XXXI CONGRESSO NAZIONALE

AIRO2021

Verso un nuovo scenario in Radioterapia Oncologica:
l'integrazione tra clinica, genomica e intelligenza artificiale

BOLOGNA, 15-17 OTTOBRE
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Radioterapia e Oncologia clinica

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LA RADIOTERAPIA NEL TEMPO DEL COVID

S. Silipigni, E. Ippolito, P. Matteucci, B. Santo,
S. Gentile, C. Greco, M. Fiore, S. Ramella

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After reporting the first case of severe acute respiratory syndrome coronavirus-2 infection in Wuhan, China, coronavirus disease 2019 (COVID-19) became a pandemic in a short time and hit all over the world.

There has been noteworthy concern about the impact of COVID-19 pandemic on essential health services including the management of cancer and among the restrictive and containment measures put in place, quarantine seems to have had the most significant and long-term negative psychological effects on the population. It has been recognized that cancer patients are at greater risk than the general population of developing psychological distress.

Cancer patients are more susceptible to COVID-19 infections because of their often compromised immune system resulting from systemic therapies. Furthermore, patients with indication for radiotherapy often undergo extended treatments and are in close contact with staff for positioning, heightening the potential for nosocomial transmission; for this reason, bringing cancer patients to the hospital for daily radiation therapy treatments must be done in a carefully controlled environment that limits the potential for viral transmission.

During this extraordinary time, the oncology community faces unprecedented challenges and the pace of scientific publication related to the coronavirus and its effects also exponentially increased.

Numerous expert groups, professional societies, and other institutions early on in the COVID-19 pandemic proposed serious consideration of delay or alterations of regular radiation schedules.

Radiation oncology community had to reorganize their activity trying to find a hypothetical trade-off between the risk of cancer progression in case of RT interruption and the likelihood of infection in case of RT initiation or continuation.

We conducted a literature search using PubMed to identify articles published in English language that reported on care recommendations for cancer patients during pandemic, using the terms "(radiotherapy) and (COVID-19)". Articles were selected for relevance and split into four categories:

- Risk management (flow optimization, developing telemedicine/telehealth service, applying safer patients' setup and preparation protocols).
- Adaptation of guidelines (hypo-fractionated regimens, delaying radiotherapy, omitting radiotherapy).
- Detection of initial coronavirus lung disease during radiation treatment and follow up.
- Radiotherapy for COVID-19 pneumonia treatment.

THE BATTLE FOR COLD TUMOR MICROENVIRONMENT: THE BOARD IS SET, RADIOTHERAPY IS MOVING

F. Iori[1,2], S. Cozzi[1], P. Ciammella[1], G. Timon [1], G. Blandino [1], L. Giaccherini [1], M. Augugliaro [1], M.P. Ruggeri [1], B. Alessio[2], L. Frank [2], C. Iotti[1]

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Radiotherapy (RT) is a fundamental resource for oncological patients since it can effectively kill cancer cells, once that target tumor area is precisely localized. RT had historically a complementary limited role in metastatic cancer, which tended to be managed predominantly by systemic therapies (*i.e.*, chemotherapy, target therapy, immunotherapy). Notwithstanding this, RT combination with immunotherapies - in particular immune checkpoint blockades (ICBs) - has shed an interesting light on radiation treatment potential in metastatic disease, to attain a complete regression. Evidence stresses how even diverse combinations of immunotherapies may have a reduced efficacy in patients affected by so-called cold tumors. These are characterized by an immunosuppressive tumor microenvironment (cold TME) and a worse treatment response than hot tumors, which conversely present an inflammatory and immunogenic TME (hot TME). Cold TME constitutes a comfortable habitat where carcinogenesis and cancer progression can persist and widespread.

Although literature underlines how RT can have both an immunosuppressive and an immunostimulant action on TME, several studies have shown how cold TME radiomodulation can enhance host immune response against cancer cells. Thereby, RT combined with immunotherapy, enable host immune system to reach metastatic cancer complete eradication

Thus, since TME is a chess board which continuously and dynamically mutates, RT can be a decisive move in the match against metastatic cancer.

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INTRODUCTION REPORT

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Artificial Intelligence (AI) relies on machine learning (ML) and deep learning (DL) algorithms to perform tasks that would normally require human intelligence, but in a much more efficient and less time-consuming way. Along with radiomics and genomics, AI is a promising research field in oncology, playing an important role both in diagnosis and prognosis; in radiation oncology, AI usually refers to autocontouring and autoplanning procedures.

Huge amounts of data can be analyzed by using ML algorithms; it is also possible to create virtual datasets from real ones, in order to generate more data for the learning process. In a more complex way, DL uses Artificial Neuronal Networks to mimic human brain and allow the extraction and the analysis of data from different and heterogeneous sources.

Both ML and DL have been employed for predicting Quality of Life (QoL). In breast cancer patients ML and DL can be used to objectively assess the aesthetic outcome of locoregional therapies or to study the impact of postoperative persistent pain to psychological wellness. In prostate cancer patients, ML algorithms may contribute to find the dosimetric parameters that can best correlate to patient-reported toxicities. Furthermore, secondary data sets can be obtained from big data; with AI and natural language processing techniques, important information can be collected from support social media, so as to improve understanding of QoL and identifying patients who mostly need for support.

QoL is also an outcome of interest in multifactorial decision support systems (DSSs), AI platforms that integrate various kind of oncological data and compare several outcomes of different therapeutic strategies to find both effective and economical therapeutic solutions. This could be a matter of particular interest, since the use of DSSs is already fundamental to obtain reimbursement of certain therapies in some countries.

