treatment Planning System). Set up -uncertainties were verified with Exactrac® Xray system image guided RT. Two X-ray images with Exactrac X-Ray 6D system were used to verify set-up before each treatment. We evaluated overall survival (OS), progression free survival (PFS), acute toxicities according RTOG and neurological function. Prognostic factors were also evaluated using the Cox proportional Hazard model.

Results. With a median follow-up of 11 months (5-

24), the median OS was 9 months (3-19), the median brain- PFS was 6,2 months (2-10) and intracranial failure was 80% out-field. Treatment was well tolerated and only 30% of patients showed low acute toxicities. According neurological evaluation, 7 patients (47%) had improved neurological function and 8 patients had stable neurological function. According to univariate analysis, KPS and long interval between WBRT and SRT were prognostics factors of OS and brain free-disease survival. According to multivariate analysis, the time between WBRT and SRT longer than 14 months was associated with longer brain free-disease survival.

Conclusions. Despite the low number of patients, this study show that SRT- reirradiation is safe and effective treatment in patients with recurrent brain metastasis and improve neurological function. Accuracy with dedicated IGRT system is crucial.

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IMAGE-GUIDED STEREOTACTIC BODY RE-IRRADIATION IN LOCALLY RECURRENT PROSTATE CANCER: TERNI'S EXPERIENCE

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Aims. Management of locally recurrent prostate cancer after definitive radiotherapy remains controversial . The aim of this study is to explore the efficacy and safety of prostate re-irradiation with image-guided stereotactic volumetric modulate arc radiation therapy (VMAT-IGRT). We present our preliminary results.

Methods. Men affected by isolated local recurrence of prostate cancer, proven by a 18F-Choline or PSMA positron emission tomography and 3Tmultiparametric magnetic resonance, who underwent previous prostate external beam radiation therapy were enrolled in this study. Between may 2018 and June 2023 a cohort of 29 pts were re-irradiated to the prostate with stereotactic VMAT-IGRT, the total dose was 30 Gy in 5 daily fractions. Pts were followed by clinical examination and PSA value 1 month after treatment and every 3 months thereafter. Toxicity incidence was registered according to Common Terminology Criteria for Adverse Events version 4.03. The efficacy of salvage stereotactic VMAT-IGRT was estimate in terms of biochemical relapse-free survival (bRFS,), local control (lC), and androgen deprivation therapy free interval (aDTFI).

Results. After a median follow-up of 23 months (range 15-48), 26 of 29 pts accrued were evaluable. Only one case of grade ≥ 2 acute genitourinary (GU) toxicity was recorded while gastrointestinal (GI) acute toxicity was negligible. No grade ≥ 2 late GU and GI toxicity events occurred. In the first six months all but two pts had a biochemical control with decrease in serum level PSA, three pts had a progressive increase in serum PSA at the ninth, twelfth and fifteenth months, respectively. All the pts with biochemical failure showed bone or nodal progression without evidence of local recurrence at choline or PSMA PET.

Conclusions. Our preliminary report showed that stereotactic V-MAT-IGRT re-irradiation could be a safe and effective treatment in selected pts with local recurrence prostate cancer, with an excellent toxicity profile.

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FEASIBILITY OF REPEATED LINAC-BASED FRACTIONATED STEREOTACTIC RADIOTHERAPY AND STEREOTACTIC RADIOSURGERY FOR PATIENTS WITH MULTIPLE BRAIN METASTASES

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Aims. Linac-based fractionated stereotactic radiotherapy (fSRT) and stereotactic radiosurgery (SRS) are increasingly being used to manage patients with multiple metastases. This retrospective cohort study aimed to evaluate safety and feasibility for linac-based fSRT and SRS in patients with multiple brain metastases (BMs).

Methods. From January 2021 to April 2023, patients with BMs were treated with Linac-based fSRT and SRS. Volumetric modulated arc therapy with Hyperarc were performed for all patients. The cumulative incidence with competing risks was used to estimate local control (LC), distant intracranial failure (DIF), and radiation necrosis (RN).

Results. 80 patients and 451 BMs were treated (SRS:3 patients, fSRT:77 patients). Thyrty-six out 80 patients (45%) were male and 44 were female, median brain mets were 6 (range 2-20). Primary tumors were as follow: 30% breast, 33% lung, 10% melanoma. Five patients had prior RT treatment: 3 of them whole brain RT and 2 FSRT. Median PTV in cc was 10 (0.5-66cc). Median dose was 24Gy (range 18-30) in 3 fractions (range 1-5). Median GI were 0.7 (range 0.3-1). No acute side effects were reported. 26 patients (27,5%) reported a progression of disease out of field and 23 out 26 underwent to a second course of stereotactic radiotherapy with the new brain metastases (median 8, range 1-16), Four patients out 23 underwent to another course of brain fSRT (median brain mets 10, range 3-20).

Conclusions. It seems reasonable to use linac-based fSRT and SRS in patients with multiple BMs due to the

high feasibility and safety of the procedure without side effects. Second and third stereotactic RT could be proposed. Surely, robust data are needed.

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TREATMENT OF BREAST CANCER PATIENTS RECURRENCE WITH SECOND SURGERY AND REIRRADIATION: A RETROSPECTIVE EVALUETION

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Aims. Breast reirradiation (reRT) after breast conserving surgery (BCS) or mastectomy poses a distinct therapeutic challenge for treatment of recurrence of breast cancer in the ipsilateral breast. Data on safety of different fractionation regimens are limited. This study report our experience with reirradiation for locoregional recurrent or second primary breast cancer.

Methods. Between 2014 and 2022, all patients with breast cancer treated with breast or chest wall reRT at our institution were identified. A retrospective analysis of clinical data of this patients was performed (type of surgery, pTNM, staging disease, receptor expression and associated systemic therapy). Adverse events were assessed using the Common Terminology Criteria for Adverse Events v5.0.

Results. Fourteen patients were reviewed with median follow-up of 4.5 years (range: 1-8 years). Median age at time of first breast cancer was 48 (range 38-46) and 69 (range 49-75) at time of recurrence. About recurrence, 7.1% had invasive carcinoma with a ductal carcinoma in situ (DCIS) component, 78.6% had invasive carcinoma alone and 14.2% had DCIS alone. A total of ten patients (71,4%) tested positive for estrogen receptor, 9 (64.3%) for progesterone receptor, and 2 (14.2%) for HER2/neu overexpression. All were clinically node negative. For the reirradiation course, median dose delivered was 45 Gy (range 36.9-50 Gy) with 1.8 Gy daily. Five patients (35.7%) was treated with adjuvant chemotherapy and seven (50%) with adjuvant endocrinotherapy. About normal tissue tollerance, seven patients (50%) experienced grade 1 erythema, three (21.3%) grade 2 erythema, two patients (14.2%) dysphagia, one patient (7,1%) experienced grade 1 eczema. None had grade 3 or higher late adverse events. At median follow-up of 4.5 years, OS was 92.9%, one patient (7.1%) had second homolateral breast relapse, two patients (14.2%) had suspected lung micronodules and another patient (7,1%) had bone metastases.

Conclusions. Re-irradiation can be considered for local recurrence to achieve durable local control for patients with cancer who have otherwise few therapeutic options. With the use of new radiotherapy techniques, which allow for conformal treatment plans, image guidance, and short fractionation schemes, the use of re-irradiation for different sites is increasing in clinical settings. Our analysis showed that reRTwas effective with good OS and local recurrences rate and an acceptable toxicity profile. Future studies and longer follow up is required.

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RE-IRRADIATION THERAPY FOR LOCALLY RECURRENT PROSTATE CANCER AFTER EXTERNAL-BEAM RADIATION THERAPY

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Aims. Optimal management of locally recurrent prostate cancer after definitive radiation therapy is still problematic. The development of highly accurate radiotherapy devices could offer precise irradiation while sparing healthy tissues. The aim of this study is to evaluate the efficiency and the toxicity of re-irradiation in patients with recurrence of prostate cancer after external- beam radiation therapy.

Materials and Methods. From October 2015 to June 2022, reirradiation was administrated to 12 patients for isolated local recurrence of prostate cancer. The patients were previously treated with external-beam radiation therapy to a dose of 70-78 Gy. After a median time of 80 months (range 13-185 months), the patients had a intraprostatic recurrence confirmed by multiparametric MRI and total body 18F-fluorocholine PET-CT. The target delineation was performed on plan CT-MRI fusion to limit the normal tissue toxicity especially for rectum wall and bladder. The VMAT treatment was delivered by 6MV beam modulator Linac with 4mm MLC. Patient set-up and isocenter position were controlled before each fraction by CBCT. The most commons fractionation used at the time of reirradiation were 30Gy/3ff and and 25Gy/5ff. Toxicity was evaluated according to CTCAE v. 5.0 and the treatment response was evaluated by PSA. No patients were subjected to systemic therapy.

Results. Median follow-up was 15 months (range 2-58 months). At data analysis (June 2023) 4 patients are still free of disease after a median time of 27 months. During follow-up we reported 8 cases of biochemical failure with a median median disease-free survival of 13 months. Treatments were well tolerated, no G3-G4 acute nor late toxicities were reported.

Conclusions. Re-irradiation of intraprostatic recurrences after external beam RT showed favorable results in terms of disease control. The re-irradiation can be considered for intraprostatic recurrence instead of brachytherapy, surgey or pharmacological approach. Toxicity was low and acceptable.

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REIRRADIATION OF BRAIN METASTASES (BM): RADIATION NECROSIS (RN), OVERALL SURVIVAL (OS) AND QUALITY OF LIFE (QOL)

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Aims. Patients with limited BM are eligible for Stereotactic Radiosurgery (SRS) or whole brain radiation therapy (WBRT). Among patients who receive reirradiation SRS for recurred/progressed disease, RN is a clinically relevant complication with variable development timing, generally occurring from 6 months to several years after treatment. RN can lead to cognitive decline and worsening QoL.

Methods. Between 2017 and 2022, 21 pts (18 women and 3 men) received reirradiation with SRS and/or WBRT at our institution. Median age was 61 years (range: 32 - 71). The most common primary sites were breast and non-small cell lung cancer (NSCLC) (9 and 8 respectively) and 4 with other localization (2 pts endometrial cancer, 1 pt with colon-rectal cancer and 1 pt with urothelial cancer). Patients and treatment characteristics: KPS (Karnofsky Performance Status) and NFS (Neurological Function Score), local control, OS and toxicity were analyzed before and after treatment. RN was diagnosed by clinical evaluation, magnetic resonance imaging (MRI) and, in some cases, tissue evaluation.

Results. 52 BM were treated. 11 pts underwent WBRT as upfront treatment, 10 pts SRS. Mean range between prior treatment and reirradiation was 14 months and mean dose of treatment was 20 Gy (range 7-27,5 Gy); 46 in single fraction, 6 with fractionated SRS (FSRS) (3, 4 or 5 fr). 10 pts received post-SRS WBRT (30 Gy/10 fr). The post re-irradiation median survival was 12 months. 8 pts developed evidence of PD at SRS treated sites. Response was obtained in 95% of lesions with 1-year. 12 pts died (8 for systemic PD, and 4 pts brain PD). The majority of the pts had a good KPS and NFS after reirradiation. 1 pt had asymptomatic RN and 3 had symptomatic RN (treated with corticosteroid and 1 with surgical excision). Local control was better for breast and lung metastases as compared with other primitives metastases.

Conclusions. Our study demonstrates durable local control and, although rates of RN are significant, reirradiation of BM with SRS or WBRT resulted feasible and effective in selected patients. A correct pts selection and an accurate evaluation of the cumulative irradiation dose are suggested.

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STEREOTACTIC RE-IRRADIATION OF LOCALLY RECURRENT PROSTATE CANCER AFTER RADICAL PROSTATECTOMY AND RADIATION THERAPY: THE EXPERIENCE OF RADIOTHERAPY UNIT OF UNIVERSITY HOSPITAL OF FERRARA

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Aims: To evaluate the efficacy and safety, in terms of acute and late toxicity, in patients with recurrence prostate carcinoma (PCa) treated with re-irradiation.

Methods. From September 2019 to September 2022, 8 consecutive recurrence PCa patients were treated with hypofractionated stereotactic VMAT with daily on-line IGRT based on CBCT images. All patients showed a relapse in prostatic bed previously treated with conventional or VMAT Radiotherapy, with a mean time to recurrence of 82.5 months (range: 36-108). Previous bladder catheter placement for urethral identification and bladder filling, recurrence was delineated on fusion CT/MRI and choline/PSMA PET. All patients were asked to empty their bowels. The prescribed dose was 25-30 Gy in five consecutive fractions. Clinical follow-up with PSA test was performed 45 days after treatment, and there after every 3 months. Acute and late toxicities were prospectively recorded using RTOG-EORTC scale. Androgen suppressive therapy was prescribed based on risk categories.

Results. All patients completed the treatment without interruption. Four patients were treated also with androgen suppressive therapy. Acute genitourinary (GU) toxicity was grade 1 in four patients and grade 3 in one patient with hematuria and AUR. No acute gastrointestinal (GI) toxicity occurred. Late GU toxicity was grade 1 in three patients (urinary urgency). With a median follow-up of 20 months (range: 10-36) four patients had stable PSA reduction; three patients showed biochemical recurrence after a median of 14 months (range 10-22) and one patient developed distant metastases after 18 months.

Conclusions. Our experience confirms that re-irradiation of PCa recurrence localized in the prostatic bed with hypofractionated stereotactic IGRT/VMAT is a safe and effective strategy with potentially curative with a low toxicity profile and a good results in disease control; can also postpone the start of systemic therapies and thus slow down the natural course of the disease.

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STEREOTACTIC RADIOTHERAPY: IS IT ONLY FOR OLIGOMETASTATIC PATIENTS? SIMULTANEOUS IRRADIATION/REIRRADIATION OF 18 BONE/NODAL METASTASES IN HEAVILY-PRE-TREATED CASTRATION-RESISTANT PROSTATE CANCER: A CASE REPORT

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Aims. Stereotactic radiotherapy (SBRT) is an effective treatment of oligometastatic prostate cancer (PCa) patients. However, SBRT is typically used in patients with ≤ 5 metastases. Here we report the case of a PCa patient who simultaneously underwent SBRT on 18 metastatic lesions, as bridge therapy pending the availability of Lutetium (^{177}Lu) vipivotide tetraxetan therapy.

Methods. In June 2022, a 74-year-old patient with castration-resistant PCa followed up in our center had further disease progression after the following treatments: radical prostatectomy, adjuvant androgen deprivation therapy (ADT), postoperative radiotherapy, salvage ADT, para-aortic lymphadenectomy, postoperative radiotherapy on the para-aortic nodes, abiraterone, enzalutamide, taxotere, and 7 subsequent SBRTs to bone or lymph node metastatic sites. A ^{68}Ga-PSMA PET/CT showed 18 new or progressive bone/nodal metastases (4/18 previously irradiated) while the total PSA value was 3.7 ng/ml. After multidisciplinary discussion, the patient was a candidate for therapy with ^{177}Lu. However, this treatment was not available for at least 6 months. Therefore, also considering the excellent general conditions (ECOG PS: 0) and the results of the VISION Phase III trial, SBRT was planned on all visible metastases, with variable dose and fractionation (from 25 to 40 Gy in 5 fractions) according to the proximity to the Organs at Risk and previously delivered doses.

Results. SBRT was delivered without interruptions and without any patient reported side effect. One month after the end of SBRT, a reduction of PSA to 2.6 ng/dl was recorded (remaining below pre-treatment levels for the next 6 months) while a ^{68}Ga-PSMA PET/CT performed 3 months after SBRT showed a partial or complete metabolic response at all irradiated sites (Figure 1). The patient remained asymptomatic and in good general condition until May 2023 when therapy with ^{177}Lu was initiated after ^{68}Ga-PSMA PET/CT showing further multi-metastatic progression still only in bone/nodes. Fifteen days later a reduction in PSA from 8.2 to 3.4 ng/dL was recorded.

Conclusions. This report suggests that, in selected patients, SBRT can be safely delivered as first local treatment or reirradiation on a large number of metastases with potential benefits on tumor control and quality of life.

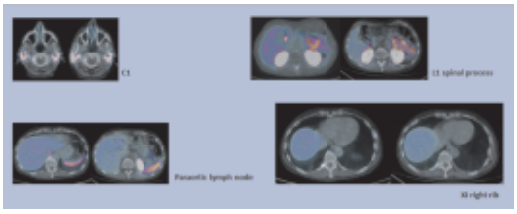

Figure 1. Pre and post-RT PSMA-PET in some irradiated targets.

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PULSAR IN METASTATIC REFRACTORY CANCER PATIENTS TO RESTORE SENSITIVITY TO IMMUNOTHERAY. PRELIMINARY DATA

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Aims. PULSAR is a new palliative ablative RT delivery in conjunction with immunotherapy, allowing for an immune response in adaptation of radiation fields based upon tumor response. In metastatic cancer patients in progression mainly in liver and bones and refractory to immunocheckpoint inhibitors, PULSAR may act as a booster to restore tumor microenvironment (TME) sensitivity to immunotherapy. Herein our preliminary experience on two patients.

Methods. Two metastatic patients Head and Neck (case A) and renal cancer (case B) developing progressive disease during immunotherapy were enrolled. Case A was refractory to pembrolizumab, Case B was resistant to avelumab. Sites of refractory metastatic lesions were lung, bones, nodal areas spread in the neck, thorax, abdominal vessels. Patients were treated s with SBRT on

these areas for significant and symptomatic metastatic progressive (2-4) lesions consecutively with 6 Gy/fr every one-two weeks for 3- 5 fractions on alternate days and timely treated with the same immunocheckpoint inhibitors. Replanning was performed after 1-3 fractions according to the new reached volume as detected on the cone-beam CT images. At baseline, before every fraction and immunotherapy cycle, a sample of serum and fresh peripheral blood were collected to assess changes in adaptive and innate immunity cells with immunophenotype by flow cytometry. PD-L1 expression on circulant tumoral extracellular vesicles (cEVs) together to the quantification of soluble form of PD-L1 (sPD-L1) by ELISA assay was done. Clinical outcome was scored according iRECIST criteria.

Results. After one month off PULSAR, both patients recorded a response on irradiated sites in terms of iPR and iSD as confirmed by CT and PET scan images on irradiated lesions. Immunophenotype showed the increase of CD3-CD8 and NK, NK-like lymphocytes with a reduction of T-regs. A weak improvement of sPDL1 level and in cEVs was also detected from baseline. Thus they are alive with stable metastatic disease still continuing the same immunotherapy.

Conclusions. Sensitivity to acquired immunotherapy resistance in metastatic patients could be restored with PULSAR to continuate an effective palliative care

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ANALYSIS OF PATTERN OF PRACTICE IN USE OF ABLATIVE SPINAL STEREOTACTIC BODY RADIOTHERAPY

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Aims. Spinal Stereotactic body radiotherapy (SBRT) may yield superior pain relief and local control as compared to conventional palliative radiotherapy (PR). However, heterogeneous schedules are used in clinical practice, ranging from high-dose intensive to more bland regimens that are iso-intensive as conventional PR: for instance 24 Gy/3 fraction result in an EQD2(10) of 36, that is equivalent to 30 Gy/10 fractions(fx). An institutional protocol was enforced from January 2021 to harmonize clinical practices toward preferred use of high dose-intensive regimens (HDI) such as 24Gy/2fx (EQD2=44) for pain control and 27-30Gy/3fx (EQD2=43-50) for local ablation. We hereby analyze the impact of this protocol on regimen choice.

Methods. We included patients treated with SBRT to 3 or fewer involved spine segments from January 2021 to December 2022 in our center. Dose prescriptions were retrospectively reviewed: in case of deviation from the internal protocol, treatment plan was reviewed to analyze the causes of non-dose intensive (NDI) prescriptions. Descriptive and analytical statistics using the chi-square test were performed.

Results. We identified 231 patients: treatments were delivered with robotic-arm linac or VMAT in 140 and 91 cases, respectively. Dose prescriptions are summarized in Figure 1. HDI accounted for 80% of delivered SBRT spinal treatments (n=186). NDI accounted for 35/140 (25%) and 10/91 (9%) prescriptions in 2021 and 2022 respectively. Main reasons for NDI included (a) prior dose received in case of reirradiation (n=15/45) and (b) risk of major violation of dose constraints to organs at risk (n=24/45). Physician's preference accounted for 6 cases. Use of NDI significantly declined in 2022 as compared to 2021 (p=0.009).

Conclusions. HDI spinal SBRT is feasible in the majority of cases. NDI is mainly dictated by previous dose or organ at risk proximity, while physician preference is rare. Use of NDI significantly declined over time following implementation of an institutional protocol.

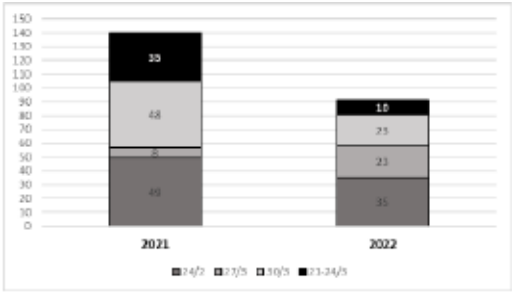

Figure 1.

P295

LOCAL CONTROL AND LONG TERM TOXICITY IN SPINAL METASTASES TREATED WITH STEROTACTIC BODY RADIATION THERAPY

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Aims. In recent years, stereotactic body radiotherapy (SBRT) has made extensive use for the treatment of spinal metastases. Compared to conventional radiotherapy, this technique has achieved a good local control with similar pain control and no added toxicity. The aims of

the study were to evaluate the disease local control following stereotactic radio□therapy to spinal metastases and the onset of chronic toxicities.

Methods. We conducted a retrospective review of patients treated at our Institution between January 2021 to December 2022 with stereotactic radiotherapy in spinal metastasis. Local control at the treated site was evaluated at baseline and during radiological and clinical follow-up after treatment. Statistical analysis was performed to identify predictors of disease control. Toxicity was monitored during follow up. Descriptive was performed; Kaplan Meier analysis was carried out to estimate local control.

Results. From a cohort of 226 patients treated with stereotactic body radiotherapy in spinal sites we included 109 patients for whom radiological follow up was available. Cervical, dorsal and lumbosacral spine were involved in 3, 74 and 32 cases. In total, 29 treatments were delivered in VMAT and 80 with robotic-arm linac. Most represented primary tumors were prostate (n=) and colorectal (n=) carcinoma. Treatment schedule mostly consisted of 24 Gy in 2 fractions (n=49) and 27-30 Gy in 3 fractions (n=60); median BED was 53 (51.3-60). The median follow-up was 10 months (2-27). The 12 and 18-months local control rates were 99% and 96% (Figure 1). Late toxicity occurred in 2 patients. One patient developed G3 neuropathic pain 8 months after S1-S2 radiotherapy: dose constraints to cauda and sacral roots were respected at plan review. Following radiological review, one case of vertebral fracture was identified 3 months after SBRT.

Conclusions. SBRT in spinal metastasis yielded satisfying and durable local control with minimal rate of severe toxic effect. A follow up of at least 6 months is necessary to better assess local failure rate and incidence of late toxicity.

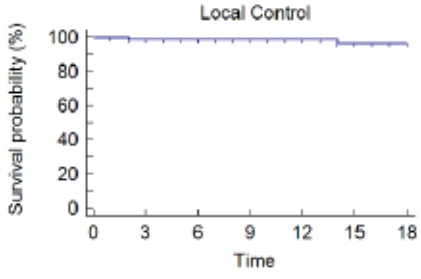

Figure 1.

P296

SPATIALLY FRACTIONATED RADIATION THERAPY: FIRST EXPERIENCES WITH THE LATTICE TECHNIQUE

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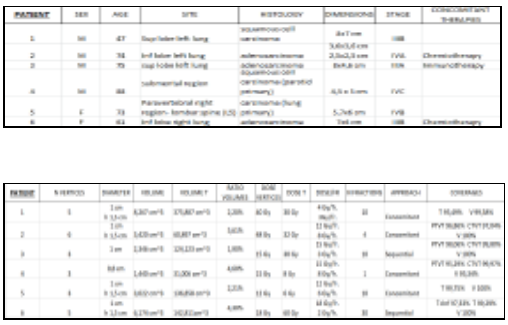
Spatially Fractionated Radiation Therapy (SFRT) is a radiation therapy technique (also know as GRID therapy) that allows a heterogeneous high-gradient dose distribution and a safe dose escalation to unresectable bulky cancers in palliative settings. Modern linear accelerators with multi-leaf collimators and Image-Guided Radiotherapy (IGRT) make possible to use its newer 3D version: Lattice Radiotherapy (LRT). With LRT we create, within the tumor volume, multiple localized high-dose islands (vertices) with a certain degree of separation and lower dose regions (valleys). LRT enhances its action inducing bystander and abscopal effects. We present our first experiences. From January to May 2023, we treated 6 symptomatic patients (pts) with bulky tumors. We used a geometric arrangement (through a grid tool of the Treatment Planning System) to create from 3 to 6 cylindrical vertices, each with a diameter of 1 cm and a separation of 1.5/2.0cm between each vertex and the next in the axial plane. We used Montecarlo algorithm and VMAT radiotherapy. We applied a concurrent approach in 4 cases and a sequential one in 2 cases. Total doses ranges from 18 Gy to 40 Gy to the vertices (V) and from 6 Gy to 60 Gy to the entire tumor (T) (Table 1 LRT). We planned to achieve ≥95% prescription dose coverage to at least 95% of the targets and we used the constraints for Organs At Risk (OAR) normally employed. LRT permits to deliver ablative doses to bulky tumors, when Stereotactic Body Radiation Therapy (SBRT) is not feasible but limiting the dose to OAR and avoiding excessive toxicity to the surrounding normal tissues. It's mandatory that radiation oncology team have experience with SBRT plans. Our pts completed the treatment without toxicities and interruptions. We observed relief of initial symptoms (dyspnea, pain) and reduction of the tumor volume at some first controls: the CT control, at 1 month after RT, of a patient with an adenocarcinoma of the right lung (stage IIIB) showed an impressive reduction of the tumor (20 mm *vs* 70 mm). LTR has proven to be a safe and effective technique. It can be used for the treatment of bulky cancers, allowing the delivery of a very high dose inside the tumor. This means a higher local control without adding any extra toxicity in the peripheral normal tissues. Currently, we are recruiting more pts to increase our

experience and confidence with this technique, with the goal to shift palliative treatments into curative ones.

Table 1.



P297

PAIN CONTROL IN BONE METASTASES AFTER RADIOTHERAPY: A PROSPECTIVE ANALYSIS

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Aims. To analyze the efficacy of different fractionation regimens of radiotherapy (RT) in managing painful bone metastases (BM) and identify predictive factors for pain control.

Methods. From Feb 2022 to Feb 2023, 44 patients with 65 symptomatic BM were evaluated. Pain analysis using the Brief Pain Inventory (BPI) tool was conducted at baseline, 1 and 3 months after RT. Analgesic intake was recorded and converted to morphine-equivalent doses (OME). The International Consensus on Palliative Radiotherapy Endpoint (ICPRE) was used to assess pain response. Multivariate logistic regression analysis examined patient-related factors (sex, age, PSECOG, pretreatment and 1-month pain score, morphine intake), tumor-related factors (primary tumor type, lesion site, systemic therapy), and treatment-related factors (technique, dose, fractions, target coverage) predicting BM pain control at 3 months after RT.

Results. Breast (32%) and lung (24%) cancer were the most common primary disease sites. Treatment plans included 3DCRT (60%) and VMAT (40%) using single or multiple fractions. Median biological effective dose was 29 Gy (14-108). Median CTV and PTV were 87.5 cc (0.3-562.2) and 274.1 cc (1.7-1216.0), respectively. All 44 patients completed the 3-month follow-up and reported no grade > G2 toxicity. Baseline median BPI was 15 (4-40) and median OME was 26.5 mg/day (0-265). At 1 month after RT, median BPI was 5 (0-26) and median OME was 35 mg/day (0-450). After 3 months, median BPI and OME were 4 (0-28) and 36 mg/day (0-450), respectively. Pain response rates (partial+complete response) were 61% (44%+17%) at 1 month and 60% (34%+26%) at 3 months. Most responders had a PS ECOG score of 0-1 (67%; P=0.008) and received active systemic therapies (67%; P=0.036). Non-responders had lower pretreatment BPI (mean: 13.7 *vs* 58.2; P=0.032) and OME (mean: 19.2 *vs* 62.5; P=0.827), with significantly higher values after 1 month (mean: 9.1 *vs* 5.3, P=0.033; 109.6 *vs* 48.9, P=0.037). Mean PTV dose was 99.3% in the former group and 97.5% in the latter (P=0.055). Multivariate analysis indicated that baseline BPI (OR: 1.171; 95% CI: 1.032-1.327; P=0.014) and BPI at 1 month (OR: 0.826; 95% CI: 0.698-0.976; P=0.025) were significant independent predictors of BM pain response at 3 months.

Conclusions. RT effectively and safely controls short-term pain in BM, regardless of tumor type and dose-fractionation scheme. Multidisciplinary approach is recommended to optimize morphine use during treatment.

P298

IMMUNOTHERAPY AND LATTICE TECHNIQUE. PRELIMINARY DATA IN PATIENTS WITH TUMOR BULKY DISEASE

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Aims. To evaluate clinical outcomes in patients treated with LATTICE technique and immunotherapy.

Methods. We evaluated metastatic patients with bulky disease within Lattice_01 protocol treated using lattice technique concurrent with immunotherapy.

Results. From October 2020 to December 2022, we evaluated eight patients with different histological diagnosis underwent to radiotherapy with SFRT-Lattice technique. Enrolled patients had metastases from the following primitive tumors: cutaneous melanoma, cutaneous squamous cell carcinoma, urothelial carcinoma, renal cell carcinoma and squamous cell lung cancer. Eight patients and nine lesions were treated. Concurrent immunotherapy was Pembrolizumab in three patients, Nivolumab in four patients and Cemiplimab in a patient. One of these patients with metastatic urothelial carcinoma was irradi-

ated on two lesions. The other seven patients had bulky disease on: lung, bone, scalp (two), adrenal gland and pelvic wall. We delivered a median dose of 12 Gy (range 10-15 Gy) on vertices (median 1, range 1-4) followed by a median of 20 Gy (range 8-30) in 4-10 fractions (range 1-10). We observed: a complete remission in a patient with cutaneous squamous cell carcinoma; a partial remission in six patients; a stable disease in a patient with scalp lesion from melanoma. Clinical benefit was reported in 8/8 patients.

Conclusions. these preliminary data seem to support the safety of association between immunotherapy and Lattice technique. To the best of our knowledge there are few case reports on this issue. The present case series is the first reported in literature.

P299

STEREOTACTIC RADIOTHERAPY (SBRT) FOR PAIN CONTROL IN SPINAL METASTASES

B. Bettazzi[1], V. Lorenzetti[1], M. Loi[1], D. Cela[1], G. Simontacchi[1], D. Greto[1], G. Francolini[1], E. Olmetto[1], P. Garlatti[1], L. Visani[2], B. Detti[1], V. Scotti[1], L. Livi[1]

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Purpose: Despite evidence from recent prospective trials, stereotactic radiotherapy (SBRT) is not yet recognized as a standard of care for antalgic purpose. We therefore analyzed pain control after SBRT on spinal metastases.

Materials: We retrospectively collected data on palliative SBRT, done in our center between 2021 and 2022 on a cohort of consecutive patients. SBRT performed both with the VMAT and CyberKnife (CK) techniques. All SBRT were performed on bone lesions secondary to primary tumors of various histologies (prostate, breast, lung, kidney, larynx, thyroid, colon, salivary glands, ovary, pancreas, bladder). CTCAE v. 5 for adverse events.

Results: Among 226 spinal metastases treated with SBRT, 72 were performed for antalgic purpose. Pain control data were available for 63 of these. Treatment sites were cervical, thoracic and lumbosacral spine in respectively 2, 37, 24 cases. Oligometastatic disease was found in 18 cases. SBRT was carried out with CK or with VMAT in 35 and 28 cases respectively. Treatment schedules were 24 Gy in 2 fractions (n=32) or 27-30 Gy in 3 fractions (n=31), with a median BED of 52.8 Gy (range 51.3-60). At a median follow-up of 10 months, pain response was achieved in 38 patients, consisting of complete pain relief in 28 cases and partial response in 10. Stability of the symptom was obtained in 24 patients. Only 1 patient experienced increased pain after treatment, possibly in relation with vertebral fracture after radiologic review. Pain flare was observed in 11 patients, while G $\geq$ 2 nausea/vomit was observed in 3 patients. χ^2 test was used to compare categorical values to correlate pain control with clinical and treatment related data. No difference in terms of pain control was observed according to treatment schedule or primary tumor.

Conclusion: According to our experience, SBRT on spinal metastases with a median BED of 52.8 Gy results for pain control with an excellent safety and efficacy profile.

P300

HIGH-DOSE LATTICE RADIOTHERAPY IN LARGE TUMORAL MASSES

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Aims. Lattice Radiotherapy (LRT) is a compelling therapy for palliation in bulky tumors. Most of the cases in the literature are stage IV lung cancer patients. LRT is particularly interesting for the immunogenic stimulation that can be achieved with different mechanisms.

Materials and Methods. Six patients (pts) were treated between 2017 and 2021. The median age was 76 (range 46 - 80 years) and all the patients pts were stage IV patients. The treatment regions were heterogeneous (iliac common node, right armpit, left psoas muscle, lung left, right emithorax and sacro-iliac region). All pts had tumor maximal measure ranging from 8 cm to 15 cm. Follow-up median was 26.5 months (range 1 - 52 months). All pts were treated with one initial fraction of LRT on small spheres of 1 cm in diameter with separation of about 2 cm created inside the tumor with dose of 15 Gy with volumetric modulated arc therapy (Figure 1). Two weeks after the end of LRT, the treatment was continued with standard palliative moderate hypofractionated external beam radiotherapy (EBRT) using 10 daily fractions of 3 Gy with tridimensional conformal radiotherapy (3D). All patients received radiotherapy during interval between systemic therapy cycles.

Results: Three months after the end of radiotherapy 5 out 6 pts (83%) obtained a significant reduction in tumor volume, between 30% and 60%, respect to CT baseline. Before radiotherapy treatment, not all patients reported pain symptoms assessed through the Numeric Pain

Rating Scale. (NSR). The acute toxicity included only worsening in pain 4 out 6 pts (66.5%) that disappeared the subsequent follow-up. No other acute symptoms were reported.

Conclusion: LRT can be a safe and effective treatment for bulky tumors in every part of the body. It is effective palliation treatment to reduce the tumor volume. It can be performed also during systemic therapies. This approach deserve further investigation in prospective trials, to understand also the immunogenic effects that can be achieved.

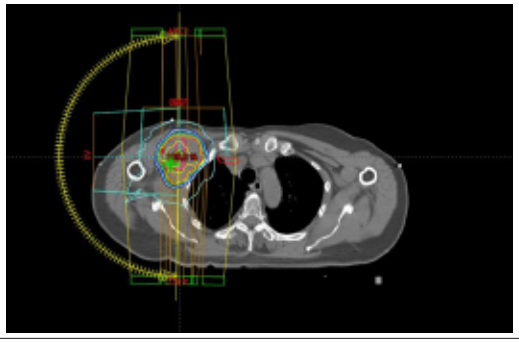

Figure 1.

P301

TREATING NODAL METASTASIS WITH PALLIATIVE INTENT: STEREOTACTIC BODY RADIOTHERAPY (SBRT) TO POSITIVE CHOLINE PET / CT LYMPH NODES FOR OLIGOMETASTASIZED PROSTATE CANCER (PCA) PATIENTS

P. Ziccarelli[1], I. Bonetti[2], A. Chirillo[1], D. Cosentino[1], M. Di Stefano[1], P. Indrieri[1], V. Lauria[1], G. Lecce[1], F. Piro[1], F. Ranuio[1], E. Spadafora[1], L. Ziccarelli[1], L. Marafioti[1]

[1]U.O.C. Radioterapia A.O. Cosenza; [2]U.O. S. Fisica Sanitaria A.O. Cosenza, Italy

Aims. The purpose of this study is to evaluate the feasibility and toxicity of based stereotactic body radiotherapy (SBRT) for oligometastatic prostate cancer (PCa) patients.

Methods. In this study, oligometastasized PCa patients with nodal (≤ 3 lesions) were treated using SBRT in association with androgen-deprivation therapy. All patients were studied with Choline PET/CT before RT. The prescribed SBRT to pathologic lymph nodes was 8 Gray (Gy), delivered in three fraction to have a better control of organ motion (bowel above all) and normalized so that the 80% isodose covers 100% of the PTV.

Results. Between January 2019 and December 2022, 149 oligometastasized PCa patients with nodal metastasis were treated stereotactic on positive choline PET / CT lymph nodes. At a median follow-up of 4 (1-10) months, no toxicity was observed and a reduction in the volume of irradiated lymph nodes in 60% of patients. Only 5%of the disease progressed, while the remaining lymph node volume was stationary. All patients were re- evaluated with PET/CT.

Conclusions. SBRT to positive choline PET / CT lymph nodes for oligometastic prostate cancer is a feasible treatment modality with minimal toxicity . Further studies with a longer follow-up are needed to better evaluate late toxicity and local control.

P302

SPINE INSTABILITY NEOPLASTIC SCORE (SINS) AS A PREDICTIVE TOOL IN RADIOTHERAPY: A NARRATIVE REVIEW

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Aims. This narrative review seeks to identify the SINS score application in the radiation oncology field, In particular we tried to focus on the possible usefulness of SINS for three different setting: vertebral painful lesions, adverse event or failure prediction after RT, SINS changes after RT.

Methods. This literature review was performed searching papers on MEDLINE published from January 2010 (year of the SINS score introduction) to August 2022. Keywords used were SINS AND radiotherapy OR RT AND metastases OR spine. The computer search was supplemented manually using reference lists for all available review articles, primary studies, meeting abstracts, and bibliographies of books to identify studies not encountered in the computer search. Full text articles, written in English language, prospective and retrospective studies, case reports/series, and reviews focusing on the eventual correlation between SINS and radiotherapy were included in this paper.

Results. In terms of vertebral painful lesions and RT symptomatic responses, the SINS score could be an interesting aid in order to choose the right therapeutic approach. Being pain caused by three main components (mechanic, tumor-related and inflammatory), accordingly, we found that lesions with higher level of instability, and therefore higher SINS score, could did not find any significant benefit from radiation therapy which is more effective on the tumor-related pain component. On the other hand, regarding SINS score as predictor of adverse event after radiotherapy and its changes after radiotherapy, the available experiences showed contrasting results, probably due to study limitations, such as sample size, different primary histology, and bone matrix status.

Conclusions. The few experiences investigating the possible uses of SINS score an instrument for the evaluation of radiotherapy outcomes show ambiguous conclusions. Further prospective studies in selected series are needed to obtain more precise and definitive results.

P303

WIDE FIELDS RADIOTHERAPY WITH IMRT/VMAT: THE GOOD PALLIATION

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[1]Radioterapia Oncologica, IRCCS-CROB; [2]Fisica Sanitaria, IRCCS-CROB, Italy

Aims. Radiotherapy is an effective tool for cancer palliation to alleviate disease symptoms and to stop enlarging secondary masses with a little time investment by the patients (pts). The classic technique involved for Palliative Radiotherapy Treatments (PRT) is the 3D-conformal radiotherapy (3DCRT), with two or three static beams which assure rapid and adequate PRT. In the recent years, more advanced techniques, such as intensity-modulated (IMRT) and volumetric modulated arc therapy (VMAT), have been applied to PRT in order to spare organs at risk (OARs), although the prescribed doses are relatively low. Considering the increasing indication for retreatments and the need to treat pts with high disease burden, these new techniques are even more attractive. We present our experience using advanced techniques (IMRT/VMAT) for PRT compared with traditional 3DCRT.

Methods. We included consecutive pts with bone metastases treated with 3DCRT versus IMRT/VMAT for PRT (15-30Gy) in wide Planning Target Volumes (PTV): the sites of metastases were vertebral column, (cases with ≥ 4 vertebrae) and pelvic bones (whole- and hemi-pelvis) cases. Overall treatment time (OTT), mean PTV coverage (V95%), doses at OARs and relief of pain adopting the Numerical Rating Scale (NRS) were considered.

Results. Between January 2022 to January 2023, 65 pts matching the large PTV volumes criteria underwent PRT to our Institute: for vertebral column 18 were treated with IMRT and 15 with 3DCRT, obtaining a mean PTV coverage of V95%=98.3% *vs* 94.2%, respectively. For pelvic bones, 8 pts were treated with IMRT/VMAT and 24 with 3DCRT, with a mean PTV coverage of V95%=98.0% *vs* 93.7% respectively. Sparing of OARs was greater with the IMRT/VMAT, although with longer OTT (from 3 to 4 times longer), as expected. However, the pain ameliorated in the IMRT/VMAT pts treated group (3/4 NRS points reduction *vs* 2/3 of 3DCRT pts).

Conclusions. Both 3DCRT and IMRT/VMAT are effective techniques in PRT. The choice is based on careful assessment of various factors, like tumour size, location, logistics, proximity to OARs, OTT and need for further re-irradiations. Furthermore, it should be considered that this approach is appropriate in view of re-irradiation and future treatments to near target regions. In this scenario, the policy of dose saving even for fractions typical of PRT can certainly help pts who are undergoing systemic therapy.

P304

STEREOTACTIC BODY RADIOTHERAPY FOR BONE METASTASES: OUR EXPERIENCE

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Aims. Stereotactic body radiotherapy (SBRT) is a promising approach in treating bone metastases particularly in oligometastatic disease and re-irradiation. We evaluated local control and toxicity in patients treated with SBRT in our Centre.

Methods. From March 2021 to November 2022 seven pts with bone metastases (median age:65-78 years) who underwent SBRT were retrospectively evaluated: 4/7 (57%) pts presented metastatic disease at diagnosis and 3/7 (43%) pts were oligometastatic on bone site. The number of spinal and extra-spinal lesions was 3 and 4, respectively, two of which were in-field re-irradiation. The primitive tumor was prostate (2 pts), breast (2 pts), lung (2 pts) and kidney (1 pts). All patients were immobilized with stereotactic devices to ensure reproducible positioning. A computed tomographic (CT) scan with 3 mm slice thickness was performed. The gross tumor volume (GTV) was defined on the simulation of CT fused with RMN or PET/CT. The planning target volume (PTV)

was obtained by adding a 3-5 mm isotropic margin to the GTV, depending on the site of irradiation and whether first or second irradiation. The treatment was administered with Volumetric Modulated Arc Therapy (VMAT)-SBRT technique and the fractionated schemes consisted of 30-35 Gy/5Fr and 24-27 Gy/3Fr. Acute and late toxicities were scored according to Common Terminology Criteria for Adverse Events version 4.0.