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"LE EVIDENZE E GLI APPROCCI ATTUALI - IL PUNTO DI VISTA DEL RADIOTERAPISTA"

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In modern oncological approach, radiotherapy plays an important role in the management of uterine endometrial carcinoma, especially in the adjuvant setting. Indeed, adjuvant treatment is currently based on the presence of clinical-pathological risk factors. In medium-high risk, interventional radiotherapy (brachytherapy) is recommended, while for high-risk endometrial cancer pelvic external beam radiotherapy is the best choice as adjuvant approach. Four molecular groups of cancer can be identified: POLE ultra-mutated, microsatellite unstable hypermutated, copy-number-low, and copy-number-high. In order to define the best group of patients eligible for radiotherapy, big-data analysis, also using large databases and artificial intelligence, could offer useful decision support tools based on predictive models. Moreover, radiotherapy requires quality assurance and training due to the technological complexity of the procedure. In order to offer the best treatment to the patient, the introduction of the Intelligence Artificial Guided Procedure (IAGP) and automation in clinical practice could be very useful. The impact of this introduction will not be negligible and could improve all phases of the radiotherapy workflow: 1) first consultation of the patient with indication for radiotherapy 2) delineation 3) planning 4) treatment 5) follow-up and other therapeutic indications. Thus, the support of big data analysis and deep learning process could improve the overall quality of healthcare. Regarding the "contouring process", self-segmentation solutions, based on big data analysis, have been introduced in routine clinical practice. In addition, the implementation of large databases based on consortia, such as COBRA (consortium for brachytherapy data analysis) and radiomics archives provide a lot of very useful data for the analysis of predictive models that integrated in Decision Supporting Tool can reduce the impact of knowledge gaps between experts and non-experts, improving personalized cancer care. The aim of this talk is to present and discuss how the introduction of big data analysis and artificial intelligence could impact clinical practice and radiotherapy workflow in the treatment of endometrial cancer.

UNMET NEEDS AND CHALLENGES IN ENDOMETRIAL CANCER:

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Endometrial cancer represents the fourth most common cause of cancer in the female sex. For a long time, patients have been categorized into low, intermediate, intermediate/high and high-risk classes based on specific prognostic factors, such as FIGO stage, type of histology, involvement of vascular spaces, and grading. Nonetheless, in 2013,[1] a new classification of endometrial tumors into 4 molecular subgroups was introduced (POLE ultramutated hypermutated MSI, low copy number, high copy number), with significant diagnostics, prognostic and predictive implications. These subclasses help in accurately assessing the risk stratification and improve patient care. Also, these categories are slowly making the transition from purely theoretical to being implemented in clinical settings. Our better understanding of the molecular mechanisms of the carcinogenic process, together with the identification of biomarkers with prognostic and predictive value, allows for a better use of current drugs and for the the development of several novel targeted drugs, which are likely to bring radical changes in patients treatment.

Therefore, we now recognize that endometrial tumors need more complex and personalized approaches to avoid under- and overtreatment in an already comorbid population, including diversified surgical

procedures, adjuvant settings and the management of recurrent and metastatic lesions

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PROGNOSTIC AND PREDICTIVE FACTORS OF OUTCOMES AND TOXICITY IN RECTAL CANCER: THE STATE OF THE ART

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The standard of care for locally advanced rectal cancer (LARC) is neoadjuvant chemoradiation (nCRT) followed by a total mesorectal excision. At the time of surgery ~30% of patients present a complete response to nCRT, 8%–20% a partial response and a large subset of tumors reveals resistance to treatments. In addition, despite the development of more robust techniques and the optimal use of neoadjuvant and adjuvant therapies, the reported rates of locoregional recurrence range between 3 and 10% after curative resection, with devastating consequences, increased morbidity and mortality and a poor prognosis with a 5-year survival rate of around 50%[1] Similarly, nCRT also carries significant morbidity.[2] Then, the ability to predict the response to nCRT could crucially inform the decision when considering treatment for rectal cancer. Moreover, proper risk-stratification of patients with poor response and/or who are at higher risk of recurrence would help to customize therapeutic strategies and follow-up. In the last few years, scientific literature focused on the detection of new histopathological, molecular genetics, and immunological biomarkers, pretreatment morbidities and nutritional states able to predict clinical outcomes, efficacy of treatments and toxicities (Table). Hopefully, the integration of different types of systemic inflammatory scores, blood biomarkers, tumor biology, clinicopathological and imaging features will deliver a personalized multimodal treatment for LARC, through sophisticated prognostic modeling.

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L'INTEGRAZIONE DEI DATI NELLA PREDIZIONE DELL'OUTCOMES PER IL TUMORE DEL RETTO: DOVE LA BIOLOGIA INCONTRA LE SCIENZE INFORMATICHE

G. Chiloiro, L. Boldrini, D. Cusumano, A. Romano, E. Meldolesi, S. Reina, V. Valentini, M.A. Gambacorta

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Objectives: Locally advanced rectal cancer (LARC) represents a heterogeneous group of neoplasms with different prognosis.

Current trends suggest that neoadjuvant chemoradiotherapy (nCRT) benefits patients with earlier stages of rectal cancer who are more likely to develop a complete response (CR), allowing organ preservation and avoiding potentially unnecessary surgery. Recently, data indicate that more advanced tumours with poor characteristics require nCRT prior to total mesorectal excision (TME) for local and distant disease control. Indeed, several new nCRT strategies use consolidation or induction chemotherapy and dose-escalation in order to increase response. The aim is therefore to detect early markers of both aggressiveness and response to treatment in LARC patients at the time of diagnosis, during nCRT or after surgery.