Results. After 6 months to SBRT a reduction in pain was achieved by all patients, which was complete in 5 patients (71,4%) and partial in 2 pts (28,5%) with a reduction in pain relieving drugs. The radiological response was evaluated by PET/CT or TC-RMN and 4 pts (57,1%) had complete remission (RC) and 3 pts (42,8%) had partial response (RP).

Conclusions. In our experience bone SBRT results feasible and safe; the majority of patients presented complete remission of symptoms and an acceptable radiological response.

P305

PROSPECTIVE DOUBLE ARM PHASE 2 RANDOMIZED TRIAL FOR PATIENTS WITH MULTIPLE BRAIN METASTASES AND/OR LEPTOMENINGEAL CARCINOMATOSIS: COMPARISON OF WHOLE BRAIN RADIATION THERAPY (WBRT) ALONE AND WBRT PLUS SILIBININ

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Aims. Incidence of brain metastases (BMs) is rising due to a greater detection rate of small brain lesions related to increased Magnetic Resonance Imaging (MRI) use and because of more effective systemic therapies contributing to extra-cranial disease control. Approximately 20% of cancer patients develop BMs along their disease course. In case of limited spread, either single fraction or hypofractionated radiosurgery are considered treatments of choice. In case of extended brain disease and/or leptomeningeal carcinomatosis, Whole Brain Radiation Therapy (WBRT) might be required. Since the 1950s, WBRT has been widely used in case of multiple BMs. Nevertheless, median overall survival (OS) is limited to 3 months. Recent studies demonstrated that an increased activity of Signal Transducer and Activator of Transcription 3 (STAT3) in reactive astrocytes correlates with reduced survival in patients with BMs. By experimentally blocking STAT3 signaling, BMs development was reduced. Silibinin, a flavonoid isolated from milk thistle, can impair STAT3 activation showing an anticancer effect in preclinical studies. We thus designed a double arm phase 2 randomized trial aimed to compare WBRT alone versus WBRT plus Silibinin. Primary endpoint is OS, while secondary endpoints are Progression Free Survival (PFS), Brain Failure (BF) and toxicity in term of corticosteroid therapy use.

Methods. Forty-four patients are expected to be enrolled in 2 years. Enrolled patients have a histological or cytological solid tumour diagnosis, clinical indication for WBRT and a Karnofsky performance status (KPS) ≥60. In experimental arm A, WBRT is delivered concomitantly to Silibinin; in control arm B, WBRT is delivered alone. Patients in both arms will receive a dose of 30 Gy in 10 fractions. Quality of life and corticosteroid therapy use will be assessed before RT, at the end of RT, and at follow-up. Disease outcome will be evaluated 2 months after treatment with MRI or CT and every 3 months afterward.

Results. From March to May 2023, 14 patients were enrolled in the study (five patients in Arm A, and 9 patients in Arm B). Primary histology was breast cancer in 5 patients (35%), NSCLC in 6 patients (43%), SCLC in 2 patients (14%), and colon cancer in 1 patient (7%). One patient in Arm A was unable to complete RT due to lung progression.

Conclusions. WBRT alone or with Silibinin was well tolerated in all patients, in absence of acute toxicities or modulation of corticosteroid therapy.

P306

ONLINE ART, WHEN OFF-LINE ART IS NOT ENOUGH: A CASE REPORT FOR A PALLIATIVE TREATMENT IN THE MEDIASTINUM WITH EXTREME ANATOMIC VARIATIONS

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Aim. This study reports the benefits of online adaptive radiation therapy (ART) for a peculiar patient treated with palliative intent.

Methods. We present the case of a 61-year-old patient with metastatic serous ovarian cancer who was undergoing carboplatin-doxorubicin chemotherapy. Following the latest CT restaging in April 2023, which revealed disease progression in multiple organs the patient was referred to our radiotherapy department. Specifically, the mediastinal lymph nodes were compressing the right bronchus and esophagus, although the patient was asymptomatic. However, due to the rapid disease progression, the prognosis was unfavorable. During the first treatment session consisting of 30 Gy in 10 sessions, the patient exhibited significant mobility of the mediastinum caused by hyperinflation of the affected

right lung. As a result, we modified the initial image-guided radiation therapy (IGRT) protocol to an off-line adaptive RT approach, with three replans for the first 6 fractions, followed by an on-line ART for the remaining 4 fractions. This extreme case was utilized to compare the differences between the 3 treatment protocols: IGRT, off-line adaptive RT, and on-line ART. The primary parameters analyzed included variations in lungs and clinical target volume (CTV), CTV V98%, as well as the mean dose to the lungs and heart.

Results. In this particular clinical case, employing an IGRT protocol for all treatment sessions would have resulted in inadequate coverage of the target volume (CTV V98%<70%). The off-line adaptive ART approach enabled acceptable target coverage for the initial 6 fractions (CTV V98%>98%). However, without 2 additional replans, the same level of coverage could not be achieved for the final 4 fractions (CTV V98% ~ 83%). By transitioning to online ART, optimal target coverage (CTV V98%>99%) was achieved, even in the presence of significant anatomical variations, while maintaining the same dose to the organs at risk.

Conclusions. The implementation of CBCT-based online ART is a relatively new development in the field of external RT, and its full range of applications have yet to be fully defined. We present a case study that showcases the safety and efficacy of this technique, even in the context of palliative care, when pronounced anatomical inter-fraction variations are present. These findings highlight the potential of online ART for these patients; further research and clinical exploration in this area are needed.

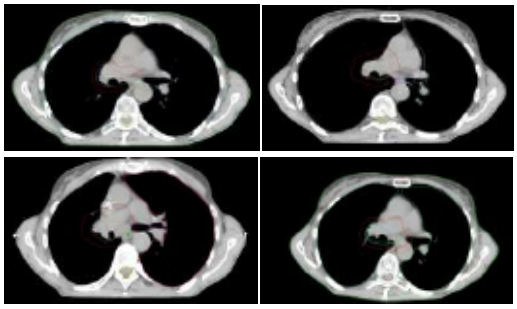

Figure 1. From top left to bottom right: Planned radiotherapy treatment; first offline adaptive treatment, second offline adaptive treatment, first online ART treatment.

P307

RADIOTHERAPY OF ORBITAL METASTASES: A SYSTEMATIC REVIEW OF MANAGEMENT AND TREATMENT OUTCOMES ON BEHALF OF PALLIATIVE CARE STUDY GROUP OF ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY (AIRO)

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Aims. We search the current literature on data regarding the role of RT in OM treatment, focusing on improvement of symptoms and patient quality of life.

Methods. This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations.

Results: From 340 citations, 60 papers were finally selected: 45 case reports and 15 case series. The case reports accounted for 47 patients. In 37/39 cases (95%) EBRT was done. Patients were mainly treated with 3DCRT, IMRT, and with SBRT. The most used RT regimens were 30Gy in 10 fractions (23%) and 20-25Gy in 5fx (13%). No sever toxicity was reported. One year- and two year-LC were 97.3% and 86.5% respectively. One year- and two year- OS were 73.0% and 51.0%, respectively. Among the case series, a total of 457 patients were examined, 227 of whom underwent RT. The main used techniques were 3DCRT, CK, GK, SBRT, and BRT. RT doses could vary from 30 Gy/10 fractions to 60 Gy/30 fractions, 50 Gy/5 fractions, or 16.5-21 Gy in single fraction. No toxicity above G2 was reported. ORR could vary

between 75% and 100%. Only two study provided information on response duration: a mean LC time of 22.8 months and a mean time to local progression of 5 months (range: 3-7). Regarding OS, the data were heterogeneous, ranging between 1 and 54 months.

Conclusions. RT for OM seems to be a safe and feasible option. More information on the RT ideal techniques and dose are still needed.

P308

STEREOTACTIC RADIOTHERAPY AND AUTOMATIC TABLE REPOSITION IN THE METASTATIC DISEASE

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Aims. Analyze and correct the positioning errors in the 6 freedom degrees of the treatment table, translation (Y, X, Z) and rotation (coronal, sagittal, transversal), in patients with intra and extracranial metastatic disease treated with stereotactic radiotherapy.

Methods. From March 2019 to april 2022, 78 patients were treated with stereotactic radiotherapy for metastatic disease. 31 patients were treated with stereotactic radiotherapy for intracranial metastatic disease. 39 patients were treated with stereotactic radiotherapy for lymphnodal or visceral extracranial disease. 8 patients were treated with stereotactic radiotherapy for bone extracranial disease. The number of metastases treated simultaneously was a maximum of 3. All patients underwent daily IGRT verification and in all patients automatic table translation and rotation correction were performed for each radiotherapy session. All patients had a specific immobilization system and all patients were treated with the "Elekta VERSA HD" linear accelerator equipped with the "HexaPOD" automatic table rotation system.

Results. All freedom degrees were recorded for each single fraction of stereotactic radiotherapy delivered. An average was made of the movements in all freedom degrees for every radiotherapy fraction effectuated. The three groups of patients were analyzed separately for localization of metastatic disease. Group 1 patients with intracranial metastatic disease: avg translation Y=0.12cm, X=0.15cm, Z=0.1cm; avg rotation coronal 0.92°, sagittal 1.12°, transverse 1.37°. Group 2 patients with lymphnodal or visceral extracranial disease: avg translation Y=1.26cm, X=0.22cm, Z=0.62cm; avg rotation coronal 1.62°, sagittal 1.87°, transverse 0.9°. Group 3 patients with bone extracranial disease: avg translation Y=1.1cm, X=0.32cm, Z=0.46cm; avg rotation coronal 1.28°, sagittal 1.84°, transverse 0.46°.

Conclusions. In our experience, the automatic movement of the table, in the 6 degrees of freedom, is a valid support to guarantee a more accurate positioning of the patient with metastatic desease treated with stereotactic radiotherapy. Due to type of different errors linked with the patient collaboration, operator experience, to the immobilization system used and indifferently to the irradiated body district, it's necessary use this process for every single session.

P309

TIME TREND IN THE USE OF SINGLE-FRACTION (SF) AND VMAT -BASED PALLIATIVE RADIOTHERAPY

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Purpose: Recent meta-analyses demonstrate that single-fraction (SF) palliative radiation treatments result in equal analgesia as multi-fractionated treatments (MF), with benefits in terms of costs, compliance and efficacy. However, in clinical practice the use of SF palliative treatment is underused for fear of insufficient efficacy or greater toxicity. In our study we therefore evaluated the time trends in the use of palliative SF and MF palliative radiotherapy.

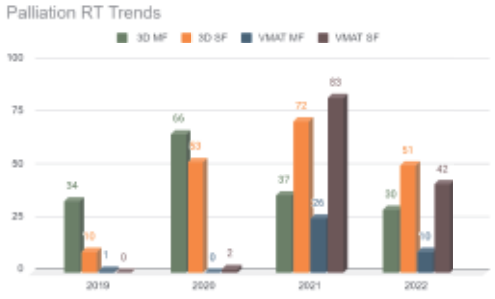

Figure 1.

Materials. We retrospectively collected data on palliative radiotherapy treatments performed in our center on a cohort of consecutive patients from 2019 to 2022. Treatments performed with both VMAT and 3D conformal techniques were included. Treatment schedules were grouped as follows: MF, which included 30 Gy in 10 fractions of 3 Gy each and 20 Gy in 5 fractions of 4 Gy each, and SF, which corresponded to 8 Gy in a single session. We compared the time trend of MF *vs* SF treatments use

by analyzing the data for the two-year period 2019-2020 *vs* the data for the two-year period 2021-2022.

Results: We report our results in Figure 1.

After statistical analysis, we have found a trend towards preferred use of SF (p< 0.00001, significant at p> .05) and VMAT (p< 0.00001, significant at p> .05) in the 2021-22 as compared to 2019-20.

Conclusion: In the time window we examined, there has been a significant increase in the use of SF palliative radiotherapy with a concomitant significant increase in use of VMAT technique. Use of VMAT strategy may possibly have impacted on wider application of SF due to improved sparing of organs at risk.

P310

PALLIATIVE RADIOTHERAPY OF BONE METASTASES IN LOW/MIDDLE-INCOME COUNTRIES: A SYSTEMATIC LITERATURE REVIEW

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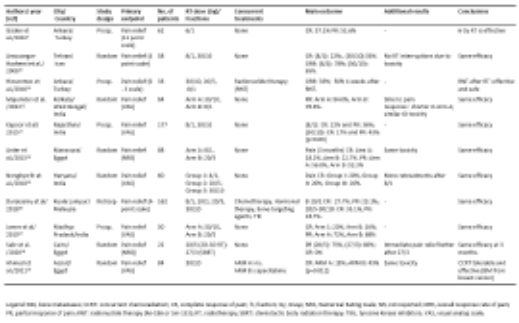
Aims. Palliative radiotherapy (RT) effectively relieves pain in patients with bone metastases (BMs). Furthermore, several clinical trials, in most cases conducted in high-income countries (HICs) , proved that single-fraction RT is equally effective compared to multi-fractionated RT. However, the evidence is scarce regarding low/middle-income countries (LMICs), where the diagnosis of BMs could be later and RT techniques less advanced. Therefore, we conducted a systematic literature review to evaluate the efficacy of palliative RT of BMs in the LMICs setting.

Methods. A literature search was performed independently by two authors on PubMed, Cochrane, and Scopus databases based on PRISMA guidelines. Overall, 333 records were screened and after the selection process only 11 papers were included in the analysis.

Results. Complete pain response rates ranged from 0.0% to 37.1% (median: 22.5%) for single fraction RT and from 0% to 43% (median: 20.1%) for multi-fractionated RT. Partial pain response rates ranged from 23.6% to 76.9% (median: 56.5%) for single fraction RT and from 24.7% to 84.6% (median: 55.3%) for multi-fractionated RT (Table 1). Four randomized trials compared single-fraction RT with multiple-fraction RT and none of them showed significant differences in terms of pain relief.

Conclusions. Our analysis showed that response rates after palliative RT recorded in LMICs are similar to those reported in studies performed in HICs. Even in this setting, RT in single fraction is confirmed as equivalent to multi-fractional RT.

Table 1.



P311

LADIES PROJECT: LARGE DATABASE IN ENDOMETRIAL CANCER

R.M. Rinaldi[1], R. Autorino[1], V. Vavassori[2], S. Lucci[1], G. Macchia[3], M. Boccardi[3], I. Mihoci Roshanian[4], R. Sebastiani[4], B. Santo[5], D. Russo[5], M. Ferioli[6], A. Benini[7], E. Perrucci[8], A. Raguso[9], S. Cossa[9], P. Matteucci[10], C. Talocco[10], F. Trippa[11], L. Draghini[11], A. Augurio[12], F.C. Di Guglielmo[12], P. Cocuzza[13], L. Vicenzi[14], F. Pistis[15], F. De Felice[16], S. Meregalli[17], M. Tamburo[18], M.A. Gambacorta[1], C. Aristei[8]

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Aims. To evaluate the role of radiotherapy for endometrial cancer in a retrospective multicentric Italian study.

Methods. A large database was built by 3 of the authors and then shared with other 5 collegues to create a project's core group. A protocol for the restrospective study was designed and approved by the coordinator centre ethical committee and by the single participating centres ethical commitee. So far, 39 centres asked to participate in the study.

Results. Data of one thousand eight hundred forty eight patiens were analyzed. They were treated between 2010 and 2020 with surgery, post-operative external beam radiotherapy and/or brachytherapy preceded or not by adjuvant chemotherapy, which was delivered on the basis of histological risk factors. A minimum of 12 months follow-up was required. Patients were enrolled in 16 Italian Radiation Oncology Centres (3 was in the North Italy, 6 in the Center and Isles, 7 in the South) . Each centre enrolled a mean of 108 patients (range 390-14). Stages were from IA to IIIC. Patients were classified according to the 2021 classification based on stage, histology, grade, LVSI, and myometrial invasion into three risk classes, low-intermediate-high, for a total of 115 low-risk, 1055 intermediate-risk, and 503 high risk. Each risk class was correlated to the type of radiotherapy treatment performed, with prevalence of IRT for the low risk group, EBRT+IRT for the intermediate and high risk group; clinical outcomes are similar to current guidelines.

Conclusions. We create a large database based on the Italian data in the management of endometrial cancer in Radiation Oncology Centres. These data allow a picture of the real word use of adjuvant radio- and systemic therapy for endometrial cancer and to compare them with current guidelines.

P312

NEOADJUVANT VERSUS EXCLUSIVE RADIOCHEMOTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER PATIENTS

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Aims. To compare outcomes in FIGO stage I-IVA cervical cancer patients treated with neoadjuvant radiochemotherapy (NAD RTCT, according to LARA4 protocol) versus definitive radiochemotherapy (EXC RTCT).

Methods. Between 2020 and 2022, 162 FIGO STAGE I-IVA cervical cancer patients were treated:

83 (Group A) patients were submitted to NAD RTCT (concomitant platinum-based chemotherapy plus a median dose of 45 Gy of external beam on the whole pelvis and 50 Gy on T or positive N) followed by radical surgery according to the LARA4 protocol. 79 (Group B) patients underwent EXC RTCT (concurrent platinum-based chemotherapy plus a median of 45 Gy of external beam radiation on the whole pelvis plus a simultaneous integrated boost on positive lymph nodes of 55 or 57.5 Gy and 28 Gy in 4 fractions of High Dose Rate brachytherapy).

Results. The baseline characteristics of the two groups are summarized in Table 1. In group A, pathological complete response was documented in 30 cases (36%); in group B, the radiological complete response at 6 months from the end of brachytherapy was in 60 patients (77%). With a median follow-up of 40 months, the 1- and 2-year disease-free survival rates were 96% and 76% for patients treated in the LARA4 protocol *vs* 77% and 71% for patients treated with exclusive RTCT (p=0.01). It could be caused by a different distribution of the stages, age, and comorbidity between the groups with a recurrence outside of the radiotherapy field or distant metastases. One- and 2-year overall survival were 97% and 93% *vs* 93% and 80%, respectively, in the two groups (p=0.05).

Conclusions. In this preliminary comparison, NAD RTCT carried out encouraging pathological response and a favorable trend in terms of overall survival when compared with standard EXC RTCT. Longer follow-up is needed to confirm these results and to find out more about long term side effects.

Table 1.

	NEAODJUVANT RTTCT (LARA 4)	DEFINITIVE RTCT	P value
Patients (N°)	83	79	P= 0.05
AGE (MEDIAN)	49 (26-77 yrs)	55 (25-81 yrs)	P= 0.05
HISTOLOGY			P= 0.54
SQUAMOUS CELL	73	72	
CARCINOMA	9	7	
ADENOCARCINOMA	1	0	
ADENOSQUAMOUS			
GRADING			P= < 0.001
G1	2	2	
G2	30	27	
G3	31	23	
NA	20	27	
STAGING			P= < 0.001
IB1	1	0	
IB3	2	0	
IIA2	1	4	
IIB	13	21	
IIIA	1	2	
IIIC1	65	37	
IIIC1	0	20	
IVA	0	5	
RESPONSE	pCR 30 (36%) pR1 27 (32.5%) pR2 23 (28%) PD 3 (3.5%)	RC 61 (77%) RP 2 (2.5%) SD 4 (5%) PD 11 (15.5%)	P= <0.001

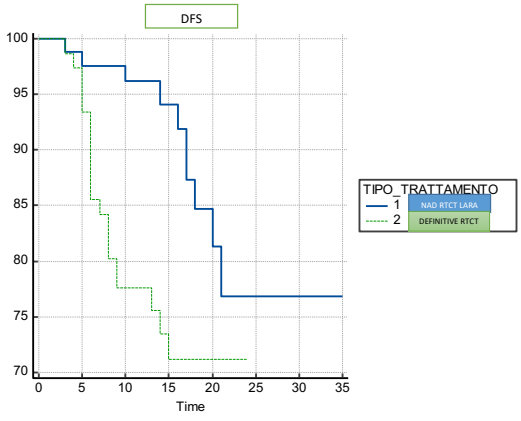

Figure 1.

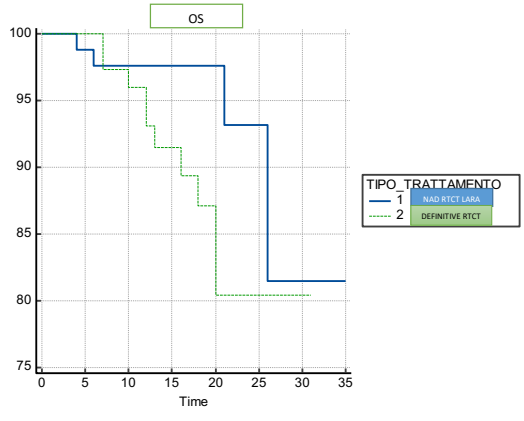

Figure 2.

P313

CARBON ION RADIOTHERAPY FOR RECURRENT, REFRACTORY AND OLIGOMETASTATIC OVARIAN AND FALLOPIAN TUBE CANCERS

A. Barcellini[1,2], K. Murata[3], G. Fontana[4], A. Vai[4], S. Molinelli[4], C. Cassani[5,6], S. Secondino[7], J. Franzetti[1], S. Yamada[3], N. Okonogi[3], E. Orlandi[1]

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Aims. To assess the efficacy and safety of carbon ion radiotherapy (CIRT) for recurrent, refractory and oligometastatic ovarian /salpinx cancer (RR-OSC) treated in two international institutions

Methods. The first endpoints of this explorative analysis were the objective response rate (ORR) to CIRT (defined as the sum of complete response (CR) and partial response) and 1-2-year (y) local control (LC) on "per-lesion" basis. The secondary aim was acute/late toxicities (scored using RTOG/EORTC or CTCAE scales according to centre policy). Actuarial outcomes were evaluated using the Kaplan-Meier method. Logistic and log-rank test/Cox regression were used for the analysis of factors (total dose, dose per fraction, age, GTV, tumor site) predicting clinical CR and actuarial outcomes(α=0.05) adjusted for radiobiological models applied along with differences in ethnicity.

Results. 26 women (58% Asian and 42% Caucasian), for a total of 36 lesions, underwent CIRT for RR-OSC. In 5 cases CIRT was delivered as re-irradiation. The median age at CIRT was 59.5 years (range:44-81) and the most common histological type was high-grade serous carcinoma (42%). Parenchymal lesions accounted for 58% (abdominal=14;pelvic=5,brain=2) followed by lymph node ones (42%; N=15). Lesions were treated with a median total dose of 52.8 Gy[RBE] (range:39-64 Gy[RBE]) and no concomitant systemic therapies were administered during CIRT. Overall, the ORR was 97% and 15 (41%) lesions achieved CR within 12 months after CIRT. The dose per fraction > 4.2 Gy[RBE] was associated with a higher chance of CR (OR: 10, 95% CI: 2.23 - 58.3, p=0.005). The 1- and 2-y LC rates were 92% (95% CI: 81%- 100%) and 79% (95% CI: 57%-100%) respectively and the GTV $\leq$ 14 cc (p=0.034) impacted the LC on the Log-rank test. We recorded only one case of G3 EORTC/RTOG enterocolitis in the acute and late phases

and no G≥3 toxicities in re-irradiated patients. 4 patients received PARP-i and 6 anti-VEGF (before and/or after CIRT), which did not seem to increase the risk of severe toxicities.

Conclusions. For the first time we described the efficacy and safety of CIRT in patients with RR□OSC, even in the case of re-irradiation. To better select patients for CIRT, prospective and randomized studies are recommended, taking into account the CIRT advantages as well as the radiobiological hallmarks of these malignancies.

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SALVAGE STEREOTACTIC RADIOTHERAPY IN OLIGOMETASTATIC GYNECOLOGICAL CANCER: COMPARISON BETWEEN OUTCOMES OF LYMPH NODE VS OTHER SITES METASTASES

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Aims. In this retrospective study we analyzed the different clinical outcomes of stereotactic radiotherapy (SRT) to lymph node (LN) metastases versus parenchymal lesions, in gynecological cancer patients (pts).

Methods. From 4/09 to 5/23 137 lesions of 76 pts were treated with SRT. In 27 pts (35.5%) multiple SRT were prescribed on synchronous and metachronous lesions. Twelve lesions were treated with Image Guided-helical Intensity Modulated Radiotherapy (IG-IMRT) to a median dose of 40(27-63) Gy in a median of 5 (3-10) fractions prescribed at 95% of PTV. One hundred twenty-five lesions were treated with robotic SRT to a median dose of 40(18-60) Gy in a median of 5(1-8) fractions, prescribed at a median isodose of 80% (67-84%). Primary tumor was: uterus in 38.7%, ovary/Fallopian tubes in 39.3%, cervix in 15.3% and vagina/vulva in 6.5% of patients. Fifteen nodal PTVs (21.4%) were in the same field of previous adjuvant or salvage RT. The sites of oligometastatic disease were LN 51.1%, lung 30.6%, central nervous system 6.5%, liver 5.8%, and bone and soft tissue 5.8%. GTV was defined on the merged image of CT, PET and MRI. Toxicity was assessed using CTCAE v 5 criteria.

Results. Median follow-up was 19.5 (1-75) months. Ten pts died before first evaluation. In the LN SRT group, 14pts (20%) presented grade (G) 1 or 2 acute toxicity (nausea, pain) and 2 pts G2 late toxicity (rib pain, paraesthesia). In the other sites SRT group 7 pts presented G1 acute toxicity and 5 pts G1 late toxicity. Only one patient had G3 late toxicity (spine fracture and related neuropathy). SRT responses in 64 LN evaluable lesions *vs* 58 other targets were: complete response (CR) 78.1% *vs* 70.7%, partial response (PR) 9.4% *vs* 18.9%, stable disease 0 *vs* 1.7%, and progressive disease (PD) 12.5% *vs* 8.6%, respectively. The 12, 24, and 36-month Overall Survival (OS), analyzed on all lesions, was: 76.9%, 65%, and 47.5%, respectively (Figure1a). OS of nodal *vs* other sites groups, at 12, 24, and 36-month , were 87.1% *vs* 66.4%, 65.5% *vs* 64.4%, and 58.4% *vs* 36.1%, respectively(p = 0.01) (Figure 1b). Cancer Specific Survival (CSS) of LN *vs* other sites group, at 12, 24, and 36-month, were: 90.3% *vs* 69.8%, 71.1% *vs* 67.8%, and 68.6% *vs* 41.3%, respectively(p=0.003)(Figure1c).

Conclusions. As in the MITO 1 study, in our experience LN oligometastatic disease demonstrated significantly better OS and CSS than extra-LN sites group in long term follow up, despite a 90% local control in the latter group.

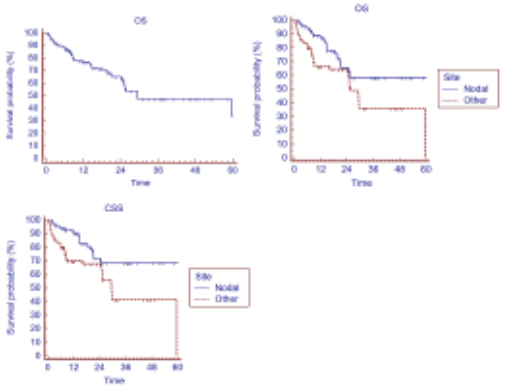

Figure 1. Kaplan Meier estimate of: a) Overall Survival in all patients; b) Overall Survival in lymph-nodal vs other sites patients; c) Cancer Specific Survival of lymph-nodal vs other sites patients.

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TUMOR VOLUME SHRINKAGE EVALUATED ON MAGNETIC RESONANCE IMAGING AFTER EXTERNAL BEAM RADIO-CHEMOTERAPY AS POTENTIAL PREDICTIVE FACTOR OF COMPLETE RESPONSE IN A PROSPECTIVE SERIES OF 30 PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER

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Aims. The aim of the study was to evaluate tumor volume shrinkage as a predictive factor of complete response to definitive chemo-radiotherapy and High Dose Rate Brachytherapy (HDR-BT) boost, measured on magnetic resonance images (MRI) both at diagnosis and at re-evaluation before HDR-BT in patients (pts) with locally advanced cervical cancer.

Methods. From December 2020 to December 2022, 30 pts with locally advanced cervical cancer underwent pelvic External Beam Radiotherapy (EBRT) treatment associated with concurrent chemotherapy (CHT) and subsequent HDR-BT boost. All pts underwent MRI at diagnosis (T0), after EBRT-CHT before starting the HDR-BT boost (T1) and on follow-up at 3 months after the end of treatment. Tumor volume and its variation were contoured, calculated and evaluated on T2-sequence MRI at T0 and T1. Tumor local response was assessed by MRI at first follow-up. Patients with MRI evidence of residual tumor at first follow-up underwent biopsy for histological confirmation.

course.

Table 1.

AGE	YEARS
Median	51,17
Range	29-72
HISTOLOGY	
Squamous cell	27
Adenocarcinoma	3
FIGO stage	
I B3	1
II B	23
III C1	6
TREEATMENT RESPONSE	
Complete Response	24
Residual Disease	6
TUMOR SRHIKAGE %	
100- 71.5%	Complete Response
68.3 – 31.7%	Residual Disease

Results. In 24/30 pts follow-up MRI at 3 months after the end of treatment, showed complete remission (CR) tumor while in 6 pts a local residual disease was observed. Tumor persistence was confirmed by histological examination only in 3/6 pts. For the 24 pts in CR, tumor volume shrinkage was greater than 70% (range: 100%-71.5%), in the 6 pts with positive MRI it was less than 70% (range: 68.3%-31.7%). A complete response to treatment was observed for patients with a tumor volume reduction from diagnosis of at least 71.5%. The analysis was performed with MedCalc Statistical Software using Mann-Whitney test for independent samples; our observational study revealed a statistically significant correlation between the percentage of tumor volume change and treatment complete response ($p<0.0001$). Our preliminary data do not reveal a statistically significant correlation between initial tumor volume and complete response ($p=0.1138$). The relationship between the tumor volume before HDR-BT boost and treatment complete response was not statistically significant ($p=0.0148$).

Conclusions. Our preliminary data showed that early response to EBRT-CHT might be a potential predictive factor of treatment complete response in patients with locally advanced cervical cancer. A tumor volume shrinkage of less than 70% after EBRT-CHT was associated with disease persistence at the end of whole treatment

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DOSIMETRIC IMPACT OF AUTOMATIC SEGMENTATION OF OARGANS AT RISK IN CERVICAL CANCER RADIOTHERAPY

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Aims. This study aimed to evaluate if the dosimetric effects of organ at risk (OAR) automatic contouring (AC) inaccuracies confirm the previous findings in terms of geometric indexes where deep learning (DL)-based tools outperformed traditional algorithms in AC for cervical cancer (CC).

Methods. Four AC tools were evaluated: MVISION (MV) and LIMBUS AI (LI) (DL-based tools), Atlas-Based Auto Segmentation (STAPLE, ST), and Random Forest algorithm (RF). A total of 40 consecutive CC patients from a single institution were retrospectively selected. Twenty structure sets (SS) were randomly chosen as the atlas set for STAPLE and RF. The remaining 20 SS (testing) were auto-segmented by STAPLE, RF, MV, and LI. Original target volumes were added to the AC sets. A total of 100 SS were used to optimize 100 plans (20 patients x 5 SS each) delivering 50 Gy in 25 fractions using Monaco research v.59 (Elekta). The plans obtained from the manually contoured SS (gold standard, GS) were used as the planning GS. Dose distributions were superimposed on the GS SS to register OAR dose differences caused by delineation variations. Plan complexity was measured in terms of monitor units (MU) and Modulation Degree (MD). Statistical significance was assessed using the Wilcoxon test ($p<0.05$).

Results. Planning failed with 2 out of 100 SS: 1 ST and 1 MV, due to the PTV-bowel intersection issue. Results are presented in Table 1. Although no statistical significance was observed with small median deviations, dose deviations could be significant at an individual patient level, affecting the clinical plan acceptability (e.g., PTV $V_{95\%}$ -38.9%, bowel V_{45Gy} -90.7%). Acceptable plans were achieved in all but one GS plan and were preserved in LI SS. ST, RF, and MV showed unacceptable target coverage in 3 out of 20 cases each but preserved OAR sparing. The variation in MUs demonstrated the influence of AC variation on planning. A not statistically significant increase in median MD was observed in RF and ST SS, but not in DL SS.

Conclusions. The dosimetric effect of AC inaccuracies did not confirm the superior performance of DL tools. Although AC reduces contouring time, the control and validation by radiation oncologists remain crucial to avoid significant dosimetric effects. Further investigation on a larger cohort is warranted to study the correlations between geometric indexes and dose deviations.

Table 1.

	ST vs GS	RF vs GS	MV vs GS	LI vs GS
PTV $D_{95\%}$	0.0 [-0.8 – 0.5]	-0.1 [-1.4 – 0.2]	0.1 [-1.1 – 0.3]	0.0 [-0.6 – 0.4]
PTV $V_{95\%}$	-0.5 [-19.5 – 4.0]	-0.5 [-38.9 – 4.5]	-0.2 [-22.8 – 4.0]	0.0 [-4.5 – 16.8]
Rectum D_{mean}	1.3 [-21.9 – 23.4]	1.0 [-13.8 – 18.5]	1.8 [-11.0 – 24.3]	0.5 [-14.6 – 11.2]
Rectum $D_{50\%}$	1.8 [-32.9 – 26.8]	0.3 [-17.6 – 26.4]	2.8 [-16.5 – 33.3]	1.0 [-24.1 – 17.1]
Bladder D_{mean}	2.8 [-14.5 – 28.7]	1.6 [-16.2 – 17.6]	0.0 [-24.6 – 9.2]	2.7 [-35.1 – 14.3]
Bladder $D_{50\%}$	3.1 [-20.7 – 22.8]	1.4 [-26.7 – 18.1]	-0.1 [-36.6 – 7.9]	3.7 [-22.2 – 16.2]
Bowel V_{45Gy}	-6.7 [-57.5 – 57.9]	-6.4 [-90.7 – 33.1]	-2.2 [-75.0 – 124.8]	-0.9 [-25.2 – 195.6]
Right Femoral Head $D_{5\%}$	-0.8 [-15.3 – 15.4]	-0.4 [-12.1 – 17.5]	0.9 [-6.4 – 16.1]	0.0 [-9.7 – 19.6]
Left Femoral Head $D_{5\%}$	0.3 [-23.8 – 17.2]	0.6 [-15.6 – 16.6]	0.7 [-19.5 – 14.9]	0.1 [-34.5 – 13.9]
MU	7.5 [-7.4 – 27.3]	0.1 [-26.9 – 13.2]	-3.5 [-18.7 – 19.0]	2.6 [-12.4 – 21.7]
MD	10.7 [-17.7 – 26.7]	5.0 [-15.6 – 22.0]	2.1 [-19.7 – 32.9]	3.3 [-6.1 – 22.8]

Table 1 – Percentage deviations in dose and complexity metrics caused by inaccuracies in DAR automatic contouring. The reference plan is the plan obtained with the manual gold standard contours. Median and ranges are reported. Abbreviations: GS: manual gold standard, ST: STAPLE, RF: Random Forest, MV: MVision, LI: LimbusAI. $D_{x\%}$: dose received by the x % of contoured volume, D_{mean}: mean dose, $V_{x\ Gy}$: volume receiving more than x Gy, MU: Monitor Units, MD: Modulation Degree.

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DEFINITIVE RADIO-CHEMOTHERAPY AND INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY) IN INVASIVE VAGINAL CARCINOMA: A MONOCENTRIC EXPERIENCE

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Aims. Vaginal carcinoma (VC) is a rare malignancy accounting for 1% to 2% of all gynecological cancers. Although surgery yields good local control (LC) and overall survival (OS) in selected cases of vaginal intraepithelial neoplasms and early (I–II) stages of VC, definitive radio-chemotherapy (RCT) followed by interventional radiotherapy (IRT, also called brachytherapy, BT) is considered as an excellent option. The aim of this study was to report the results of our mono-institutional series of vaginal cancer patients treated with radio-chemotherapy followed by IRT.

Methods. We retrospectively analyzed 21 patients with primary vaginal cancer who received RCT followed by IRT with curative intent between January 2019 and December 2021. The primary study end-point was the local control (LC), secondary end-points were the metastasis free survival (MFS), the overall survival (OS), the cancer specific survival (CSS), and the rate and severity of acute and late toxicities. To analyze actuarial outcomes, we used the Kaplan-Meier method; differences among subgroups were evaluated by log-rank tests. Statistical analysis was carried out by SPSS statistical software (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp).

Results. All patients were treated with radio-chemotherapy with complementary IRT. Fourteen patients were stage II, 5 patients' stage III and 2 stage IVB (International Federation of Gynecology and Obstetrics stages). The median total dose of external beam RT was 45Gy (range 45Gy-60Gy). OncentraBrachy treatment planning system and a Flexitron (Elekta, Stockholm, Sweden) afterloading machine with a 192-Ir source was used for IRT treatment. The median IRT total dose was 28 Gy (range 10Gy-28Gy) over four high dose rate (HDR) fractions in order to achieve between 85Gy - 95 Gy EQD2α/β10 to the high risk (HR)-clinical target volume CTV and 60 Gy EQD2α/β10 to intermediate risk (IR)-CTV. All patients received additional cisplatin chemotherapy. The median duration of follow-up was 20 months (10-56 months). The two-year actuarial LC, MFS and OS rate were 79.4%, 90.5% and 79.4%, respectively. Acute toxicity G2 was recorded in 11 patients, four gastrointestinal, one genito-urinary, four skin and two vaginas. One patient developed G3 skin toxicity. Late G3toxicity was recorded in one patient (vaginal stenosis).

Conclusions. Definitive radio-chemotherapy followed by IRT is an effective treatment modality for primary vaginal cancer.

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THE PREDICTIVE AND PROGNOSTIC VALUE OF FIGO STAGING DEFINED BY COMBINING MRI AND [18F]FDG PET/CT IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER

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Objective. In the last version of the FIGO classification, imaging tools have been recommended to complete the clinical assessment in patients with cervical cancer. However, which imaging approach should be preferred is still unclear. Thus, we aimed to explore the prognostic power of Magnetic Resonance Imaging (MRI), contrast-enhanced Computed Tomography (ceCT), and [18F]-Fluorodeoxyglucose Positron Emission Tomography ([18F]FDG-PET)/CT findings in terms of recurrence-free survival (RFS) and overall survival (OS) in patients staged for locally advanced cervical cancer (LACC).

Methods. We retrospectively recruited thirty-six LACC patients submitted to MRI, ceCT and [18F]FDG-PET/CT for primary staging before receiving concurrent chemoradiotherapy plus endouterine brachytherapy boost and simultaneous-integrated boost guided by [18F]FDG-PET/CT. The predictive and prognostic value of imaging findings were measured considering RFS and OS as the study endpoints.

Results. The involvement of pelvic lymph nodes at MRI independently predicted RFS (HR 13.271, 95% CI 1.730-101.805; p=0.027), while the presence of metastatic paraaortic lymph nodes at [18F]FDG-PET/CT independently predicted both RFS (HR 11.734, 95% CI 3.200-43.026; p=0.005) and OS (HR 13.799, 95% CI 3.378-56.361; p<0.001). Based on these findings we incorporated MRI and [18F]FDG-PET/CT findings together with clinical evidences into the FIGO staging system. With respect to the classification accounting for clinical, MRI and ceCT data, the use of next-generation imaging (NGI) determined a stage migration in 10/36 (27.7%) of patients. Patients belonging to different NGI-based FIGO classes showed remarkably different median RFS (stage IIB: not reached; stage IIIC1: 44 months; stage IIIC2: 3 months; p<0.001) and OS (stage IIB: not reached; stage IIIC1: not reached; stage IIIC2: 14 months; p<0.001).

Conclusions. NGI findings provide prognostic insights in the primary staging of LACC. Incorporating MRI and [18F]FDG-PET/CT findings together with clinical data into the FIGO staging system provide a stage migration compared to the use of ceCT and MRI and significantly stratify the long-term oncological outcome.

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COMPARING RESULTS OF HIGH-DOSE RATE BRACHYTHERAPY VERSUS STEREOTACTIC BODY RADIATION THERAPY IN THE TRATMENT OF LACC PATIENTS (PRELIMINARY DATA FROM STARBACS STUDY)

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Aims. To evaluate toxicities and Local Control (LC) of stereotactic body radiation therapy (SBRT) compared to HDR brachytherapy (HDR-BT) in non-metastatic locally advanced cervical cancer (nmLACC) patients after concomitant chemo-radiotherapy.

Methods. We enrolled all patients with diagnosis of nmLACC observed in our center. External beam radiation therapy (EBRT) combined with chemotherapy (CT) was followed by either endocavitary brachytherapy (BT) or SBRT-boost. Efficacy and toxicities were compared between the two groups.

Results. From February 2020 to May 2023 we treated 30 patients with FIGO-stage IIB-IIIC1 LACC. Median age was 49 (range 29-74). Squamous cell carcinoma was the most common histology (93,3%). All patients were submitted to platinum-based CT at 40 mg/mq weekly concurrent with EBRT on pelvic nodes (Clinical Target Volume) and uterus (Gross Tumor Volume) using intensity modulated technique. We delivered a total dose of 45/50.4 Gy in 25/28 fx. Metastatic pelvic nodes were treated using simultaneous integrated boost (SIB) technique to a total dose ≥54 Gy. An isotropic margin of 2mm (PTV1-2) both on CTV and GTV has been applied. For contouring delineation matched simulation-CT with contrast-enhanced MRI using the software MIM for deformable imaging fusion and for the precise patients' set-up the daily onboard Cone Beam-CT (CBCT) have been used. After restaging with contrast-enhanced MRI and 18-FDG-PET, 13 patients underwent to BT (group A) and 17 to SBRT-boost (group B). Group A patients were submitted to BT technique using Fletcher applicator

delivering a median total dose =20 Gy in 3-4 fx (range 14-26). Group B patients were submitted to SBRT-boost using robotic arm linear accelerator delivering a median total dose =15 Gy/3 fx (range 12-24). For both groups the aim was to deliver a total EQD2 dose ≥80 Gy. Acute toxicities observed in A group *vs* B group were the following: dysuria G1-2 (31% v 41%), vaginitis G1-2 (31% v 30%), and edema G1-2 (15% v 6%). One group A patient had edema G3; one group B patient had vaginitis G3. The median Follow-Up was 8 months (range 1-32) in A group and 9 months (range 1-21) in B group. Up-to-date we reported: LC of 69% in group A and 65% in group B. Two patients in both groups underwent pelvectomy.

Conclusions. SBRT-boost showed similar disease outcomes and toxicities rate as those seen with BT in LACC patients. Our data suggest that this kind of RT could represent an option in patients unsuitable to intracavitary BT.

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ENDOMETRIAL CANCER ELDERLY PATIENTS TREATED WITH ADJUVANT RADIOCHEMOTHERAPY: OUTCOMES AND TOXICITIES

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Aims. Although the vast majority of women diagnosed with uterine cancer are postmenopausal, information on the tolerability and outcomes of radical therapy in elderly women is scarce. The aim of the present study is to evaluate gastrointestinal and genitourinary toxicities (CTCAE 5.0) in elderly women with endometrial cancer treated with curative intent out of clinical trial.

Methods. Fifty-two women aged >65 years treated with surgery, radiotherapy and chemotherapy, for stage I-IV endometrial carcinoma were included. Baseline characteristics of all patients included age at diagnosis, comorbidities, diagnosis date, grade, histology, FIGO stage, RT, CHT, outcomes, hematological toxicity, GI, and GU toxicity.

Results. The majority of women (31/62 patients) had stage III or IV disease, with (21/52 patients) having stage I or II disease with high-risk features. Most tumors were high-grade. The most common (49/52 patients) histology was endometrial adenocarcinoma followed by serous papillary carcinoma. Almost all women had an excellent functional status; ECOG PS score was 0 in 80%, 1 in 15%, and 2 in 5%. Chemotherapy regimens included two or three drugs: carboplatin and paclitaxel, carboplatin, paclitaxel, and doxorubicin, or carboplatin monotherapy. The treatment was associated with significant toxicity, with 60% experiencing grade 2 and 3 hematological toxicity (leukopenia, neutropenia, and thrombocytopenia) at least once during chemotherapy and radiotherapy. GI toxicity (nausea, vomiting, diarrhea, constipation, abdominal pain) was present in 73.2% of women, and GU toxicity (dysuria and cystitis) in 40.5%. DFS was 70% at 1 year and 60% at 3 years.

Conclusions. Based on the findings described so far, it can be concluded that chemoradiotherapy in elderly women with endometrial carcinoma is feasible in daily clinical practice. A significant rate of toxicities have been observed.

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IMPACT OF MOLECULAR ANALYSIS FOR ADJUVANT TREATMENT OF ENDOMETRIAL CANCER

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Aims. Recently, four molecular sub-classes with different diagnostic, prognostic and predictive implications have been identified for endometrial cancer: ultra-mutated cancer with mutations in the exonuclease domain of the DNA polymerase epsilon (POLE), hypermutated cancer with microsatellite instability, copy-number-high with frequent TP53 mutations, and the copy-number-low group. Aim of our analysis was to analyze the molecular pattern of patients with endometrial cancer and to evaluate how the molecular classification has guided adjuvant treatment decisions.

Methods. From January 2022 to May 2023, samples from 51 patients with surgically treated endometrioid endometrial cancer received genomic analysis. Molecular analysis of microsatellite loci was performed classifying microsatellite instability as follows: MSI-high for microsatellite instability of 2 or more loci, MSI-low for microsatellite instability of 1 locus, MSS for none microsatellite instability. Analysis was performed by DNA extraction following microdissection, amplification by PCR end-point and hybridization of marker-specific probes. Moreover, multiple genetic analyses were performed by Next Generation Sequencing by extracting DNA. Results were expressed according to the Human Genome Variation Society v 20.05.

Results. Mean age was 64 years (range: 40-82 years). At diagnosis, FIGO stage was IA for 43.2%, IB for 39.2%, II for 11.7% and IV for 5.9% of patients. Grading was G1 for 50.9%, G2 for 31.4% and G3 for 17.7% of patients. Lymph-vascular space invasion was present in

three patients with IV stage disease. Five per cent (5.9%) of patients had POLE mutations, 17.6% of patients had TP53 mutations and 15.7% of patients had microsatellite instability. Of these, four patients had multiple-classifier endometrial cancer. The other 60.8% of patients had a copy-number-low tumor. One third of the metastatic patients had TP53 mutations. Patients without POLE/TP53 mutations were treated according to their staging and histopathologic characteristics. Indeed, patients presenting TP53 mutations, although with low-staged cancer, were proposed for chemoradiotherapy treatment, validating the molecular analysis as informative for the prognosis and treatment choice.

Conclusions. Treatment of endometrial cancer has become risk-based and the molecular analysis is necessary in order to select and compare adjuvant treatments based on the molecular group. Our analysis suggests molecular analysis also for patients at apparently low risk in order to better define the treatment choice.

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ADJUVANT EXTERNAL-BEAM PELVIC RADIATION (EBRT) FOLLOWED BY VAGINAL BRACHYTHERAPY (VB) BOOST IN ENDOMETRIAL CARCINOMA (EC)

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Aims. Toanalyze the impact on local control and toxicity ofadjuvant VB boost to EBRT in ECconsidering age,stage,histology, grade, risk group, lower uterine segmentinvolvement (LUS), cervical stromal infiltration (CSI) andlymphvascular space invasion (LVSI).

Methods. One hundred and eighteen EC patients (pts) were treated from 2012 to 2019 with postoperative EBRT and VB+/- chemotherapy (CT).The median age was 63years (41-83 years). All pts underwent primary surgery, 75 with and 43 without lymphadenectomy.50,8%pts received chemotherapy.FIGO stage I was 37,3%, stage II 39,8% and stage III 22,9%. Endometrioid and high risk hystology were 83,9% and 16,1% respectively. The tumor grade was 54,2% G1-G2 and45,7% G3. LUS was present in48,3% of tumors, CSI in 49,2% and LVSI in 42,4%. The risk stratification was: intermediate risk 16,1%, high-intermediate risk 50% and high risk 33,9%. All pts received EBRT:45,8% with IMRT and 54,2% with 3 DCRT. The median dose was45 Gy (range 43.2-50.4 Gy) in 25-28 fr. All ptsriceivedhigh dose rate VB. The upper half of vagina was treated with10-15 Gyin 2-3fr. Latetoxicity was graded according to CTCAE5.0 scale. Association of variables with local control and late toxicity was assessed by Fisher's extact test. The Kaplan-Meier method estimated outcome rates.

Results. The median follow-up was 65 months (4-132 months). The 5-years OS, LC, DFS and DSS were 87,9%, 90,9%, 83,3%,90%.Univariate analysis showed histology ($p<0.0001$), grade ($p=0.05$) and risk group ($p<0.002$) significantly correlated with local control. Tumor relapsed in 15/118 pts (12,7%). The median time to recurrence was 21,8 months (1-78 months).Local recurrences (1 vagina, 1 central pelvis) were in 2(1,7%) cases, distant(1both pelvis, 1 both vagina, 3 both lymph node, 5 other sites) in 10 (8,5%), retroperitoneal lymphnodal in 3 (2,5%) (1 para-aortic, 1 para-aortic and pelvic, 1 para-aortic and vagina). Late G2 toxicity was observed in22/118 (18,6%): 1 costipation, 1cystitis, 8 (6,8%) vaginal atrophy, 12 (10,2%) vaginal stenosis. There was 1 urinary incontinence G3.

Conclusions. The traditional adverse features (histology, grade, risk groups) impactcontrol in our patients cohort. Furthermore, our study population experienced a high local control rate of 90.9%. Distant failure was 8,5%. Late G2 vaginal toxicity was 16,9%.However, the role of a VB boost needs further investigation to understand the incremental benefit beyond pelvic RT.

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EARLY DETECTION OF TREATMENT FAILURES IN LOCALLY ADVANCED CERVICAL CANCER: WHAT IS THE TIMING OF TUMOR RELAPSES AFTER CHEMORADIATION PLUS BRACHYTHERAPY BOOST?

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Aims. International guidelines (NCCN v. 1.2023) recommend post-treatment 18F-FDG-PET/CT in patients

with locally advanced cervical cancer (LACC), possibly supplemented by pelvic MRI. However, the indications for subsequent imaging checks are rather vague. On the contrary, the current possibility of effectively treating patients with oligorecurrent disease makes the possibility of early detection of relapses very relevant. In order to identify the optimal timing for intensive imaging-based follow-up of LACC patients, we performed a secondary analysis of a single-center observational study.

Methods. One hundred and sixty LACC patients with follow-up > 12 months were treated in our institution from 2007 to 2021 and enrolled in an observational study. All patients underwent definitive CRT plus brachytherapy boost. FIGO stage was IB-II and III-IVA in 83.1% and 24.9% of cases, respectively. Median follow-up was 36 months (range: 12-151 months)

Results. The results of this analysis are shown in Table 1. Overall, 60 patients (37.5%) experienced treatment failure. In summary, 85% of relapses were diagnosed in the first two years after therapy. Furthermore, local recurrences and regional lymph node failures were diagnosed in the first two years after treatment in 93.3% and 92.8% of cases, respectively. Instead, only 76.2% of metastases were diagnosed in the first two years. Furthermore, the rate of local-regional recurrences and distant metastases after ≥3 years of treatment was 6.9% and 23.8%, respectively. Finally, only 5% of the patients presented disease recurrence between 5 and 10 years after treatment, while none of the patients showed relapse ≥10 years after treatment.

Conclusions. Most LACC recurrences, and in particular local-regional recurrences, are diagnosed in the first two years after treatment, while treatment failures after five years are very rare (5.0%). Further studies would be useful to identify the patient groups for which intensive follow-up may allow an early diagnosis of LACC recurrence when patients are still in an oligorecurrent/metastatic stage.

Table 1.

Table 1: timing of the diagnosis of tumor relapse (numbers in brackets indicate percentages per line)

		Failure detected during					
	No.	1st year	2nd year	3rd year	4-5th years	6-10th years	>10th years
Local failures	30	19 (63.3)	9 (30.0)	1 (3.3)	0 (0.0)	1 (3.3)	0 (0.0)
Regional failures	28	17 (60.7)	9 (32.1)	1 (3.6)	1 (3.6)	0 (0.0)	0 (0.0)
Distant metastases	42	13 (31.0)	19 (45.2)	4 (9.5)	2 (4.8)	4 (9.5)	0 (0.0)
Treatment failure (all)	60	29 (48.3)	22 (36.7)	3 (5.0)	3 (5.0)	3 (5.0)	0 (0.0)

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INTENSITY MODULATED RADIATION THERAPY IN VULVAR CARCINOMA (VC): SURVIVAL OUTCOMES AND TOXICITY PROFILE ANALYSIS OF A MONO-INSTITUTIONAL EXPERIENCE

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Aims. To evaluate outcomes and toxicity of cohort of VC patients (pts) treated with Intensity Modulated radiation therapy (IMRT).

Methods. We retrospectively analysed VC pts who underwent IMRT at our institution. Toxicities were graded using the CTAE v5.0. The Kaplan–Meier method was used to estimate the rates of survival outcomes. The risk factors were performed with the log-rank test. The chi-square test (or Fisher's exact test) for ordinal and nominal variables was used to evaluate the association between toxicities and treatment.

Results. 17 pts were treated between May 2018 and August 2022. Median actuarial follow-up 31 (95%CI: 15.1-46.8) (range 6-58). Median age was 79 years (range 62-98). FIGO stage were IB in 6 pts, II in 2 pts, IIIA in 4 pts, IIIB in 2pts, IIC in 1 pts and IVA in 2 pts. Eleven pts received adjuvant RT, and 6 received definitive RT. Median RT dose to the vulva/vulvar bed and loco-regional nodes were 55 Gy (range 45-64) and 50.4 Gy (range 45-64) delivered in 28 fractions (range 25-33). Concurrent chemotherapy was used in 3 pts. Median treatment time was 43 days (range 33-77). Due to intercurrent acute toxicities 2 pts interrupted temporarily the RT for 4 and 5 days. Two and 7 pts experienced severe (>G3) gynaecological (vaginal mucositis) and skin acute toxicity (erythema), respectively. We reported only one late skin sever toxicity (cutaneous fistula). The use of concomitant chemotherapy was related to worst acute skin toxicity (p-value 0.026). Definitive treatments were related to worst GU and GI acute toxicity (p-value 0.041). Median OS was 37 months (95%CI:17.5-54.4). Six-months, 1 year- and 2 year- OS were 94.1%, 76.5% and 67% months, respectively. OS for histological grade 1-3 was statistically significant different (p<0.001). Five pts had local failure, median LC was 33.8 months (95%CI: 1-100) and 6 months- LC was 76.5 months. Histological grade G1-3 and unifocal *vs* multifocal were related to

worst LC with a p-value of 0.032 and 0.024. Eight pts had progression with a median PFS of 45 months (95%CI: 5.8-84.1), 6 months- 1 year- and 2 year-LC were 70.6%, 64.7% and 57.5%. Histological grades were statistically related to PFS: 6 months-PFS was 50%, 44.4% and 20% for grade 1, 2 and 3, respectively with a p-value 0.004. One patient developed lung metastasis.

Conclusions. IMRT for VC is well tolerated. Further studies with larger cohorts are encouraged in order to establish strategies to improve survival outcomes.

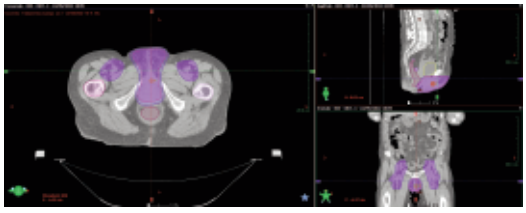

Figure 1.

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PELVIC INSUFFICIENCY FRACTURES IN CERVICAL CANCER AFTER DENITIVE RADIATION THERAPY

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Aims. The aim of this study is to correlate the incidence of Pelvic Insufficience Fractures with clinical and dosimetric factors in patients affected by cervical cancer treated with definitive radiochemotherapy.

Patients and Methods. Magnetic resonance imaging (MRI) of patients with cervical cancer treated with external-beam RT for the entire pelvic area between 2020 at 2021 in our institution were reviewed. Pelvic bone marrow was contoured for each patient and divided into three subsites: lumbosacral spine (LSBM), ilium (IBM) and lower pelvis (LPBM). The volume of each region receiving 10,20,30 and 40 Gy (V10, V20, V30, V40, respectively) and Dmean was collected. The clinical data such as age, BMI, comorbidity, steroid therapy before radiotherapy, menopausal state, smooking status, vitD dosage before and after radiotherapy were analyzed.

Results. A total of 78 patients were reviwed. Twenty-two patients (28 %) developed PIF in the irradiated field. Median age at onset of PIF was 51 (range 36-86). Thrity-two patients (41%) were in post menopausal state. We can find any correlations with dosiemtrica analyzed factors. Only clinical factors significantly correlated with PIF were BMI and age (p=<0.01 and p=<0.03, respectively).

Conclusions. In this prelimary study we can find some clinical factors (BMI and Age) correlated with PIF, without any dosimetric value. Further studies could be necessary to find other correlations.

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LOCALLY ADVANCED CERVICAL CANCER IN THE ELDERLY PATIENT, A SIGNIFICANT SUBGROUP THAT DESERVES OPTIMIZATION OF TREATMENTS

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Aims. With a prospective to personalized medicine that guarantees access to safe and effective oncological treatments, we have an exploratory evaluation of a sample of elderly patients treated at our Center for locally advanced cervical cancer, whose treatment was modulated according to age, comorbidities, geriatric assessment evaluated with the G8 scale.

Methods. We focused on 10 consecutive patients trated from January 2021 to December 2021 for locally advanced cervical cancer, 7 (70%) of whom with ≥75 years (range 75-88). HPV-correlated tumor was recorded in all the selected patients. All the patients were evaluated in a multidisciplinary meeting, the final clinical decision was taken also taking into account the geriatric evaluation with the G8 scale. In patients with G8 ≥14, a standard treatment was proposed, *i.e.* external beam radiotherapy (EBRT) concomitant to chemotherapy with weekly Cisplatin followed by brachytherapy boost (BCT) with high-dose rate (HDR); in patients aged ≥80 years and/or G8 <14 (2 (29%) for each category) exclusive EBRT+BCT treatment was chosen. We deliver a dose of 50Gy (normofractionation) for external beam radiotherapy (EBRT), with a helical modulated intensity technique, the second phase of treatment with brachytherapy previewed the use of RM-compatible endouterine applicators, that allow us to take also MRI for the HR PTV definition, the patients receveid 2800 cGy in 4 fractions of 700 cGy (EQD2 84Gy)

Results. Treatment tolerance was good, in patients who received multimodal treatment the total duration of treatment was 10 weeks, due to chemo-related G3 haematological toxicity which obliged treatment suspension. In the remaining patients, the treatment was completed within the expected 8 weeks. Regarding toxicity (CTCAE

v5.0), all patients complained of G1 dysuria, G1 tenesmus and G1 diarrhea, all resolved in 3 weeks with dietary modifications and probiotics alone. Of the late toxicities, 2 (29%) patients over 80 years developed significant vaginal stenosis which prevented the introduction of the vaginal speculum. At the last follow-up evaluation all the patient are NED.

Conclusions. Despite the relatively low incidence of cervical cancer in elderly patients, a patient-tailored approach may equally guarantee a great tolerance and oncological outcomes in this subgroup. A short geriatric evaluation with easy-manageable screening tools like G8 scale may help to offer the more appropriate, cost-effective, therapeutic approach.

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LOCAL CONTROL OUTCOMES USING SBRT-VMAT IN THE MANAGEMENT OF ENDOMETRIAL CANCER

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Aims. To determine long term outcome after Stereotactic Body Radiation Therapy (SBRT) using Volumetric Modulated Arc Therapy (VMAT) technique in patients with endometrial cancer.

Methods. Twenty-three patients (pts) with stage I and II endometrial cancer where selected for this study:10 pts underwent post-operative RT to the whole pelvis (WP) (prescribed dose of 50 Gy/25 fractions), followed by a sequential boost on the vaginal cuff, delivered with VMAT-SBRT (15Gy/3 fractions on alternate days); the remaining 13 pts were considered eligible for adjuvant vaginal brachytherapy (BV) but medical or other reasons prevented all of them from BV and they were therefore treated with VMAT-SBRT (30Gy/5fractions on alternate days). During treatment simulation, all pts were positioned in supine position with arms on the chest and with full bladder and empty rectum. A soft radiopaque transvaginal probe was used to define the vaginal cuff on CT scans. All plans were optimized in Monaco TPS using the Monte Carlo algorithm so that at least 99% of PTV would receive the prescription dose. Doses at OARs were kept as low as possible, respecting the constraints suggested in the AAPM TG 101. For each patient, daily CBCT was performed before each treatment fraction to correct for translations and rotations of patient positioning. Each patient underwent follow-up (FU) every six months. Late toxicity was scored according to the common Terminology Criteria for Adverse Events version 3.0 (CTCAE). Transvaginal ultrasound and pelvic MRI were used to assess local control at two years.

Results. Two over 23 pts died for secondary lung cancer; 3/23 pts were lost at FU. For the remaining 18 pts: 17/18 had G0 late GI and GU toxicities, while only one pts referred occasional rectal bleeding. No local recurrence was revealed at transvaginal ultrasound and pelvic MRI for 18/23 pts.

Conclusions. The SBRT-VMAT in management of endometrial cancer is feasible with a good profile in terms of acute and late toxicity with an excellent 2 years local control.

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ADJUVANT HIGH-DOSE-RATE VAGINAL BRACHYTHERAPY (HDR-VB) AS MONOTHERAPY IN EARLY STAGES ENDOMETRIAL CANCER (EC) WITH INTERMEDIATED AND INTERMEDIATED-HIGH RISK FACTORS WITH A SCHEDULE OF 25GY IN 5 WEEKLY FRACTIONS OF 5 GY

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Aims. to evaluate the toxicity and the outcomein I-II FIGO stage EC treated with high-dose-rate-brachytherapy (HDR-VB)withschedule of 25 Gy in 5weekly fractions of 5 Gy.

Methods. from 2014 to 2019seventy-oneconsecutive EC patients (pts) received adjuvant HDR-VB. The median age was 65 years (38-87yrs). All pts underwent primary surgery, 56,3% with and 43,7% without lymphadenectomy. Endometrioid was the prevalent histology(95,8%). FIGO stage distribution was: IA 25,4%, IB67,2% and II 7,4%.Tumor grade G1-2 was in 55 (77,5%) and G3 in 16 (22,5%) pts. Lymph-vascular space involvement (LVSI) in 8 (11,3%) pts. The pts risk was: 6 (8,5%)low, 48 (67,6%) intermediate,14(19,7%) intermediate-high and 3 (4,2%) high. Brachyvision treatment planning system and GammaMed device (HDRIr192) were used to plan and treat the pts.The median vaginal cylinder diameter was 3 cm. All pts were treated with schedule of 25 Gy in 5Gyx 5 weeklyfr at 0,3-0,5 cm depth from the vaginal surface. The CTV was the upper half of vagina (median =4.5 cm).Bladder, rectum and bowel were the OARs. Vaginal, gastro-intestinal and genito-urinary toxicity was graded according CTCAE 5.0 scale.

Late toxicity and recurrence were evaluated against age, grade, LVSI, stage, risk group,BMI, number of nodes removed, dose prescription depth. The Kaplan-Meier method was used to estimate rates of five-years LC,OS, DFS and CSS.

Results. The median follow-up was 65,3 months (14-97 months). Tumor relapsed, within the first 3 yrs, in 10 (14%) pts:3 (4,2%) vaginal, 1 (1,4%) pelvic, 5 (7%) distant and 1(1,4%) pelvic both distant.Late toxicities G2 were: 1 (1,4%)costipation, 1 (1,4%) incontinence, 2 (2,8%)vaginal dryness and 8(11,3%) vaginal stenosis. Age, BMI,>10 nodes removed, doseprescription depth, risk group,LVSI were not correlated with toxicity at univariate analysis. Only the stage IA and IB versus stage II (p=0.0001) were significantly correlated with DFS: 92,7% and 26,6% respectively. The 5-year OS, DFS, CSSand LC were 88.3%, 90%, 96,4% and 96,7% respectively.

Conclusions. There are no prospective data on the best schedule ofVB alone in EC, however our experience,produced similar results to the other studies. We reported 3 (4,2%) vaginal recurrences and 8 (11,3%) late G2 vaginal stenosis. No late G3-G4 toxicities were registered.Furthermore, our study population experienced a high vaginal control rate of 96,7%, with fractionation scheme of 25 Gy in 5Gy x 5 weekly fr

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INTRAOPERATIVE ULTRASOUND GUIDANCE DURING INTERVENTIONAL RADIOTHERAPY (BRACHITERAPY) IN LOCALLY ADVANCED CERVICAL CANCER: A MONOCENTRIC EXPERIENCE

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Aims. The standard of care for women diagnosed with IB2 to IVA cervical cancer (locally advanced cervical cancer- LACC) according to the Federation of Gynecology and Obstetrics staging (FIGO), is concurrent chemoradiation followed by intracavitary brachytherapy (BT). A Single session of BT for LACC is carried out using a specific applicator,according to the patient's anatomy and disease characteristics . The applicator is usually made up of two components: a vaginal applicator and an intrauterine tandem that is inserted through the cervical orifice. The insertion procedure can lead to uterine perforation. Intraoperative ultrasound (IUS) guidance can be a valid support to avoid this complication. Aim of this study is to show the role and benefits of IUS in cervical BT implants as experienced in our istitution.

Methods. Between January 2018 and December 2022, 240 patients with LACC were treated with primary radiation therapy including BT guided by IUS. The BT procedure in the operating room includes several stages: a pelvic examination of the patient, placement of a urinary catheter with a 100 ml bladder filling of saline solution for better uterine visualization and tandem's positioning by real-time ultrasound guidance. The ultrasound scanning with sagittal and or transverse sections allows verification of tandem that can be repositioned if it is shorter or more advanced, or stacked against the lateral, anterior or posterior walls of the uterus.

Results. In the period of observation 960 uterine insertions for BT were performed with US guidance. Only 23 of those insertions had a uterine perforation that was undetected with US (2 % rate). The perforation sites were the anterior, lateral and posterior wall. Uterine perforations occurred in patients with uterine fibromatosis, retroverted uterus, adherence to previous abdominal surgery, and interfraction changes in uterine position (anteverted to retroverted). When these complications were detected during the the CT or MRI simulation, the applicator was removed and, after a short period of observation, the patient was discharged. In all cases, no major complication such as a bowel or bladder perforation occurred.

Conclusions. Limitation of this retrospective study is that it does not compare US guided insertions with blind tandem insertions. However, in our experience, Intraoperative ultrasound is an essential tool for optimizing the placement of the uterine tandem and reducing the rate of uterine perforation.

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USE OF CONSCIOUS SEDATION IN INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY) FOR LOCALLY ADVANCED CERVICAL CANCER - OUR EXPERIENCE

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Aims. In patients with locally advanced cervical cancer (LACC), high–dose-rate brachytherapy (HDRBT) after chemoradiation (CRT) represents an efficient method for treatment delivery. During the treatment, there are multiple causes of considerable discomfort. Intrauterine tandem stimulates sympathetic autonomic afferents that enter the spinal cord at the T10-L1 level; this produces lower abdominal pain of cramping nature,

associated with nausea and vomiting. Vaginal packing and distension of the cervix and upper vagina stimulates somatic afferents via the pudendal nerves of S2-4 that cause lower back pain. For these reasons, the anaesthetist is a vital member of the HDRBT team for LACC in our institution. Aim of this analysis is to evaluate our experience of pain relief procedures.

Methods. All patients with LACC undergoing HDRBT at our institution were analyzed. Midazolam and an opioid were the main agents used to achieve conscious sedation. The procedure is repeated in the same way about 4 times. Drugs doses were personalized according to body weight and individual resistance. All dosages were registered at the end of each procedure. For each session, NRS pain scores ranging from 0 to 10 were registered by asking the patient at different times during the procedure. Procedure duration and recovery time for each patient were also recorded.

Results. From Jan 2019 to Dec 2022, 190 patients underwent 760 HDRBT procedures. The median duration of the whole BT procedure was 3,6 hours. Duration of the sedation was about 15 minutes, and no significant cardiovascular events during this period were noted. Total dose of intravenous (IV) midazolam used ranged from 0.5 mg to 8 mg (median: 2 mg). Total dose of IV morphine equivalent used ranged from 2.5 mg to 65 mg (median: 8.5 mg). Mean and median pain scores during the procedures were 1.6 and 1 respectively. Brief moments of moderate to severe incidental pain were associated to specific parts of the procedure. Maximal pain score during the entire procedure ranged from 0 to 10 (median: 4.9). Recovery period from conscious sedation was brief (median discharge time: 1 hour).

Conclusions. HDRBT for patients with LACC is usually completed in a few hours; good pain control with conscious sedation with fentanyl and midazolam was achieved. Relatively brief periods of moderate to severe incidental pain were noted at times of applicator manipulation. Once the applicators are withdrawn, there are no further analgesic requirements.

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POST-OPERATIVE KELOIDS IRRADIATION (POKER): DOES THE SURGERY/HIGH-DOSE INTERVENTIONAL RADIOTHERAPY ASSOCIATION MAKE A WINNING HAND?

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Aims. Keloids are common following surgeries, traumas, or minor skin stimulations. Radiotherapy has been used for over a century to treat keloids, and recent studies have supported the use of post-operative interventional radiotherapy (POIRT) as an adjuvant treatment. The aim of our work is to report the results involving POIRT approach in a homogenous cohort of patients affected by keloid and treated at a single institution with the same fractionation schedule.

Methods. Inclusion criteria were as following: 1) surgery with a histopathological diagnosis of keloid, 2) subsequent high-dose rate interventional radiotherapy (HDR-IRT) with prescription dose to clinical target volume of 12 Gy in 4 fractions (3 Gy/fr) administered twice a day with at least 6 hours between, 3) follow-up period of at least 24 months.

Results. One-hundred and two patients and a total of 135 keloids were eligible for the analyses. The median follow-up was 64 [interquartile range: 25 - 103] months. In our cohort 36 (26.7%) recurrences were observed, 12-months and 36-months cumulative incidence of recurrence were 20.7% (95% CI: 12.2 - 28.5) and 23.8% (95% CI: 14.9-31.7) respectively. History of spontaneous keloids (HR=7.00, 95% CI: 2.79 -17.6, p<0.001), spontaneous cheloid as keloid cause (HR=6.97, 95% CI: 2.05 - 23.7, p=0.002) and sternal (HR=10.6, 95% CI: 3.08 -36.8, p<0.001), ear (HR=6.03, 95% CI: 1.71-21.3, p=0.005) or limb (HR=18.8, 95% CI: 5.14-68.7, p<0.001) keloid sites were significantly associated to a higher risk of recurrence.

Conclusions. The findings support the use of surgery and POIRT as an effective strategy for controlling keloid relapses. Further studies are needed to identify the optimal Biologically Effective Dose (BED) for keloid treatment and to establish a scoring system for patient selection for surgery and radiotherapy.

P332

EXCLUSIVE OR ADJUVANT HIGH DOSE RATE BRACHYTHERAPY FOR EARLY-STAGE LIP CANCER IN THE MODERN ERA OF INTERVENTIONAL RADIOTHERAPY, A SINGLE CENTRE EXPERIENCE

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Aims. Interventional radiotherapy (IRT), also known as brachytherapy, has proven its utility in the treatment of localized tumors. The aim of this paper is to evaluate efficacy of modern IRT in early-stage lip cancer, in terms of clinical outcome and safety.

Methods. Between December 2011 and February 2023, a series of 24 patients with 25 lip cancers were treated by exclusive or adjuvant interstitial high-dose-rate IRT. Twenty-two patients with 23 tumors were evaluable for the analysis, the other 2 were lost at follow-up. The median age and KPS of the patients were 75.5 years (range, 46-91), and 90% (range, 80-100), respectively. Adjuvant IRT was performed in 11 patients for 11 tumors with close or positive margins, radical treatment in the other 11 patients for 12 tumors. Stages were cT2N0 in 3, cT1N0 in 2, recurrent disease in 8, pT1-2 with close or positive margins in 11 cases, respectively. Site of disease was superior lip in 5, commissure in 1 and inferior lip in the last 17 lesions, respectively. Histology was squamous cell carcinoma in 20 cases and basocellular carcinoma in other 3 cases. In adjuvant setting IRT was performed with 8 fractions of 4 Gy, in radical setting with 9 fractions of 4 Gy. Two fractions per day with a minimal gap of 6 h was delivered.

Results. After a median follow-up of 31 months (range, 6-124), the 5 years cancer specific and overall survival was 87 % and 58% respectively. The local control was 86% al 74% at 1 and 2 years, respectively. Pain and oedema were registered during treatment in all patients, acute G1-G2 mucositis in 5 patients, no severe acute and chronic toxicities were recorded.

Conclusions. High-dose-rate IRT is effective and safe for patients with early stage lip cancer both in adjuvant than radical settings. Our results are slightly lower respect to literature, to increase clinical outcome we will explore higher doses and a better selection on patients with really initial early stage lip cancer.

P333

HDR BT TREATMENT OF NON-MELANOMA SKIN CANCER: OUTCOME AND FEASIBILITY IN A RETROSPECTIVE ANALYSIS

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Aims. To evaluate local control, toxicity, and cosmetic outcomes in NMSC treated with high-dose-rate BT (HDR-BT).

Methods. From October 2007 to January 2023, 56 lesions in 48 elderly eligible patients were analyzed. The histological subtypes were: 76.8% squamous cell carcinoma, 12.5% basal cell carcinoma, 3.6% Sarcoma and 7.1% other hystologies (2 cases of mycoses fungoides, 1 case of cutaneos lymphoma and 1 case of mixed squamous cell carcinoma and basal cell carcinoma). Median age at the diagnosis was 78,5 (48,5-102,4) years. A surface flap was customized to the size of each target lesion and the catheters were embedded; every treatment was optimized with 3D planning using CT imaging. Different prescribed doses and fractionation have been chosen: 24-31.5 Gy in 8-12 fractions for palliative treatment (6 cases, 11%), 34-52 Gy in 10-20 fractions for adjuvant treatment (33 cases, 59%) and 36,75-60 Gy in 7-30 fractions for radical treatment (17 cases, 30%); the average biological effective dose (BED) was 35.7, 51 and 60.9, respectively. The treatment was mostly delivered with daily fraction and some schedules were accelerated with 2 fractions a day. Acute and late toxicity were recorded according to CTCAE 4.0.

Results. At a mean follow-up of 27,2 (2 – 145) months local control was 91%. Fifteen out of 17 lesions (88%) who received a radical dose showed a complete response, one had a partial response and one showed progression disease. One patient with squamous cell carcinoma had local recurrence after 2 years. Among the patients treated with an adjuvant BRT 2 patients (6%) had local recurrence (after 4 months and 1 year). In both cases the histology was squamous cell carcinoma. In the palliative group 3 lesions (50%) had a partial response and just 1 case developed a progression. No severe acute toxicity was recorded; just 30% of the cases presented G2 acute toxicity, recovered within 2 months from the end of BRT. Late toxicity was G2 in 23% of the lesions and G3 in 4% of the lesions, no greater late toxicity was recorded. Excellent cosmetic results were observed in 50% of the lesions; only 4 cases (7%) reported a fair cosmetic result and no poor cosmetic result were observed.

Conclusions. HDR-BRT represents an effective and safe solution for the treatment of NMSC, even in elderly population, with excellent clinical outcome and very low toxicity. More data with a longer follow-up are necessary.

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ELDERLY PATIENTS WITH NON MELANOMA SKIN CANCERS (NMSC) TREATED BY CONTACT HIGH DOSE RATE BRACHYTHERAPY(CHDR BRT) AND INTERSTITIAL HIGH DOSE RATE BRACHYTHERAPY (IHDR BRT)

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Aims. Non Melanoma skin cancers(NMSC) are the

most common human malignancy in the world with increasing incidence in recent years. In this study shows the data concerning elderly patients affected by NMSC treated with high dose rate interstitial and contact brachytherapy (contact High Dose Rate Brachytherapy , cHDR – BRT , interstitial High Dose Rate Brachytherapy, iHDR - BRT).

Methods. Patients with NMSCs enrolled in the study underwent cHDR BRT or iHDR – BRT. Applicators were used: Freiburg Flap or silicone mold in the cHDR BRT, flexible catheters and needles for the iHDR – BRT. The source used is I'192 with remote afterloading.

Results. From May 2021 to May 2023, 22 patients aged between 65 and 98 years were treated: 18 with cHDR BRT and 4 with iHDR – BRT, 10 patients with primary BRT, 9 patients with adjuvant BRT and 3 patients with palliative/cytoreductive BRT, for a total of 27 lesions, with the following histological types: basal cell carcinoma, squamous cell carcinoma, pleomorphic sarcoma, Merkel cell carcinoma. The fractionation schemes used were the following: 45/40 Gy in 9/8 fractions, 35/30 Gy in 7/6 fractions, 50 Gy in 10 fractions bid. Three patients had acute G3 toxicity with resolution within three months. Twenty patients are currently in the absence of local recurrence. Two patients died of causes unrelated to the oncological disease in the absence of local recurrence.

Conclusions. cHDR BRT is a safe and effective therapeutic option well tolerated for elderly patients with NMSC with good results in terms of toxicity and local control disease.

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PSMA-PET AND PCA: AN EXPLORATORY ANALYSIS BEYOND THE NUMERICAL DEFINITION OF OLIGOMETASTATIC STATE

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Aims. Oligometastatic disease usually relies only on the number of radiological localizations. The aim of this study is to evaluate the predictive value of volumetric parameters derived from prostate-specific membrane antigen/PET (PSMA-PET) in oligorecurrent PCa patients. The study is a spin-off analysis of the ongoing phase II randomized trial RADIOSA (NCT03940235).

Methods. Patients enrolled within the RADIOSA trial who underwent PET-PSMA at first biochemical recurrence were included. Two experienced nuclear medicine specialists retrospectively reviewed PSMA-PET images blinded to all histopathological and clinical data. PSMA-PET quantitative parameters PSMA tumor volume (PSMA-TV) and Maximum standardized uptake values (SUVmax) were collected. Patients were stratified according to these two parameters, PSA at the first diagnosis and at the first recurrence, time between the diagnosis and the first recurrence and the site of oligometastases (bone or lymph nodal).

Results. A total of 46 patients were included. Median PSA values at the first diagnosis and at the oligorecurrence were 7.62 ng/mL and 1.27 ng/mL, respectively. Median time between first diagnosis and oligorecurrence was 46 months. A total of 29 patients had only lymph nodal localization, while 17 had at least one bone localization. Considered variables across the different subgroups are shown in Table 1. When stratified according to the median PSA at diagnosis, Median SUVmax resulted higher in patients with a PSA above the median value while median PSMA-TV and time to recurrence were comparable in both groups. When stratified according to the median PSA at recurrence, Median SUVmax resulted higher in patients with an higher PSA (> 1.27) ng/ml, while patients in the lower PSA group had a smaller PSMA-TV (1.75 *vs* 2.28 cm3). Patients with a longer median time to recurrence had a higher median PSA at the recurrence. When grouping patients according to the metastatic site, those with at least one bone metastases had a shorter time interval between first diagnosis and recurrence and a lower median SUVmax.

Conclusions. Patients with higher PSA values both at first diagnosis and at the recurrence have an higher median SUVmax, and patients with a lower PSA at the oligorecurrence had a lower lesion volume (median PSMA-TV 1.75) and a shorter time at the recurrence. These very preliminary data suggest that PSMA-PET-derived quantitative indexes could be useful for staging, in particular the volumetric parameters.

Table 1. Median MaxSUV, PSMA-TV and time to recurrence for patients stratified according to PSA and lesion site.

	PSA at diagnosis* ≤ 7.62 ng/ml (n = 22)	PSA at diagnosis* > 7.62 ng/ml (n = 22)
Median SUVmax (total, all lesions)	9.08	15.60
Median PSMA-TV (cm³)	2.17	2.03
Median time to recurrence (months)	49.6	45.3
	PSA at recurrence ≤ 1.27 ng/ml (n = 23)	**PSA at recurrence > 1.27 ng/ml (n = 23)**
Median SUVmax (total, all lesions)	9.56	13.87
Median PSMA-TV (cm³)	1.75	2.28
Median time to recurrence (months)	45.3	69.9
	Lymph node lesions (n = 29)	**Bone lesions (n = 17)**
Median SUVmax (total, all lesions)	14.30	10.97
Median PSMA-TV (cm³)	2.05	2.20
Median time to recurrence (months)	47.9	40.4

*List of abbreviations: PSMA-TV (PSMA tumor volume); PSA (prostate specific antigen); SUV (standardized uptake value). *Missing data for 2 patients*

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STEREOTACTIC RADIOTHERAPY IN BRAIN OLIGOMETASTATIC PATIENTS

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Aims. Brain metastases are common metastases in adults, accounting for more than half of all intracranial tumors. They are commonly associated with breast, lung cancer, melanoma and, occasionally colorectal and kidney carcinoma. Stereotactic radiotherapy (single or multi fractions) could be an option for patients with good performance status and controlled primary disease.

Methods. The standard treatment in our Istitution for oligometastatic pts is stereotactic radiotherapy. From 2018 to 2023, we treated 417 pts with brain metastases, 85 pts (156 lesions) had brain oligometastatic disease. The median age was 64 yrs, KPS between 100-70%, all pts had controlled primary disease and a life expectancy more than 3 months. Primary tumor sites are summed in Table 1. 75% pts received immunotherapy, 20% target agent and 5% chemotherapy. The single brain metastases were observed in 267 pts (64%) and multiple brain metastases in 108 (26%). Doses prescriptions were 18-21 Gy in Stereotactic Radio-Surgery (SRS), 24-27Gy in fractionated stereotactic radiotherapy (fSRT). Plan CT slice thickness was 1.25-2.5 mm. MR sequences (1–3- mm slice thickness, enhanced T1) were used to define the target and organs at risk. The planning target volume was defined by 1 mm margin expansion from GTV. VMAT plan was generated using two no coplanar volumetric modulated arcs and 6MV.FFF energy and IGRT treatments were delivered using robotic couch with 6 degrees of freedom. In case of progression of disease (PD) a fSRT/SRS retreatment was often considered.

Results. At time of the first follow up (interval: 2-6 mth) 271 pts (65%) had partial remission (PR), 104 pts (25%) had complete response (CR), 42 pts (10%) PD. At time of the second FUP (6-12 mth) 83 pts were lost, 167 pts presented PD. At least, between 12-36 mth, 17 pts were alive but in PD.We reported as acute toxicity within six months, according to the Common Terminology Criteria for Adverse Events version 5.0, edema in 95% and convulsion in 5% of pts. Chronic toxicities (from six months to last follow-up or death) were repeated seizures in 50%, radionecrosis in 40% and panhypopituitrism in 10% of pts.

Conclusions. In our experience, both SRS and fSRT has provided a satisfactory local control rate with a low toxicity profile According to a rigid follow-up protocol, any PD was early detected and a possible re-irradiation proposed, delaying a possible palliative whole brain irradiation and granting a slower neurocognitive decline.

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OLIGOMETASTATIC SARCOMA TREATED WITH CURATIVE INTENT ABLATIVE RADIOTHERAPY (OSCAR): A MULTICENTER STUDY ON BEHALF OF THE AIRO (ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY) "BIOLOGY AND TREATMENT OF OLIGOMETASTATIC DISEASE" STUDY GROUP

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Aims. Stereotactic Ablative Radiotherapy (SABR) is emerging as a valid alternative to surgery in the oligometastatic setting in soft tissue sarcomas (STS), although robust data are lacking due to the rarity of the disease. The aim of this retrospective multicentric study is to evaluate toxicity and efficacy of SABR in oligometastatic (≤ 5 lesions) STS.

Methods. This is a retrospective multicentric study including adult patients (≥18 years) affected by stage IV STS, treated with stereotactic radiotherapy for a maximum of five cranial or extracranial metastases in up to three different organs. SABR had to be delivered with ablative purposes (50Gy EQD2/10 delivered in a maximum of 12 fractions as per Oligocare definition). Primary endpoint is overall survival (OS). Secondary endpoints are local control (LC), distant progression free survival

(DPFS), time to polymetastatic progression (TTPP) and toxicity.