Methods: In this context, there is a growing interest in identifying as early as possible those patients who have a high probability of reaching pCR, ideally before or at least during therapy, in order to have the possibility to tailor the treatment according to the prediction of the patient's response. Several predictive models have recently been proposed for this purpose, involving clinical data, genetic parameters and radiomic features extracted from diagnostic images. However, this type of approach needs dedicated economic and professional resources. In response to these limitations, there is a new interest in investigating the potential of image features that may be more widely applied and with a clear clinical and/or biological significance.

Results: An increasing number of studies have focused on the possibility of predicting pathological CR by analysing magnetic resonance imaging (MRI), as this modality is generally the gold standard diagnostic imaging technique for rectal cancer. Some MRI-based models have revealed the predictive value of images acquired before or during nCRT, thus providing a clinical opportunity to modulate thetreatment itself. In addition, delta radiomics and early regression index may allow prediction of survival outcomes. The idea is to create a panel of the most significant clinical, biological, molecular, genomic and radiological features to stratify LARC patients into high, intermediate and low risk.

Conclusion: predictive models should be integrated into clinical practice in order to modulate therapies to increase response and reduce treatment-related toxicities in LARC patients.

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CURRENT EVIDENCES AND CLINICAL APPROACHES FOR METASTASIS DIRECTED THERAPY IN PROSTATE CANCER

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Aims: Oligometastatic prostate cancer patients represent a complex population in which different different nosological entities coexist (e.g Pelvic oligorecurrence, oligometastatic hormone sensitive disease, non-metastatic/oligometastatic castration resistant disease). In this scenario, next generation imaging and following metastasis directed therapy play an important role for integrated management of disease.

Methods: A narrative overview of literature data about use of Next generation imaging and metastasis directed therapy was conducted

Results: For pelvic oligorecurrence, next generation imaging showed to have significant impact on post-RT event free survival.[1] Elective nodal radiotherapy actually plays a pivotal role in this setting, but metastasis directed therapy is an attractive alternative for selected patients.[2,3] Metastasis directed therapy has been shown to improve both ADT free survival and PFS in Oligometastatic hormone sensitive disease.[4-5] Prospective data are available for use of metastasis directed therapy in this setting. In non metastatic/oligometastatic castration resistant prostate cancer, use of NGI currently represent a debated issue. Many retrospective series have been published, but early prospective data are availabl.[6-7]

Conclusions: Pelvic oligorecurrence is the only setting in which next generation imaging showed to influence event-free survival after postoperative radiotherapy. However, role of metastasis directed therapy in this scenario should be defined. Oligometastatic hormone sensitive disease currently represents the main setting in which MDT showed to improve ADT free survival and PFS in prospective trial, allowing «curative» approach in selected cases. In oligometastatic mCRPC (or m0CRPC N+), SBRT should be used to improve response to ARTA, promising data are already available, comprehensive of molecular CTC profiling

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URO-ONCOLOGY – IMAGING AND GENOMICS IN OLIGOMETASTATIC PROSTATE CANCER: INNOVATIONS AND FUTURE PERSPECTIVES

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There is increasing evidence of an oligometastatic state in which patients may experience prolonged survival with multimodality combinations of local and systemic therapy. Prostate cancer (PCa) has become a paradigm for the oligometastatic state due to a relatively indolent disease course and early detection of metastatic disease using PSA screening and next generation imaging. Currently, the diagnosis of metastatic PCa is based on 99mTc bone scan and CT. However, these conventional imaging modalities may underestimate the burden of disease. For this reason, a wide range of other imaging modalities may be applied to complete diagnosis, including PSMA-PET and whole body MRI. Because oligometastatic PC includes a wide range of disease biology and clinical presentations, the optimal management of oligometastatic disease remains unclear. The impact of genetic factors is as well elusive, as their role and prevalence need to be better defined and the genomic landscape is extremely complex, remarkably in the oligometastatic castration resistant setting. This gap could be partially fulfilled by the adoption of liquid biopsies, that offer a rapid, non-invasive mean to identify specific hallmarks of neoplastic cells. Although promising, currently this approach is not standardly part of routine clinical practice, as more research is needed to determine the most appropriate markers and to arrange the optimal processing and isolation methods for specific biomarkers. The most advanced novel areas of research pertain to CTCs, cell-free DNA, and miRNA. The challenge is that in the future oligometastatic PC patients will receive "patient-tailored treatments" based on molecular characterization of the tumors and next generation imaging information.

EVIDENCES AND ACTUAL APPROACHES FOR DEFINITION OF TARGET VOLUMES REIRRADIATION

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A growing and symptomatic tumor that has been previously irradiated is one of the most challenging clinical scenarios that radiation oncologists can face. The key issue for reirradiation is an accurate definition of target volumes and organs at risk (OARs) to precisely calculate the spatial dose distribution, and select the optimal radiation dose fractionation schedule. It is unquestionable that the imaging has a crucial role for treatment planning in re-irradiation. For reirradiation of prostate cancer, multiparametric magnetic resonance imaging (MRI) allows the visualization of recurrent nodule(s) in pre-irradiated prostate[1-2] The French Association of Urology (Afu) recommend the use of a choline PET, and of an MRI if negative, for any suspicion of local recurrence after radiotherapy.[3] The European Association of Urology (EAU) guidelines recommend PSMA.

Currently, the definition of target volume is very variable, corresponding to the whole gland, a subpart of the gland only or the recurrent macroscopic disease after prostatectomy.[4] For Glioblastoma reirradiation, MRI with contrast-enhanced T1-weighted and T2-weighted sequences, are used because of their more accurate depiction of tumor extension compared to computed tomography (CT). The gross tumor volume (GTV) is generally defined as the visible lesion on MRI contrast-enhanced T1-weighted sequences. The clinical target volume (CTV) is then generated by adding a variable margin of 0–5 mm to the GTV. No GTV-to-CTV margins are usually utilized during SRS, where margins up to 5 mm are commonly applied during hypofractionated and conventionally fractionated SRT.[5] Positron emission tomotherapy (PET)/CT imaging with radiolabeled amino acids may help to improve target volume delineation accuracy by revealing tumor infiltration in regions with a non-specific MRI appearance.[6-8]

In the head and neck cancer reirradiation, the target delineation should include the use of MRI and PET. PET integration in planning has demonstrated a clearer differentiation with fibrosis and post treatment changes and a reduction of GTV size based on PET-derived metabolic information. MRI helps in the identifying fibrosis and identifying carotid vessel ulceration and encasement.

The optimal treatment volume for reirradiation is uncertain. Popovtzer et al. reported the appropriateness of limited field irradiation (GTV plus a margin of 5 mm) avoiding prophylactic treatment of the neck.[9] In case of a nodal recurrence, the target volume will include the involved nodal level or in few cases only the gross node with a 0.5–1 cm margin.[8]

With a more adequate imaging it is possible to obtain an accurate and smaller target volumes aiming at limiting the risk of toxicity and allowing to use higher doses and improving local tumor control rates.

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OMICS AND RE-IRRADIATION

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Re-irradiation is being increasingly considered as a treatment option for recurrent tumors in view of the advances in the ability to document doses, overlay plans, intensity modulation, and image guidance. Notwithstanding, unlike first-line radiation regimens, which have been tested in several large prospective randomized trials, re-irradiation studies suffer from lack of homogeneity and much smaller numbers to draw any statistically sound conclusions. New developments in omics science and, in general, in artificial intelligence are revolutionizing cancer radiotherapy, with breakthroughs in treatment accuracy and efficacy.[1] Methods from the fields of artificial intelligence not only support the radiation oncologist, resulting in increased productivity, but can also help to automatically detect small lesions which are frequently overlooked otherwise. In addition, radiomics and machine learning have been shown to efficiently classify tumor sub-regions with different metabolic pattern[2] and to identify resistant sub-volumes with different levels of radiosensitivity as a possible target for radiation dose intensification[3] in order to improve the local control rate, reduce the risk of local recurrence and eventually a second course of irradiation. In this scenario, it has been recently developed a prognostic model based on FET-PET radiomics features in recurrent glioblastoma multiforme that could significantly distinguish re-irradiation responders from non-responders.[4] However, developed classifiers for predicting tumor radiation response have focused mainly on radiomics and gene expression data, rather than the integration of multiple omics modalities, owing in part to a lack of available omics datasets for individual patient tumors. More recently, the integration of machine learning and genome-scale metabolic modeling methodologies has allowed for improved biomarker identification and prediction of radiation response in individual patient tumors.[5] Despite significant interest in methodologies for the a priori prediction of radiation response, the number of studies evaluating the potential of omics datasets for clinical application in radiation oncology is increasing slowly. We believe that, in the future, the synergistic integration of machine learning and omics data modeling will inevitably yield additional insights for improving precision medicine and long-term care of cancer patients who may benefit from reirradiation.

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MOLECULAR TESTS WITH PROGNOSTIC AND THERAPEUTIC IMPACT ON THE TUMOR CARE

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Technological improvement in high-throughput next-generation sequencing and the advances in computational processes have opened new opportunities for precision oncology in the genomic medicine era. Patients may be guided to therapy with genomically targeted agents, radiotherapy, hormone modulators and immunotherapies, based on the characteristics of their tumor and of the tumor molecular profile. Molecular tumor boards (MTBs) are the logical evolution of these new strategies. The characteristic of a MTB is the interdisciplinary team performing of radiation oncologists, radiologists, pathologists, surgeons, and also including geneticists, bioinformatics specialists, basic/translational scientists, immunology experts. The aim of MTBs is to identify and discuss all potential therapeutic strategies, based on genetic tests, for patients who are not responding to standard-of-care systemic therapies. The MTB is a vehicle by which precision immuno-oncology can be accomplished. In today's precision oncology era, liquid biopsies is rapidly evolving. Liquid biopsies are characterized by the extraction and analysis of circulating tumor DNA (ctDNA), to evaluate somatic mutations, copy number alterations, and gene fusions to select the right immunotherapies to cancer patients. Genetic tests and immunotherapy has transformed cancer therapy with impressive responses most notably in melanoma, renal cancer, and non-small cell lung cancer (NSCLC). The use of both molecular tumour board and liquid biopsy has already been described in the clinical practice. In this scenario, technological advance in the field of imaging and molecular biology have led to radiogenomics which aims to establish a correlation between quantitative or qualitative imaging features and the genomic data obtained from a molecular analysis of different type of tumors. Radiogenomics represents another promising novel approach to permit a personalized patient care. These imaging surrogates can be used to predict response to specific the right therapy and the potential for early metastasis and for personalize treatment options present the current data in glioblastoma multiforme, non-small cell lung cancer, hepatocellular carcinoma, intrahepatic cholangiocarcinoma, breast cancer, prostate cancer, renal cell carcinoma, cervical cancer, and ovarian cancer. This important consideration expose the multi-disciplinary nature of this emerging applications, where radiologists, oncologists, biologists and statistical scientists work together to obtain practical insights for personalized medicine. These technological advancements have performed new research opportunities in predictive diagnostics, precision medicine, virtual diagnosis, patient monitoring, drug discovery and also direct the option of a targeted therapy based on specific molecular features of different tumors.