Table 1.

Patient and primary disease		
Variable	Number	Percentage
Sex: male	56	40.6%
female	82	59.4%
Performance status: 0	81	58.7%
1	44	31.9%
2	13	9.4%
Age (median/range)	54 years (18-88)	
Primary site: Limbs	50	36.3%
Trunk	38	27.5%
Pelvis	37	26.8%
Other	13	9.4%
Histology: Lipo/leio/Sinovial/UPS	98	71%
Ewing/RMSA/small cell	3	2.2%
Other	37	26.8%
Grading: G1	10	7.2%
G2	29	21,1%
G3	82	59.4%
Missing	17	12,3%
Metastatic disease characteristics		
Disease Free Interval (median/range)	3 years (0-21)	
Oligometastasis classification: de novo	77	55.8%
Induced	46	33.3%
Oligopro	15	10.9%
Previous metastasectomy: no	61	44.2%
yes	77	55.8%
Previous systemic therapy: no	53	38.4%
1 line	53	38.4%
≥ 2 lines	32	23.2%
SBRT		
Number of irradiated lesion(s): 1	88	
2	36	
≥3	12	
Irradiated site(s): lung	93	
Liver	14	
Nodes	6	
Other	25	
BED (median/range)	98.9 Gy (35.7-180)	

Abbreviations: UPS undifferentiated pleomorphic sarcoma; RMSA rabdomiosarcoma; BED biologically effective dose

Results. From 10 Italian RT centers, 138 patients were enrolled in the study. Patients were treated between November 2010 and October 2022. Patients and treatment characteristics are shown in Table 1. Treatment was generally well tolerated. Only 13 patients (9.4%) experienced acute toxicity, no G3 or G4 toxicity was recorded. Most common side effects were asthenia, esophagitis and pain. Toxicity profile was excellent also for late toxicity, with 3 cases of G1 cough, 2 patients with dyspnea (G1 and G2) and one case of pneumonitis G2 and esophagitis G2. At last follow up, 60 (43.4%) patients died (all but 7 due to sarcoma). Median OS was 39.7 months. Rates of OS at 1 and 2 years were 91.5% (84.9-95.3) and 72.7% (63.3-80.1). At multivariate analysis, PS and grading were correlated with OS. Sixteen patients had in field recurrence (11.5%), while 111 (80.4%) relapsed in distant sites. Rates of LC at 1 and 2 years were 94.8% (95%CI 88.8-97.6) and 88.0% (79.7-93.1). Grading was the only factor impacting on LC at multivariate analysis. Median DPFS was 9.7 months. Rates of DPFS at 1 and 2 years were 40.8% (31.9-49.4) and 19.4% (12.8-27.2). Again grading was statistically correlated with DPFS. Seventy-five patients (54.3%) had a polyprogression during follow up. Median time to polyprogression (TTP) was 27.8 months. Rates of TTP at 1 and 2 years were 72.1% (63.4-79.2) and 53.9% (44.3-62.6).

Conclusions. SABR is a safe and effective approach for the treatment of oligometastatic sarcoma. One out of 5 patients is free of progression at 2-years.

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STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR BONE METASTASES: COMPARISON BETWEEN SINGLE AND MULTIFRACTIONS TREATMENT

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Aims. Metastatic bone involvement is a frequent event in cancer patients (pts). Stereotactic Body Radiation Therapy (SBRT) is increasingly used for spinal and non-spinal bone metastases in clinical practice, due to good pain and local control. The aim of this study is to report our experience with robotic SBRT delivered with CyberKnife™ (Accuray, Sunnyvale, CA, USA), comparing different fractionation schedules, in terms of efficacy and toxicity.

Methods. Between October 2017 and March 2023 210 treatments were delivered in 133 pts. Median age at SBRT was 72 (21-91) years. Primary tumor was prostate in 76 pts, breast in 20 pts, lung in 14 pts, and other histologies in the remaining pts. For spine metastases, Clinical Target Volume (CTV) was defined according to the International Spine Radiosurgery Consortium consensus guidelines. Single fraction (SF) SBRT was delivered in 128 treatments and Multi Fraction (MF) schedules were used for 82 treatments. Median prescribed dose was 18 Gy (18-21) at a median isodose of 79% (69%-83%), for SF, and 25 Gy (12-35) in 2 to 5 fractions at a median isodose of 78% (67%-82%), for MF. Prophylactic steroid therapy was administered to 66 pts. Toxicity was assessed with CTCAE version 5.0 criteria.

Results. Median follow-up was 33 (0.4-65.4) months. Acute toxicity was as follows: one patient presented G2 hyposthenia and paresthesia of the lower limb, 4 pts G1 back pain, 2 pts G1 nausea. Two late lumbar spinal fractures were registered, at 20 and 60 months after SBRT, respectively. Local relapse free survival (LRFS) was 87.1% at 12 months, 78.8% at 24 months and 72.6% at 36 months. Median distant metastases free survival (DMFS) was 9.8 months (3-66.6). Among pts who experienced distant progression after spine SBRT, 26.2% were

oligoprogressive. Overall Survival (OS) at 12, 24, and 36 months was 83.3%, 61.9%, and 51.2%, respectively. A trend for a significant difference in OS in favor of single *vs* multiple SBRT fractions was observed (Figure 1): 38.9 *vs* 28.4 months (p=0.06). Of the 37 patients who reported pain, 81% presented a complete pain response after SBRT.

Conclusions. SBRT of bone metastases is an effective and well tolerated therapy, with both good local control and pain control. A low risk of late fracture was observed in our cohort. A higher number of patients and a longer follow-up are needed to show a difference between different SBRT schedules.

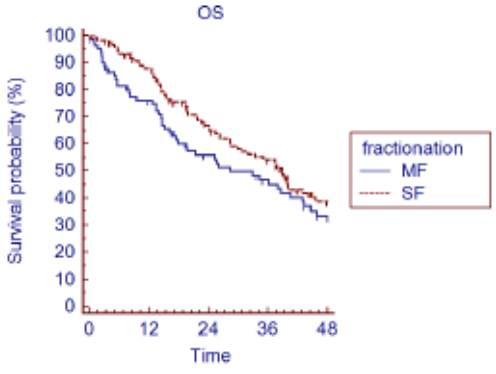

Figure 1. Overall Survival in the single fx *vs* 3-5 fx treatments.

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CLINICAL EFFICACY OF STEREOTACTIC BODY RADIOTHERAPY AS ADRENAL GLAND METASTASIS-DIRECTED THERAPY IN OLIGOMETASTATIC PATIENTS

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Aims. Adrenal gland metastases (AGMs) represent a common manifestation of metastatic tumor spread. In oligometastatic patients (OMPs), effective treatments for AGMs are needed. Aim of the present study was to evaluate the clinical efficacy of Stereotactic Body Radiotherapy (SBRT) as adrenal gland metastasis-directed therapy in OMPs.

Methods. Oligometastatic patients treated at our Institution with SBRT for AGMs were retrospectively analyzed. All patients were clinically and radiologically evaluated during and after completion of SBRT. Study endpoints were local progression-free survival (LPFS), disease free survival (DFS), overall survival (OS), and toxicity. Survival was estimated by the Kaplan-Meier method and factors potentially affecting outcomes were analyzed with Cox regression analysis.

Results. From January 2017 to December 2022, 32 OMPs according to ESTRO-EORTC criteria, accounting for 35 AGMs, received SBRT as metastasis-directed therapy (Table 1).

Table 1. Patients and lesions characteristics.

Patients, n		32
Treated AGMs, n		35
Sex, n (%)	Female	12 (37.5)
	Male	20 (62.5)
Age, median (IQR)		68 (62.7-74.5)
Primary tumor, n (%) *	Lung	26 (81.2)
	Renal	5 (15.6)
	Other	1 (3.1)
Histology, n (%) *	Adenocarcinoma	20 (62.5)
	Clear cell	5 (15.6)
	Small cell	4 (12.5)
	Other	3 (9.4)
AGM classification, n (%) ^	De-novo	9 (28.1)
	Repeat	13 (40.6)
	Induced	10 (31.2)
AGM timing presentation, n (%) ^	Synchronous	8 (25.0)
	Early metachronous (6-24 months)	9 (28.1)
	Late metachronous (> 24 months)	15 (46.9)
AGM side, n (%) ^	Right	15 (42.9)
	Left	20 (57.1)
Patients at high risk of adrenal insuffiency, n (%) °		4 (12.5)
Pre-SBRT systemic therapy, n (%) *	Chemotherapy	3 (9.4)
	Immunotherapy	11 (34.4)
	Target therapy	5 (15.6)
	Combination	7 (21.9)
	No systemic therapy	6 (18.8)
Total number of OM, n (%) §	1	22 (68.8)
	2	3 (9.4)
	3	2 (6.2)
	4	3 (9.4)
	5	2 (6.2)
Dose and fractionation, n (%) ^	30-35 Gy/5 fractions	9 (25.7)
	40-50 Gy/5 fractions	16 (45.7)
	Other	10 (28.6)
BED_{10}, Gy, median (IQR) ^		70 (48-72)
GTV, cc, median (IQR) ^		11.8 (8.9-23.9)
PTV, cc, median (IQR) ^		41.7 (29.3-61.4)

AGMs: adrenal gland metastases; IQR: interquartile range; OM: treated oligo-metastases; Gy: gray; BED: biological effective dose GTV: gross tumor volume; PTV: planning target volume; cc: cubic centimeters.
* per patient
^ per lesion
§ per radiotherapy course
° 3 patients with bilateral AGMs irradiation, and 1 patient treated after contralateral adrenalectomy

Most AGMs originated from non-small cell lung cancers (71.9%). SBRT was prescribed to a median biological effective dose (BED_{10}) of 70 Gy (IQR 48-72 Gy), delivered in 5 fractions (IQR 5-5). Median gross tumor volume (GTV) and median planning target volume (PTV) were 11.8 (IQR 8.9-23.9) and 41.7 (IQR 29.3-61.4) cc, respectively. Median estimated follow-up was 16.3 months (95% CI 7.4-18.5). Overall local control rate based on RECIST criteria was 80% (CR = 17.1%, PR=45.7%, SD=17.1%), with a 1- and 2-year LPFS rates of 81.2% (95% CI 62.7-91.1) and 73.1% (95% CI 48.0-87.4), respectively. A PTV BED_{10} dose >70 Gy was correlated with improved LRFS (2-year LPFS 83.3% BED >70 Gy *vs* 61.9% BED <70 Gy, *p*=0.027). One- and 2-year DFS rates were 36.6% (95% CI 18.8-54.5) and 32.0% (95% CI 15.2-50.2), respectively, and the corresponding OS rates were 62.8% (95% CI 40.0-79.0) and 51.4% (95% CI 28.6-70.2), respectively. At univariate analysis, less than 3 SBRT-treated oligometastatic sites correlated with survival (HR for DFS 0.30 [95% CI 0.11-0.80], *p*=0.016, and HR for OS 0.24 [95% CI 0.07-0.82], *p*=0.023). No SBRT-related adverse events G>2 occurred, and no cases of adrenal insufficiency were recorded (hormonal and electrolytes testing showed only transient vari-

ation within the reference range).

Conclusions. SBRT represents an effective option as metastasis-directed therapy for adrenal gland metastases in OMPs. A prescribed dose corresponding to a BED_{10} >70 Gy correlates with improved local control.

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THE EFFICACY AND FEASIBILITY OF STEREOTACTICT BODY RADIATION THERAPY IN OLIGOMETASTATIC PATIENTS WITH HEAD AND NECK TUMOR: A RETROSPECTIVE STUDY

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Aims: Oligometastatic disease affect up to 40% of head and neck cancer (HNC) patients who develop metastases. Local treatment of all oligometastatic sites may prolong survival in selected patients. The SBRT is a non-invasive alternative local approach with encouraging data in HNC. The objective of this study was to assess the efficacy of SBRT and identify predictive factors in oligometastatic HNC patients.

Methods. Patients with oligometastatic HNC treated with SBRT between 2013 and 2022 were retrospectively collected. Local control (LC), progression-free survival (PFS), overall survival (OS) were evaluated.

Results: In total, 72 lesions were treated with SBRT in 36 patients. The lung was the common site of metastases. In most cases, patients had oligorecurrent disease. The median prescription dose was 48 Gy in 4 fractions, with a biologically effective dose (BED) of 100 Gy considering α/β of 10. Characteristics are reported in Table 1. The median follow-up was 26.9 months. Median OS was 59.3 months; 1- and 3-year OS rates were 80.3% and 59.9%. At univariate analysis, gender (p=0.007), disease-free interval (p=0.008), primary tumor histology (p=0.000), systemic therapy before SBRT (p=0.021), site of lesions (p=0.014), time to SBRT (p=0.037) and multiple SBRT course (p=0.005) were associated with OS. At multivariate analysis, salivary primary histology (p=0.004) and systemic therapy before SBRT (p=0.015) remained positive predictors of OS. Median LC was not reached; 1- and 3-years rates were 83% and 74.5%. At univariate analysis, number of treated lesions (p=0.035) and previous local treatment (p=0.000) were predictive factors for LC. At multivariate analysis, number of lesions (p=0.003) remained statistically significant. The PFS rates at 1 and 3 years were 45.7% and 13.4%. None of the analyzed factors was associated with PFS. Median time to next systemic therapy (TTNS) was not reached; 1- and 3-years rates were 84% and 66%. Salivary histology (p=0.018), oligorecurrent disease (p=0.025) and complete ablation (p=0.048) were independent predictive factors of TTNS at multivariate analysis.

Conclusions. SBRT is feasible and effective in oligometastatic HNC patients. This approach has an acceptable toxicity profile and may improve survival, especially in the presence of salivary primary histology and in patients who received systemic therapy before SBRT.

Table 1. Patients' and disease's characteristics.

	N. (%)
Age, median (range)	71 years (32 – 85)
Sex	
Male	29 (80.6%)
Female	7 (19.4%)
Primary tumor site	
Oral cavity	5 (13.9%)
Larynx	14 (38.9%)
Nasopharynx	4 (11.1%)
Oropharynx	5 (13.9%)
Salivary glands	7 (19.4%)
Paranasal Sinus	1 (2.8%)
Primary tumor histology	
Squamous cell carcinoma	24 (66.7%)
Salivary	10 (27.8%)
Others	2 (5.5 %)
Metastases treated with SBRT	72
Lung	46 (63.9%)
Nodes	8 (11.1%)
Liver	9 (12.5%)
Bone	7 (9.7%)
Adrenal	2 (2.8%)
Pattern of metastases	
Oligorecurrent	63 (87.5%)
Oligoprogressive	9 (12.5%)
Dose of **SBRT** (Gy), median (range)	48 (30-75)
fractions, median (range)	4 (3-8)
BED_{10}, median (range)	100 (60-262.5)
Systemic Therapy before SBRT	
Yes	13 (36.1%)
No	23 (63.9%)

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STEREOTACTIC BODY RADIATION THERAPY (SBRT) IN PATIENTS WITH PANCREATIC OLIGOMETASTASES FROM RENAL CELL CARCINOMA: A SINGLE-CENTER EXPERIENCE

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Aims. The pancreas represents an uncommon site of metastasis in renal cell carcinoma (RCC) and it is associated with a favorable prognosis in the oligometastatic disease. Stereotactic body radiation therapy (SBRT) is an effective and safe non-invasive local therapy for inoperable oligometastatic patients from various primary tumors. The purpose of this study was to evaluate the safety and efficacy of SBRT in selected RCC patients with pancreatic oligometastases unfit for surgery.

Methods. A retrospective study focused on inoperable RCC pancreatic oligometastases treated with SBRT from January 2017 to February 2023 in our Institution was performed. All patients were treated with a prescription dose of 45 Gy in 6 consecutive daily fractions using the technique of modulated arc volumetric therapy (Figure 1). The biologically effective dose (BED) of the total prescribed dose was 78.7 Gy, considering an α/β of 10. Local control (LC), progression-free survival (PFS) and overall survival (OS) were calculated. The univariate analysis was performed to identify variables associated with outcomes.

Results. In total 24 patients were included in the analysis. Most of them were male (n=20). The median age was 67 years (51-81). Thirty-one pancreatic lesions were treated with SBRT. Median lesion size was 1.6 cm (0.5-7.7). The pancreatic metastasis was the single site of disease in 54.2% of cases. Eight patients (33.3%) received systemic therapy before SBRT. The median follow-up was 17 months (3-60). The median time from diagnosis of primary RCC to pancreatic metastasis was 11 years (2-30). Local failures were observed in 3 patients. The LC rates at 2 and 4 years were 100% and 75%, respectively. Median PFS was 23 months, with a rate at 1 year of 77%, 2 years 48% and at 4 years of 32%. At time of analysis, 87.5% of patients were alive (n=21). The OS rates at 2 and 4 years were 94% and 82%, respectively. At univariate analysis, the size of lesions treated with SBRT was significantly correlated with LC (p=0.008) and OS (p=0.014). No Grade 3 or higher adverse effects were observed.

Conclusions. SBRT for pancreatic lesions in oligometastatic RCC was feasible with acceptable toxicity. Considering the excellent local control especially in small lesions, this approach appeared to be an effective treatment paradigm for patients unfit for surgery. However, more data are needed to evaluate the factors that may aid in the patient selection to improve outcomes after SBRT.

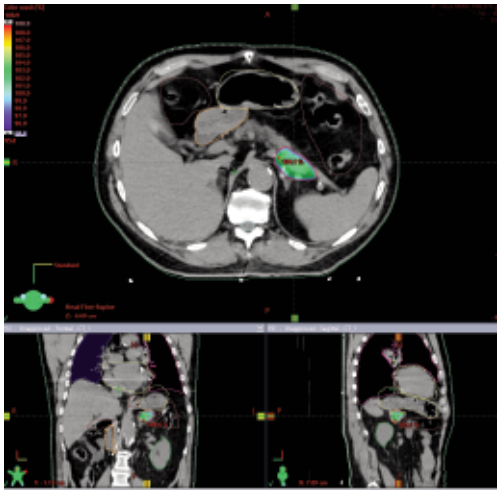

Figure 1.

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STEREOTACTIC RADIATION THERAPY AND IMMUNOTHERAPY IN OLIGOPROGRESSIVE AND OLIGOPERSISTENT PATIENTS OUTCOMES AND PROGNOSTIC FACTORS: OLIGOPROIMMUNO RETROSPECTIVE STUDY

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Aims. Few evidences are available about the combination of immune checkpoint inhibitors (ICI) and stereotactic radiation therapy (SRT) in oligoprogressive and oligopersistent patients. The aim of this study was to evaluate clinical results and prognostic factors in oligometastatic patients treated with SRT during ICI.

Methods. This mono-institutional retrospective study including oligoprogressive and oligopersistent patients treated with SRT during ICI from February 2015 to August 2022. Overall Survival (OS), Progression free survival (PFS), Local control (LC) and time to the next treatment at progression (TTNT) were evaluated. Acute and late toxicities were recorded.

Results. Between February 2015 and August 2022, 45 patients were treated with SRT on oligoprogressive or oligopersistent site(s) during administration of immunotherapy. Median age was 61 years. Most of patients were treated in an extracranial organ. Median BED was 81,6 Gy. No patient had G2 or higher acute toxicities. Patients and disease characteristics are summarized in Table 1.

Table 1. Patients and disease characteristics.

Characteristics	Individuals	Percentage
Gender		
Male	18	40%
Female	27	60%
Presence of comorbidities		
Yes	28	62.2%
No	17	37.8%
PS		
0	39	86.7%
1	6	26.7%
Smokers		
Active	9	20%
Ex	18	40%
No	18	40%
Site of primary disease		
Kidney	4	8.9%
Cervix	1	2.2%
Bladder	1	2.2%
Melanoma	18	40%
Colon	2	4.5%
Esophagus	1	2.2%
Lung	18	40%
Histology		
Adenocarcinoma	19	42.3%
Clear cells carcinoma	4	8.9%
Melanoma	18	40%
Small cell lung cancer	1	2.2%
Neuroendocrine	1	2.25
Squamous cell	1	2.2%
Urothelial	1	2.2%
Timing of mestases		
Sincronous	20	44.4%
Metacronous	25	55.6%
Oligometastatic type		
Induced oligopersistence	11	24.5%
Repeat oligopersistence	2	4.4%
Repeat oligorecurrence	1	2.2%
De novo metacronous oligorecurrent	1	2.2%
Induced oligorecurrence	2	4.4%
De novo metacronous oligoprogression	3	6.7%
Repeat oligoprogression	4	8.9%
Induced oligoprogression	21	46.7%
Previous local ablative treatment		
Yes	21	46.7%
No	24	53.3%

Median follow-up was 12.9 months. Median OS was 34.2 months (range 17.0-54.7), 1, 3 and 4 years OS was respectively 72.4 %, 48.5% and 34.7%. At univariate analysis, previous chemotherapy (yes *vs* no [P<0.0001], HR 0.085, 95%CI 0.0023-3.203), number of irradiated lesions (1 *vs* 2 or more [P<0.0296], HR 0.403, 95%CI 0.1635-0.9974) and BED > 75 Gy (yes *vs* no [P<0.0394], HR 0.4119, 95%CI 0.1418-1.1961) correlated with OS. Median PFS was 7.4 months (range 5.5-17.2), 1, 3 and 4 years PFS was respectively 40.9%, 21.5% and 7.2 %. At univariate analysis, previous chemotherapy (yes *vs* no [P<0.0001], HR 0.07032, 95%CI 0.0012-4.1845) and oligo *vs* induced status (HR 3.2308, 95%CI 0.9845-10.6029, P=0.0016) correlated with PFS. Patients received IT for a median time of 10.4 months after SBRT (range 7.9-21.4). Considering only living patients at last follow up and/or patients who changed systemic therapy before death, median TTNT was 33.5 months (range 24.1-56.1), 1, 3 and 4 years TTNT was 77.2%, 48.3% and 48.3% respectively.

Conclusions. SRT is a valid, non invasive, well tollerated treatment for oligoprogressive and oligopersistent patients during ICI with promising TTNT, PFS and OS. New studies are needed to better study the interaction between SRT, immune system and ICI in the big scenario of the oligometastatic patients

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SBRT OF HILAR LYMPH NODES FROM LUNG CANCER: OUTCOMES, TOXICITY AND ROLE OF CTV

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Aims. To evaluate efficacy and tolerance of stereotactic body radiation therapy (SBRT) of mediastinal and hilar lymph nodes (LN) in patients (pts) with lung cancer, in terms of clinical outcomes, toxicities and relationship between clinical tumor volume (CTV) and prognosis.

Methods. From 2009 to 2020 forty-eight patients with lung cancer underwent SBRT on LN (56 lesions overall) including 82% (46 pts) were from non-small cell lung cancer (NSCLC), 7% (4 pts) were from small cell lung cancer (SCLC) and 10% (6pts) from others histologies. The state of patients at moment of treatment was classiffied as oligorecurrent (52%), oligoprogression (27%), oligometastatic (9%) and oligopersistent (12%). The median age was 69 years (range: 54-90 years) and the Performance Status was ≤2. Thirty-eight pts underwent Intensity Modulated Radiotherapy (IMRT), while eighteen pts underwent Volumetric Modulated Arc Therapy (VMAT) technique, and the schedule of treatment most represented was 48 Gy in 8 fractions (range 23-60 Gy in 1-8 fractions). The medium BED10 was 86 Gy (range 48-120 Gy). The medium volume of CTV treated was 10 cc (range 0.74-60.3 cc). Toxicity assessment has been considered in acute and in late (more than 3 months after SBRT) for pulmonary district, according to Common Terminology Criteria for Adverse Events (CTCAE v4.0) scoring system. Survival outcomes were calculated through Kaplan-Meier curves.

Results. Median survival was 23 months. The acute and late toxicities was < Grade 2 for all parameters for all pts. At 1- and 3-years survival probability were as follows: local control (LC) 89% and 83%, loco regional nodal control (LRNC) 81% and 70%, distant nodal control (DNC) 92% and 88%, distant metastasis free survival (DMFS) 49% and 36%, overall survival (OS) 66% and 35% respectively. At univariate analysis, the volume of CTV (> 10 cc) was associated with worst results in terms of DMFS and OS with statistically significant data (P=0,0281 and P=0,0015 respectively).

Conclusions. The application of SBRT for mediastinal and hilar LN, especially in the oligometastatic patient with lung cancer, improve local control (LC) and other outcomes with limited toxicity, with evidence that CTV volume is an unfavorable factor in terms of DMFS and OS.

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OUTCOMES OF STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR) FOR LIVER DE NOVO OLIGOMETASTATIC, REPEAT OLIGOMETASTATIC, AND INDUCED OLIGOMETASTATIC DISEASE

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Aims. Non-surgical local ablative approaches for liver metastasis are increasingly used for patients (pts) not eligible for surgery. The role of Stereotactic Ablative Radiotherapy (SABR) in the management of oligometastatic cancer pts have been widely investigated confirming its safety and efficacy. Here we report our results based on the ESTRO-EORTC definition of oligometastatic disease (OMD).

Materials and Methods. All pts with OMD treated at our institution with SABR from 02/2016- 02/2023, were retrospectively investigated. SABR was delivered with Helical Tomotherapy® (HT) or CyberKnife® (CK). For CK pts a median number of four (3-8) radiopaque gold fiducials were implanted before the treatment. All pts underwent contrast-enhanced simulation CT scan. Based on the metastatic disease history all pts were divided into 3 groups. Group 1 includes de-novo OMD (NOMD) (32 pts), group 2 repeat OMD (ROMD) (14 pts),and group 3 induced OMD (IOMD) (10 pts). Kaplan-Meyer estimate was used to report Overall survival (OS) and Local Relapse Free Survival (LRFS). Toxicity was registered according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

Results. A total of 56 lesions in 40 pts were treated. Median age of the patients at diagnosis was 66 years (29-83). Median follow up was 14.5 months (0.6-81.9). Twenty-five lesions were treated with CK, the remaining 31 with HT. Median number of liver metastases/patient was 4 (1-6). Median GTV was 16.65 (0.3-631.7) cc. a/b coefficient, was 100 (59.5-378) Gy. No ≥ G3 toxicities and radiation-induced liver disease (RILD) were recorded. OS at 6- and 12-months of NOMD, ROMD and IOMD were 90%, 84.6%, 80% and 73%, 75.2%, 70% (p=0.4), respectively. Six- and 12-month LRFS for NOMD, ROMD and IOMD was 85.9%, 100%, 100% and 85.9 %, 77.8% and 100%, respectively (p=0.48).

Conclusions. SABR for liver metastasis in OMD is an effective and well-tolerated in all settings of pts. In our cohort no statistical difference was observed in the 3 main OMD groups. Probably larger cohorts and longer follow-up are needed to observe a difference in groups of patients who theoretically have different prognostics.

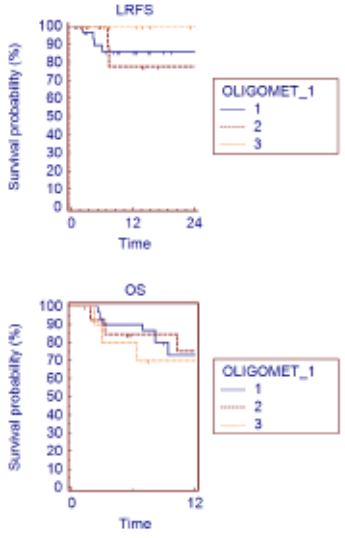

Figure 1. LRFS and OS in the three groups of Oligometastatic Disease.

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CLINICAL OUTCOME OF PATIENTS TREATED WITH SBRT FOR LUNG-ONLY OLIGOMETASTATIC HEAD AND NECK SQUAMOUS CELL CARCINOMA

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Aims. Oligometastatic disease in head and neck squamous cell carcinoma (HNSCC) is an atypical scenario. Although no evidence-based recommendations are currently available regarding the use of local ablative treatments which are the most widely adopted strategies to postpone the start of first-line or further systemic treatments. The purpose of our analysis was to update and report on long-term clinical outcomes of a cohort of HNSCC patients treated with stereotactic body radiother-

apy (SBRT) for lung-only oligometastatic disease.

Methods. Patients with 1 to 5 pulmonary lesions undergoing treatment with curative intent of the primary disease were enrolled in this retrospective study. The oligometastatic pattern was defined as "de novo" if susceptible to SBRT only or "oligoprogressive" if detected after first line of systemic therapy. We evaluated time to progression (TTP) as the time from the last day of SBRT to disease progression or death from any cause. Predictive factors of better clinical outcome and survival analysis were performed by Cox regression and Kaplan Meier methods, respectively.

Table 1. Predictive factors at univariate analysis.

Covariate	Median TTP months (95%CI)	P value
Gender		
Male	18.00 (4.96-31.03)	0.23
Female	Not reached	
Age		
< 65 years	28.00 (5.94-50.06)	0.28
≥ 65 years	13.00 (4.01-21.99)	
< 70 years	9.00 (1.94-16.06)	**0.013**
≥ 70 years	Not reached	
ECOG PS		
0-1	22.00 (8.02-36.00)	0.34
2	8.00 (0.00-16.59)	
Oligometastatic pattern		
De novo	26.00 (13.75-38.24)	0.13
Oligoprogressive	4.00 (0.00-10.00)	
p16/HPV status		
negative	18.00 (7.28-28.72)	0.22
positive	Not reached	

Results. A cohort of 45 patients and 46 metastases were retrospectively evaluated. The median age was 67 years (range 37-86) and 87% of patients had a ECOG PS 0-1. HPV negative status (78%) and "de novo" oligometastatic pattern (80%) were reported by the majority of patients. After a median follow up of 28 months (range 2-88), median TTP was 18 months (95% CI 4.8 – 31.2) and median overall survival (OS) was 62 months (95%CI 10,8 - 113.2). At univariate analysis, patients aged > 70 years reported a better TTP (p 0.013). No statistically significant correlation was observed in respect with gender, ECOG PS, oligometastatic pattern and p16/HPV status (Table 1). Out of 26 histologically proven metastases, 18 distant sites were not tested for p16/HPV status. We collected only 2 patients reporting concordance between p16/HPV positive status of primary tumor and lung metastases. Overall, 6 patients reported grade (G) 1-2 acute toxicity and no acute G3 adverse events were observed.

Conclusions. In appropriately selected HNSCC patients with lung-only oligometastatic disease, SBRT may improve clinical outcome prolonging time to progression and to systemic treatments. Distant metastases from HPV-related primary HNSCC should be tested for p16/HPV status given the clinical implications of HPV positivity for diagnosis and treatment.

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SABR ON MEDIASTINAL AND HILAR LYMPHADENOPATHY

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Aims. Mediastinal and hilar lymphadenopathies (MHL) are a frequent pattern of cancer spread, most common in lung cancer, but can occur also in others primary disease. In that situation Stereotactic Ablative Radiation Therapy (SABR) can have an important role in the therapeutic management, however the safety and efficacy have not yet been established. SABR treatment on ultra central localizations has been found to be associated with higher rates of severe toxicity. Aim of this study is to evaluate clinical outcomes and toxicities of MHL treated by SABR.

Methods. This is a retrospective study that analyzes a group of patients treated by SABR on MHL from different primary tumors (the tumor most frequent is lung in 49% of cases). The criteria of inclusion are: ECOG performance status ≤2; primary cancer disease under control; maximum 5 metastases of which one is the lymph node treated by SBRT; maximum lymph node diameter ≤5 cm.

Results. One hundred eighteen MHL were treated in 99 patients from 2007 to 2022 by SABR (<8 fractions). In 24% of treatment the concomitant treatment was allowed. The schedule most represented was 30 Gy in 5 fractions (range 23-60 Gy in 1-8 fractions). The Local Control was obtained in 88% of NMs treated by SABR with rates at 1- and 3- years of 90% and 82% respectively. The rates of Progression Free Survival at 1- and 3- years were 57% and 47% respectively. The rates of Overall Survival at 1 and 3 years were 71% and 41% respectively. Acute toxicities were seven cases Grade 1 (in form of pain, fatigue, nausea, vomiting and cough), one case with anemia G2, one case died 3 days after treatment on mediastinal lymph node by esophageal bleeding, G5. One case presented late toxicity with dyspnea Grade 2.

Conclusions. SBRT to mediastinal and hilar lymph node metastases is feasible and the risk for serious toxicity appears to be acceptable in the modern era. More prospective studies are needed to confirm these results.

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FRACTIONATED STEREOTACTIC RADIOTHERAPY FOR BRAIN METASTASES: RESULTS OF A SINGLE CENTER RETROSPECTIVE ANALYSIS

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Aims. Multi-fraction Stereotactic Radiotherapy (mSRT) delivered in 3-5 fractions has been used in patients (pts) with brain metastases as an alternative to single-fraction radiosurgery with the aim to obtain high local control rate and reduce radiation-induced toxicity. In the present analysis, we have evaluated the results and toxicity of mSRT in pts with 1-5 brain metastases.

Methods. Data of 103 consecutive pts (median age of 62 years, range 42-84) treated for 1-5 brain metastases were extracted from case records and analyzed. All metastatic tumors were treated with linear accelerator-based multi-fraction SRT using a commercial stereotactic mask fixation system. This retrospective analysis evaluated the incidence of toxicity and the local progression free survival (LPFS), the distant brain progression free survival (DBPFS) and the overall survival (OS), using the Kaplan-Meier method.

Results. Between July 2018 and December 2022, 103 consecutive pts (69% men and 31% women) showing 1-5 brain metastases received mSRT and were included in this analysis: 64% of pts presented lung cancer, 11% colon-rectal cancer, 9% breast cancer, 6% melanoma, 6% renal carcinomas, 4% other primaries. A total number of 199 brain metastases were irradiated according to the following schedules: 3 × 9 Gy (93% lesions), 5 × 6 Gy (4%) and 5 x 5 Gy (3%). At a median follow-up of 6.4 months (range 5-33), 10.3% of the treated lesions recurred locally. The 1-year local control rate was 89%. The 1-year DBPFS and 1-year OS rates were 49% and 53% respectively. Forty-seven percent of pts experienced some grade of neurological toxicity according to the RTOG score: 35% pts G1, 10% G2. Only two pts with brain metastases larger than 3 cm presented G3 neurological toxicity for symptomatic radiation-induced brain necrosis. Post-radiation imaging changes suggestive of radionecrosis occurred in 12 pts.

Conclusions. Multi-fraction SRT (at a dose of 27 Gy in 3 daily fractions) seems to be a safe and effective treatment modality for the management of brain metastases. The lasting local control of brain metastases and the low rate of late radiation-induced sequelae following stereotactic radiotherapy are becoming increasingly relevant since new systemic treatment options constantly improve the prognosis of pts in this setting.

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STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN NON-SPINE BONE OLIGOMETASTASIS: A SINGLE-INSTITUTION RETROSPECTIVE STUDY

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Aims. To retrospectively analyze treatment outcomes and toxicity of SBRT for non-spinal bone oligometastasis.

Methods. Between July 2018 and April 2023, 40 patients (pts) with 48 non-spinal bone oligometastasis were treated with SBRT. Primary endpoints were local recurrence-free survival (LR-FS) and overall survival (OS); secondary endpoint was acute and late toxicity. LR was defined as lesions not classified as progressive disease on RECIST criteria. Acute toxicity (defined as toxicity < 90 days) and late toxicity (defined as toxicity ≥ 90 days) were graded according to CTCAE 4.0 criteria. The GTV was defined as the gross visible lesion on diagnostic imaging. A 3-5 mm margin was added for the PTV. Treatment was delivered by volumetric-modulated arc therapy and daily image-guidance was performed using a kilovoltage cone-beam CT.

Results. The median age was 70 years (yrs), range 44-83 yrs. Median PSK was 100 (range 50-10). The most common primary site was prostate (51%), followed by lung (22%), breast (16%), and other (11%). BM sites were: pelvis (72%), rib (10%), femur (6%), sternum (6%), shoulder (2%), and skull (2%). Lesions were lytic in 28 (58%) cases and sclerotic in 20 (42%) cases. The most used SBRT regimen were: 33 Gy in 3 fractions. Diagnosis of disease was made with PET/CT in 41 (85%) cases, CT in 6 (13%) cases, and MR in 1 (2%) case. In 20 (42%) of cases, pts received concomitant systemic therapy. Fifteen (37%) pts underwent SBRT for >1 synchronous lesion. Median follow-up was 15 months (range 1-47). At time of analysis, 29 (73%) pts were alive. Cause of death was progression of disease in 8 (20%) pts. The 1- and 2-yr LR-FS rates were 86% and 66%, respectively. Median OS was 31 months (95% CI, 21-29 months). The 1- and 2-yr OS rates were 90% and 59%, respectively. LR occurred in 5 (13%) pts with a median time to failure of 13 months (range 3-31). Sixteen (40%) pts had systemic progression after SBRT at a median time of 5 months

(range, 1-31). Neither acute nor late toxicity have been reported.

Conclusions. Our retrospective study confirms the role of SBRT in the treatment of non-spinal bone oligometastasis with high LR-FS rates. Moreover, SBRT is associated with acceptable acute and late toxicity.

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STEREOTACTIC RADIOTHERAPY FOR PROSTATE CANCER LYMPH-NODAL OLIGOMETASTASES: A MULTICENTER EXPERIENCE

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Background. The favorable role of SBRT for lymph-nodal oligometastases from prostate cancer has been reported by several retrospective and prospective experiences, suggesting a more indolent natural history of disease when compared to patients with bone oligometastases. This retrospective multicenter study evaluates the outcomes of a cohort of patients treated with stereotactic body radiotherapy for lymph-nodal oligometastases.

Methods. Inclusion criteria were as follows: up to 5 lymph-nodal oligometastases detected either with Choline-PET or PSMA-PET in patients naïve for ADT or already ongoing with systemic therapy, at least 6 Gy per fraction radiotherapy regimens for SBRT were considered. Only patients with exclusive lymph-nodal disease were included for the purpose of the study. The primary endpoint of the study was LC; toxicity assessment was retrospectively performed following CTCAE v4.0

Results. A total of 100 lymph-nodal oligometastases in 69 patients have been treated with stereotactic body radiotherapy between April 2015 and November 2022. Median age was 73 years (range, 60-85). Oligometastatic disease was mainly detected with Choline-PET in 47 cases, while the remaining were diagnosed by PSMA-PET, with most of the patients treated to a single lymph-nodal metastasis (48/69 cases), 2 in 14 cases, 3 in the remaining. Median PSA prior to SBRT was 1.35 ng/ml (range, 0.3-23.7 ng/ml). Patients received SBRT with a median total dose of 35 Gy (range, 30-40 Gy) in a median number of 5 (range, 3-6) fractions. With a median follow-up of 16 months (range, 7-59 months), our LC rates were 95.8% and 86.3% at 1- and 2-years. DPFS rates were 90.4% and 53.4%, respectively at 1- and 2- years, with 9 patients developing a sequential oligometastatic disease treated with a second course of SBRT. Polymetastatic disease-free survival (PMS) at 1- and 2-years were 98% and 96%. Six patients needed ADT after SBRT for a median time of ADT-free survival of 15 months (range, 6-22 months). Median OS was 16 months (range, 7-59) with 1- and 2-years rates of both 98%. At multivariate analysis, higher LC rates and the use of PSMA-PET were related to improved DPFS rates, and OS was significantly related to a lower incidence of distant progression. No G3 or higher adverse events were reported.

Conclusions. In our experience, lymph-nodal SBRT for oligometastatic prostate cancer results as a safe and effective option for ADT-delay with no severe toxicity.

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STEREOTACTIC RADIOSURGERY WITH VOLUMETRIC MODULATED ARC THERAPY (VMAT): LOCAL CONTROL AND TOXICITY PROFILE RESULTS OF A MULTI-ARM PHASE I TRIAL (DESTROY-2)

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Aims. To present the interim results of a phase I trial on stereotactic radiosurgery (SRS) delivered using volumetric modulated arc therapy (VMAT) in patients with primary or metastatic tumours in different extracranial sites.

Materials and Methods. Patients were enrolled in different arms according to tumour site and clinical stage, and sequentially assigned to a given dose level. Toxicity profile, tumour response and early local control (LC) were investigated and reported.

Results. 230 lesions in 207 consecutive patients (male/female: 120/87, median age: 66 years; range: 29-92) were treated. The most represented primary tumors were: breast cancer (40 patients), colon cancer (47 patients), and prostate cancer (62 patients). The prescribed dose ranged from 12 (BED(2Gy,α/β:10) = 26.4 Gy) to 28 Gy (BED(2Gy,α/β:10) = 106.4 Gy) to the planning target volume. Twenty-two patients (10.6%) experienced grade 1-2 and only one grade 3 acute toxicity, which was a pulmonary toxicity. In terms of late toxicity,

we registered only 6 toxicity>G2: a G3 gastro-intestinal one, three G4 bone toxicity, a G3 laryngeal toxicity, and a G5 pulmonary toxicity (haemoptysis). Regarding LC, the 1-, 2-, and 5-years LC were 90.6%, 81.6%, and 69.7%, respectively

Conclusions. The maximum tolerable dose has been reached in any study arm with a safe toxicity profile and promising LC rates

Table 1. Patients characteristics.

Patients		N (%)
Gender		230
	Male	134 (58)
	Female	96 (42)
Age (median, range)		68 (29-92)
ECOG		
	0	167 (73)
	1	40 (17)
	2	20 (8)
	3	3 (2)
Primary tumor		
	Prostate	62 (27)
	Colon	47 (20)
	Breast	40 (17)
	Gynaecological	22 (10)
	Head & Neck	14 (6)
	Pancreas	10 (5)
	Other	35 (15)
Comorbidities		
	Cardiovascular	43 (31)
	Diabetes	27 (20)
	Lung diseases	8 (5)
	Renal Diseases	2 (2)
	Other	58 (42)

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ENDOBRONCHIAL ULTRASOUND (EBUS)-GUIDED FIDUCIAL PLACEMENT FOR STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN INTRATHORACIC NODAL OLIGOMETASTASES: A CASE SERIES AND PRELIMINARY OUTCOMES

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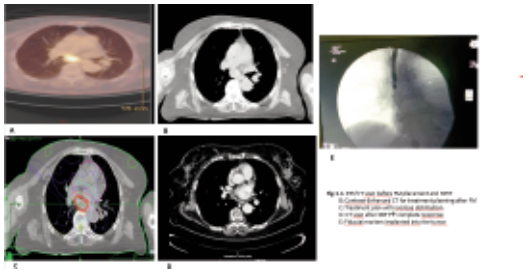
Aims. The role of SBRT in the setting of oligometastatic disease is well established, but its applicability in ultra-central lesions is debated, due to proximity of mediastinal OARs and uncertainty in dose deliver due to respiratory motion. Real-time tumor tracking (RTTT) under guidance of fiducial markers (FM) implanted via EBUS may improve treatment delivery. We present preliminary data from patients treated with SBRT following EBUS-guided FM placement.