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MOLECULAR TUMOR BOARD: DEFINIZIONE DEI CRITERI PER LA SELEZIONE DEI PAZIENTI

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Since the introduction of high throughput cancer genes evaluation, it was recognized that this new powerful tool required the implementation of new cultural skills often distant from the clinical practice for the majority of operators. The molecular tumor board (MTB) is a new tool collecting and revising the multiplicity of new data provided by the genetic dissection of a neoplasm aimed at a personalized therapeutic approach.[1] Next generation sequencing, with the array of opportunities from targeted genes analysis to whole genome sequencing, augmented the possibility to personalize the treatment in many "orphan" cases. To fully appreciate the power of the tool some drugs, such as pembrolizumab and larotrectinib, have already an FDA approved "tissue-agnostic" indication, namely microsatellite instability (MSI)/ deficient mismatch repair (dMMR) and neurotrophic tyrosine

kinase receptor (NTRK) fusion, respectively).[2] However, the process of a fine molecular characterization and the consequent clinical evaluation requests logistics and dedicated professional figures involved in the evaluation, with a substantial rise of time and costs. Moreover, although the identified target may recognize a specific drug, it might not be available to the patient for approval, costs, reimbursement, and specific local regulatory problems. Thus, in this frame, it is of crucial importance to identify the patients that could have a concrete advantage from this more costly evaluation. In general patients that are affected by advanced (unresectable or metastatic) rare neoplasms, or refractory to standard therapies disease, or diseases for which it is not defined a clear therapeutic pathway, are the best candidates for MTB. Of course, the amplitude of the molecular assessment should vary according to the contest: usually targeted genes sequencing is used for exclusive clinical contest, while a more wide molecular evaluation is applied in the research field. Furthermore, the clinical contest has to consider all the specific practical problems above mentioned that could restrict the implementation of the therapy suggested by the MTB. For instance, the evaluation of NTRK fusion for advanced tumors refractory to previous treatments or the evaluation of Microsatellite Status (MS) status and dMMR in patients with colorectal cancer may be considered mandatory, but it could be not appropriate for patients with extremely poor conditions in which the probability to end the molecular evaluation with a possible therapy is extremely low. In conclusion, while the wide molecular analysis of cancer has all the features to be the next "standard" approach in the diagnostic characterization of the disease on the clinical field, at the present time, it is wise considering the limits in which MTB can be applied, and to enroll in clinical trials as many MTB evaluated patients as possible to enrich the knowledge in the field and further empower this useful tool.

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MOLECULAR TUMOR BOARD (MTB) E ONCOLOGIA DI PRECISIONE

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The access to genomic profiling tests based on Next-Generation Sequencing (NGS), the development of new mutation-driven drugs, "agnostic approval" processes of the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA) ("under evaluation" practice) represent a considerable phenomenon in the development of oncology and precision medicine. These have started the mutational oncology model that supports and integrates the traditional histological one.

This new model, although still preliminary, is deeply different from the histological method. Its very complicated management affects several variables concerning scientific, organizational and re-organizational, ethical and privacy aspects. It inevitably requires the activation of inter-disciplinary groups (MTB-Molecular Tumor Board), in order to govern clinical and decisional processes for appropriateness. New oncological target therapies can be an additional value in the treatment of rare tumors and of patients without therapeutic alternatives. Nevertheless, there is a documented risk that an uncontrolled use of NGS tests and of mutation-driven drugs can compromise their appropriateness compared to standard and consolidated medicines and can determine the economic unsustainability. In order to overcome these problems, a central governance (AIFA and Regions) of criteria for using tests and selecting target therapies is essential. The concept of precision medicine in oncology has been redefined through molecular profiling, which has revealed that certain somatic genomic alterations or signatures are often represented in different cancers, regardless of the primary tumour origin. At the same time, a single type of cancer may involve multiple genomic alterations, leading to genetically defined subsets. The journey towards redefining cancer by genomic profile rather than primary organ location has led to an increased number of cancer tumour–agnostic clinical development programs. NGS testing comprises a variety of technologies, including multigene hotspot testing, medium-size gene panels, comprehensive genomic profiling of several hundreds of genes, whole exome sequencing (WES) and whole genome sequencing (WGS). Large panels, WES and WGS can also be used to examine genomic signatures, such as the overall tumour mutational burden (TMB), microsatellite instability (MSI) and hologous recombination deficiency (HRD) status (Frampton *et al.* 2013; Dong *et al.* 2015; Schrock *et al.* 2017). Many genomic alterations are rare and occur at frequencies of 5% or less across advanced cancers (Meric Bernstam *et al.* 2015). Precision medicine, through NGS-based genomic profiling tests in clinical studies and routine patient care, has allowed tailoring treatments to each patient's feature and each cancer genomic alteration. Considering this changing paradigm in oncology, a consolidated platform that collect high-quality real-world data (RWD) on solid tumours is essential to support the future of the healthcare system. A standardised data collection strategy at a global level would provide the opportunity to acquire RWD of high quality and interchangeable across countries. In the light of the constantly evolution of precision medicine, together with the introduction of new targeted therapies, there is a need to capture the most up-to-date data from patients receiving molecularly-guided treatment options (MGTO), thus making prospective and dynamic data collection crucial. Real-world evidence on

patients who have received a genomic profile-based MGTO can provide valuable information for various stakeholders that are patients, physicians involved in the treatment choice, Regulatory Authorities, payers, researchers and the pharmaceutical industry. Major Regulatory Authorities, such as EMA and FDA, have recognised the importance of RWD as a source of complementary evidence for regulatory decisions (EMA 2015; FDA 2018; EMA 2019).

INTERVENTIONAL RADIOTHERAPY IN SKIN AND GYNECOLOGICAL CANCER: STATE OF THE ART

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Aims: In the past two decades, major new developments have taken place in the field of Interventional radiotherapy (IR): in this report, we analyzed the most important changes occurred in these years concerning gynecological and skin cancer.

Methods: An exhaustive research of published articles has been performed, to look for changes occurred in gynecological and skin cancer IR.

Results: The introduction of CT and MRI into the field of IR allowed a better target dose optimization while sparing the adjacent surrounding tissues, using 3-D based volumetric planning. Therefore, in 2000, the GEC-ESTRO GYN Working Group was established to support the emerging field of gynecological image-guided adaptive brachytherapy (IGABT), by publishing 4 recommendations on MRI contouring, dose reporting, applicator reconstruction and imaging. In 2008, the same Group founded the "IntErnational study on MRI-based BRachytherapy in locally Advanced CErvical cancer" (EMBRACE), to evaluate the outcome of IGABT in a multicenter setting. Afterwards, the new ICRU Report 89, based on the Gyn GEC-ESTRO recommendations, was published in 2013. Even if MRI is the best imaging to optimize dose distribution, its availability is limited, as opposed to TC scan. Consequently, CT based contouring guidelines have been recently proposed and published. Various IR techniques and recommendations have been improved even for skin cancer treatment. A progressive development and personalization of superficial modalities, interstitial techniques and the use of treatment planning CT/MRI based, have led to additional implementation of good control and cosmesis. All these improvements and the creation of a large database, have led to a detailed analysis of possible constraints to avoid severe complications such as osteoradionecrosis of the mandible or soft tissue necrosis, recently proposed by the head and neck and skin GEC ESTRO Working Group. Recently, a potential alternative as electronic brachytherapy has been emerged. As such, the American Brachytherapy society has lately released a consensus statement concerning this treatment modality as well as an update regarding skin IR guidelines previously published.

Conclusions: IR is drastically evolved in the last years. Technology improvement, 3D imaging implementation and new applicators development have led to an increasing personalization and accuracy in gynecological and skin cancer treatment.

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BACK TO THE FUTURE: NEW TECHNOLOGIES AND ARTIFICIAL INTELLIGENCE APPLIED TO INTERVENTIONAL RADIOTHERAPY

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Aim: Artificial intelligence (AI) applications, in the form of machine learning and deep learning, are being incorporated into practice in various aspects of medicine, including radiation oncology. Several evidence from publications explores its utility and future use in external beam radiotherapy. However, its role in interventional radiotherapy (IRT, also called brachytherapy) is sparse. The aim of this presentation was to define the role of AI in interventional radiotherapy.

Method/result: AI has been applied for interventional radiotherapy procedures starting from decision-making till treatment completion. AI use has led to improvement in efficiency and accuracy by reducing the human errors and saving time in certain aspects. AI also contributes to advancements in radiology and associated sciences that can affect interventional radiotherapy decisions and treatment. There is a renewal of interest in IRT as a technique in recent years, contributed largely by the understanding that contemporary advances such as intensity modulated radiotherapy and stereotactic external beam radiotherapy cannot match the geometric gains and conformality of IRT, and the integrated efforts of IRT societies to promote interventional radiotherapy training and awareness. Use of AI technologies may consolidate it further by reducing human effort and time. Prospective validation over larger studies and incorporation of AI technologies for a larger patient population would help improve the efficiency and acceptance of IRT.

Conclusions: AI may contribute to improve clinical outcomes through the application of predictive models and decision supporting systems optimization. This approach could lead to reducing time-consuming, healthcare costs, and improving treatment quality assurance and patient's assistance in IRT.

STEREOTACTIC RADIATION THERAPY AT RADICAL DOSE IN HEPATIC OLIGOMETASTASES: STATE OF THE ART AND FUTURE PERSPECTIVES

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Aims: The condition of oligometastatic is an intermediate tumor state for most cancers, somewhere between purely localized lesions and a largely metastatic disease.[1,2] Our aim is to analyse the state of the art and future perspectives of stereotactic radiotherapy in oligometastatic liver disease.

Methods: Analysis of the scientific literature regarding hepatic stereotactic radiation therapy in the oligometastatic patient.

Results: The liver is a common site of metastasis. Multiple prognostic criteria related to survival were identified including, age, general clinical condition, disease-free interval between tumor resection and occurrence of metastases, number and size of lesions and satellite lesions. Historically, radiotherapy had a limited role in the treatment of liver metastases for which other therapeutic approaches such as surgical resection, radiofrequency ablation (RFA), cryotherapy, laser-induced thermotherapy and high-intensity focal ultrasound has been preferred.[1-2-3] The modern experience of stereotactic radiotherapy for liver metastases at radical doses have competitive results with more invasive techniques traditionally used for local control.[4,5,6] Among radiation modality, excellent results can also be achieved with proton therapy.[7]

Conclusions: Liver stereotactic radiation therapy can fully enter among the therapeutic possibilities in an oligometastatic setting. Further studies also randomized with longer follow-up using stereotactic body radiation therapy (SBRT) vs more traditional techniques (surgery and radiofrequency ablation) are needed to confirm the value and role of SBRT in this therapeutic setting.