Materials and Methods. We retrospectively collected data of oligometastic patients with miscellaneous metastatic primary tumours treated with Cyberknife robotic radiosurgery system for ultracentral nodal metastases from December 2021 to February 2023. Golden 25G FM were placed intralesionally via EBUS under general anesthesia and via rigid bronchoscopy. After 1 week patients underwent blank and contrast-enhanced CT for the treatment planning; a 4D-CT was acquired to verify the solidarity between FM and the tumor along respiratory cycle. 8/9 lesions were treated with an ablative dose in 5 fractions (EQD2 $\geq$ 50 Gy). Preliminary outcomes and acute and late toxicities were assessed.

Results. Data from 8 patients accounting for 9 lymph nodal metastases are reported. Median age was 68 years (48-76) and median follow-up 3.5 months (2-12). Primary tumor was lung, breast and gastric in 3, 2 and 3 cases, respectively. Treatment site was station 7, 10R, 11R, 3 and 8 in 3, 3, 1, 1 and 1 cases, respectively. Median number of FM was 3 (2-3); no migration or malfunction were observed. Median dose delivered was 35Gy (30-40) in 5 fractions. No acute toxicities were reported. Treatment resulted in partial response (PR) in 3 cases and complete response (CR) in 3 cases (Figure 1). 3 patients resumed chemotherapy after SBRT, 3 continued surveillance, 1 died of intracranial progression and 1 patient experienced local failure. One case of aortoesophageal fistula, possibly correlated to treatment, was observed.

Conclusions. EBUS-implanted FM is a minimally invasive and well tolerated procedure which may mitigate the impact of tumor motion on treatment delivery with promising results. Caution is required in case of suspicion of mediastinal organ infiltration, particularly esophagus.

Table 1.



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STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR): A PROMISING CHANCE FOR OLIGOMETASTATIC (OLIGO-M) BREAST CANCER (BC) PATIENTS

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Aims. Multidisciplinary management of oligo-M BC with local therapy could improve disease control and defer systemic treatment, therefore SAbR may improve the prognosis of oligo-M BC patients. In the literature, there is very little data available that is specific to breast cancer.

Methods. We conducted a monoistitutional retrospective analysis on oligo-M BC patients treated with LINAC-based SAbR in combination with systemic medical treatment. The primary objective was to estimate local control and toxicity of the combined approach.

Results. 35 patients with 50 oligo-M BC (less than 5 lesions in the same organs with maximum diameter <5cm) were irradiated from June 2015 to February 2023. Median age and KPS were 60 years (35-84) and 100% (90-100), respectively. The patients mostly had one to four lesion(s) whose most widely represented site was bone (34/68%), lymph nodes (10/20%), lung (4/8%) and liver (2/4%). The primary tumor expressed estrogen receptors in 27 patients (77%); the status was HER2+++ in 7 patients (20%). All patients were studied with PET/TC before SAbR and during follow-up to detect oligoprogression. 33(94%) patients developed metastasis during active systemic therapy (oligo-progressive patients), while 2(6%) developed metastasis without an active treatment (oligo-recurrent patients). The median prescribed dose was 35 Gy (21-45) in median 5 fractions (3-5). Median volume of treated lesions was 31cc (5-189). Radiotherapy was administered concomitant with systemic therapy only in patients receiving Cdk 4/6 inibitors a 7-day stop was performed before and after SAbR. After a median follow-up of 20 months (3-96) only one patient with liver metastasis developed local recurrence after 7 months from SAbR, 98% of irradiated lesions showed a complete or partial response to treatment. 12 (34%) patients with progression outside the irradiated lesion were retreated with a second course of SAbR continuing the same systemic therapy. No grade ≥3 toxicity was reported. At the time of analysis 31(88,5%) of patients were alive.

Conclusions. This retrospective analysis of oligo-M BC patients showed an excellent local control after SAbR with a good toxicity profile. This advantage can probably translate in a PFS and OS, with a not negligible, although still theoretical, chance of cure, especially if local therapies are integrated with efficient systemic treatments.

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SBRT LINFONODALE: UNO STUDIO MONOCENTRICO RESTROSPETTIVO

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Aims. Lymph node metastases (NMs) are a common site of tumor spread with variable incidence based on the primary tumor site, stage, histology, and grading. NMs can occur at the different time of disease, at moment of diagnosis, during systemic therapy or during follow-up. Sometimes lymph nodes can be the only site of metastasis. The oligometastatic disease (OMD) is an intermediate stage between limited disease and metastatic dissemination. In that setting Stereotactic body Radiation Therapy (SBRT) can be a therapeutic option. Aims of our study is to evaluate the outcomes of NMs treated by SBRT in terms of Local Control (LC), Progression Free Survival (PFS) and Overall Survival (OS). The secondary end point is to identify predictive factors of response.

Methods. This is a retrospective study that analyzes a group of patients treated by SBRT on NMs from different primary tumors (31% lung, 22% prostate, 13% colon rectal, 10% gynecological, 7% breast, 6% upper GI, 5% genitourinary, 2% H &N, 4% others). The criteria of inclusion are: ECOG performance status ≤2; primary cancer disease under control; maximum 5 metastases of which one is the lymph node treated by SBRT; maximum lymph node diameter ≤5 cm.

Results. From November 2007 to September 2021, 229 NMs were treated in 174 patients by SBRT (<8 fractions). In 34% of treatment the concomitant treatment was allowed. The single fraction was administered in the 22% of cases and multiple fractions in the 78% of cases. The schedule most represented was 30 Gy in 5 fractions. The LC was obtained in 90% of NMs treated by SBRT with rates at 1-, 3- and 5- years of 93%, 86% and 86% respectively. The rate of PFS were 44%, 23% and 13% at 1-, 3 - and 5- years respectively. At univariate analysis a pelvic lesion site was a favorable prognostic factor (p-value: 0.005), the CTV>4.82cc was a negative statistically significant prognostic factor for PFS (p-value: 0.037). The rates at 1-, 3- and 5- years of OS were 78%, 48% and 36% respectively. At univariate analysis having more than one lesion (p-value: 0.035) and a CTV>4.82cc (p-

value: <0.001) were statistically significant negative prognostic factor, in contrast a lesion site in the pelvis was a positive statistically significant prognostic factor (p-value: 0.001).

Conclusions. SBRT is an option for the treatment of NMS, whit high rates of LC, improving the data of survival. Prospective studies are required to further confirm the benefit of this treatment.

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NON METASTATIC CASTRATION RESISTANT PROSTATE CANCER: IS THERE A ROLE FOR PSMA-PET GUIDED METASTASES DIRECTED THERAPY IN THE ERA OF ARSI? A SINGLE CENTER RETROSPECTIVE ANALYSIS

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Aims. Regarding non-metastatic castration-resistant phase (nmCRPC), 3 randomized trials explored androgen-receptor signaling inhibitors (ARSI) role, but only one showed that a II line with ARSI is feasible, while many patients might receive cytotoxic treatments. In this setting, the role of PSMA-PET instead of conventional imaging is controversial. A recent study showed that up to 40% of high-risk nmCRPC cases could be oligorecurrent disease, potentially amenable of MDT. We report our experience on PSMA-PET-guided MDT.

Methods. This is a single center retrospective study. Inclusion criteria were: biochemical progression of prostate cancer with serum testosterone levels below 50 ng/dl; PSA doubling time < 10 months; PSMA-PET positivity for no more than five non-visceral lesions; SBRT to all lesions. Exclusion criteria were: de novo metastatic disease; previous systemic treatments for metastatic disease. First line systemic therapy for (mCRPC) was chosen after multidisciplinary discussion, in patients no more amenable for MDT. The primary outcome of this study was time to first line systemic therapy (stPFS) for mCRPC. Secondary outcomes were radiological progression free survival (rPFS), defined as evidence of new lesions after first SBRT, local control (LC) and PFS after subsequent MDTs (PFS2, PFS3).

Results. 35 patients affected by 64 metastases were included. Median follow-up was 33 months (range 8-71). Median PSA doubling time was 5.2 mo (1-9.8). SBRT was delivered in 3-6 fractions with a median BED of 150Gy (α/β ratio 1.5). Metastases were divided as follows: 8.5% prostatic bed relapse, 25.7% pelvic nodes, 31.4% extra-pelvic nodes, 34.2% bone metastases. Median number of treated lesions was 2 (1-4). After first SBRT, median rPFS was 5 mo (2-34). 25 patients had a second SBRT course, 14 patients had 3 or more. In total, 169 metastases were treated through all SBRT courses, with a median of 3 (1-13). Median PFS2 was 5 mo (2-32) and median PFS3 was 4 mo (1-15). LC was 98%. 20 patients developed mCRPC and 18 started systemic therapy. Median stPFS was 17 mo (2-35).

Conclusions. The possibility of delivering multiple SBRT courses and the high rates of LC lead to clinically meaningful results in terms of stPFS. This analysis, albeit on a small cohort of patients, shows the potential of SBRT in delaying the start of systemic therapy in patients with oligomCRPC, thus possibly increasing the time free from cytotoxic therapies. More evidence from randomized trials is needed.

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PSMA-PET/CT-BASED STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN THE TREATMENT OF UNCOMPLICATED NON-SPINAL BONE OLIGOMETASTASES FROM PROSTATE CANCER

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Background and purpose. Stereotactic body radiotherapy (SBRT) has a consolidated role in the treatment of bone oligometastases from prostate cancer (PCa). While the evidence for spinal oligometastases SBRT is robust, its role in non spinal-bone metastases (NSBM) is not standardized. In fact, there is no clear consensus about dose and target definition in this setting. The aim of our study was to evaluate efficacy, toxicity, and pattern of relapse of SBRT delivered to NSBM from PCa.

Materials and Methods. From 2016 to 2021, we treated a series of oligo-NSBM from PCa with 68Ga-PSMA PET/CT-guided SBRT. The primary endpoint was local progression-free survival (LPFS). The secondary endpoints were toxicity, pattern of intraosseous relapse, distant progression-free survival (DPFS), polimetastases-free survival (PMFS), and overall survival (OS).

Results. 150 NSBM in 95 patients were treated with 30-35 Gy in 5 fractions. With a median follow-up of 26 months, 1- and 3-years LPFS were 96.3% and 89%, respectively. A biological effective dose (BED) ≥198 Gy correlated with improved LPFS (p=0.007). Intraosseous relapse occurred in 8 (5.3%) cases. Oligorecurrent disease was associated with better PMFS compared to de

novo oligometastatic disease (p=0.001) and oligoprogressive patients (p=0.007). No grade ≥3 toxicity occurred.

Conclusions. SBRT is a safe and effective tool for NSBM from PCa in the oligometastatic setting. Intraosseous relapse was a relatively rare event. Predictive factors of improved outcomes were defined.

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THE ROLE OF RADIOTHERAPY IN OLIGOMETASTATIC MERKEL CELL CARCINOMA

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Aims. Merkel cell carcinoma (MCC) is a rare neuroendocrine skin cancer, approached with a standardized multimodal treatment. Nowadays, immunotherapy has been shown to be effective in patients with advanced disease, and there has been considerable interest in combining immunotherapy with external beam radiation therapy (EBRT) to improve local control. Our aim was to clarify the role and possible use of conventional fractionated (cEBRT) or stereotactic body radiotherapy (SBRT) in oligometastatic MCC, with or without concomitant systemic therapy (ST) focusing immunotherapy treatments.

Methods. In this multecenter retrospective analysis we included patients treated with cEBRT (median dose of 40 Gy) or SBRT (median dose of 35 Gy) on oligometastases from MCC. Any site of the body was allowed, with a maximum of 5 metastases in up to two organs. Concomitant ST was allowed. End-points were the evaluation of local control, survival and pattern of toxicity.

Results. The study included twenty-two patients with a diagnosis of oligometastatic MCC treated from July 2019 to January 2023 with metastases-directed radiotherapy. The time to recurrence ranged from 4 to 60 months from the primary treatment. The site of recurrence was mainly located in lymph nodes (fifteen, 68%). Nine (41%) patients were treated on a solitary metastasis, nine (41%) on two metastases, two (9%) on three lesions and two (9%) on four lesions. The diagnosis of oligometastases was performed through combined CT and PET scans in 41% of patients, with PET only in 41%, with CT only in 13%, and 5% with other imaging modalities. Seven (32%) patients underwent SBRT and 15 (68%) patients underwent cEBRT. Concomitant ST was administered in 45% of patients, 41% received sequential ST and 14 % no ST at all. Median follow up was 6 months. The study found that no patient experienced any toxicity above grade G1 both in the acute setting: 23% of patients experienced skin G1 toxicity, and 5% gastrointestinal G1 toxicity. No late toxicity was recorded. At the follow-up, two to three months after treatment, 36% of patients experienced a partial response, and 55% had a complete response. One patient died and one patient was lost at follow-up.

Conclusions. Radiotherapy for oligometastatic MCC is a safe and effective option which can obtain an excellent disease control. Both cEBRT and SBRT can be delivered alongside ST without evidence of severe side effects. Further research is required to refine the optimal treatment approach.

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STEREOTACTIC RADIOTHERAPY IS SAFE AND EFFECTIVE IN OLIGOMETASTATIC CANCER: RESULTS OF DIFFERENT SCHEDULES OF A SINGLE CENTRE

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Purpose. To assess the effect of stereotactic ablative radiotherapy (SABR) on oncological outcomes and toxicity in oligometastatic cancer patients (pts) treated with SBRT using different schedules.

Materials and Methods. From January 2017 to January 2023, records of 49 pts (56 lesions) with oligorecurrent disease treated with SBRT were retrospectively reviewed. Median age at the treatment was 71 (51-84) years. Primary tumor was prostate for 31 pts, lung for 10, ovary for 10, breast for 2, colon for 1, melanoma for 1 and stomach for 1 pt. The treated lesions consisted on lymph nodes 60.5%, lung 19.6 %, brain 3,6%, bone 12.5 %, vagina and prostate 1.8% All pts underwent TC or PET/TC simulation on supine position and 2.5-3 mm slice thicknesses. The GTV was defined as the visible tumor extent on CT simulation; image-fusion software were used if clinical indicated. For lung cancer 4D simulation was performed in order to create an ITV. PTV was obtained by adding a margin of 3-5 mm to the GTV. Median PTV was 17,8 (3,7-90,5) cc.

Prescription dose was 24-27 Gy in 3 fractions (ff) / 30 Gy in 5 ff and for lung lesions 50 Gy in 5 ff given every other day; it was prescribed at PTV isodose line of 80% or isocentric with PTV dose coverage of 95/105 %. The treatment was performed with Versa HD™ linear accelerator of Elekta Company using VMAT technique. OS, PFS and LC control were calculated using Kaplan- Meier curve and SPSS 22 version software.

Results. after a mean follow up of 23 (3–73) months, local response was CR in 63%, PR in 33%, and SD in only 4 %. During follow-up only 3 (5.4 %) pts experienced local recurrence in the treated site with a LC of 94.6 %. PFS at 1, 3 and 5 years was 58 %, 46 % and 26%; OS was 86%, 83%, and 80% respectively. Overall, 16 pts (28.6%) received systemic treatment before and during treatment, in remaining 40 pts SBRT managed to delay systemic treatment by 25 months. Pts with a PTV < 8 cc had statistically significant advantage in PFS compared to pts with PTV ≥ 8 cc (p-value < 0,05). We did not observe any other factor influencing PFS. No toxicities ≥G3 were recorded.

Conclusions. SBRT proved to be a safe and effective treatment in oligometastatic cancer and it contributes to delay start of systemic treatments. More data with higher number of pts and longer follow-up are necessary to define the optimal dose for fraction, considering physics features, kind of lesions and site of treatment.

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LOCOREGIONAL TREATMENTS IN OLIGOMETASTATIC LUMINAL BREAST CANCER

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Aims. Metastatic breast cancer has been historically considered as an incurable disease. Radiotherapy (RT) has been traditionally used for only palliation of the symptoms caused by metastatic lesions. However, in recent years the concept of oligometastatic disease has been introduced as a clinical scenario with a limited number of metastases (≤5) and involved organs (≤2) with controlled primary tumor. The main hypothesis in oligometastatic disease is that locoregional treatment of primary tumor site and metastasis-directed therapies with surgery and/or RT may improve outcomes. Recent studies have shown that not all metastatic breast cancer patients have the same prognosis, and selected patients with good prognostic features as those younger than 55 years, hormone receptor-positive, limited bone or liver metastases, a low-grade tumor, good performance status, long disease-free interval (>12 mo), and good response to systemic therapy may provide maximum benefit from definitive treatment procedures to all disease sites.

Methods. According with literature in the last two years the multidisciplinary breast cancer group selected 30 patients diagnosed with breast cancer and oligometastatic disease. All patients presented with luminal subtype breast cancer. 23 had only bone sites metastatic involvment, 3 had both liver and bone metastases, 2 had lung metastases, 2 had single brain metastastases. 23 pts were treated with first line systemic therapy and underwent locoregional treatment only if imaging confirmed stable disease for more than 12 months or partial response was demostrated. 7 pts were treated with surgery of the breast according to the locoregional exetension of disease and were treated with stereotactic radiotherapy on bone/brain metastases and one with termoablation on the liver. 17 pts received locoregional radiotherapy on breast/chest wall and regional node according with definitive histology report.

Results. All patients, median age 53 years, well tolerated the loco-regional treatment. 4 patients developed distance progression disease 6 month after locoregional treatment.

Conclusions. Retrospective and prospective trials on locoregional treatment in oligometastatic breast cancer have been shown conflicting results, althogh there is an increasing trend in favor of locoregional treatment.

Longer follow up and more randomised trials is needed to clarify the role of locoregional treatment on survival improvement in metastatic breast cancer.

P359

MONO-INSTITUTIONAL EVALUATION OF RESPONSE AND OF LOCAL CONTROL IN OLIGO METASTATIC PROSTATE CANCER PATIENTS TREATED WITH STEREOTACTIC RADIOTHERAPY

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Aims. Since the formulation of the concept of oligometastatic disease, loco-regional treatment by stereotactic radiotherapy (SBRT) has proved its efficacy to metastatic cancer patients with limited disease burden, for delivering of ablative radiation doses with limited toxicity. The aim of the study was to investigate response, local control (LC) and overall survival (OS) in oligo-metastatic prostate cancer patients undergoing SBRT for lymph node and bone metastases.

Methods. We retrospectively reviewed 30 oligometastatic patients treated with SBRT for lymph node and bone metastases between 2019 and first quarter of 2023.

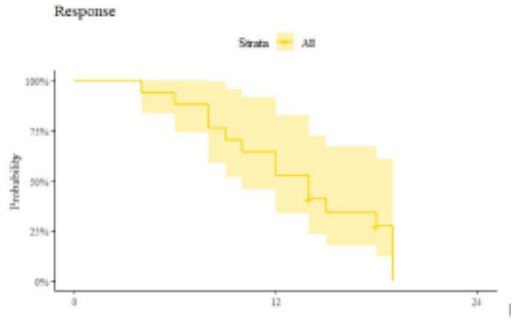
The histological type of the primary lesion, the previous radiotherapy and/or surgery, the number of metastases and the concomitant systemic therapies were considered. Response, local control (LC) and overall survival (OS) were determined. The responses were divided in complete (CR) and in partial (PR). Treatment outcomes were evaluated using Kaplan–Meier analysis. A P-value less than 0.05 was considered statistically significant.

Results. The median age was 72 years old. All patients were adenocarcinoma tumours. 77% of patients were on hormone therapy: 53% with LH-RH agonistic analogue and 42% with antiadrogens. Treatment on lymph node metastases was performed in 23 patients and on bone metastases in 7 patients. The most used RT schedules were the following: 27 Gy (9 Gy/day) for lymph node oligo-metastatic site, 30 Gy (10 Gy/day) for bone oligo-metastatic disease. For both treatments, an alternate day schedule was used. The median follow-up was 12 months while 5 patients were lost to follow-up. Overall, 72% of patients achieved a lesion response of which 69% a complete response. The 1-year and 2-year LC rates were 83%, and 29%, respectively. Median OS was 11 months with the 1-year rates were 51%. The Kaplan-Meyer analyses for response showed 88% at 6 months and 52% at 12 months, as described in Figure 1. Particularly, a good correlation between response and local control seems to be evident with patients in CR who showed a 6 months LC of 100% and patients in PR who showed a 6 months LC of 50%.

Conclusions. SBRT confirms a high Response Rate in Oligometastatic prostate cancer disease with a good correlation between Response and Local Control.

Table 1.

Figure 1. Kaplan-Meyer analysis for response in the studied group.



P360

STEREOTACTIC ABLATIVE RADIOTHERAPY FOR LYMH NODE OLIGOMETASTASES IN PROSTATE CANCER PATIENTS

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Aims. Stereotactic Ablative Radiotherapy(SABR) for Lymph node oligometastases(LNO) in prostate cancer(PC) patients(pts) is a modern therapeutic option supported by the rational of tumor cells sensitivity to high dose per fraction.The optimal timing for the combination of systemic agents (according to standard of care) should be evaluated on a case-by-case basis.Here we report results from our experience.

Methods. Between January 2021 and December 2022, 35 PC pts affected by LNO were treated at our Radiation Unit.All pts underwent simulation with BlueBag body immobilizer and specific preparation according LNO site. CTVs contouring was PET-based.The prescription radiation dose ranged between 24 Gy in 3 daily fractions(df) and 36Gy in 6 df - requiring that 98%of PTV was covered by 80% or 90-95% isodose, according to PTV extension and distance from critical structures.VMAT plans and daily IGRT with CBCT were performed in all cases. Biochemical disease control(PSA reduction),local control(PET response of irradiated LNO),toxicity profiles(RTOG scale) and time to disease progression (PD) requiring systemic agents were evaluated during follow up.

Results. 34 pts had oligometastatic hormone-sensitive PC (1 had de novo oligometastatic disease and 33 had oligoprogressive disease after prior treatments), while 1 pt was castration-resistent with LNO. Concomitant androgen deprivation therapy (ADT) was prescribed for 8 oligoprogressive pts. Second line therapy was prescribed for the castration-resistent pt. 7 pts had more than one LNO, that were treated with multiple isoecenters in selected cases. Mean follow up is 17 months(range 6-27). At 3 months follow up, Complete Biochemical Response was early obtained by 12 pts, which still confirm disease control with no systemic therapy changes. Among 13 pts with PD during follow up, 6 pts underwent reirradiation for novel LNO.Local control (restaging PET was performed only for PD) was obtained for every treated lesion.Time to PD requiring changes in systemic approach was 6 months (3-12).No significant radiation-induced toxicities were reported.

Conclusions. The reported experience on SABR for the management of LNO confirmed published data supporting its application for PC pts(good LC an tolerance).The role of systemic agents in this setting is

well-known, but optimal timing/sequence of combined therapies has to be agreed in multidisciplinary meetings, in order to optimize tumor control and offer advantages to these long-surviving pts.

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STEREOTACTIC BODY RADIOTHERAPY IN METASTATIC PROSTATE CANCER PATIENTS TREATED WITH SYSTEMIC THERAPY AND UNDERGOING TO OLIGOPROGRESSION: REPORT ON 10 CONSECUTIVE CASES

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Aims. Stereotactic body radiotherapy (SBRT) directed to the metastatic sites of disease progression has been suggested as a possible therapeutic strategy in oligoprogressive prostate cancer. This modality, in principle should allow to delay the dismission of a systemic line of treatment prolonging the global control of the disease. However, a clear benefit has yet to be demonstrated. We report the experience with this treatment approach in our institution.

Methods. From april 2018 to november 2022, 10 patiens affected by oligoprogressive prostate cancer were treated with SBRT targeting the nodal or bone sites of progression, while maintaining the on-going systemic therapy. Three patients were assuming a single agent ADT, while the other 7 were in treatment with a successive line of systemic therapy. All patients were evaluated with a pre-treatment 68Ga-PSMA or 18F-Choline PET/CT, which demonstrated from one to five localizations of disease. All the active sites were treated with SBRT in one (15-24 Gy) or three (21-27 Gy) fractions. PSA serum levels were tested at baseline, one month after RT and then at least every 3 months; all patients underwent a post treatment 68Ga-PSMA or 18F-Choline PET/CT, except for one patient evaluated with bone scan and CT. Endpoints were: PSA response, defined as a post-treatment decrease > 50% from baseline measured within 6 months, local control (LC), biochemical progression-free survival (bPFS), radiological progression-free survival (rPFS) and freedom from polymetastatic progression (FPP).

Results. A total number of 18 lesions were treated (6 nodal and 12 bone). At a median follow-up of 16.5 months (6-61), 8 of the 10 patients had PSA response; all patients had local control of the treated metastases. Biochemical progression of disease occurred in 5 patients with a median bPFS time of 11.5 months. Radiological progression of disease occurred in 6 patients with a rPFS time of 12 months; 2 patients had polymetastatic progression with FPP time of 16.5 months (Table 1). The toxicity of SBRT resulted negligible.

Conclusions. Although with the limits of a small sized sample and a short follow up time, our data support the benefit of treating with SBRT the sites of oligoprogressive disease before switching to a subsequent line of systemic treatment in patients affected by metastatic prostate cancer. Prospective studies to assess the possible impact on overall survival of this approach are warranted.

Table 1.

	FUP (months)	PSA resp	bPFS (months)	LC (months)	rPFS (months)	FPP (months)
Pt1	57	Yes	23	57	25	57
Pt2	19	Yes	9	19	9	19
Pt3	6	No	4	6	4	6
Pt4	32	Yes	18	32	19	19
Pt5	14	No	6	14	10	10
Pt6	14	Yes	14	14	14	14
Pt7	50	Yes	50	50	50	50
Pt8	7	Yes	7	7	5	7
Pt9	8	Yes	8	8	8	8
Pt10	61	Yes	61	61	61	61
Median time	16.5		11.5	16.5	12	16.5

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NODULAR LEPTOMENINGEAL DISEASE AFTER POSTRESECTION STEREOTACTIC RADIOTHERAPY FOR BRAIN METASTASES IN A PATIENT WITH TRIPLE NEGATIVE BREAST CANCER

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Aims. The advent of postoperative stereotactic radiotherapy (SRT) for brain metastases minimized the neurocognitive side effects of WBRT leading to a paradigm shift in oncology. However, SRT is associated with a novel pattern of intracranial recurrence, termed nodular leptomeningeal disease (nLMD), especially in patient with breast histology. This case report illustrates nLMD in a patient affect by breast cancer who underwent brain metastases surgery and subsequent SRT to surgical cavity.

Materials and Methods. A 56-year-old female experienced headache and postural instability in March 2023. Her past medical history was known for a triple-negative

breast cancer (Stage IIB, cT2N1M0) which was diagnosed 2 years prior. After multidisciplinary evaluation she underwent neoadjuvant chemotherapy (4 cycles of EC Q3W and 12 cycles of weekly paclitaxel) followed by right mastectomy and axillary lymphadenectomy in August 2021. The histological examination revealed persistence of disease [NST invasive G3 carcinoma ER-PgR 0%, MIB-1 38% HER2 negative and ITC in 4 out of 24 nodes, ypT1aN0 (i+)]. Then the patient received adjuvant radiotherapy on chest wall and lymphatic drainage at a total dose of 50 Gy (2 Gy per fraction /25 fraction). In July 2022 she presented to the emergency department with neurological symptoms and a brain MRI demonstrated an expansive lesion in the right parieto-temporo-occipital site with a profuse perifocal edema. The histological report after brain surgery suggested "metastasis of poorly differentiated carcinoma compatible with breast cancer" and received adjuvant SRT on postoperative cavity (27 Gy in 3 fractions). In January 2023 she started chemotherapy (CT) with myocet + cyclophosphamide Q3W. Two months after initiation of CT, a brain MRI detected disease progression with apparently diffuse dural involvement characterized by multiple nodular thickenings.

Results. Our patient developed a characteristic nodular dural pathological infiltration after postsurgical SRT boost to the resection cavity.

Conclusions. This is a representative case of nLMD after brain adjuvant SRT possibly related to iatrogenic dissemination of tumor cells at the time of resection. nLMD is potentially can be avoided via a change in treatment sequencing. In fact, neoadjuvant SRT approach would seem to reduce the risk of post-surgery tumor spillage and LMD. Thus we await the results of prospective randomized trials of neoadjuvant versus adjuvant SRT for a brain metastasis

P363

RADIOTHERAPY STEREOTACTIC IN PATIENTS WITH OLIGOMETASTATIC BONE DISEASE FROM BREAST CANCER: ARCHIVAL RESEARCH ON 14 PATIENTS TREATED WITH SBRT

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Aims. Stereotactic body radiotherapy (SBRT) is assumed to be an effective radiotherapy technique to improve local control rates, with benefits in terms of progression-free survival and low toxicity rates. Due to the high incidence of secondary-onset bone lesions in breast cancer patients, nowadays it's necessary to direct research toward the implementation of validated procedures that can guide daily practices. To this purpose, we conducted a retrospective analysis on breast cancer patients with oligometastatic bone disease treated at our institution from 2015 to 2022

Methods. We retrospectively selected 14 breast cancer patients treated at our institution from 2015 to 2022 with SBRT on bone metastasis, regardless of the type of concomitant systemic treatment. Age ranged from18 to 65 with median age 52 SBRT was delivered in single or multiple fractions, with median dose of 16 Gy/1 fraction to the bone metastasis. To assess safety, patients have been clinically and haematologically evaluated before, during and after the end of the treatment. Toxicities have been collected according to CTCAE 5.0. To assess efficacy, patients have been radiologically evaluated both before and after the end of the treatment. Median follow up is 30 months.

Results. Out of the 14 patients selected, at a median follow up of 15 months all patients (100%) had good local control, at median follow up of 30 months, 6 patients (42%) had stable disease, at a median follow up of 60 months, 3(21%) patients had stable disease, at a finale follow up of 84 months 2 patients (13%) had stable diseas. No patients treated with SBRT manifested G2-G3 toxicities.

Conclusions. The clinical data analysed suggest that early treatment in oligometastatic breast cancer patients with involvement of only the bone district increases PFS with poor toxicity, no G3-G2 toxicity, good treatment tolerance, and improves local disease control.

Table 1.

• N patients	• PFS at 15 months	• PFS at 30 months	• PFS at 60 months	• PFS at 84 months	• N re-irradiated patients	• Toxicity
• 14	• 14	• 6	• 3	• 2	• 3	• G0-G1

P364

ROLE OF RADIOTHERAPY IN OLIGOMETASTATIC NEUROENDOCRINE BLADDER CANCER

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Aims. This is an evaluation of the role of radiotherapy in a patient with oligometastatic neuroendocrine bladder cancer, in partial response after first-line chemothera-

py. Neuroendocrine tumor of the bladder is a rare entity with a non-standard therapeutic pathway.

Methods. Our case is about a 78-year-old patient in excellent conditions with a history of multiple low-grade urothelial bladder tumors. During TURB for a 3 cm bladder dome lesion the Urologist found a non-resectable disease with a pathological diagnosis of neuroendocrine carcinoma of the bladder infiltrating the detrusor bundles, pT2 classification (AJCC 8th edition, 2017). CT scan demonstrated known bladder lesion, 27 mm enlargement of right adrenal gland and numerous subcentimeter lung micronodules, thus the patient started 6 cycles of chemotherapy with Carboplatin-Etoposide. At restaging CT pulmonary state was stable, bladder lesion was 20x26 mm and there was a reduction of right adrenal nodule. Moreover FDG-PET scan showed metabolically active bladder and right adrenal lesions and non-active bilateral pulmonary micronodules. Then Tumour Board was done: no indication for second line chemotherapy, according to histotype, thus locoregional treatment of bladder and right adrenal gland was proposed. The patient, initially asymptomatic, developed macrohematuria before starting RT.

Results. Radiation treatment was performed on both lesions with radical intent. It was delivered to bladder lesion an early boost of 9 Gy in 5 fraction (1.8 Gy/fraction) with full bladder, then to whole bladder organ 45 Gy in 25 fraction (1.8 Gy/fraction) with empty bladder. SBRT was performed on the right adrenal gland with a dose of 35 Gy in 5 fractions at 80% isodose. Each treatment was performed with VMAT technique with daily IGRT-CBCT. For SBRT no breath hold was fulfilled for poor patient compliance. Set up was obtained with vacuum pillow plus abdominal compressor for adrenal gland and pelvis immobilization system for bladder.

Conclusions. The patient well tolerated the treatment on both sites, with resolution of macrohematuria after the boost. It was reported no pain and nocturia two times per night. Additionally, it was noted an initial size reduction of bladder lesion during daily CBCT evaluation. The patient is now waiting for restaging. The proposed treatment has shown excellent tolerability thus radiotherapy can be considered a therapeutic option in this type of bladder neoplasm.

P365

MR-GUIDED STEREOTACTIC ARRITHMYA RADIOABLATION FOR VENTRICULAR TACHYCARDIA

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Aims. The purpose of this study is to report the feasibility of magnetic resonance imaging-guided stereotactic arrithmya radioablation (MRgSTAR) in patients suffering from ventricular tachycardia (VT).

Methods. An interdisciplinary decision was made to perform radioablation to minimize repetitive implantable cardiac electronic device (ICD) shocks in patients suffering from recurrent VT, despite maximal antiarrhythmic therapy and previous endocardial radiofrequency catheter ablations or with intolerance/contraindications to invasive ablation. All patients had a MR compatible ICD. The planning target volume (PTV), consisting in the interventricular septum plus 2mm margin, was delineate on a true fast imaging (TRUFI) MR scan acquired during simulation and prior to RT delivery. An IMRT treatment plan of 25Gy to 85% isodose (Figure 1) was on-table adapted and delivered in a single fraction on a dedicated MR-linac (MRIdian, ViewRay). Treatment simulation, planning and delivery for inpatients were performed on-table in a single workflow. Interfraction motion was managed using real-time MRI tracking, based on acquisition of a sagittal cine MRI during the whole delivery time and automated gating. The primary safety endpoint was treatment-related adverse effects during acute follow-up (FU). The primary short term efficacy endpoint was the reduction at 3 months of VT episodes.

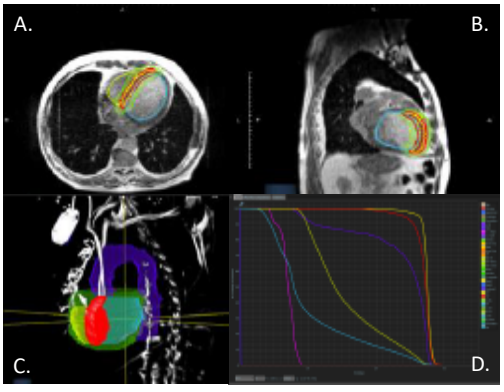

Figure 1. *MR-guided adaptive stereotactic arrhythmia radioablation (MRgSTAR) treatment plan.* Final target volume including inter-ventricle septum (PTV: red; CTV: yellow) treated with 25Gy (82% isodose: red line, 50% isodose: light green line). On simulation axial (A) and sagittal (B) MR- scan, great vessels and cardiac substructures are easily distinguished: left (cyan) and right (light yellow) ventricle, pericardium (green) and aorta (purple). 3D imaging reconstruction (C) shows the location of ICD leads. Dose to ICD (blue line) was 0,25Gy; dose to left (purple line) and right (magenta line) ICD lead was 28,9Gy and 9Gy, respectively, as shown by DVH (D).

Figure 1.

Results. From September 2022 to April 2023, five male patients (pts), affected by ischemic (2 pts) and non-ischemic (3 pts) cardiomyopathy, underwent MRgSTAR. Median age was 69 years (range 53-82). The mean left ventricular ejection fraction was 34% (range, 18-47). The mean PTV was 99cc (range, 30.6-114.7). The maximum total dose to ICD was <2 Gy, varying according to loca-

tion. Treatment times varied from 25 minutes for outpatients to 4 hours for inpatients, including the entire workflow; the mean beam-on time was 21 min (range 15-29). At a median 3-month FU (range, 1-10), no treatment-related serious adverse event occurred and a reduction of number of VT episodes was observed.

Conclusions. Stereotactic radioablation for VT can be considered a non-invasive alternative option for patients with drug-refractory cardiac arrhythmias. The use of a modern hybrid MR-Linac, enabling visualization of intracardiac structures on MR imaging and interfraction motion control by automatic gating, may increase accuracy and safety of STAR. Further clinical evaluation in larger populations of patients is needed.

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EVALUATING THE EFFICACY OF RADIATION THERAPY IN PREVENTING RECURRENCE OF HETEROTOPIC OSSIFICATION AFTER TOTAL XSHIP ARTHROPLASTY: CLINICAL AND RADIOLOGICAL OUTCOMES

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Aims. This study aimed to evaluate clinical and radiological outcomes, risk factors and complications in patients undergoing surgical removal of heterotopic ossifications (HO) after total hip arthroplasty (THA). The role of radiotherapy was analyzed.

Methods. A retrospective study was conducted, including patients who underwent surgical removal of periprosthetic calcifications after THA surgery. Patient demographic characteristics, imaging, previous surgery, clinical scores, and surgical parameters were analysed. Radiotherapy and pharmacological prophylaxis (NSAIDs and COX-2 inhibitors) were evaluated. Multivariable logistic regression analysis was used to assess the association of the presence of HO with age, sex, and all those variables, which differed significantly ($p<0.05$) in univariate analyses.

Results. Twenty-six patients with HO and 156 THA patients without HO (control group) were included. Patients with HO had a lower burden of comorbidities, lower BMI and lower ASA scores than controls. Out of 26 patients with HO, 10 (38.5%) underwent radiotherapy prophylaxis, administered as a single dose 24 hours before surgery. The total dose of 7 Gy was administered as single fraction on the volume defined by the extension of the prosthesis. Only one patient who underwent radiotherapy had a recurrence while new ossifications were found in 3 patients without prophylaxis (11.5%). Logistic regression analysis showed a significant inverse association between the presence of HO and ASA scores. Surgical approaches and radiographic classifications improved after surgery. Radiotherapy prophylaxis and pharmacological treatment showed positive results. Complications were recorded, including local and systemic complications, but overall, patients reported physical improvement following surgery.

Conclusions. Surgical removal of HO in symptomatic patients with high-grade disease resulted in good clinical and radiographic outcomes. Radiotherapy was an effective perioperative and preventive strategy for recurrence of HO, also associated with NSAIDs and COX-2 inhibitors. However, additional large-scale studies are needed to validate and further establish these findings.

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VENTRICULAR TACHYCARDIA ABLATION THROUGH RADIATION THERAPY (VT-ART) CONSORTIUM: SET-UP RESULTS OF AN OBSERVATIONAL MULTICENTRIC TRIAL VIA MATCHED PAIR ANALYSIS

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Aims. Ventricular tachycardia ablation through radiation therapy (VT-ART) for sustained VT seems promising. Still, definitive data are lacking, and no direct comparison with standard procedures is available. Aim of this multicenter observational study is to evaluate the efficacy and safety of VT-ART, comparing the clinical outcome of patients undergone to VT-ART to patients not having received such procedure.

Methods. The two groups will not be collected by

direct accrual to avoid randomization among the innovative and traditional arm: a retrospective selection through matched pair analysis will collect patients presenting features similar to the ones undergone to VT-ART within the consortium.

Results. The project has just been launched at the promoting Center. Currently, only the promoting Center is recruiting patients. Multicentric National Center inclusion has started. The first 10 patients have been enrolled by the promoting Center. All patients were male, with a mean age at the time of the procedure of 69 years (range, 60-75). Pretreatment mean left ventricular ejection fraction was 33% (range, 22-50). All patients had at least grade 1 heart failure according to the New York Heart Association (NYHA) classification, mean grade 2 (range 1-3). Patients had previously undergone an RFCA (range 0-3) for VT on average, with a median time between the most recent RFCA attempt and the STAR session of 20 days (range 0-67). The mean CTV volume of the was 96.09 cc (range 32.50-238.50). The mean PTV volume was 135 cc (range 44 -303). For all patients, SBRT was performed with a dose of 25 Gy (80% isodose) in a single fraction. In no case did the dose administered to OARs exceed the threshold reference values. Two patients died before reaching the 3 month follow-up for progressive heart failure. Four patients had a dramatic reduction in arrhythmic burden. The recruitment of similar patients to the irradiate group through matched pair analysis, did found 1 matches along the first month of retrospective active evaluation. Further details about radiotherapy planning, delivery and IGRT; patient matching and clinical comparison would be reported at the congress.

Conclusions. Our trial will provide insight into the efficacy and safety of VT-ART through a matched pair analysis, via an observational, multicentric study of two groups of patients with or without VT-ART in the multicentric consortium (with subgroup stratification into dynamic cohorts).

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PILOT TRIAL OF LOW DOSE WHOLE BRAIN RADIOTHERAPY IN EARLY ALZHEIMER'S DISEASE

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Aims. Alzheimer's disease (A.D.) is the most common form of dementia and accounts for at least 60-80% of dementia cases. Estimated 6.2 million Americans, ages 65 and older, are living with this disease. Barring the development of any novel therapeutics to prevent, slow, or cure A.D., this number continue to increase with an approximated 13.8 million Americans being diagnosed with A.D. by 2060. Therefore, new strategies must be developed to combat this very important disease. One field of medicine that has garnered significant interest from researchers to potentially treat A.D. is low-dose ionizing radiation. Various reports suggest that the brain's exposure to low doses of ionizing radiation can oppose the mechanism of accumulation of beta amyloid, neuroinflammation and cerebral vasculopathy.

Methods. In the initial stage of A.D. we want to compare two arms of different dosage of radiotherapy to verify the better effect of more dosage in A.D.. Arm one consist in drug administration (Donepezil 10 mg) and W.B.I. of 10 gray in 10 fractions. Arm two consist in Donepezil administration with same dose and W.B.I. of 20 gray in 10 fractions. We planned 20 patients per arm. We prepared neurocognitive and psychometric tests and bioumoral marker's dosage. Every patient is planned to receive positron emission tomography before and after W.B.I., psychometric and neurocognitive tests and umoral markers. We utilize W.B.I. with 3DCRT and we will explain criteria for elegibility and for exclusion, informed consent will be administered. The follow-up is planned at 6 weeks and at 3, 6, 9 12 months with PET and neurocognitive tests and umoral markers.