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LE RICHIESTE DEL RADIOTERAPISTA AL RADIOLOGO NEI TUMORI DEL DISTRETTO TESTA COLLO

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HNCs are a rare disease that often arise in different subsites of an anatomically complex region. Multimodality strategies are today the standard of care in locally advanced cancer and discussion in disease management teams (DMT) has be shown to bring several advantages and better oncological outcome. DMT generally has a weekly schedule and involves radiation oncologists, radiologists, ENT surgeons, medical oncologists and other specialists engaged in HN cancer.The role of radiologist has become part in every step of the clinical history of the single patient. Imaging help clinicians both in diagnostic setting and during FU. To define the better approach radiation oncologists ask to radiologist: to discriminate between malignant and benign lesions; to stage cancer; to indicate the relationships between structures such as infiltration of a vessel or muscle. A new rule for radiologist could be during contouring. The radiation oncologist outlines the GTV using clinical information and diagnostic images. If there are questions related to the definition of the GTV, a radiologist could be consulted on an ad-hoc basis. In UK the Royal College of Radiologists in a ' recent document 'Imaging for Oncologists' has suggested that "the clinical oncologist and clinical radiologist should work together to define the GTV", but there is little evidence to guide how this should occur. Working together provided a teaching/learning opportunity. During FU we ask to radiologist to discriminate if there is a persistence disease after treatment; local or distance progression disease; second tumor; to discriminate between PD or sequele. On the other hand radiologists complain about the lack of sufficient clinical data available. For example the vocal cord mobility or a superficial mucosal extension in oral cavity change the T stage. An important issue is the surveillance imaging in asyntomatics patients treated definitively without clinically suspicious findind behond a few years, this could have a low clinical impact and a high cost. Last but not least there is the need of more structured radiology reports including all relevant staging information.

HYPO- AND ULTRA-HYPOFRACTIONATION IN BREAST CANCER

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Moderate hypofractionation with 15–16 fractions of 2.6– 2.7 Gy has been accepted as the standard of care for wholebreast external beam radiotherapy (EBRT) for invasive breast cancer in many countries.[1] This was based on the results from several well-powered randomized controlled trials showing comparable outcomes with regard to the risk of recurrence and chronic toxicity and with potential advantages in terms of reduced acute toxicity and improved cost-effectiveness.[2-4] First results on hypofractionated post-mastectomy radiotherapy have been published[5-7] with multiple trials on this topic and on hypofractionated regional nodal irradiation still ongoing. While there may be residual areas of debate, such as very young patients, large breast size,[8] there is now a broad consensus that moderate hypofractionation should be used preferentially after breast-conserving surgery when regional nodal irradiation is not indicated. Recently, results from FAST and FAST-Forward, two large randomized controlled trials testing 5-fraction regimens for adjuvant whole breast radiotherapy, have been published [9-10 . Brunt AM, Haviland JS, Wheatley DA et al (2020) Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial. Lancet 395:1613–1626. https://doi.org/10.1016/S0140-6736(20)30932-6 27. Brunt AM, Haviland JS, Sydenham M et al (2020) Ten-year results of FAST: a randomized controlled trial of 5-fraction whole-breast radiotherapy for early breast]. FAST and FAST-Forward represent the next generation of hypofractionation trials. The trials were well-designed and conducted in a similar manner to its predecessors with a systematic approach to total dose, fractionation and overall treatment time. Thus, they provide valuable insight into radiation biology of breast cancer as well as clinical results regarding tumor recurrence and late adverse events. Based on the results of FAST and FAST-Forward, adjuvant whole-breast radiotherapy in 5 fractions should be used with caution in patients with a favorable long-term prognosis. However, it may be regarded as an additional option in the radiation oncology armamentarium, especially in elderly frail patients and in settings with limited health care resources. Nevertheless, in light of the excellent results of adjuvant breast cancer treatment nowadays, the bar is set high and a reduction in overall treatment time of two weeks should generally not be the only motivation to adopt a new standard of care. Tumor control and toxicity remain pivotal in the consideration of treatment options. Thus, shared-decision making regarding ultra-hypofractionated whole-breast radiotherapy in 5 fractions should include a discussion of residual uncertainties regarding long-term tumor control and a potential increase in late toxicity. To date, ultra-hypofrac-

tionated radiotherapy should not be used in patients who underwent mastectomy or who require regional nodal irradiation. Furthermore, in the absence of further data, caution is advised.

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TREATMENT OF RHINOPHARYNGAL CARCINOMA: LIMITS OF THE PAST AND PRESENT AWARENESS

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Nasopharyngeal cancer (NPC) is one of the greatest challenges for oncologists and it is associated with a poor prognosis, largely attributed to lack of relevant symptoms. Because of the anatomic location, radiotherapy plays a key role in the treatment of this disease, while surgical resection is hardly feasible. Most of NPCs, both limited and loco-regionally advanced, show good response to radiotherapy, either alone or in combination with chemotherapy. Since the publication of the findings of the 0099 (INT-0099) trial, concurrent chemo-radiotherapy (CCRT) has been the standard therapy for locally advanced NPC, and further clinical trials have demonstrated that the 5-year overall survival (OS) rate for patients receiving CCRT is 11.7% higher than that for patients receiving radiotherapy alone. The high radiochemosensitivity of NPC allowed to obtain longer survival. The first reports of long survivors (25% at 5 years) in the mid-1960s marked the first major goal. Megavoltage RT has since become the mainstay of treatment, but its limitations both in terms of therapeutic margin and toxicity, are now known. Two-dimensional techniques were used for nearly three decades, but treatment failure and locoregional disease recurrence occurred in> 25% of patients. Over the past decade, advances have been made in RT technology (with the advent of intensity modulated radiotherapy) and diagnostic imaging, enabling cure rates > 70% with RT alone. When using an increasingly conformal technique, every single step in RT process and several factors implicated in RT planning are involved in the therapeutic ratio improving. The first fundamental step is accurate *delineation of the gross tumor extent*: fusion of magnetic resonance images with planning computed tomography such as of positron emission tomography are indicated. *Optimization of dose fractionation and dose escalation* is another crucial point. Although NPC is radiosensitive, a significant dose-response correlation has been suggested. The general consensus is that a total dose of 70 Gy or higher is needed for the gross tumor. Simultaneous integrated boost, brachytherapy, stereotactic RT or radiosurgery can represent methods to achieve dose escalation, giving an additional boost. Alternative radiation schedules were also investigated. Although meta-analyses have suggested improved outcomes with accelerated or hyperfractionated regimens for head and neck cancers in general, these have not been widely adopted in NPC. Furthermore, late toxicity remains a concern, with the risks of temporal lobe necrosis, fatal epistaxis and excessive incidence of neurologic damage in case of over-acceleration.