Results. We will show the protocol of this trial and preliminary results and tolerance of radiation therapy and side effects and finally the experience of other centers worldwide.

Conclusions. We propose, in this trial, the use of W.B.I. with a total low dose with the intention to slow down the evolution of A.D., and to ameliorate the patients quality of life reducing the progression of this disease.

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ONTHOLOGY AND STANDARDIZED DATA COLLECTION FOR STEREOTACTIC NONINVASIVE CARDIAC RADIOABLATION FOR REFRACTORY VENTRICULAR TACHYCARDIA: SETTING A STANDARDIZED WORKFLOW ON THE BASIS OF A SINGLE CENTER CASE SERIES

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Aims. Stereotactic cardiac radioablation (RA) for ventricular tachycardia (VT) is promising but controversial. Methods and details about RA procedure aren't univocal. We aimed to a standardized, sharable RA procedure to facilitate homogeneity of treatment and data collection among different centers.

Methods. After a first enrollment of RA case series, a planned systematic retrospective evaluation of multiple clinical and technical features was performed. Feedbacks were incorporated into the regular flow for SBRT treatments. RT specialist data were analyzed according to the following elements: i)Workflow (simulation setting, target definition, organs at risk(OAR) contouring, treatment planning, quality assurance, and treatment delivery); ii)Tools for target definition (cardiac CT, cardiac MRI, ECG, EAM); iii)Characteristics of RT machines (CBCT- and MR-guided Linac); iv)RA Prescriptive features (dose, fractions, isodose %, PMK simulation notes); v)Contouring details (CTV, PTV, OAR); vi) Delivery characteristics (image guidance, inter-/intra-fraction motion, delivery techniques, treatment timing).

Results. After the first 6 consecutive patients(pt), RA recruitment was stopped to set the dedicate process. The following pt have been treated according to the implemented standard. Were implemented in standardized manner dedicated to RA: a) organigram of doctors involved in indication and prescription of the treatment and process to rule the relative responsabilities (sharable figures available); b)workflow (figure available); c)pt assessment and initiation of the clinical pathway (clinical draft for RT's chart available); d) RA prescription and scheduling (table available); f) simulation (checklist with notes for procedure, pt safety, PMK management and pt specific cardiological setting available); e)contouring (CTV delineation and OAR setting and atlas notes available); g) planning; h) delivery (checklist with notes for workflow procedure, pt safety, PMK management, IGRT setting, procedural timing standardized collection) (tables available); i) standardized data collection (an internally validated,by both RTst and cardiologist, sharable excel file to indicate and collect across Centers the relevant feature for this peculiar type of patients was developed).

Conclusions. Outcome of RA can be affected by inhomogeneous data collection, and RT variability. The proposed approach can provide improvement homogeneity in the current increasing spread of a nonunivocal procedure.

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RADIOTHERAPY FOR ATYPICAL FIBROXANTHOMA OF THE SCALP

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Aims. Atypical fibroxanthoma is a rare skin cancer that usually arises from sun-exposed areas. The typical presentation is a nodular lesion of the head and neck skin in elderly patients. It is often difficult to differentiate it from other soft tissue sarcomas, such as dermatofibrosarcoma protuberans and malignant fibrous histiocytoma. Surgery is considered the standard treatment with wide local excision of at least 1 cm margin. Adjuvant radiotherapy is strongly suggested in case of non-radical excision due to high risk of local relapse and metastases. Two cases of elderly patients treated with adjuvant radiotherapy with scalp fibroxanthoma are presented.

Methods. The first case was an 83-year-old man who received primary excision of a 2 cm mass of the scalp. Histology revealed an atypical fibroxanthoma with incomplete excision, with the tumour involving the deep and lateral resection margins. Surgeons judged the patients as inoperable and, after a staging CT, he underwent adjuvant radiotherapy. The second case was an 86-year-old man who received primary excision of a 3 cm mass of the scalp histologically proven as atypical fibroxanthoma with tumour involving deep margin. The second patient refused to undergo surgery again and he accepted to be treated with adjuvant radiotherapy. Both patients were treated with external 6 MeV electron beam radiotherapy with a bolus of 0.5 cm and with a total dose of 60 Gy in 30 fractions (2 Gy per fraction). Acute and late toxicities were evaluated.

Results. Follow-up time was sixty-three months for the first case and ten months for the second patient. Both patients were alive and without disease until May 2023. Acute skin toxicity was G0 for the first patient and G1 for the second patient. No late toxicities were observed.

Conclusions. Adjuvant radiotherapy is a safe and effective option for patients with surgical atypical fibroxanthoma who received an incomplete resection of tumour in order to avoid local recurrence and to improve outcome.

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NON-MELANOMA SKIN CANCER IN ELDERLY PATIENTS: HYPOFRACTIONATED RADIOTHERAPY IMPROVES OUTCOMES AND CLINICAL MANAGEMENT

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Aims. In non-melanoma skin cancer (NMSC) hypofractionated radiotherapy is an established strategy of treatment in order to provide long-term local disease control and slow down the growth of the lesions. The aim of the study is to evaluate the regimen of 24Gy in 3 fractions in terms of tumor response and safety in elderly patients with NMSC who also have logistic difficulties or poor performance status in dealing with daily radiotherapy treatment.

Methods. The population study consisted of 17 patients (5 females - 12 males) with a median age of 82 years old (range 59-96) with a ECOG range of 0-2, treated from April 2018 to March 2023. All patients had a histologically proven non-melanoma skin cancer and were unsuitable for surgery or underwent R1 resection. Radiotherapy was delivered using electrons beams with energies of 6-9-12-15 MeV. The dose prescribed was 24Gy in 3 fractions, 8Gy a week for three weeks. A bolus was used to ensure full dose to skin surface. Toxicities were graded according to CTCAE 4.0. RECIST criteria were used to evaluate the treatment response.

Results. 17 patients (18 lesions) were included in the analysis. Lesions were classified according to histology (11 squamous cell carcinoma - 7 basal cell carcinoma) and to their location (15 head and neck, 1 trunk, 2 of the limbs). Considering patients' risk factors (age, PS and comorbidities) and tumor characteristics (size, location and depth of invasion), 11 patients were unsuitable for surgery and they were treated with radiotherapy with radical intent. The other 7 patients, who underwent R1 resection, received post-operative radiotherapy treatment. All patients completed the radiation protocol. All lesions were evaluable for response: complete response was achieved in 11 sites (61.1%), partial response in 5 sites (27.7%) while there were 2 local progression (11.1%). Median FUP was 18.3 months (range, 3-44 months). To date, 4 patients had no disease evidence (23.5%), 4 are alive with disease (23.5%) and 9 are dead of other causes (53%). Treatment was well tolerated and only two toxicities were observed: a G1 erythema and G2 conjunctivitis both managed with topic agents.

Conclusions. The regimen of 8 Gy in 3 fractions administrated once a week for three weeks allows elderly patients with non-melanoma skin cancer to complete the treatment and it combines a good toxicity profile with an impressive response rate in terms of local control both in radical and post-operative setting.

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COMPARISON OF HDR-BRACHYTHERAPY AND TOMOTHERAPY FOR THE TREATMENT OF NON-MELANOMA SKIN CANCERS OF THE HEAD AND NECK

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Purpose. Non-melanoma skin cancer (NMSC) has increased significantly over the last few decades, with surgical excision being the preferred form of treatment however external beam radiotherapy and HDR brachytherapy (HDR-BT) are an option. This study aimed to investigate and compare HDR-BT treatment plans with Helical Tomotherapy VMAT (HTV) treatment plans in small target volumes close to radiationsensitive organs of the head and neck to evaluate technique advantages in the treatment of NMSC lesions.

Methods. Patients who underwent skin cancer HDR-BT Freiburg flap treatment between 2019 and 2022 were included in this retrospective observational analysis. The clinical target volumes (CTVs) were contoured by an expert radiation oncologist from the skin surface to 5mm or 3mm depth, and its visible extension was marked with a radio-opaque tin wire. Each patient had two treatment plans, one using an individually shaped HDR-BT surface mould and the other HTV calculated for this study. Quality assurance of treatment plan was performed in HDR-BT through EBT3 gafchromics. HTV treatment plans were verified through Delta4 Phantom+. Plans were then compared employing organ at risk (OAR) maximum doses and the conformity index CI. Expert radiation oncologists assessed the quality of both plans using their routine workflow for plan evaluation.

Results. All patients had complete remission, excellent or good cosmetic outcome and no toxicities were reported. HTV delivered a better target coverage uniformity and lower OAR doses than HDR-BT, with a statistically significant difference ($p<0.05$). HTV showed higher CIs and maximum dose for the optic nerve, optic chiasm, and lens in the homolateral part. From clinical evaluations HTV shows a better overall plan quality. Despite this HDR-BT performs better when in CTVs concave surfaces are present.

Conclusions. HTV offers more conformal treatment and better OAR sparing, but HDRBT may be superior for complex geometries and faster treatment times.

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HDR BRACHYTERAPY IN THE TREATMENT OF SKIN KAPOSI SARCOMA: A MONO-INSTITUTIONAL SERIE

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Aims. Kaposi sarcoma (KS) is a multi-focal, angioproliferative neoplasm that usually appears on the skin, but can also involve the visceral organs. Since KS lesions are considered very radiosensitive, the most widely advocated type of treatment, with excellent local control is radiotherapy based. HDR brachytherapy is considered superior to EBRT in terms of dosimetric coverage that is related to lower complication rates. In order to choose between these two techniques, characteristics of the patient, Karfnosky performance status (KPS), and patient's delivery comfort would be considered.

Methods. Between June 2010 and February 2023, we treated 11 patients for a total of 39 lesions patients with KS with HDR-IRT. Patients underwent brachytherapy treatment for a total dose ranging from 10 to 30 Gy (10 Gy per fraction). Toxicities were recorded using the Common Terminology Criteria for Adverse Events scale (CTCAE) v. 4.03. Median follow up was 41.1 months.

Results. Median age was 61,8 years. Acute toxicity was recorded in 22 lesion treated (53.8%). Grade 1 erythema appeared in 15 cases with late persistence in 5 cases, despite the application of eudermic cream in all cases; Grade 2 erythema appeared in 5 cases, with regression to grade 1 in two cases and progression to superintensive ulcer from Pseudomonas Aeruginosa in one case, treated by specialist. Towards the end of each treatment schedule, epidermolysis developed which was resolved within 3 weeks; Grade 3 skin toxicity apperars in 1 case (2.6%) and was managed with dressings and close outpatient follow-up until grade 1 toxicity. At last follow-up, 64.1% (25/39 lesions) patients were disease free and 35.9% (14/39) recorded a partial response.

Conclusions. HDR brachytherapy could be a good option in the treatment of KS. Brachytherapy, using hypofractionated regimen, provides excellent results, in terms of cosmetic and local control, and compliance, very relevant in elderly patients. HDR brachytherapy results in a very good toxicity profile.

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CUSTOMIZED 3D-PRINTED BOLUS FOR HIGH-DOSE-RATE BRACHYTHERAPY IN FACIAL BASAL CELL CANCER

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Aims. Basal cell carcinoma (BCC) is the most common form of skin cancer and the standard treatment is complete surgical removal. Radiotherapy, particularly high-dose-rate (HDR) brachytherapy, is a treatment option for inoperable tumors or in postoperative setting in case of positive/close margins after surgery. Skin lesions are usually treated with flap-style Flexible Freiburg Applicator (FFA) but in anatomical site FFA could not perfectly adhere to patient skin leading to non-optimal treatment outcome. Emerging 3D printing technology allows the creation of customized bolus and catheter trajectories. Aim of this study was to analyze our clinical experience of HDR brachytherapy with 3D-printed bolus for patients with BCC.

Methods. Five patients with histologically proven BCC were enrolled in this analysis. Median age was 78 years (range between 68 and 88 years) and they all were judged inoperable. The site of lesions was nose/perinasal region for two patients, external ear for two patients and cheek for one patient. All patients received a computer tomography scan and target volumes and OARs were delineated. The CT data set was imported into a 3D Slicer software to define applicator shape and an Autodesk Fusion 360 software has been used to design the desired catheter paths. For each patient, channels were created and their paths optimized in order to cover PTV. The designed applicator exported in .stl file format has been printed with an ultimaker 3D printer by using a TPU filament. Patients received a second CT scan with the 3D-printed bolus fixated to the face and than a treatment plan was generated with a prescribed physical dose was 39 Gy in 13 fractions.

Results. The 3D printed applicator matched its design and could be stably placed over the patient's surface. Moreover, it shows better adhesion against standard FFA. The size of the largest air gap at the interface of the 3D-printed structure was 1-2 mm against 6-9 mm for the FFA. All treatment plans had 95% isodose line covering 98% of the PTV and patients were successfully treated with skin toxicity of G0 for 3 patients and G1 for 2 patients.

Conclusions. HDR brachytherapy with customized 3D-printed bolus for facial skin cancer is a safe and well-

tolerated option for patients with inoperable basal cell cancer. The proposed workflow for 3D printing patient-specific surface applicators is feasible and it offers dosimetric advantages.

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HIGH FREQUENCY ULTRASOUND (HFUS) IN PATIENTS WITH NON MELANOMA SKIN CANCER (NMSC) AS A POST RADIOTHERAPY ASSESSMENT TOOL

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Aims. Cutaneous non-melanoma skin cancer (NMSC) can be effectively treated using radiation therapy (RT) in cases of inoperability, patient preference, or in an adjuvant setting. However, the decision to use RT for patients with other risk factors, such as PNI invasion, T3, G3 degree of differentiation, should be made based on the discretion of the radiation oncologist and the tumor board multidisciplinary (TBM) as the side effects may outweigh the benefits. HFUS (US ultra-high frequency, 48MHZ) is the latest generation ultrasound technique that provides an accurate and reliable analysis of the skin structure from the epidermis to the hypodermis. In this study, we aimed to evaluate the effects of RT treatment on the skin structure clinically and using HFUS, record adverse effects and severities, and detect any disease recurrence that may not be clinically evident.

Methods. Between July 2022 and April 2023, we enrolled 20 patients who underwent RT in our institute to evaluate toxicities clinically and using HFUS. Out of these patients, 13 had cSCC, while 7 had BCC, and 10 received RT for radical treatment, while the other 10 had adjuvant RT. The dosage used for both groups was 55/60 Gy in 10/20 fractions, respectively, using electron beam with 6MeV energy. We followed up every 3 months using clinical examination and HFUS.

Results. At the first follow-up after 3 months, 4 patients developed erythema G1 according to the CTCAE toxicity scale, while only 1 patient developed erythema G1 at the second follow-up after 6 months. None of the remaining patients showed any acute toxicities during the follow-up at 3/6/9 months. Using HFUS, we observed alterations in the skin layers' echogenicity immediately after RT treatment, but after 3 months, there was a restitutio ad integrum of the treated skin region, and the skin layers' echogenicity returned to normal.

Conclusions. Our study confirms that RT for NMSC is a safe and well-tolerated treatment, both in the radical and adjuvant modality, with minimal toxicities. Adjuvant therapy with RT should be considered in high-risk cases of NMSC.

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3D PRINTED BOLUS FOR RADIOTHERAPY OF SKIN TUMORS. A PRELIMINARY PLANNING AND FEASIBILITY STUDY

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Aims. 3D printing technology can be applied to create individually customized shapes for 3D printed boluses (3Db) for radiation therapy (RT). Irregular surface of the patient's skin, mainly in head and neck (H&N) skin tumors, often cause some air gap effects when using commercial boluses, with second skin sparing effect, thus reducing both maximum and surface doses. Customizable 3Db reproducing the complexity of human anatomy in skin H&N tumors are designed to compensate these irregular surfaces. In this study we evaluated the feasibility of using printed patient-specific 3Db to irradiate H&N skin tumors.

Methods. From June 2021 to March 2023 we retrospectively analyzed clinical, pathological and dosimetric characteristics of patients treated in our Institution with RT using 3Db in the postoperative and radical setting, for H&N cutaneous malignancies, including several histological types. 3Db were drawn on a first CT-simulation with our treatment planning system and then 3Db were printed on a CE marked stereolithography 3D printer (Form 3B, Formlabs, Somerville, MA, USA) using a CE marked photosensitive clear rigid resin (density: 1.15 g/cm^3). Thereafter, patients underwent CT simulation wearing a 3Db under the immobilization system mask and then planned for RT.

Results. Twenty patients with H&N skin tumors, enrolled in an observational study (PORTO-1), were treated with customized 3Db fabricated for RT at the nose, cheek, or periorbital or scalp region both in postoperative and radical setting. Clinical and pathological characteristics are shown in Table 1. Patients were mainly treated with volumetric modulated arc technique, including flattering filter free beam technology or stereotactic body radiotherapy for tumor diameter ≤ 4 cm in radical setting, (prescription dose: 36 Gy/6 fraction every other day) using 6 MV energy. The planning target volume coverage achieved with 3Db was optimal (median D95%= 96.6%, range: 94.7%-99.3%, mean V95%= 96.44% ± 2.83% SD) while maintaining high minumum doses (mean Dmin= 58.13% ± 29.47% SD).

Conclusions. Printed customized 3Db are effective build-up devices that could potentially improve treatment efficiency in H&N skin tumors. In particular, resin 3Db are cost-effective compared to the commercial ones: i) having suitable dosimetric properties, ii) perfectly fitting against the irregular face shape, and iii) significantly increasing build-up region doses.

Table 1.

Patients		No (%)
Treatment setting	Radical	4 (20)
	Postoperative	16 (80)
Region	Nose	13 (65)
	cheek	3 (15)
	periorbital	3 (15)
	scalp	1 (5)
Histological type	squamous cell carcinoma	15 (75)
	basal cell carcinoma	2 (10)
	angiosarcoma	1 (5)
	Merkel cell carcinoma	1 (5)
	malignant peripheral nerve sheath tumor	1 (5)
Technique	VMAT X 6 MV	7 (35)
	VMAT FFF X 6 MV	9 (45)
	SBRT	4 (20)
Total dose (cGy)	median (range)	5460 (3600-6250)
Dose/fraction (cGy)	median (range)	215 (150-600)
D_{95} (cGy)	median (range)	5791 (3603-6601)
	mean (± SD)	5310 (±1000)
V_{95} (%)	median (range)	96.6 (94.7-99.3)
	mean (± SD)	96.44 (±2.83)

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NON MELANOMA SKIN CANCER IN THE ELDERLY: HYPOFRACTIONATED RADIOTHERAPY AND CASE REPORTS

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Aims. Non Melanoma skin Cancer (NMSC) is a radiation therapy (RT) responsive cancer and this therapy remains the first choice in inoperable patients or for unresectable lesions. Many elderly patients have medically or technically inoperable NMSC that could be cause pain or bleeding. In these patients extended daily treatment may be not recommended for logistically difficult or inappropriate performance status (PS). In this group of patients a shorter course of RT, called hypofractionated RT (HRT), delivered in less of 10 fractions either daily, every other day or once weekly, should be strongly indicated. In literature most HRT schedules utilize a dose fraction range of 4-12Gy, according to the tumor dimension and/or PS, until a total dose of 30Gy-60Gy.

Methods. Case 1: A 100-year-old female was referred with a rapidly growing four centimeters lesion of the nose. The biopsy confirmed a moderately differentiated squamous cell carcinoma (SCC). Surgery was excluded because it was impossible to achieve complete resection. HRT was evaluated and the patient consented to receive six fractions of 7Gy delivered to the lesion with a 1cm margin, twice a week with 6MeV electron beam. Total dose 42Gy. Case 2: A 94-years old man was referred with a biopsy proven 2cmx2.5cm bleeding SCC of the left temporal fossa. The patient was unfit to the surgery, so was recommended RT and he accepted to receive 10 fractions of 5Gy to the lesion with a 1cm margin delivered three times a week with 6MeV electron beam. Total dose 50Gy.

Results. Both patients had a good local control with non-residual disease at six month from the end of HRT. The progression free survival (PFS) and the overall survival (OS) are 18 months. They only refer a G1 cutaneous toxicity with dyschromia as unique collateral effect.

Conclusions. Hypofractionated course of RT is an effective treatment option and can be safely administered in elderly patients, with low toxicity rate and optimal results.

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RADIOTHERAPY IN PRIMARY ORBITAL NON HODGKIN LYMPHOMA: A SINGLE INSTITUTION CASE SERIES

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Aims. Orbital non-Hodgkin's Lymphomas (NHL) are rare tumors, comprising only 1% of all NHL, with an annual incidence of 1 case per million. Primary radiotherapy (RT) with conventional doses is the standard therapy for localized indolent lymphomas of the orbit resulting in

high response rates and good local control. The aim of this study was to describe treatment outcome and toxicity in patients with orbital NHL treated with RT.

Methods. In this retrospective analysis, case records of patients with a diagnosis of orbital NHL treated at our institute were analyzed from 2002 to 2022. Patients were worked up and staged according to Ann Arbor system. Diagnosis was confirmed by surgical biopsy using incision, excision or orbitotomy. The median radiation dose was 36 Gy (4-36 Gy) in 2-20 fractions.

Results. A total of 79 patients were included in this study. Median age at diagnosis was 64 years. In 36 cases (45.6%) there was involvement of the right orbit, in 40 cases left orbit (50.6%) and in 3 cases synchronous bilateral eye involvement (3.8%). The most common histology was extranodal marginal B-cell lymphoma (n=56, 70.9%). Patients presented with typical symptoms like periorbital swelling. At a median follow-up of 38 months (1-226), 53 patients were alive (3y-CSS 90%), with 10 patients relapsed (1 locally, 1 in contralateral eye, and 8 distant, 3y-PFS 86%). Three-years local control resulted 98.6%. Acute ocular radiotherapy-related complications (grades 1–2) were detected in all eyes treated, like conjunctivitis, and periorbital edema. No grade 3–4 acute toxicity occurred. Late eye toxicity was reported in 30.4% of cases. Grade 1 cataracts were detected in 17 patients (21.5%), grade 1 dry eye in 16 (20.3%), reduction of visual acuity in 8 (10.8%; all cases grade 1, except of 2 cases grade 3) and grade 1 maculopathy in 2 (2.5%).

Conclusions. Radiotherapy was very effective in disease control in patients bearing localized orbital lymphoma. Although the doses utilized in this series are higher than that recommended at the present (20-24 Gy), the toxicity profile was tolerable.

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10 YEARS MONO INSTITUTIONAL EXPERIENCE IN MYELOABLATIVE TOTAL BODY IRRADIATIONS – A CLINICAL DOSIMETRY ANALYSIS

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Aims. Myeloablative total body irradiation (TBI) is a well-established practice used in the conditioning of hematopoietic stem cell transplantation in patients with hematological diseases. At our Institution, an extended-distance supine technique has been implemented using a 15 MV LINAC beam. Lung lead compensating filters together with PMMA and water bolus were used to increase dose homogeneity. This study aims to review in-vivo dose (IVD) measurements over 10 years of treatments assessing the technique's robustness and accuracy.

Methods. In 2012 we improved our TBI technique by introducing complete CT planning with Oncentra TPS (Elekta AB, Stockholm, Sweden). A 2-lateral opposite fields plan (with source-to-midline distance ranging from 3.65 m to 3.90 m) was calculated with a collapsed-cone algorithm to estimate the shape and thickness of lung compensators and monitor units (MU) to give 100% of the prescription dose to the patient midline. IVD is performed during each fraction at 6 different anatomical locations (groin (G), oral cavity (C), neck (N), apical (AL) and basal lung (BL), hips (H)) with silicon diodes or thermoluminescent dosimeters (TLD) and used to adjust the MUs. The IVD data of 109 TBI patients treated between 2012 and 2023 were retrieved. Data are related to different schedules (12 Gy in 6 bi-daily fractions, 9.9 Gy in 3 daily fractions) for a total of 558 fractions and included the variation of total delivered MUs from the TPS estimate (ΔMU) and dose deviations at the end of the treatment.

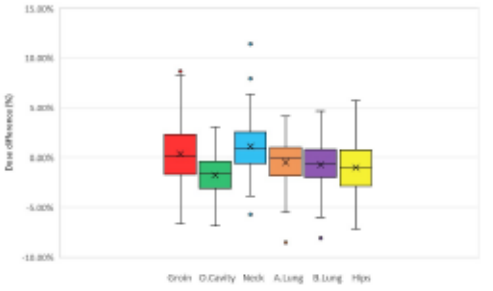

Fig. 1 – Boxplot of percentage dose difference in six anatomical regions considered in this study. Mean, maximum and minimum values are shown, together with percentiles and outliers.

Figure 1.

Results. Pediatric patients represent the majority (87%) and the diagnosis most represented is acute lymphoblastic leukemia. The pediatric and adult median age was 10 and 45 years respectively. The ΔMU and minimum and maximum range is -1.2% [-7.1% - 3.6%] and in only 5% of patients the thickness of lung compensators was changed. Median deviation and minimum and maximum range between measured and prescribed doses are G 0.1% [-6.7%, 8.7%], C -1.6% [-6.9%, 3.0%], N 0.8% [-5.8%, 11.4%], AL -0.1% [-8.6%, 4.1%], BL -0.6% [-8.1%, 4.7%] and H -1.0% [-7.2%, 5.7%]. No evident inter-fraction fluctuation was registered.

Conclusions. It is possible to confirm the implemented technique's robustness and validity in delivering the prescribed dose under IVD monitoring. Nevertheless, this technique and associated IVD are strongly time-consuming. An ongoing study focuses on the possible adoption of a new efficient TBI method exploiting modern radiation therapy techniques.

P380

WHOLE BODY MRI FOR CONTOURING OF TOTAL MARROW AND LYMPH NODE IRRADIATION

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Aims. Total Marrow and Lymph Node Irradiation (TMLI) is a modulated RT technique delivered as a conditioning regimen for bone marrow transplantation, aiming to spare organs at risk from high doses. The TMLI target includes bones, lymphatic system, and spleen. The use of contrast agents in whole body CT (WB_CT) is limited by long acquisition times, affecting lymph node clinical target volume (CTV_LN) definition. Our aim is to evaluate the potential of whole body simulation magnetic resonance imaging (WB_MRI) in optimizing lymph node delineation.

Methods. Since 2010, 126 patients were treated in our center using VMAT based on WB_CT without contrast media, using a margin of 5 mm around CTV_LN. Since March 2022, 15 patients underwent WB_MRI without contrast agent, co-registered with WB_CT and two CTV_LNs were defined on the two series (Figure 1). Deformable registration was performed using various ROIs for better position accordance, and MR-based segmentation was mapped on WB_CT that was used for planning optimization. Customized scripts assessed CTV_LN topological similarity, volume comparison, and dosimetric coverage.

Results. Mean difference between CT-based and MRI-based CTV_LN was 175 cc with larger volumes for MRI, indicating CT underestimation. Mean Dice Similarity Coefficient (DSC) for CTV_LN was 0.76 (range 0.68-0.81), while Hausdorff Distance (HD) was 3.0 mm (range 2.2-3.8). Pelvic lymph nodes showed the best geometric similarity (DSC: 0.81, range 0.79-0.82; HD:1.5 mm, range 1.4-1.6 mm), while the abdominal region had the worst (DSC: 0.72, range 0.55-0.83; HD: 2.8 mm, range 1.6-3.8 mm). Mean V95% were 100% (range 100-100%) for WB_CT and 98.1% (range 95.5-99.4%) for WB_MRI.

Conclusions. Geometric similarity between segmentation was observed with slight differences, mainly due to CT underestimation of specific lymph node areas and imperfect co-registration of anatomical regions. Target volume coverage remains clinically reasonable considering historical margins around CTV_LN. MR-based contouring may enable more accurate lymph node segmentation, reducing required margins. This study was supported by grant AuToMI (GR-2019-12370739, funded by the Italian Ministry of Health).

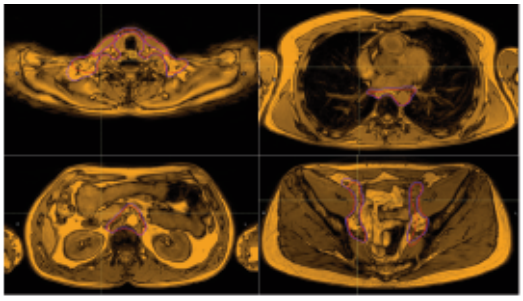

Fig.1 Axial view of CT-based (red line) and MRI-based CTV (blue line) for H&N, thoracic, abdominal and pelvic regions.

Figure 1.

P381

DOSIMETRIC BENEFITS OF DEEP INSPIRATION BRETAH-HOLD TECHNIQUE IN MEDIASTINAL LYMPHOMA RADIOTHERAPY

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Aims. Deep inspiration breath-hold (DIBH) is a radiotherapy technique that has demonstrated dosimetric advantages in the treatment of thoracic tumors. However, limited information is available regarding the use of DIBH in patients with mediastinal lymphoma. This study aimed to evaluate the potential dosimetric benefits of the Breath-Hold technique by comparing free breathing (FB) plans to DIBH plans in patients with mediastinal lymphoma.

Methods. Six lymphoma patients with mediastinal involvement were included in this study. All patients underwent chemotherapy followed by radiotherapy. CT simulation scans were acquired for both FB and DIBH, with contrast administered during the FB phase. Patients were immobilized using 4-5 point thermoplastic shells when the neck was involved. Contours and treatment plans were generated for both FB and DIBH data sets, and dosimetric data were compared. Radiotherapy was delivered in breath-hold for all patients, except one, using

a Varian True Beam and two or three full arcs in VMAT technique (energy 6MV), combined with voluntary deep inspiration breath-hold. Breath-hold amplitude during CT simulation, setup check and irradiation was monitored using a surface monitoring system (Varian RGSC System).

Results. In the comparison of treatment plans between DIBH and FB, we observed in DIBH a mean heart dose reduction of 0.86 Gy (p=0.3), a mean right ventricle dose reduction of 1.06 Gy (p = 0.3), a mean left ventricle dose reduction of 1.06 Gy (p = 0.2), while the mean right and left breast doses were reduced by 0.65 Gy (p=0.2) and 0.61 Gy (p=0.08), respectively. DIBH also resulted in a decrease in mean right lung dose (9.13 *vs* 10.19 Gy, p = 0.3) and mean left lung dose (7.43 *vs* 9.1 Gy, p=0.16).

Conclusions. The administration of radiotherapy in a breath-hold setting for mediastinal lymphoma patients is feasible and safe. Although not statistically significant due to the small sample size, our findings demonstrate a trend of dose reduction in all analyzed organs at risk. DIBH offers the potential to decrease the radiation dose to the heart, lungs, and breasts in this patient population. Further investigation with a larger cohort is warranted to validate these promising results.

P382

ROLE OF TOTAL SKIN ELECTRON BEAM RADIOTHERAPY AT RELAPSE AFTER ALLOGENEIC TRANSPLANT IN MYCOSIS FUNGOIDES AND SÉZARY SYNDROME

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Introduction. Based on current literature, about 50% of patients affected by mycosis fungoides (MF) and Sezary syndrome (SS) relapse after allogeneic transplant (AT). Despite this, spare evidence is available for the management of relapsed disease, above all for the use of radiotherapy (RT). The aim of this study is to evaluate the role of total skin electron beam radiotherapy (TSEBI) in the post-HT setting.

Materials and Methods. We retrospectively analyzed data from 10 consecutive patients affected by MF or SS, who underwent AT and were treated with TSEBI after relapse. All patients were treated at Italian centers. Given the small number of patients, we only performed an observational analysis on outcomes after TSEBI and its safety.

Results. Each patient received several therapies before AT, including systemic therapy, phototherapy and RT, both local RT and TSEBI. The AT was performed from 2013 to 2022, with a median time from diagnosis to AT of 40 months (range 10-108). The progression free survival (PFS) after AT was 3.6 months (range 1-6). The median time from AT to TSEBI was 8.7 months (range 4-18). TSEBI was performed with the schedule of 20 Gy in 20 fractions in 40% of cases (all TSEBI schedules used are shown in Table 1). The best response after TSEBI was complete response (CR) in 3 patients, very good partial response (VGPR) in 5 patients and partial response (PR) in 2 cases. With a median follow-up (FUP) of 28.8 months after TSEBI (range 2-82), we observed 9 relapses, with a median PFS of 14.4 months (range 2-60), but 6 out of 10 patients relapsed within 6 months from the end of TSEBI. Of note, patients that experienced a longer PFS were treated with higher RT doses. The overall survival (OS) of the whole cohort was 79 months (range 35-124); at the end of our FUP 3 patients had died (2 for disease progression and one for another cause). As adverse events, only 2 patients experienced acute epitheliolysis during TSEBI, graded 2 and 3 according to CTCAE score and resolved at the first follow-up visit.

Conclusions. In our cohort, despite the small number of patients and the adverse clinical characteristics, TSEBI appears to be a potential and useful treatment strategy for palliation at relapse after AT in MF/SS patients. In our experience higher doses could be required in order to obtain a durable response in this unfavorably selected patient cohort.

Table 1.

Patient	DTF	PFS POST TSEBI (months)
1	24	4
2	20	6
3	20	2
4	10	2.5
5	12	5
6	20	2
7	36	60
8	20	2
9	36	22
10	24	9

P383

TOTAL BODY IRRADIATION PLUS CHEMOTHERAPY AS CONDITIONING REGIMEN IN ALLOGENEIC HEMATOPOIETIC STEM CELLS TRANSPLANT FOR ACUTE LYMPHOBLASTIC LEUKEMIAS.

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Aims. Total body irradiation (TBI) is part of the standard conditioning regimen prior lo bone marrow transplantation (BMT) or peripheral blood cell transplantation (PBSCT) in the management of patients with acute lymphoblastic leukemias (ALL). The retrospective analysis of 90 patients (pts) treated are showed.

Methods. Between April 1999 and December 2000, a total of 90 pts are treated in combination with TBI and high dose chemotherapy followed by transplantation: 35 (38,89%) pts received a matched sibling donors, 43 (47,78%) pts received a matched unrelated donors (MUD), and finally 12 (13,33%) pts received a haploidentical donors. At the time of transplantation 33 pts (36,7%) received BMT and 57 pts (63,3%) PBSCT. All pts received an identical conditioning regimen comprising hyperfractionated TBI: 12 Gy in 6 fraction: twice-a-day (6h interval), in 3 days (12 cGy/6fr/3d). The chemotherapic conditioning regimen was endoxan in 79 (87,78%) pts, flutarabine in 11 (12,22%) pts. fractionated TB I was delivered by LINAC 6 MV. Dose homogeneity was assured by the use of four fields: pos¬terior-anterior, anterior-posterior and two lateral-laterals, with the patient alternatively assuming a supine and right or left decubitus position which was used for each fraction. The dose was calcu¬lated at the umbilical plane. At lime of TBI 47 pts (52,22%) were in first complete response (CR), 30 pts (33,33%) in second and third CR, and 13 pts (14,44%) in partial response or relapse. The median age at time of TBI was 27 years (range 6-60); 63 pts (70%) were male and 27 (30%) females. The median follow-up was 27 months (range 1-251).

Results. 47 (52,22%) pts were alive, and 43 (47.78%) pts were dead. At median follow-up (27 months) the overall survival (OS) and disease free survival (DFS) for all pts were 58,1% and 51,4%, respectively. On univariate and multivariate analysis for OS and DFS status at lime of TBI ($p<0.0001$) and type of chemotherapy ($p=0.05$), were found to be statistically significant. Acute grade I and grade > II GvHD occurred in 14 pts (15,56%) and in 11 (12,22%) pts, respectively; limited, extensive, and middle chronic GvHD occurred in 15 pts (16,67%), in 3 pts (3,33%), and in 3 pts (3,33%), respectively.

Conclusions. Our experience confirm the literature data. Different TBI parameters such as total dose, dose rate, size of fractions, fractionation, technique, and chemotherapy should be defined.

P384

BENEFIT IN DOSE ACCURANCY BY REDUCING THE SIMULATION CT TO TREATMENT TIME IN TOTAL MARROW IRRADIATION

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Aims. Total Marrow (lymph-node) Irradiation (TMI) is a challenging technique employed in the treatment of hematopoietic malignancies, with the primary goal of minimizing toxicities associated with total body irradiation by irradiating the entire skeletal structure while sparing nearby organs at risk. Due to the complexity of optimizing the treatment plan, TMI typically takes several days, leading to the simulation CT being performed more than 15 days before treatment (CT-15). In this study, we aim to evaluate the correlation between CT-15 and the delivery position.

Methods. Since 2010, our center has treated 127 patients with TMI using VMAT based on the simulation CT-15. Plans were normalized to ensure that 98% of the planning target volume (PTV) received 98% of the prescribed dose (PTV_V98% = 98%). Image-guided radiotherapy (IGRT) utilizing cone beam CT (CBCT) was employed. Shifts and the overall quality of matching (rated on a scale of 1-5) were evaluated. In the most recent 27 patients, a second CT scan was performed on day -4 (CT-4) to assess anatomical changes compared to CT-15 and evaluate their impact on the treatment plan. Non-rigid registration was used to propagate the PTV from CT-15 to CT-4, and the plan was recalculated using the same monitor units. The doses received by 95/98% of PTV (PTV_D95/98%) were calculated for both CT-15 and CT-4.

Results. A total of 693 CBCT scans were analyzed. The vector CBCT-CT matching demonstrated an average shift of 5.3±7.4mm. Image quality agreement was suboptimal (i.e., <4) in 18% of cases. For these patients, the CBCT-CT shift was 5.5±4.2mm ($p>0.05$). PTV_D95%=100.7±0.6% and PTV_D98%=97.3±1.1% in the CT-15 series but reduced to PTV_D95%=97.5±1.0% and PTV_D98%=91.3±1.2% when transitioning to CT-4. Overall, a better agreement

between CBCT and CT-4 was observed (Figure 1). In two cases (out of 27, i.e., 7% of cases), significant differences were observed between the two CT scans, leading to plan re-optimization using CT-4 and subsequent treatment delivery. This rapid optimization was facilitated by automation tools utilizing artificial intelligence (AI) developed by our team.

Conclusions. Our study highlights the potential benefits of reducing the time required for the TMI plan optimization. CT-4 exhibited improved agreement with CBCT compared to CT-15. These findings support the use of AI-based tools to expedite treatment plan optimization, enabling enhanced accuracy and efficiency in TMI delivery.

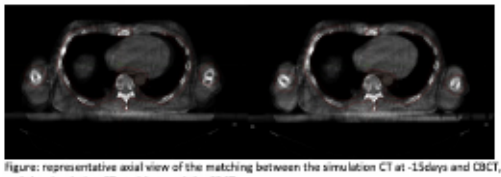

Figure: representative axial view of the matching between the simulation CT at -15days and CBCT, and the simulation CT at -4days and the CBCT.

Figure 1.

P385

RADIOTHERAPY IN PRIMARY MEDIASTINAL B CELL LYMPHOMA: A RETROSPECTIVE SERIES

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Aims. Primary mediastinal B cell lymphoma (PMBCL) represents a distinct and rare clinicopathological entity (2-4% of Non-Hodgkin's Lymphomas). Most of patients are women in the third-fourth decade with bulk mediastinal masses and extension to adiacent tissues. Immunochemotherapy with R-CHOP or R-DA-EPOCH ± radiotherapy (RT) is the standard of care despite lack of randomized studies. Concerns about RT exist specially regarding secondary malignancies and heart toxicity. Optimal dose and technique are still debated. At our institute PMBCL are currently managed with an intensified immunochemotherapy regimen (R-GMALL) in order to avoid RT related adverse events. RT is performed if metabolic active residual disease is still recognizable and is not prescribed when a bulky mass was demonstrated at diagnosis but a metabolic complete response was obtained after systemic therapy.

Methods. We retrospectively evaluated a consecutive series of 15 patients treated with chemotherapy and RT since 2014. Eleven/15 patients were female. Median age at diagnosis was 35 (range 21-55). Ten patients presented a stage I-II disease and 5 patient a stage III-IV disease. Fourteen patients had a bulky mass. Ten/15 patients were treated with R-GMALL and 4/15 patients were treated with R-CHOP immunochemotherapy due to poor performance status or comorbidities. One patient shifted to R-CHOP after 2 R-GMALL cycles because of toxicity. In 10/15 cases RT was delivered in a salvage setting with PET positive residual disease (dose 36-46 Gy) and in the other 5 cases as consolidative therapy on initial bulky mass (dose 30 Gy) after R-CHOP chemotherapy. In patients with positive PET after chemotherapy, low dose volume was defined as initial bulky mass and high dose volume as metabolic active disease. In 11 patients three dimensional conventional RT technique was used. Volumetric modulated arc therapy technique was used in the 4 most recently treated patients.

Results. With a median follow-up of 62 months(range 1-106), no recurrences and no toxicity related to radiotherapy were observed. One patient died for other causes.

Conclusions. In our experience chemotherapy followed by radiotherapy represents a safe and effective strategy in patients with PMBCL. Recent technology is helpfull to minimize radiotherapy toxicity. A better definition of optimal dose and technique is needed.

P386

RADIOTHERAPY IN THE MANAGEMENT OF OCULAR ADNEXAL LYMPHOMA: A SINGLE ISTITUTION'S EXPERIENCE OVER 12 YEARS

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Aims. Lymphoma of the ocular adnexal are a rare extranodal localization of NHL (Non-Hodgking Lymphoma). We reported our treatment techniques, complication rates and disease outcomes after radiotherapy (RT) for the management of lymphoma involving the orbits.

Methods. Between 2010 and 2021, 11 pts with confirmed histological diagnosis of lymphoma were treated in our center with RT. Median age was 59 years. The staging included: ophthalmological examination, a full blood examination (complete blood count, liver function tests and lactate dehydrogenase (LDH)), magnetic resonance

imaging (MRI) of the orbit; chest, abdomen and pelvis Computed tomography (CT) and positron-emission tomography (PET). We classified the population with Ann Arbor staging system: 8 pts with stage IE and 3 pts with IIE disease. 8 pts were treated with primary RT only, 3 pts received previous systemic treatments. 6 pts were treated with Proton Beam Therapy (PBT) and 5 pts with External Beam Radiotherapy (EBRT). Mean radiation dose was 35 Gy. Toxicities were graded according to CTCAE version 5.0. Median follow-up was 6,55 years. Patients, treatment characteristics and outcome are summarised on Table 1.

Results. 5-year local control rate was 98%; only 1 pt developed an out of field recurrence.

Acute toxicity was mild, requiring minimal intervention. 85% experienced dry eyes G1 (treated with eye lubricants), 70% acute blurred vision, 15% cataract G2. No cases of retinopathy, optic nerve injury were reported.

Conclusions. This series demonstrates that definitive radiotherapy is effective and safe in controlling stage IE and IIE primary orbital lymphomas. Based on our experience, we recommend RT as first line treatment for primary orbital lymphoma. Lens-sparing techniques should be used when possible to reduce toxicity.

Table 1.Patients, treatment and outcome summary.

Patients	Sex	Age	Stage	Site Of Involment	Sistemic Treatment	Beam Energy	Total Dose	No. Of Fractions/ Dose Per Fraction	Local Response/ Distant Relapse
1	F	38	IE	Conjunctiva RE	INF	X/6MV	39.6 Gy	22/ 1.8 Gy	CR
2	F	62	IE	Lacrimal gland LE	CHOP	p+/62MeV	36 GyE	4/ 9 GyE	CR
3	M	75	IIE	Eyelid RE	None	p+/62MeV	36 GyE	4/ 9 GyE	CR / yes
4	M	31	IE	Lacrimal gland LE	Ab monoclonal	p+/62MeV	30 GyE	3/10 GyE	CR
5	F	56	IE	Lower eyelid RE	None	p+/62MeV	36 GyE	4/ 9 GyE	CR
6	F	68	IE	Upper eyelid RE	None	X/6MV	35 Gy	14/ 2.5 Gy	CR
7	M	70	IE	Conjunctiva LE	None	X/6MV	39,6 Gy	22/ 1.8 Gy	CR
8	M	59	IE	Conjunctiva LE	None	X/6MV	20 Gy	10/ 2Gy	CR
9	F	58	IIE	Lacrimal gland LE	None	p+/62MeV	30 GyE	3/10 GyE	CR
10	F	49	IE	Upper eyelid LE	None	p+/62MeV	30 GyE	3/10 GyE	CR
11	M	65	IIE	Lower eyelid LE	None	X/6MV	20 Gy	10/ 2Gy	CR

RE: right eye; LE: left eye; INF: interferon; CR: complete response

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STEREOTACTIC BODY RADIATION THERAPY IN PEDIATRIC PATIENTS: A MULTICENTER, MULTIDISCIPLINARY LITERATURE REVIEW

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Aims. In adult patients, it is well known that hypofractionated stereotactic body radiation therapy (SBRT) is a safe and effective treatment for bone, brain, and visceral oligometastases, as well as in the retreatment of previously irradiated sites. However, SBRT is infrequently used in pediatric patients. Furthermore, randomized trials and guidelines on this topic are missing. Therefore, we planned a review of the available literature on this issue, through the collaboration between radiation oncologists and pediatric oncologists of Italian centers.

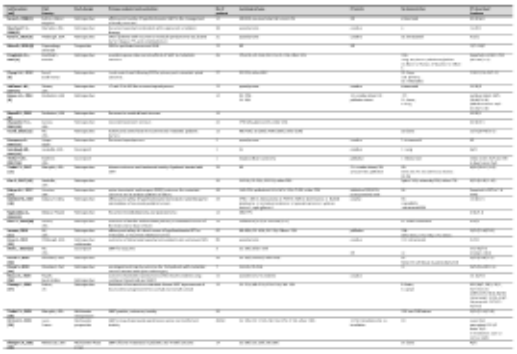
Methods. The aim of this review was to analyze the papers published in the last 15 years on SBRT of oligometastases in pediatric patients. Therefore, through a search conducted in PubMed, Scopus, and Cochrane library, the records published from 2008 to 2023 were found and the following data were extracted and collected: authors, year of publication, study design and endpoints, number of enrolled patients, histological type of primary tumor, SBRT aim, number of irradiated lesions, dose and fractionation, overall survival, progression-free survival, local control, tumor response, and symptom relief.

Results. Thirty studies were selected: 3 case reports, 24 retrospective studies, and 3 prospective studies. None of the latter was randomized. Half of the papers reported on SBRT of intracranial lesions (metastases or recurrence), while half reported on SBRT of bone or visceral lesions. Overall, 393 patients and 1074 lesions (extracranial: 66%; intracranial: 34%) were treated. Total SBRT dose ranged between 6 and 45 Gy, and the number of fractions ranged among 1 and 8. Median follow-up and median overall survival were 23.0 months (range: 1.1-240) and 26.3 (range: 5.2-147) months, respectively. The median local control, reported in 11 studies, was as follows: 6-month: 93%, 1-year: 75%, 2-year: 68%. Six papers reported symptomatic response with a relief rate ranging from 42% to 68%. Nine studies reported acute and late toxicity. The median rate of acute and late grade ≥ 3 toxicity was 13.2% and 3.8%, respectively.

Conclusions. Our review confirms the lack of high-evidence findings on SBRT in pediatric patients. The available studies suggest that the results achieved in pediatric patients are comparable to those of adult subjects. Further prospective studies, possibly multicenter, will be able to provide more reliable evidence on this topic, use-

ful for the proposal of specific guidelines for this setting.

Table 1.



P388

HIGH DOSE RATE BRACHYTHERAPY FOR CHILDHOOD SOFT TISSUE SARCOMA

G. Scarzello[1], M. S. Buzzaccarini[1], E. Pozzo, F. Salvador[1], F. Martino[1], G. Gobitti[1], S. Suresh Kallothu[1], F. Guida[2], M. Paiusco[2], M. Krengli[1]

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Aims. To evaluate the efficacy of HDR-BT in children undergoing combined modality treatment for STS.

Methods. From September 1998 to December 2022, 81 children (median age 8 years, range 1 to 18) with non-metastatic STS received HDR-BT as part of locoregional treatment. There were 35 males and 46 females, near all (77) had primary lesions, embryonal rhabdomyosarcoma (44) was the most common histological type and extremities were most commonly involved site (23); 10 children had lesions greater than 5 cm in maximum diameter. Surgical margins where positive in 25. Twenty three children have been treated according to the Italian-German cooperative protocol RMS 96 and 58 according to the European EpSSG protocol RMS & NRSTS 2005. Treatment included wide local excision and HDR-BT with or without EBRT: 76 patients have been treated with radical HDRBT alone, while 5 received a combination of HDR-BT and EBRT. All patients were treated using iridium192, by Nucletron Microselectron V3 Afterloader. HDR-BT dose has been 36 Gy, in 12 fractions, twice per day, with a minimum interfraction interval of 6 hours, with a 2 day split after the 6th application. All children receiving EBRT have been enrolled in the RMS 96 protocol, therefore they underwent irradiation up to a total dose of 32 Gy in 20 fractions of 1.60 Gy, twice per day, after a HDR-BT boost up to 18 Gy in 6 fractions twice per day. CT simulation has supplanted orthogonal films in BT planning. MRI has been used to delineate differences in soft tissues not readily seen on CT scan. Normal tissues and target volumes have been modeled using contouring on CT-MRI fused images.

Results. After a median follow up of 7 years, 67 patients are alive in first CR and 2 are alive after amputation. Two have LR and after developed lung metastasis, 2 have developed nodal and lung metastasis without LR; all of them had died for tumor progression. Patients have tolerated the HDR-BT procedure well and there has been no major acute complications directly related to the procedures. Regarding late effects, a scar on the arm that led to functional limitations and a skin necrosis on the foot required corrective surgery.

Conclusions. HDR-BT is an effective modality in the conservative management of STS in children. The high local control and acceptable toxicity is encouraging. Treatments must be executed carefully, because the short treatment times do not allow any time for correction of errors, and mistakes can result in harm to patients.

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INTENSITY MODULATED RADIATION THERAPY WITH JAGGED JUNCTION APPROACH FOR CRANIOSPINAL IRRADIATION: A RETROSPECTIVE DOSIMETRIC ANALYSIS

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Aims. Craniospinal irradiation (CSI) is the cornerstone of curative treatment for medulloblastoma (MB) in children and young adults. Even if a standard radiation therapy approach has not been established yet, many conformal techniques are at our disposal. Basing on data supporting the benefits of Intensity Modulated Radiation Therapy with jagged-junction (IMRT- JJ), we performed a dosimetric analysis to evaluate its ability to obtain an ideal panned target volume (PTV) dose coverage and organs at risk (OARs) exposure, according to QUANTEC.

Methods. We selected 10 children with low-risk MB (LR-MB) or standard-risk MB (SR-MB) treated at our institution with IMRT-JJ CSI, from 2015 to 2022, according to the SIOP-PNET 5 protocol. All plans employed 3 field sets, with 3 unique isocentres allocated at the same depth. Iso1 was placed in the cranial PTV, with a field set

consisting of 7 beams. Iso2 and Iso3 were placed in the spinal PTV with both field sets consisting of 3 beams. CSI to a total dose of 18 Gy (LR-MB) or 23.4 Gy (SR-MB) was delivered to the craniospinal axis, including the entire subarachnoid volume with a special focus on the cribriform plate, the temporal fossae intracranially, the thecal sac and the full width of the spinal subarachnoid space. In the aim to spare the temporal lobes, hippocampi, pituitary gland, and cochlea, boost to a total dose of 54 Gy was delivered only to the tumour region (defined by pre-operative MRI).

Results. All IMRT-JJ resulted in an excellent total PTV coverage, with median V95% ≥98% and V107% ≤1%. This technique has demonstrated to be less likely to produce hot and cold spots at the junctions. Optimal HI and CI values were obtained thanks to the inverse planning technique. IMRT-JJ resulted in an acceptable low-dose bath of 2 Gy, with a better sparing of healthy tissues out the PTV. Mean dose resulted <9 for right/left lens, <20.5 Gy for esophagus, <9 Gy for heart, <10 Gy for right/left kidneys and <10 Gy for right/left lungs.

Conclusions. Since literature data suggests that late toxicities after CSI may be related to the irradiation of both PTV and OARs, the application of a conformal technique such as IMRT-JJ is crucial to obtain an optimal coverage and at the same time a low dose to healthy tissues. Even if it is too early to establish a relationship between IMRT-JJ dosimetric advantages and improved clinical outcomes, in absence of a standard approach, this technique can be considered a valid option.

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CARDIAC SUBSTRUCTURES SPARING WHOLE LUNG IMRT IN PATIENTS WITH EWING PEDIATRIC TUMOR AND LUNG METASTASIS: A CASE REPORT

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Aims. Children with pulmonary Ewing' sarcoma metastases are commonly treated with whole lung irradiation (WLI); standard AP-PA WLI was linked with a cardiac dose near a prescription dose and subsequent increased risk of heart toxicity. To assess the dosimetric benefit of cardiac substructures-sparing (CSS) intensity modulated radiation therapy (IMRT) in pediatric patient undergoing WLI.

Methods. A 13- years boy affected by Ewing's sarcoma of the left humerus was treated according to ISG/AIEOP EW-1 protocol; he developed an early micronodular lung relapse treated with second-line chemotherapy, high-dose Busulfan Mephalan with PBSC rescue, subsequent WLI (15Gy, 10 fractions). To prepare WLI plan, after a breathing session training, a Simulation CT was acquired in 4D mode, using a sensor (Anzai Medical, Japan) and a belt placed in the upper abdomen to detect pressure changes due to abdominal motion. The resulting scans were binned according to respiratory phases ranging from 0 (maximum inspiration) through 100 (maximum inspiration). The Planning Target Volume (PTV) included the total internal target volume (ITV) of both the right and left lungs contoured as a composite volume and was obtained with a 1-cm expansion of the 4-dimensional lung volume. The following CS were contoured: whole heart (WH), right and left atrium (RA;LA) and ventricle (RV; LV), left ventricular myocardium, left main (LCA), left anterior descending (LAD), left circumflex (LCA) and right coronary (RCA) arteries.

Results. Treatment planning was achieved using CSS-IMRT. IMRT plan was performed with 9 beams using a step-and-shoot technique with a total of approximately 80 segments. PTV coverage was 94% (Figure 1). CSS-IMRT doses were as follows: Mean (MD) and max (Mxd) WH dose were respectively 10.6 and 16.29Gy; LV MD 11.2 and Mxd 16Gy and V14.3 (95%), V12.5 (83%) and V7.5 (50%) were respectively 11.4, 38.8, 90.8%; RV MD 8.2 and Mxd 15.5Gy and V14.3, V12.5 and V7.5 were respectively 4.1, 10.6 and 48%; LA MD 9.8 and Mxd 15Gy and V14.3, V12.5 and V7.5 were respectively 1.3, 10.5 and 99%; RA MD 12 and Mxd 15.3Gy and V14.3, V12.5 and V7.5 were respectively 8.8, 49,7 and 99%; Left myocardium MD 11.2 and Mxd 15.7Gy; LCA, LAD, LCA and RCA mean dose were respectively 12, 12, 10.7 and 11.9Gy.

Conclusions. CSS-IMRT and 4D treatment planning has the potential to reduce CS dose and consequently cardiac toxicity in children receiving WLI instead standard AP-PA WLI

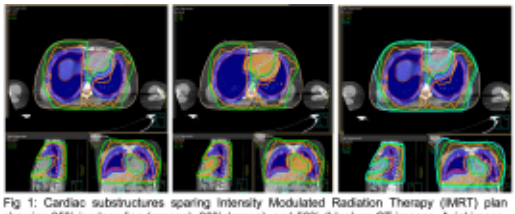

Fig 1: Cardiac substructures sparing Intensity Modulated Radiation Therapy (IMRT) plan showing 95% isodose line (orange), 90% (green), and 50% (blue) on CT images. Axial image, Sagittal and Coronal image showing biventricular sparing with IMRT.

Figure 1.

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THE BOTANICAL DRUG PBI-05204, A SUPERCRITICAL CO2 EXTRACT OF NERIUM OLEANDER, SENZITIZES ALVEOLAR AND EMBRYONAL RHABDOMYOSARCOMA TO RADIOTHERAPY *IN VITRO* AND *IN VIVO*

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Aims. Treatment of rhabdomyosarcoma (RMS), the most common a soft tissue sarcoma in childhood, provides intensive multimodal therapy, with radiotherapy (RT) playing a critical role for local tumor control. However, since RMS efficiently activates mechanisms of resistance to therapies, despite improvements, the prognosis remains still largely unsatisfactory, mainly in RMS expressing chimeric oncoproteins PAX3/PAX7-FOXO1, and fusion-positive (FP)-RMS. Cardiac glycosides (CGs), plant-derived steroid-like compounds with a selective inhibitory activity of the Na+/K+-ATPase pump (NKA), have shown antitumor and radio-sensitizing properties. We searched a molecule belonging to CGs also capable to hinder cancer cellular growth through activation of radio-sensitizing mechanisms.

Methods. The therapeutic properties of PBI-05204, an extract from Nerium oleander containing the CG oleandrin already studied in phase I and II clinical trials for cancer patients, were investigated, in vitro and in vivo, against FN- and FP-RMS cancer models.

Results. PBI-05204 induced growth arrest in a concentration dependent manner, with FP-RMS being more sensitive than FN-RMS, by differently regulating cell cycle regulators and commonly upregulating cell cycle inhibitors p21Waf1/Cip1 and p27Cip1/Kip1. Furthermore, PBI-05204 concomitantly induced cell death on both RMS types and senescence in FN-RMS. Notably, PBI-05204 counteracted in vitro migration and invasion abilities and suppressed the formation of spheroids enriched in CD133+ cancer stem cells (CSCs). PBI-05204 sensitized both cell types to RT by improving the ability of RT to induce G2 growth arrest and counteracting the RT-induced activation of both Non-Homologous End-Joining and homologous recombination DSBs repair pathways. Finally, the antitumor and radio-sensitizing proprieties of PBI-05204 were confirmed in vivo. Notably, both in vitro and in vivo evidence confirmed the higher sensitivity to PBI-05204 of FP-RMS. **Conclusions.** PBI-05204 represents a valid radio-sensitizing agent for the treatment of RMS, including the intrinsically radio-resistant FP-RMS.

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RADIATION-INDUCED SARCOMAS (RIS) IN LONG-TERM SURVIVORS-CANCER PATIENTS: OUR EXPERIENCE

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[1]Radioterapia IRCCS-CROB; [2]Fisica Sanitaria IRCCS-CROB, Italy

Aims. Radiation induced sarcoma (RIS) are rare iatrogenic malignancy occurring many years after radiotherapy (RT). They represent about 3% of all soft tissue sarcomas. These tumors are characterized by poor 5-year overall survival, ranging from 10 to 36% according to disease stage at diagnosis. The aim of this study is to describe in long term-survivors cancer patients (pts) the prevalence, the tumor characteristics, as well as prognosis and outcome of RIS in a cohort of patients treated in our center in a period of 13 years (2009-2022).

Methods. We examined all histologically documented cases of sarcoma recorded in the period 2009 -2022. There were 186 cases (85 males and 101 female pts) of sarcomas with a median age of 59.7 years (15-91 yrs). Criteria by Chanan *et al.* were used to identify RIS patients as follows: no evidence of the new tumor at RT time; sarcoma arise in the irradiated field; relatively long

latency period before sarcoma onset and histologically proven sarcoma.

Results. Among 186 sarcoma pts, we identified seven (3.8%) case of RIS. Five cases arose in the irradiated field for breast cancer while two cases in head and neck cancer pts. The mean age for RIS was 64.8 years (42-77 yrs) while the median age of primary cancer diagnosis was 57.3 years (40-61 yrs). Mean latency time was 7.3 years (2 -15 yrs). To better define RIS incidence, we retrospectively analyzed all breast and head and neck primary tumors that underwent RT. We found 0.15% of RIS incidence, in which breast cancer accounted for 0.19%, whereas for head and neck cancer was 0.1%. Histology of RIS consisted of desmoid tumor (1 pt), angiosarcomas (2 pts), chondrosarcoma (1 pt), leiomyosarcomas (2 pts), undifferentiated pleomorphic sarcoma (1 pt). Breast angiosarcoma showed the MYC immunohistochemical stain positive nuclear distribution within the atypical endothelial cells and TP53 negative immunohistochemical stain. BRCA 1 and 2 mutations were not found. Surgery was the most common treatment approach with mastectomy for breast RIS. The median overall survival was 36 months.

Conclusions. This study confirms the low incidence and the high mortality of RIS. These tumors are unique in their epidemiology and characteristics and need special research investigating for new intensive treatment strategies to improve the outcome.

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FAR-RMS PROTOCOL: NEW RADIOTHERAPY STRATEGIES

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Radiation Oncology Dpt, I.O. V. I. R.C.C. S.

Aims. To achieve the best outcomes for patients with localized, metastatic and relapsed RMS.

Methods. Local control remains the principle challenge in RMS. In the RMS 2005 study the 3-year EFS for localized disease had increased to 67.2% for high risk and to 56.2% for very high risk patients, yet local failure was still observed in the majority of relapses. The risk of long term toxicities is significantly increased when both surgery and RT are required for treatment, compared with the use of either modality on its own, so strategies to minimize these risks are needed. Preoperative RT has potential advantages over postoperative. In this protocol we propose to investigate the role of preoperative RT in operable standard, high and very high risk RMS, where there is an intended R0/R1 resection, randomizing this against standard postoperative RT. The current RT doses are based on the outcomes from EpSSG, COG and CWS studies, yet there is a lack of studies investigating the true impact of dose escalation for patients with higher risk of local failure. In this protocol we propose to investigate the role of risk adaptive RT randomizing patients with higher local failure risk to dose escalated *vs* standard RT: resectable disease where there is the intention to perform an R0/R1 resection, or tumors with a complete response to induction chemotherapy, randomizing between dose escalated RT 50.4Gy and the standard dose 41.4Gy; unresectable disease receiving primary RT alone, randomizing between 59.4Gy and the standard dose 50.4Gy. To date the standard of care for patients with metastatic disease has been to systematically irradiate all metastatic sites, but there is conflicting data. In this protocol we have undertaken to compare the outcomes of patients with extensive metastatic disease (>3 metastases extrapulmonary metastases, or lung metastases not in complete remission after induction chemotherapy), by randomizing patients to either receive RT to metastatic sites or not, in order to determine whether this actually improves the outcomes for this group of patients. In modern RT quality assurance is an essential component of all future studies. In order to reduce deviations in both target definition and treatment delivery and contributing to the ultimate aim of further improving the outcomes from local therapy, it is the intention that all RT in this protocol will be undertaken utilizing the international quality assurance platform as part of the SIOPe QUARTET project.

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EPIRUBICIN-IFOSFAMIDE REGIMEN IN SOFT TISSUE SARCOMAS: ACUTE HEMATOLOGICAL TOXICITY AND MANAGEMENT, A REAL-WORLD EXPERIENCE

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Aims. In patients receiving epirubicin-ifosfamide (EI) treatment for soft tissue sarcomas (STS), management of acute hematologic complications is often challenging, potentially leading to therapeutic delays or interruptions. We therefore analyzed the rate, severity, and impact on treatment compliance of hematologic toxicities in STS patients receiving EI with or without radiotherapy.

Methods. We gathered clinical and treatment-related data from 41 total patients who underwent chemotherapy for STS at our center from January 2018 to December 2022. The patients have been treated with Epirubicin (60

mg/m^2 day 1,2 q21) and Ifosfamide (3 g/m^2 day 1,2,3 q21). As per our institutional protocol, patients received premedication with antiemetics and corticosteroid, hydration with MESNA, and G-CSF daily as primary prevention at each cycle (day 4-9). Chi-square test was used to compare categorical variables. Toxicity Grade (G) was scored using the Common Terminology Criteria for Adverse Events (CTCAE) v 5.0.

Results. We analyzed a total of 41 patients: among these, 18/41 in neoadjuvant settings, 13/41 with postoperative intent and 10/41 for first-line metastatic treatment. Radiotherapy treatment was also associated in 26/41 cases. Hematologic toxicity consisted of anemia (36/41, but only 2/41 with G≥3), neutropenia (12/41) and thrombocytopenia (5/41).Seven patients experienced febrile neutropenia which was fatal in 3 cases. Dose reduction was required in 21 patients, and was motivated by low blood cell count at baseline and poor hematologic tolerance in 13 and 8 patients respectively. One patient started on a reduced dose as a precaution and then carried out the rest on a full dose due to good tolerance. No significant correlation was found between G≥3 hematologic toxicity and concurrent radiotherapy.

Conclusions. Despite pharmacological prophylaxis and protocol ancillary therapies, EI chemotherapy regimen may induce neutropenia which in some cases proves to be lethal. Early surveillance of the symptoms and prompt treatment in febrile episodes is advised. Grade ≥3 toxicity was not increased by concurrent radiotherapy treatment.

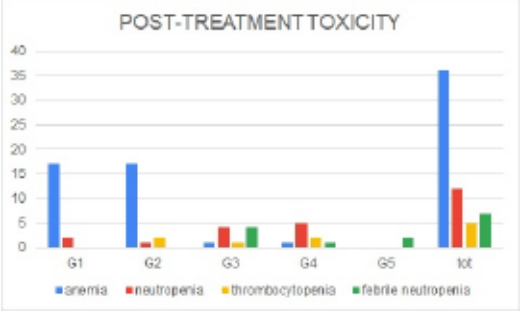

Figure 1.

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ONCOLOGICAL OUTCOMES OF NEOADJUVANT RADIOTHERAPY COMBINED WITH RADIATIVE HYPERTHERMIA IN SOFT TISSUE SARCOMA: A SINGLE-CENTER EXPERIENCE

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Purpose. This study aims to evaluate the oncological outcomes of patients with soft tissue sarcoma (STS) of the extremities and trunk who received neoadjuvant radiotherapy (RT),with or without chemotherapy, combined with radiative hyperthermia (HT).

Methods. A retrospective analysis was conducted on patients who underwent RT and concomitant HT followed by surgery. All patients received VMAT radiotherapy with a total dose of 50 Gy in 25 fractions. HT sessions were performed immediately after RT and within three hours of chemotherapy administration. The duration of each HT session rangedfrom 70 to 90 minutes,ensuring that the target temperature was maintained at or above 40°C for at least 60 minutes. BSD-500 or BSD-2000 system was used based on the depth of the lesion. Survival rates were estimated, and acute and late toxicity were reported.

Results. A total of 20 patients were included in the analysis, comprising 11 males and 9 females, all with Performance Status ECOG 0-1. The mean age was 61 years (range, 34-87). Six patients had stage II disease, while the remaininghad stage III disease. Four patients had trunk lesions, and the remaining had extremity lesions. The mean size of the treated tumor was 8.8 cm (range 2-20). Nine patients (45%) had primary lesions, and 11(55%) had recurrent lesions. The mean number of HT sessions was 7 (range 6-10). Eight patients receivedconcomitant chemotherapy, while4 patients received it sequentially.Grade 2 toxicity was observed in 5 patients (23.8%), with no cases of grade 3-4 toxicity.Nineteen patients (95%) underwent surgery after completing the treatment, with all achieving negative surgical margins except for one patient (5.2%) who had microscopic R1 margin involvement. Complete pathological response was achieved in 7 out of 19 patients (36.8%). With a median follow-up of 21.3 months, disease progression occurred in 5 patients (25%), including 2 cases of local progression and 3 cases of systemic progression (2 lung, 1 lung and liver). Median overall survival was not

reached. Three-years overall survival resulted 82%. The median disease free survival was 31.6 months, at three years it was 52%. Three-years local control and metastases free survival ware 87% and 78%, respectively.

Conclusions. These findings suggest that neoadjuvant RT combined with radiative HTholds promise in the management of STS, although larger studies are warranted to validate these results.

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PROGNOSTIC FACTORS, CLINICAL AND TOXICITY OUTCOMES FROM A LARGE COHORT OF PATIENTS WITH SOFT TISSUE SARCOMA TREATED WITH PREOPERATIVE RADIATION THERAPY

M. Banini[1], I. Bonaparte[1], M. Loi[1], D. Greto[1], E. Olmetto[1], P. Garlatti[1], M. Mangoni[1], A. Peruzzi[1], D. Campanacci[2], G. Scoccianti[2], G. Roselli[3], A. Palomba[4], C. Caporalini[4], L. Livi[1]

[1]Radiation Oncology, Azienda Ospedaliero Universitaria Careggi, Università di Firenze; [2]Oncologic Orthopedic Surgery, Azienda Ospedaliero Universitaria Careggi, Università di Firenze; [3]Radiology Azienda Ospedaliero Universitaria Careggi, Università di Firenze; [4]Histopathology and Molecular Diagnostic Unit, Careggi University Hospital, Italy

Aims. Primary therapy for Soft Tissue Sarcoma (STS) often consists of a combined surgery and radiation therapy (RT). Preoperative RT may be advantageous due to lower dose requirements and possible tumor downstaging, particularly in association with chemotherapy (CT) and modern radiation techniques. This study evaluated efficacy, toxicity and prognostic-related features in STS patients treated with preoperative RT and surgery.

Methods. Clinical and treatment related data were collected from consecutive STS patients treated at our Institution with preoperative RT followed by surgery from 1991 to 2023. Overall survival (OS), Distant-metastasis free survival (DMFS), Local control (LC) data were collected and estimated using Kaplan-Meier method. Log-rank text and Cox model were conducted to identify factors related with outcome and toxicity.

Results. 156 patients, for whom follow-up data were available, were included in our analysis. Median age was 55 years. Tumors were mostly located in the limbs (94%). Disease stage was T>=3 in 71% of cases. Most represented histotypes were liposarcoma (LPS, 34%), undifferentiated pleomorphic sarcoma (UPS) (24%) and synovial sarcoma (5%). RT prescription dose was 50 Gy in 25 daily fractions combined with CT in 82,5 % patients. IMRT was used in 34% of case. R0 and R1 resection were obtained in 93% and 7% of patients respectively. Severe surgical sequelae (wound dehiscence or sepsis) were reported in 16% of patients. Grade (G) 3 disease was observed in 69,8% patients. After a median follow-up of 32 months, OS rates at 2 and 5 years were 85% and 72%, DMFS rates were 69% and 57% and LC rates were 87% and 82%, respectively. At multivariate analysis only R1 resection resulted significant for worse LC rates (p=0.0214), whereas G3 disease was correlated with worse DMFS (p=0.0029). At Cox analysis G3 (p=0.004) and R1 (p=0.05) correlated with worse overall survival. Use of IMRT and chemotherapy didn't result in higher severe surgical sequelae.

Conclusions. In this large STS cohort, neoadjuvant treatment resulted in high RO rate and favorable outcomes. R1 resection and G3 disease correlated respectively with impaired LC and DM FS. Both factors were associated with poorer OS, highlighting the interest of treatment intensification. IMRT and concurrent CT were not correlated with surgical sequelae.

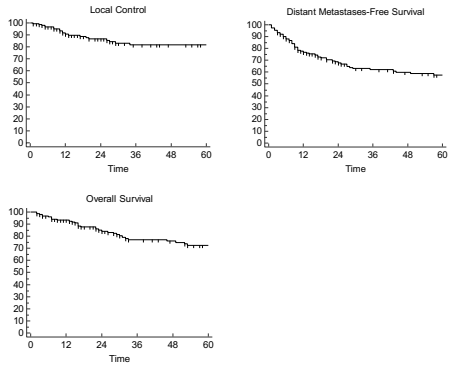

Figure 1.

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CLINICAL PATHOLOGICAL CHARACTERISTICS, PATTERN OF CARE AND SURVIVAL OF NON-METASTATIC ANGIOSARCOMA

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Aims. Angiosarcoma (AS) is a rare soft tissue sarcoma subtype that may arise de novo or in previously irradiated patients. Due to its scarce incidence, prognostic

factors and optimal pattern of care are ill-defined. The aim of this study is to investigate the clinicopathological features, treatment modalities and outcome of AS.

Methods. Clinical and treatment-related data from consecutive non-metastatic patients treated at our Institution from June 2006 to December 2020 were retrospectively reviewed. Local control (LC), Distant Metastasis-Free Survival (DMFS), Overall Survival (OS) were calculated using the Kaplan Meier method and compared with log-rank test.

Results. Twenty-two patients were included in the analysis. Median age was 60 (17-86) years. In 15 patients, AS arose in a previously irradiated field following adjuvant radiotherapy of prior breast adenocarcinoma. No information on pre-existing edema were available. All patients underwent surgery consisting of wide excision and mastectomy in 6 and 16 cases respectively.Grade 3 FNCLCC disease was identified in 7 patients. Postoperative radiotherapy and chemotherapy were required in respectively 5 (median dose 60 Gy, range 25-66 Gy) and 3 patients. At the time of our analysis after a median follow-up of 36 months disease recurrence occurred as local, distant, and concurrent distant and local failure in 3, 6 and 6 patients. Three-years LC, DMFS and OS rate were 59%, 51% and 76% respectively. At statistical analysis, only deep-seated tumors were correlated with impaired DMFS (29 months *vs* NR, p=0.0043) and OS (29 months *vs* NR, p=0.001), while no correlation was found between outcome and previous irradiation.

Conclusion. AS is characterized by poor outcomes, and may require treatment intensification with more extended surgery due to prior management and possible prognostic role of deep-seated tumor.

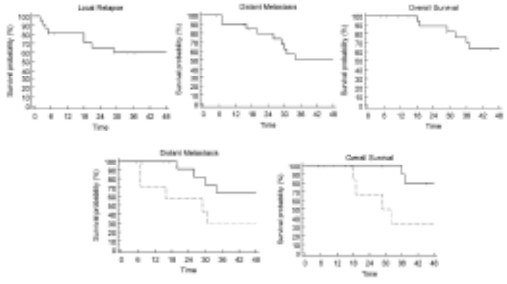

Figure 1.

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PRELIMINARY CLINICAL RESULTS OF AN ONGOING PHASE II TRIAL: SPRINT (PREOPERATIVE IMRT SIB IN LOCALLY ADVANCED SOFT TISSUE SARCOMA)

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Aims. Neoadjuvant radiotherapy is delivered in Soft Tissue Sarcoma (STS) patients to downstage the tumor and improve resectability. However, clear margin resection (R0) may not be achieved in tumors located near critical structures such as the neurovascular bundle (NVB). The aim of this study is to increase R0 rate adding an IMRT boost to the potential sites of suboptimal resection. We report results from the first 5 patients treated.

Methods. We designed a prospective monocentric single-arm phase II study enrolling locally advanced STS patients eligible for surgery. RT is administered in 25 daily fractions to the MRI-based GTV and peritumoral tissue at risk of microscopic spread (CTV1) to a dose of 50 Gy (2Gy/fraction), with a simultaneous integrated boost to the tumor/dissection plane interface (CTV2) to a dose of 60 Gy (2.4 Gy/fraction). A margin of 0.5 cm is applied to both CTV to obtain PTV1 and PTV2. Concurrent anthracyclines-based chemotherapy is allowed up to 3 cycles. Primary endpoint is the R0 resection rate. Secondary endpoints include pathologic complete response rate, objective response rate, OS, local and distant PFS, acute and chronic toxicity rate. To assess an increase in R0 rate from 81% to 97% assuming β=80% e α=0.05, 33 patients will be included. Dose constraints are shown in Table 1. At least 95% of the PTV1 and PTV2 should be covered by 95% the prescription dose up to a maximum allowed dose of 107%.

Results. Five patients were included, with a mean age of 47 years. Tumor was in the limbs and in the trunk in respectively 4 and 1 patient. Concurrent chemotherapy was performed in 2 patients. Epirubicin and ifosfamide-based chemotherapy was administered in both cases. Mean GTV size was 228.6 cm3 (range 59.8-314.5). Mean PTV coverage by the 95% of the dose prescription was 98% (95-100) and 97% (95-100) in PTV1 and PTV2, respectively. Mean PTV1 and PTV2 Dmax were 61.6 Gy (range 59-63) and 64.1 Gy (range 63-66), in both cases below the 107% threshold. Mean Bone Dmax was 55 Gy (56.6-61.8 Gy). Dmax to the skin corridor exceeded 20

Gy in 1 patient (range 12.5-58.1). The NVB was overlapping the PTV2 in all cases, but Dmax was below 66 Gy. All patients underwent surgery with a R0 resection. Two patients had a pathological complete response. One patient had wound complication requiring VAC therapy.

Conclusion. Planning goals of the first 5 treated patients are achieved in most cases. Preliminary results show a promising tumor response rate.

Table 1.

Dmax Organs at Risk	Planning Objectives
Bone	<59 Gy
Skin Corridor	≤ 20 Gy
Neurovascular Bundle	≤ 66 Gy

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NEOADJUVANT CONCURRENT GEMCITABINE AND RADIOTHERAPY FOR SOFT TISSUE SARCOMA: ASSESSMENT OF TOXICITY AND EFFICACY

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Aims. Surgery is the mainstay of treatment for Soft tissue sarcomas (STS) and is the only curative treatment option. The integration of surgery with neoadjuvant radiotherapy (RT) or chemotherapy for resectable tumor is an option that needs multidisciplinary discussion. Gemcitabine (gem) is a radiosensitizer with activity in STS. The purpose of this study was to evaluate the efficacy and toxicity of concomitant RT and gemcitabine in the neoadjuvant setting for STS.

Methods. A retrospective analysis of 19 patients treated with concurrent RT and gem from 2018 to 2022 in a neoadjuvant setting was performed. Radiative hyperthermia treatment was also performed in 9 patients since available in our Center. The RT prescription dose was for all patients 50 Gy in 25 fractions over 5 weeks. Gem was administered at 300 mg/m^2 once weekly for the duration of RT.

Results. The mean age was 61 years (range, 36-83) with ECOG Performance Status 0-1. The mean size of the treated tumor was 6.9 cm (range 2-20). Pathological response was evaluated in 17 patients. In 12 patients (70.5%) the tumor was localized in the extremities. 7 (41.2%) patients had been pre-treated with anthracycline-based chemotherapy (mean number of cycles performed 3.5, range 2-4) and 10 (58.8%) were naïve. The radiotherapy technique used was 3D-CRT, 2 IMRT, 11 VMAT in 4 patients. All patients followed 25 RT sessions in 5 weeks and the mean number of chemotherapy cycles performed was 4.4 (range 3-5). No patients reported acute and late toxicity >/= CTCAE (vers.5.0) grade 3. Six (35.2%) patients reported grade 1-2 hematologic toxicity. Of these, three had previously undergone chemotherapy and 5 also underwent hyperthermia during the integrated treatment. All patients (17/17) underwent radical surgery. An R0 resection was obtained in all but one patient (94%). 7 (41.2%) patients achieved a complete pathological response. 2/17 (11.8%) patients had post-surgical complications (anastomotic leaks). Five (29.5%) patients had disease progression, (3 local progression and 2 distant metastases). At the time of the analysis, 15/17 (88.2%) patients were alive, 3 with disease and 12 without.

Conclusions. The combination of RT and Gem in patients with STS is feasible and well tolerated, even after previous chemotherapy or in combination with hyperthermia. It might be more potent than radiation alone in achieving tumor regression and local control for high grade STS.

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ABSCOPAL EFFECT ON BONE METASTASES FROM SOLID TUMORS: A SYSTEMATIC REVIEW AND RETROSPECTIVE ANALYSIS OF CHALLENGE WITHIN A CHALLENGE

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Aims. Abscopal effect (AE) describes the ability of radiotherapy (RT) to induce immune-mediated responses in non irradiated distant metastasis. Bone represents the third most frequent site of metastasis and an immunologically favorable environment for the proliferation of cancer cells. We revised the literature, searching documented cases of AE involving bone metastases (BMs). In order to evaluate the incidence of AE involving BMs in patients treated at our department, we selected subjects requiring palliative RT on BMs or non-BMs.

Methods. Articles published in the PubMed/MEDLINE database were selected using the following search criteria: ((abscopal effect)) AND ((metastases)). Patients with BMs, who underwent performed bone scintigraphy before and at least 2–3 months after RT, were selected and screened between January 2015 and July 2022. AE was defined as an objective response according to the scan bone index for at least one non irradiated metastasis at a distance > 10 cm from the irradiated lesion. The primary endpoint was the rate of AE on BMs.

Results. Ten cases experiencing AE of BMs were identified from the literature and eight among our patients.

Conclusions. The analysis performed here suggests the use of hypofractionated radiotherapy as the only triggering factor for AE of BMs through the activation of the immune response.

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NUTRITIONAL RISK OF PATIENTS AFFECTED BY HEAD & NECK AND GASTROINTESTINAL TRACT CANCER; STRATEGIES FOR RISK ASSESSMENT AND MALNUTRITION MONITORING

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Aims. The aim of this study was to perform an early assessment of the nutritional risk of patients (pt) with H&N and digestive tract cancer by self-testing and monitor it during the oncological treatments.

Material and Methods. 53 pt treated in Manzoni Hospital of Lecco from April 2022 to December 2022 were analyzed. All pt were monitored by our Clinical Nutrition Center (CNC) at diagnosis, 30 days and 60 days after the start of oncological treatment. The nutritional risk was carried out by Screening Scored Patient-Generated Subjective Global assessment abridged version (asPG-SGA) which investigates the trend of weight loss, nutrition status, symptoms related to the disease, pt diet and daily activity. An overall index score is assigned by test evaluation to define pt nutritional status (min 0, max 37 points); pt with score ≥ 6 are defined at malnutrition risk. At baseline, 30 and 60 days evaluation, in pt with a weight loss more than 5% or a BMI < 16.9 an increase of caloric intake was prescribed by our CNC (oral intake, enteral or parenteral)

Results. Of the 53 pt enrolled (mean 68.68 years, range 48-85 year), 20 were women and 33 men. At the diagnosis 43.3% (23) pt were at risk of malnutrition. At the baseline evaluation pt with asPG-SGA score ≥ 6 had a lower kcal intake and a greater weight loss than patients with scores < 6 (p-value respectively < 0.003 and < 0.05). Moreover, at 30 days the daily kcal nutritional integration was higher in pt with asPG-SGA scale score ≥ 6 compared to pt with scale score < 6 (p-value < 0.003). There wasn't difference regarding total caloric intake (pt intake plus caloric added by the dietitian) between two groups. At subgroup analysis, pt received RT-CT treatment with weight loss > 8% had a statistically significant higher risk of hospitalization (Fisher test; p 0.0026). Finally, 4 pt (5%) interrupt oncological treatment due to side effects and/or clinical worsening, but there was not any treatment interruption due to significant weight loss.

Conclusions. The results of our study demonstrated the feasibility of asPG-SGA abridge version to identify oncological pt with nutritional risk. We found an important role of nutritional figure in this subset of patients because increasing daily kcal intake allow to complete oncological treatment despite malnutrition risk. Prospective and well-designed study with higher number of pt and test considering age, cancer stage and treatment options are necessary to confirm our results.

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INFLUENCE OF NUTRITIONAL STATUS ON SURVIVAL OUTCOMES FOR ESOPHAGEAL CANCER (EC) PATIENTS TREATED WITH NEOADJUVANT RADIOTHERAPY AND SUBSEQUENT SURGERY

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Aims. Nutritional status might impair survival outcomes in EC patients. Aim of this retrospective analysis was to evaluate the impact of nutritional assessment in EC patients undergoing preoperative RT and subsequent surgery.

Methods. We retrospectively collected data of locally advanced (LA) EC patients treated with preoperative RT with or without platinum-based chemotherapy (CT) and subsequent esophagectomy between November 2004 and April 2023. Clinical and treatment related data were collected. Acute and late toxicities were assessed. Descriptive, univariate (UVA) and multivariate (MVA) survival analysis was performed to identify correlation between enteral nutrition and survival outcomes.

Results. 54 patients (AC:n=25; SC:n=29) were included. Median age was 61 (42-82); ECOG-PS 0 in 41 patients. Jejunostomy feeding tube (JFT) was performed in 24 patients. Dysphagia was reported in 42 cases (7 cases of complete anorexia). Baseline weight loss (≥ 10% in 11 cases) was reported in 37. Median basal BMI was 21.8 kg/mq (13.6-28.2). Clinical nodal involvement was present in 21 cases. Patients received a CROSS schedule, Cisplatin-5Fluorouracil or exclusive RT in 45, 7 and 2 cases, respectively. All patients underwent planned surgery. Acute toxicity consisted mainly of grade (G) ≤2 esophagitis (n=20) or pneumonitis (n=2). Two patients developed tracheobronchial fistula after surgery, 1 stenosis and 1 experienced gastric stump necrosis. In those treated with concurrent CT, G3-4 hematologic toxicity occurred in 12 cases. After a median follow-up of 41 (2-192) months, 3-year overall survival (OS), local recurrence (LRFS) and distant metastases (DMFS) free survival was 60%, 88% and 46% (Figure 1A, B, C). ECOG PS0 only (p=0.0095) was correlated with OS at UVA. At UVA, fistula only (p=0.0065) was related to LRFS. Concerning DMFS, pCR (p=0.045) and yN0 (p=0.0078) showed a significant correlation at UVA, although only yN0 proved significant at MVA (p=0.013) (Figure 1D, E, F). Dysphagia, weight loss and the use of JFT did not affect survival outcomes neither at UVA nor at MVA analysis. Chi square test showed significant correlation between JFT insertion and dysphagia (p<0.0012) and between JFT and weight loss >5% (p=0.0001).

Conclusions. Our analysis did not show differences in survival outcomes according to nutritional status; this could be attributed to early insertion of JFT in patients with higher baseline weight loss and dysphagia.

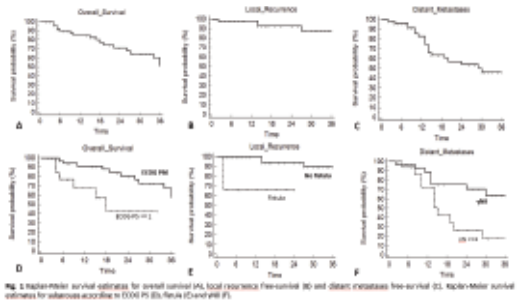

Figure 1.

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FASTING AND RADIOTHERAPY: HOW, WHICH KIND AND WHY? A REVIEW FOR CLINICIAN

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Aims. Several studies showed similar results about the association of various kind of fasting and Radiotherapy. We report a literature review of published studies evaluating this association in order to assess the results in terms of right way to use different kind of fasting associated to radiotherapy.

Methods. A systematic database search was performed on PubMed and Embase according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines. Original studies describe the use of fasting during radiotherapy and/or chemotherapy in mice models. These evaluation where done on breast or gastrointestinal tumor. Intermittent fasting was considered with an alternate day fasting (≥16h).

Results. We selected 9 studies. Fasting improves the response of tumor cells to radiotherapy in such different way. Numerous studies suggest that Calorie Restriction (CR) enhances DNA repair of sublethal damage in normal tissues and contrary to this, it is possible that (CR) impairs it in tumor cells and thus contributes to increased cell death also disregulating apoptosis, increasing sensitivity of tumor to apoptotis and depleting regulatory T cells and improving stimulation of CD8 cells.

Conclusions. Dietary manipulation through CR, especially with intermittent fasting, may enhance the efficacy of radiation therapy. The treating physician, however, must weigh the benefits and risks of each dietary intervention, as each may be suitable in varying situation.

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NUTRITIONAL STATUS AND THE WEIGHT LOSS FOR PATIENTS WHO RECEIVED RADIOTHERAPY

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Aims. Radiation therapy with chemotherapy (CCR) is currently the gold standard treatment for several oncological disease. Anatomical changes are mainly due to

weight loss. The aim of this analysis was to evaluate the nutritional status and the weight loss in our patients and to adapt the subsequent nutritional management of patients during CCR.

Methods. From August 2019 to April 2023 nutritional evaluations were performed for all patients receiving CCR. Data from interrogation, physical examination (weight [W], body mass index [BMI]), nutritional deficiencies, were collected at the beginning and during the CCR. The number of visits was adapted to the patient's needs and the initial risk class.

Results. From 2019 to 2023, 77 patients underwent nutritional assessment during radiochemotherapy. In more than half of of cases (57%) the primary tumor was head and neck cancer. Median Body Mass Index (BMI) at the beginning of radiation treatment was 24 (range 17-42). The median age of the patients was 64 years (range 21-91). The patients were visited on average 3 times during the therapy. 62 patients (80%) received a nutritional intervention (Nutritional drinks in 73% of cases and protein supplements in 37%). At the end of radiochemotherapy, 44% of patients had no weight loss or wieght gain, 34% had a weight loss < 5%, 22% had a weight loss > 5%. Twenty patients (26%) required replanning during CCR due to anatomic changes. Only 11 patients (14%) suffered treatment interruptions due to toxicity, but only in three cases the interruption exceeded 3 days.

Conclusions. Nutritional evaluation is essential in patients undergoing CCR especially for head and neck, gynecological or gastrointestinal tract neoplasms. Adequate nutritional support can reduce the extent of weight loss and consequently interruptions due to toxicity and the need for replanning of radiotherapy treatment. Careful planning of nutritional assessments should be established for all patients of this type.

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THE FELLOWSHIP OF THE HFUS (ULTRA HIGH-FREQUENCY ULTRASONOGRAPHY): COLLABORATION BETWEEN RADIOLOGISTS AND RADIATION ONCOLOGISTS IN TARGETING PRIMARY CUTANEOUS LYMPHOMAS

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Aims: Primary cutaneous lymphoma (PCL) is a rare extranodal non-Hodgkin's lymphoma confined to the skin. Radiation therapy (RT) is usually appropriate for stages T1-T3; being superficial targets, the electron beams is the recommended method of treatment. Identifying GTV (gross tumor volume) can be difficult because these lesions may not be visible during clinical examination but only detectable through palpation. Ultra High-Frequency Ultrasonography (HFUS), applying 70 MHz frequencies, offers precise and dependable insights into the skin that traditional ultrasounds (10-20MHZ) cannot match. The highest resolution of the HFUS could help to identify the morphological limits of PCL lesions and determining the field of RT treatment and evaluating local control (LC) or toxicity in future follow-up(FUP).

Methods. Between October 2022 and May 2023, we treated 5 patients (pts) with histological diagnosis of PCL median age 50 years (30-70 years). The sites of PCL were different: 3 on the scalp, 1 on the tip of the nose, 1 on the back, staging was IA for 4 pts and IB for 1 patient. With the collaboration of expert radiologists by the use of HFUS, we determined the GTV of the lesion not visually identifiable. Next, we added a margin of 2cm from the GTV to plan the electron beams treatment field, median size of PTV was 25 cm^2 (range 16-36), RT prescription was 24-30 Gray in 12-15 fractions. Toxicity was evaluated according to CTCAE v.5

Results. For patients undergoing scalp treatment (60%), HFUS played a crucial role in identifying the GTV due to the lesion being difficult to palpate. Furthermore, in one patient (20%), where the lesion was found to be superficial, we changed our treatment strategy from photons to electrons beams. HFUS is also able to reveal the eventual expansion of the lesions beyond the palpable area: for 1 patient (20%) we had to expand the treatment field to include the non-palpable portion of GTV. In the FUP at 3 and 6 months at the end of RT using HFUS, we evaluated the LC at 100% of pts; furthermore, with the high definition of the high frequency, no pts presented subcutaneous tissue changes in the ultrasonography's images.

Conclusions. The use of HFUS, as a new imaging approach for precision therapy, and the collaboration of radiologists prove to be very useful in targeting PLC's lesions that are often not clinically visible. Furthermore, this collaboration can help in the evaluation of LC, possible relapses and toxicities.

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68GA-PSMA PET/CT BEFORE EARLY SALVAGE RADIOTHERAPY IN PROSTATE CARCINOMA: IS IT USEFUL? PRELIMINARY ANALYSIS OF THE EASY-1 TRIAL (EARLY SALVAGE RADIOTHERAPY-1)

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Aims. 68Ga-PSMA PET/CT is considered an effective restaging system in patients with prostate cancer (PCa) referred to salvage radiotherapy for biochemical relapse (BCR) after radical prostatectomy (RP). However, the sensitivity of this method is still debated in patients with low PSA values (<0.5 ng/dL). Therefore, the aim of this analysis is to report the results of 68Ga-PSMA PET/CT in patients enrolled in an observational study of early salvage radiotherapy (esRT).

Methods. 721 PCa patients were enrolled in a prospective trial (EASY-1: EArly Salvage radiotherapY-1) after RP. Inclusion criteria were: PCa treated with RP, pT2 with positive surgical margins (R1) or pT3a regardless of surgical margins status or pT3b with negative surgical margins (R0), and PSA undetectable 40 days after surgery (<0.01). Patients with nodal metastases were excluded. The surveillance protocol included PSA assessment every 2 months after surgery during the 1st year, every 3 months during the 2nd and 3rd year, followed by PSA every 4 months until the 5th year, then every 6 months until the 10th year after surgery. EsRT was delivered, after 68Ga-PSMA PET/CT, in case of BCR (two consecutive values of PSA ≥0.2 ng/ml).

Results. To date, 68Ga-PSMA PET/CT results of 45 out of 60 patients referred for esRT are available. The results of 68Ga-PSMA PET/CT are shown in Table 1. 68Ga-PSMA PET/CT examination showed the presence of gross disease in one third of cases (15/45). In particular, the percentage of positive exams was 25.0% and 38.5% in patients with PSA <0.2 ng/dL and in subjects with PSA ≥0.2 ng/dL (p=0.334). The site of PCa relapse was the prostatic bed or nodal/bone metastasis in 40.0% and 60% of cases, respectively.

Conclusions. The results of this preliminary analysis suggest the sensitivity of 68Ga-PSMA PET/CT in identifying sites of macroscopic recurrence, in patients referred to esRT, even in subjects with low (< 0.2 ng/dL) PSA levels.

Table 1. Main results.

		No.	%
Patients with available ^{68}Ga-PSMA PET/CT		45	100%
PSA at ^{68}Ga-PSMA PET/CT, median (range)		45	0.26 (0.1-5.8 ng/dl)
ISUP	1	1	2.2%
	2	4	8.9%
	3	15	33.3%
	4	15	33.3%
	5	10	22.2%
^{68}Ga-PSMA PET/CT results :		45	100%
Positive		15	33.3%
Negative		30	66.7%
Site of positive ^{68}Ga-PSMA PET/CT:		15	
Prostate bed		6	40.0%
Pelvic nodes		7	46.7%
Bone		2	13.3%

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COMPARISON BETWEEN PATHOLOGICAL AND RADIOLOGICAL ASSESSMENT IN RECTAL CANCER TREATED WITH TOTAL NEOADJUVANT THERAPY

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Aims. The standard of care for Locally Advanced Rectal Cancer (LARC) is preoperative radiation (RT) with or without concurrent chemotherapy (CT). Following publication in 2020 of 2 landmark Phase III trials, integration of induction or consolidation CT to RT (Total Neoadjuvant Therapy, TNT) has been strongly advocated, particularly in high risk patients. However, treatment intensification may affect radiological evaluation, thus influencing the extent of planned intervention. We evaluated the correlation between radiological response and pathologic assessment in LARC patients' treated with TNT.

Methods. We retrospectively analysed a cohort of consecutive patients with LARC treated with TNT at our institution from June 2020 to May 2023. Indication to TNT was established by the multidisciplinary team (MDT) on an individualised base in presence of an advanced tumor stage and/or extensive nodal involvement (T4a/b and/or N≥2 according to TNM staging system) with or without positive circumferential resection margin (CRM+). All patients were treated according to the Prodige23 protocol and underwent staging MRI before treatment initiation and before surgery at 6-8 weeks after completion of RT. We collected demographics and treatment-related characteristics. Radiological

and pathological assessment was performed using the MRI Regression Criteria (MRG) [30844347] and the Mandard Tumor Regression Grade (TRG), respectively.

Results: Among 17 patients treated with TNT, pathological and radiological data were available for 11 patients. TNT was motivated by T4 disease (1 n=9%), N2 involvement (4 n=36.4%), or both (6 n=54.6%). CRM+ was found in 10 (90.9%) patients. All patients completed the planned schedule. Pathological and radiological data are summarised in Table 1. Complete agreement between MRG and TRG was found in 9/11 patients (81.8%) while minor and major disagreement was observed in 1 and 1 patient. In both patients, TRG was underestimated by MRG.

Conclusions. In patients treated with TNT for LARC, radiological post-treatment assessment using the MRG showed substantial concordance with pathological regression, particularly in patients experiencing complete pathological response. This tool may be useful to identify patients eligible for a non-surgical management following complete tumor regression.

Table 1. Pathological and radiological assessment.

Age, median		54 (range 35-66)
TNM staging at diagnosis		
T4N0		1
T3N2		4
T4N2		6
TRG		n
1	Complete regression (= fibrosis without detectable tissue of tumor)	2
2	Fibrosis with scattered tumor cells	4
3	Fibrosis and tumor cells with preponderance of fibrosis	3
4	Fibrosis and tumor cells with preponderance of tumor cells	2
5	Tissue of tumor without changes of regression	0
MRG		n
1	Complete radiologic response, no evidence of tumor	2
2	Good response, dense (<75%) fibrosis with no obvious residual tumor	2
3	Moderate response, >50% fibrosis or mucin with a minority of visible tumor	4
4	Slight response, <50% fibrosis or mucin with a majority of visible tumor	3
5	No response, no post treatment changes	0

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A RETROSPECTIVE ANALYSIS OF BRAIN ARTERIOVENOUS MALFORMATION TREATED WITH COMBINED APPROACH

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Aims. Brain arteriovenous malformations (bAVMs) are rare and congenital abnormalities composed of an abnormal tangle of blood vessels where arteries are directly connected to draining veins with no capillary bed between them. bAVMs can leads to intracranial hemorrhage, seizure and death. Therapeutic options are represented by surgery, endovascular embolization (EE) and stereotactic radiosurgery (SRS) (alone or combined). Complete nidal obliteration is the main objective of definitive treatment but, to date, there is no consensus on the treatment of bAVMs.The aim of our study is to evaluate the effectiveness of combined approaches in term of outcomes and toxicities.

Methods. We retrospectively evaluate patients underwent to SRS in combination with surgery and/or EE. The pre-treatment imaging consisted of MRI imaging system,CT angiography and digital subtraction angiography (DSA) with rotational CT angiography. Clinical and radiologic follow-up with MRI and cerebral angiography, were obtained at 3 months and then every 6 months for 2 years followed by yearly evaluations.Spetzler-Martin (SM) grading system was used.All patients received SRS treatment with a CyberKnife System.Outcomes, event free survival (EFS) and toxicities were evaluated.

Results. From 2007 to 2023,90 patients with bAVMs were treated with SRS technique. Of them, only 37 with a median age of 44 years (range 15-75y) were evaluable. The median volume was 2,75 cc (range 0,3-25,3 cc). According to SM grade score, 21 patients showed grade II, 15 grade III and 1 grade IV. Stereotactic median dose was of 20 Gy/1fraction, with median isodose line of 78%. Pre-SRS EE was performed in 55% patients (20/36): of them, 3 patients underwent to more than one EE, one in association with surgery; only one patients received prior surgery. Actuarial 3-5years EFS was of 96,55% and 88% respectively. Patients treated only with SRS had a 3y-5y EFS of 100%; in combined approach 3y EFS was of 94% and 5y EFS of 82,63%(p=0.175) (Figure 1a-b).Out of 36 patients, 47,1% developed complications: 38,8% had symptoms within 3 years post SRS (6 edema, 2 haemorrhage, 5 hemiparesis, 1 visual disturbance); 8,3%,all treated with combined approach, developed cyst after 3 years post SRS: one patient was managed both with surgery and systemic therapy with anti-VEGF; one with anti-VEGF therapy only and one conservatively.

Conclusions. Our finding,according to literature data, confirms that association of SRS and embolization leads to lower obliteration and higher long term toxicities rates.

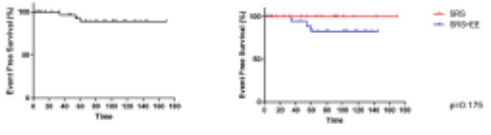

Figure 1.

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PRETREATMENT MRI IMPROVES THE BIOCHEMICAL OUTCOME OF SALVAGE RADIOTHERAPY: A CASE-CONTROL ANALYSIS

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Aims. Current international guidelines recommend choline-PET or PSMA-PET in patients with prostate cancer referred for salvage radiotherapy (sRT) to rule out nodal or hematogenous metastases. However, in our centers, we tested the efficacy of pelvic mpMRI in detecting local-regional relapses and, therefore, to optimize sRT. The aim of this analysis is to compare two matched cohorts of patients who underwent or did not undergo mpMRI before sRT in terms of biochemical relapse-free survival.

Methods. One hundred seventy-six patients from three centers were included in this study. Patients in the two cohorts were matched according to: PSA before SRT (<0.2; 0.2-0.5; 0.5-1.0; >1.0 ng/ml), pathological tumor stage, ISUP grade (1, 2, 3, 4, 5), prophylactic nodal irradiation, and adjuvant androgen deprivation therapy. Kaplan-Meier survival curves were compared using the log-rank test. This analysis is part of a multicenter observational study approved by the ethics committees of the participating centers.

Results. Macroscopic local-regional relapse was identified in 54/88 of patients (61.4%) undergoing pelvic mpMRI and therefore these patients were treated with a median total dose of 70.4 Gy (range: 66-72.6), while patients without mpMRI or with negative mpMRI received a median total dose of 66 Gy (range: 61.6-72.0). Indeed, in patients with mpMRI-detected relapse, a boost (sequential or concomitant) was delivered on the macroscopic recurrence. Overall, comparing the cohorts of patients with or without mpMRI, a significantly higher rate of biochemical relapse-free survival was recorded in the first group (4-year: 74.8% versus 60.7%; p=.039; Figure 1).

Conclusions. An unexpected and surprisingly high rate of macroscopic relapses was recorded in patients undergoing mpMRI before sRT. This allowed treatment modulation by delivering a boost to the site of recurrence. This strategy produced a significant improvement of the biochemical outcome. Our findings challenge current guidelines on pre-sRT restaging.

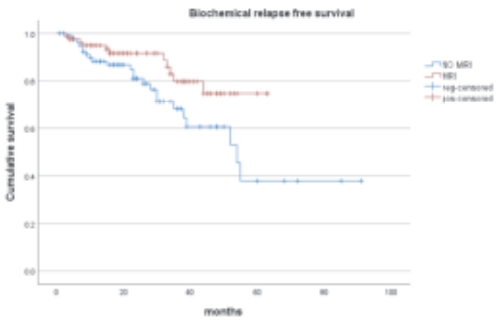

Figure 1. Biochemical relapse-free survival in patient undergoing MRI (red) and not undergoing MRI (blue) before salvage radiotherapy (p=.039).

P410

CONVOLUTIONAL NEURAL NETWORK *VS* MANUAL SEGMENTATION FOR EARLY-STAGE NON-SMALL CELL LUNG CANCER: PERFORMANCE ASSESSMENT AND CURRENT PITFALLS

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Aims. The increasing interest on automated segmentation has led to the creation of several commercial and non-commercial tools. In this work we applied an in-house developed convolutional neural network (U-net) to a dataset of candidates to curative-intent stereotactic body radiotherapy (SBRT) for early-stage non-small cell lung cancer (ES-NSCLC). The aims were to: 1) assess the performance of the U-net against a gold standard given by manual segmentation performed by a single Radiation Oncologist, and to 2) analyze which qualitative radiological parameters were associated with a decrease in the U-net performance, if any.

Methods. Pre-SBRT contrast-enhanced computed tomographies (CTs) were retrospectively retrieved. After the presence of informed consent was verified, the U-net and manual segmentations were compared by the Dice coefficient using 3D Slicer v.5.2.2, with a Dice ≥0.8

being considered as satisfactory. Qualitative radiological parameters included, but were not limited to: lesion location within lung lobes, shape (round *vs* oval *vs* complex), peri-tumor emphysema and the presence of peripheral glass opacities (pGGOs). Two classification models were built, considering the Dice coefficient as either a binary (< or ≥0.8) or continuous outcome (linear Model1 and factor regression model 2, respectively). A train:test ratio of 0.7 and a cross-validation of 10 were used in both cases. Analyses were performed with R libraries caret and glmnet.

Results. Considering the 70 available CTs, manually-segmented lesions had a higher volume than their U-net counterparts: 4.6 (IQR 2.0-12.2) *vs* 3.2 (IQR 1.3-10.3) cm3, with a median percentage difference of 21.9%. Median dice coefficient was 0.80 (IQR 0.71-0.86). Model1 showed that lesion shape and pleuric contact were the main determinants of performance, with complex shape being associated with Dice values <0.8 (Figure 1a). Conversely Model2 suggest the importance of additional variables such as the proximity to lung fissures, intra-lesion density (solid *vs* subsolid), lesion margins (regular *vs* irregular) and the presence of pGGOs (Figure 1b).

Conclusions. Overall, the U-net yielded a satisfactory performance across the dataset. However, accuracy as assessed per the Dice score is decreased in presence of some qualitative radiological features (*e.g.* irregular margins, complex shape). Further training and external validation on complex lesions may further improve model performance and open doors to clinical implementation.

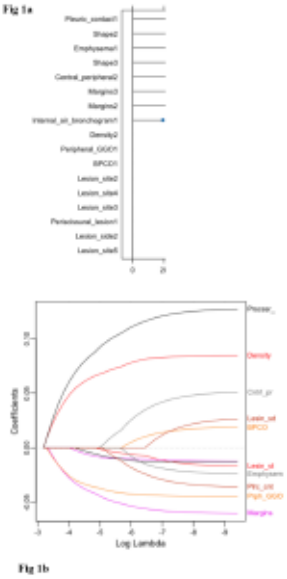

Figure 1. Variables importance per classification Models 1 (1a) and 2 (1b), considering the outcome of prediction as either binary (with Dice coefficient≥0.8 indicating a good performance) or continuous.

P411

RADIOMIC FEATURES VARIABILITY ACROSS BREATHING PHASES IN 4D-COMPUTED TOMOGRAPHY: EXPLORATORY ANALYSIS FOR EARLY-STAGE NON-SMALL CELL LUNG CANCER

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Aims. Four-dimensional computed tomographies (4D-CTs) are a gold standard in treatment planning for stereotactic body radiotherapy (SBRT) in early-stage non-small cell lung cancer (ES-NSCLC). However, dedicated investigations on the use of such images in radiomic studies are limited. This works aims to investigate if any variation exists across reconstructed respiratory phases on both original and preprocessed CTs.

Methods. Seventy 4D-CTs acquired with the same scanner and acquisition parameters at a single institution were retrieved, and the IBSI (Imagin Biomarker Initiative)-compliant software Pyradiomics v3.0.1 was used for pre-processing and features extraction. Features were subdivided into 7 classes, namely first order, gray level co-occurrence matrix, gray level dependence matrix, gray level run length matrix, gray level size zone matrix, neighboring gray tone difference matrix and shape. Following the exclusion of null features, patient-wise coefficients of variation (COV, standard deviation/average) × 100) across the ten phases and all built-in filters was calculated. Under a repeated measures model and under the hypothesis of linear variation across the inspiration/expiration phases, we assessed COV variations from phases 0-40 and from phases 50-90, with 0 and 50 being the maximum inspiration and expiration, respectively. Features with COV≤5% were considered as stable.

Results. Overall, 1967 features were available, and derived mainly belonging to the gray level co-occurrence matrix (glcm) category and deriving from lbp-3D and log-sigma filters. Of these, 1747 (88.8%) and 1744 (88.6%), were not associated with respiratory motion in phases 0-40 and 50-90, respectively, with 53 features being consistently unstable in both the analyzed time-frames. These all belonged to either the glcm or the first order categories. Different permutations of the wavelet filter yielded the highest instability. A COV>20% was observed in 33/53 cases. Further details are provided in Table 1.

Conclusions. The majority of CT-derived features

was stable across the respiratory cycle. Instability seems to affect intensity-related features more than higher-order features, as well as images processed with wavelet filtering. While, external validation will be performed to confirm the generalizability of these findings, caveats should be applied when implementing 4D-derived features in outcome modeling studies.

Table 1. Overview of unstable features sorted by instability across phase 0-40 only, 50-90 only, and both 0-40 and 50-90 phases, sorted per feature classes, filtering methods and COV intervals.

	Unstable in the 0-40 phase, n= 12 (%)	Unstable in the 50-90 phase, n= 14 (%)	Unstable in both phases, n= 53 (%)
Feature Classes			
first order	6 (50.0)	9 (63.3)	25 (47.0)
glcm	6 (50.0)	5 (35.7)	28 (53.0)
gldm	0 (0)	0 (0)	0 (0)
glrlm	0 (0)	0 (0)	0 (0)
glszm	0 (0)	0 (0)	0 (0)
ngtdm	0 (0)	0 (0)	0 (0)
shape	0 (0)	0 (0)	0 (0)
Filtering Method			
exponential	0 (0)	0 (0)	1 (1.9)
gradient	0 (0)	1 (7)	2 (3.8)
lbp-2D	1 (8.3)	0 (0)	0
lbp-3D	0 (0)	0 (0)	4 (7.5)
log-sigma	5 (41.9)	2 (14.3)	10 (18.8)
logarithm	0 (0)	0 (0)	1 (1.9)
original	1 (8.3)	1 (7)	1 (1.9)
square	1 (8.3)	1 (7)	2 (3.8)
wavelet-HHH	0 (0)	1 (7)	7 (13.2)
wavelet-HHL	0 (0)	1 (7)	6 (11.3)
wavelet-HLH	1 (8.3)	1 (7)	5 (9.4)
wavelet-HLL	0 (0)	2 (14.3)	2 (3.8)
wavelet-LHH	1 (8.3)	1 (7)	5 (9.4)
wavelet-LHL	1 (8.3)	1 (7)	3 (5.7)
wavelet-LLH	0 (0)	2 (14.3)	3 (5.7)
wavelet-LLL	1 (8.3)	0 (0)	1 (1.9)
COV Intervals			
5%<COV=<10%	0 (0)	4 (28.6)	3 (5.7)
10%<COV=<20%	3 (25.0)	3 (21.4)	17 (32.0)
COV>20%	9 (75.0)	7 (50)	33 (62.3)

P412

THE DOSIMETRIC IMPACT OF NON-COPLANAR MULTIPLE VOLUMETRIC MODULATED ARC SBRT TECHNIQUES

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Purpose. To evaluate the importance of non-coplanar VMAT SBRT in the treatment of lung lesions, an optimization algorithm for treatment planning has been developed used using commercial software. The objective is, therefore, to determine the effectiveness of these techniques on the basis of target coverage and OAR safeguard criteria.

Methods. The efficacy of SBRT with FFF non-coplanar technique (NC-SABR) for the treatment of lung lesions was evaluated through a retrospective analysis, for a cohort of 26 patients, with prescription doses between 50 Gy and 60 Gy in 3/8 Fx. The dosimetric results obtained were subsequently compared with those deduced from treatment plans elaborated in the VMAT technique with coplanar arcs (CP-SABR).. The calculation algorithm has been optimized in order to reduce radiation exposure to organs at risk (OAR), including lungs, heart and chest wall, and at the same time achieving the PTV coverage. The significance of the differences was determined using Friedman's test. The analysis was conducted on pre-estabilished subset of patients, classified according to the position of the target (wall-seated targets, island tumors and central targets).

Results. In the absence of significant differences in target coverage, our analysis revealed significant differences for Dmax in central targets and for compliance index in parietal and insular targets. In terms of OAR, our study showed a marked difference in the Dmax of the heart for central tumors (reduced with NC SABR), V13.5 of lung for insular tumors (reduced with NC SABR) and V30 of the chest wall for wall-seated targets (reduced with CP SABR).

Conclusions. The results obtained highlight the importance of considering the impact on key organs such as the heart, lungs and chest wall, underlining the need for a comprehensive evaluation of radiotherapy options. SBRT VMAT with non-coplanar arcs, can lead to lower heart Dmax levels when the target is a central area, as well as a reduction lung exposure in island tumors. Conversely, for wall-seated targets the CP SABR can achieve a reduced exposure of chestwall organs at risk. The choice of the personalized technique for the patient is essential for the reduction of specific side effects and, therefore, for greater patient compliance.

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IMPACT OF PSMA-PET/CT STAGING ON CLINICAL OUTCOMES OF PROSTATE CANCER PATIENTS TREATED WITH SALVAGE RADIOTHERAPY. A SECONDARY ANALYSIS OF AN OBSERVATIONAL MULTICENTER TRIAL

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Aims. Salvage radiotherapy (sRT) +/- androgen deprivation therapy (ADT) is the standard treatment option for prostate cancer (PCa) patients with biochemical recurrence. Moreover, PSMA-PET/CT is an effective tool for detection of local and/or distant failures and for sRT planning, while its possible correlation with clinical outcomes remains uncertain in this setting. Therefore, the aim of this case-control study was to investigate whether PSMA-PET/CT staging may have an impact in terms of biochemical and clinical outcomes in PCa patients treated with sRT.

Methods. From the database of an observational multicenter trial we retrospectively analyzed 170 patients matched based on pT stage, age, and ADT. We considered the following outcomes: biochemical relapse-free survival (bRFS), local control (LC), regional control (RC), metastasis free survival (MFS), disease free survival (DFS), and overall survival (OS). Survival curves were calculated by the Kaplan-Meier product-limit method and compared with the log-rank test.

Results. Patients were divided into two groups according to the matching criteria (cases, PSMA-PET/CT performed: 85 patients; controls, PSMA-PET/CT not performed: 85 patients). In the pooled analysis, higher DFS and OS rates were recorded in patients with lower PSA levels at sRT (both: p=.002) and higher DFS and OS rates were registered in patients undergoing adjuvant ADT (both: p=.003). By comparing cases and controls, no statistically significant differences were found for any of the considered endpoints. However, analyzing the two populations in subgroups based on potential prognostic factors (age, postoperative PSA, PSA at sRT, pT stage, nodal metastases at sRT, ISUP, adjuvant ADT) resulted, in the subgroup of pT3-4 staged subjects, higher bRFS, DFS, and OS rates in patients staged with PSMA-PET/CT (Table 1).

Conclusions. The results of our study suggest that PSMA-PET/CT before sRT may improve biochemical and clinical outcomes only in the subgroup of patients with locally advanced PCa. Therefore, further analysis on this topic seems warranted.

Table 1. Subgroup analysis on the impact of PSMA/PET-CT in prostate cancer patients treated with salvage radiotherapy.

	Value	2-year bRFS			2-year LC			2-year RC			2-year MFS			2-year DFS			2-year OS		
		Case (%)	Control (%)	p	Case (%)	Control (%)	p	Case (%)	Control (%)	p	Case (%)	Control (%)	p	Case (%)	Control (%)	p	Case (%)	Control (%)	p
AGE	Median (range)	70 (52-70<82)																	
	<65	80.6	70.6	0.247	87.5	92.3	0.715	100	92.3	0.446	100	92.3	0.455	80.0	70.6	0.390	80.0	70.6	0.398
	≥65	89.1	85.4	0.974	95.1	91.7	0.899	96.0	92.0	0.889	94.4	97.1	0.501	93.7	88.3	0.676	90.5	85.2	0.678
PSA post op	Median (range)	0.4 (0.04<0.4<9.26)																	
PSA at treatment category	≤0.39	89.3	79.5	0.672	96.2	89.2	0.908	100	95.0	0.368	90.3	100	0.189	90.9	86.3	0.531	90.6	86.1	0.532
	0.391-0.769	92.9	76.0	0.416	100	82.2	0.298	92.9	90.9	0.902	100	90.9	0.415	92.9	76.0	0.425	92.5	76.3	0.435
	0.77-2	92.3	80.0	0.801	100	100	0.594	100	86.7	0.431	100	93.3	0.655	100	86.7	0.431	100	86.9	0.433
	>2	41.7	100	0.240	nr	100	0.061	80.0	100	0.273	nr	100	1	80.0	83.3	0.240	80.3	83.0	0.242
pT stage	1-2	70.8	100	0.026	91.5	77.8	0.995	92.9	100	0.252	88.9	88.9	0.837	74.3	100	0.074	74.1	100	0.072
	3-4	100	75.3	**0.016**	100	95.2	0.868	100	90.2	0.187	100	97.3	0.406	100	80.4	**0.031**	100	80.6	**0.035**
Nodal metastases at SRT	no	81.6	86.6	0.340	93.2	91.6	0.879	98.3	92.0	0.442	94.1	95.6	0.954	91.3	92.0	0.493	93.1	92.1	0.613
	yes	90.9	100	0.307	90.9	100	0.763	90.9	100	0.763	100	100	1	90.9	100	0.763	100	90.8	0.773
ISUP	1	83.3	100	0.079	100	100	1	80.0	100	0.206	100	100	1	80.0	100	0.206	80.2	100	0.216
	2	58.3	92.3	0.517	87.5	100	0.264	nr	100	100	nr	100	1	66.7	94.3	0.932	66.5	94.0	0.942
	3	81.8	87.1	0.560	95.2	93.8	0.787	95.2	93.3	0.804	83.3	92.9	0.114	79.4	87.1	0.573	79.1	86.9	0.563
	4	100	68.8	0.061	85.7	90.0	0.988	100	72.7	0.216	100	90.0	0.127	100	77.3	0.139	100	77.5	0.142
	5	100	76.0	0.159	100	82.5	0.295	100	100	0.705	100	90.0	0.229	100	76.0	0.159	100	76.2	0.161
ADT	yes	94.9	86.2	0.971	nr	nr	1	96.8	93.7	0.819	95.0	97.7	0.968	88.1	88.6	0.913	88.3	88.1	0.923
	no	100	26.7	0.212	92.7	91.2	0.730	100	66.7	0.564	100	66.7	0.564	100	26.7	0.212	100	27.1	0.223

Legend: bRFS: biochemical relapse-free survival; DFS: Disease-free survival; ISUP: International Society of Urological Pathologists; LC: Local Control; MFS: Metastasis-free survival; OS: Overall survival; PSA: Prostate Specific Antigen; RC: Regional control; pT stage: pathological stage, ADT: Androgen Deprivation Therapy; SRT: Stereotactic Radiotherapy, post op: post prostatectomy.

P414

THE ROLE OF PORTABLE ULTRASOUND IN ASSESSING BLADDER FILLING

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Aims. Optimal management of radiotherapy patients with prostate, ano-rectal, and gynecological cancers relies on proper bladder filling. While standardized instructions are typically given to patients regarding water intake, reproducing the same bladder filling as during simulation CT can be challenging. This study aims to explore the potential of portable ultrasound in evaluating bladder filling.

Methods. Between March 2023 and May 2023, all patients receiving treatment for pelvic malignancies underwent ultrasonography on the LINAC couch to

assess bladder filling. Measurements of bladder volume were taken in three dimensions, and the volume was calculated using both ultrasonography and cone-beam CT. The reliability of bladder volume measurements was determined using the Intraclass Coefficient Correlation test. Additionally, a retrospective analysis of cone-beam CT scans from September 2022 to February 2023 was conducted to determine the percentage of failed scans due to inadequate bladder filling.

Results. 23 patients were included in this analysis. Ultrasonography evaluation was easily performed, requiring a median of 2 minutes after a week of experience. A total of 45 ultrasonography evaluations were compared with cone-beam CT, yielding an Intraclass Coefficient Correlation (ICC) of 0.85. Conversely, the ratio of failed cone-beam CT scans due to inadequate bladder filling was 15%.

Conclusions. Ultrasonography evaluation offers a convenient technique that can be incorporated into the radiotherapy workflow for pelvic malignancies. It allows for easy measurement of bladder filling without the need for ionizing radiation. However, further research is necessary to establish standardized methods for evaluating bladder filling using ultrasonography, which can be readily adopted in clinical radiotherapy practice.

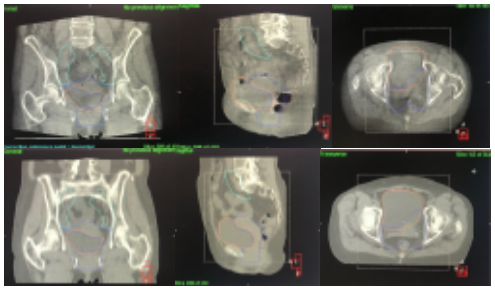

Figure 1. Coronale, sagittal and trasverse section of a CBCT scan of a patient with inadequate bladder preparation.

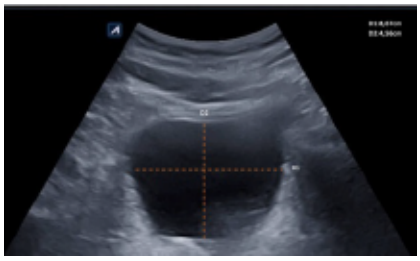

Figure 2. Bladder ultrasound performed 10 minutes later on the same patient showing adequate bladder filling.

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PREDICTIVE MODEL OF HEMATOLOGIC TOXICITY IN BONE-MARROW-SPARING RADIATION TREATMENTS

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Aims. Patients affected by Prostate cancer (Pca) may undergo radiotherapy (RT) and experiment reduction of blood cells levels, due to the involvement of the bone marrow (BM) in the field of treatment. This study was conducted to assess if bone marrow sparing techniques may determine an abatement in hematologic toxicity (HT).

Methods. Data included patients treated for Pca from July 2021 to August 2022.

Bone marrow was considered as divided into three different sections: • Lumbosacral-BM (LSBM): extending from the superior margin of L5 somatic body to whole sacrum; • LowerPelvis-BM (LPBM): including bilateral pubic bones, ischium bones, acetabula and proximal portions of femurs, from the upper limit of the femoral heads to the lower limit of the ischial tuberosities; • Iliac-BM (IBM): extending from the iliac crests to the upper border of femoral heads. The sum of LSBM, LPBM and IBM determined the creation of the BM structure. Hematologic Toxicity was assessed and reported according to Common Terminology Criteria for Adverse Events (CTCAE) v5.0. The correlation between presence of HT and dosimetric bone marrow parameters was determined using the Wilcoxon Mann–Whitney test, setting a value of $p<0.05$ as significance level. The predictive performance of the model was determined by calculating the Area Under Receiver Operating Characteristics (ROC) Curve (AUC), obtained using a linear regression model.

Results. Twenty-seven patients were enrolled: 20 (74%) of them were subjected to Whole Pelvis Radiotherapy (WPRT), while 7 (26%) to Prostate-only RT. Seventeen (63%) patients were treated using Intensity Modulated Radiotherapy (IMRT), 10 (27%) were treated with Volumetric Modulated Arc Therapy (VMAT). A statistically significant correlation ($p<0.012$) was found between D50% IBM and the probability of developing grade 2 lymphocytopenia at the end of RT. This correlation results in a predictive model with an AUC of 0.74 (Figure 1). A value of D50% IBM>34Gy correlates with

a probability of HT of 52% at the half of RT and 64% at the end of the treatment.

Conclusions. BM delineation could be a valid option to reduce hematologic toxicity. IBM dose may predict, according to constraint (D50%>34Gy), the probability of developing grade 2 lymphocytopenia. Further studies are still necessary to determine the benefits of bone marrow sparing radiotherapy.

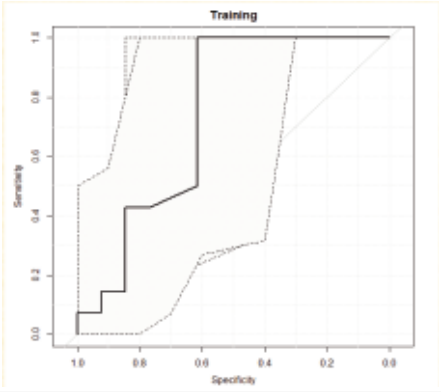

Figure 1.

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ENHANCING STUDENT PERCEPTION OF RADIATION ONCOLOGY THROUGH AN INTERACTIVE CLERKSHIP PROGRAM

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Aims. Despite the growing interest in oncology, the field of radiation oncology in Italy is not adequately represented. Many students may be unaware of radiation oncology as a potential career path and the important role it plays in cancer treatment. This study aims to examine students' perception of the radiation oncology specialty before and after completing a clerkship program at our institution.

Methods. From 08/05/2023 to 23/06/2023, seven groups of fourth-year medical students will participate in a 5-day program at the Instituto Europeo di Oncologia. The program involves spending 5 hours daily in the radiation oncology department, where they will receive an orientation session, tour the facility, and gain clinical experience alongside staff radiation oncologists and residents. During the program, the students will also engage in the contouring lab, learning about organ segmentation in radiation oncology. They will perform the contouring task twice: once at the start of the program and again after an introductory lecture on organ segmentation. Participants will complete two questionnaires: one before the contouring lecture and another after the contouring session. At the end of the program, the accuracy of their contours will be evaluated by comparing them to a reference contour. The questionnaires aim to gather information about the students' demographics, their initial perception of the difficulty of segmentation tasks, the adequacy of their anatomical and radiological knowledge, and their interest in pursuing radiation oncology as a future career.

Results. As of the present abstract, 14 students have participated in the contouring workshop and completed the two questionnaires. The study is currently ongoing, and we are awaiting the analysis of final results after all students have had the opportunity to participate. However, preliminary results indicate an increase in interest in radiation oncology after the program, with a median score of 3 and three students scoring 5. The interactive contouring activities received overall high satisfaction, with a median score of 4. Additionally, all students strongly recommend that this activity be offered to other fourth-year medical students.

Conclusions. Student perception of a medical specialty is a factor that can significantly impact career decisions. This study aims to demonstrate that an interactive clerkship experience can enhance student perceptions of radiation oncology as a potential career path.

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ARTIFICIAL INTELLIGENCE AND RADIONICS APPLIED TO IMAGE-GUIDED RADIATION THERAPY (IGRT): A SYSTEMATIC REVIEW

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Introduction. The workflow of radiation treatments has changed following the advent of Image-guided Radiation Therapy (IGRT) ensuring highly collimated treatments. Artificial intelligence (AI) and radiomics are emerging tools that have shown promising results for diagnosis, treatment optimization and outcome prediction. Aim of this review is to assess the impact of AI and radiomics on modern IGRT modalities in RT.

Methods. A Pubmed/MEDLINE and Embase systematic review was carried out to investigate the impact of radiomics and AI to modern IGRT modalities. The search strategy was "Radiomics" AND "Cone Beam Computed Tomography"; "Radiomics" AND "Magnetic Resonance guided Radiotherapy"; "Radiomics" AND "on board Magnetic Resonance Radiotherapy"; "Artificial Intelligence" AND "Cone Beam Computed Tomography"; "Artificial Intelligence" AND "Magnetic Resonance guided Radiotherapy"; "Artificial Intelligence" AND "on board Magnetic Resonance Radiotherapy" and only original articles up to date to 01.11.2022 were considered.

Results. Using the search strategy a total of 402 studies were obtained on Pubmed and Embase. Following the complete selection process a total of 84 papers were obtained. Radiomics application to IGRT was analysed in 23 papers, while a total 61 papers were focused on the impact of AI on IGRT techniques.

Discussion. AI and radiomics seem to significantly impact IGRT in all the phases of RT workflow, even if the evidence in the literature is mainly based on retrospective data. Further studies are needed to confirm these tools' potential and provide a stronger correlation with clinical outcomes and gold-standard treatment strategies.