The *adaptive radiotherapy* is another interesting chapter but not without controversy. The clinical benefit of adaptive radiation therapy in IMRT for NPC is emerging, but predictive model for optimal timing of re-planning, should be investigated.

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STEREOTACTIC ABLATIVE RADIOTHERAPY SINGLE FRACTION FOR OLIGOMETASTATIC PATIENTS

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Aims: Stereotactic ablative radiotherapy (SABR) is an effective and safe local treatment options in patients with oligometastatic disease. SABR is currently used to treat oligometastases, but the optimum dose/fractionation schedule is unknown. Single fraction radiosurgery (SFRS) is especially attractive as an outpatient procedure in terms of patients' compliance, cost effectiveness and limited treatment time. However, evidence on choice of fractionation schedules for oligometastatic disease is lacking. The aim of this study was to review the clinical outcomes after single fraction (SF) stereotactic ablative radiotherapy (SABR) in patients with oligometastatic disease.

Study	No. of lesions	Dose	Site of RT	Rate of Local control	Rate of Toxicity
Muacevic et al 2013[3]	64	Mean 20 Gy	Bone	95.5% at 2 y	No significant toxicities reported
S.Gandhidasan et al 2018[4]	186	18-28 Gy	Mixed	90% at 1 y	No grade ≥ 4
Osti et al 2013[5]	103	23 and 30 Gy	Lung	89.1% at 1 y	2 cases of Grade 3 toxicity
David et al 2020[6]	19	20 Gy	Bone	100% at 2 y	No grade 3 or 4 toxicities
Michelle P Li et al 2020[7]	10	20 Gy	Sternal	90% at 32 mo	No grade 3 or 4 toxicities.
Sogono et al 2021[8]	494	16-28 Gy	Mixed	96% at 1 y	3% grade 3 or 4 toxicity
Kalinauskaite GG et al 2020[9]	94	17-26 Gy	Lung	89% at 1 y	No grade ≥ 3
Filippi et al 2014[10]	90	26 Gy	Lung	88.1 at 2 y	little acute toxicity and limited late toxicity (<15%)
Folkert et al 2021[11]	39	35-40 Gy	Liver	96.6% at 4 y 100% at 1 y	No grade ≥ 3

Methods: A literature review was performed to identify and summarize the findings of key prospective and retrospective studies that have shaped the field of SF SABR for oligometastases to the lung, liver, lymph nodes, bone and spine.

Results: Criteria used for selection of patients with oligometastases included: metastases limited to ≤ 2 organs and in total ≤ 5 metastases at the time of treatment. The most common target sites were lung and bone. The median planning target volume dose for SF SABR was 26 Gy (range: 17–40). SF SABR regimens can achieve 1 and 2 year local control rates of 89–100%, and 64–100% respectively. Rates of grade 3 or 4 toxicity are consistently low, no grade 5 toxicity were presented The descriptive data is shown in the Table 1.

Conclusions: SBRT offers an excellent management option for patients with oligometastases. SF SABR, using both a dedicated accelerator and a conventional accelerator associated with specific systems of control and dosimetric planning techniques[1], offers adequate toxicity profiles with good rates of local control. However, additional research is still needed to optimize dose to improve rates of local control while limiting toxicity to normal structures.

CRITICITÀ CLINICHE, TECNICHE E RADIOBIOLOGICHE: CONTRA

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Due to the increasing number of patients deserving an ablative approach with Stereotactic Body Radiation Therapy (SBRT), the appeal of single fraction is undeniable, being convenient both for patients and for radiation oncology departments. However, there are still some controversies and open issues that, in my opinion, make single shot SBRT not yet ready for prime time. From a technical point of view, it is evident that reducing the number of fractions also reduces the safety margin. Indeed a random error could be negligible in a 30 fractions treatment, while it could have dramatic consequences in case of single fraction. In this modern era, this should not be regarded as a definitive obstacle for such treatments and it also partially applicable also to fractionated SBRT. However, safe single shot treatment, particularly for mobile targets, requires advanced technologies (like for instance real time tracking or fiducials positioning inside the tumor) that can limit its applicability in the "real life". From a radiobiological point of view, it should be acknowledged that the mechanisms of action of SBRT are still partially unknown. However, there is certainly one big criticism concerning the use of single shot SBRT: hypoxia. Indeed, one of the historical reasons for fractionation is the possibility of tissue reoxigenation, making tumor cells more susceptible to RT in the subsequent fractions. Preclinical data and models agree in the prediction of a lower tumor control probability (TCP) of single fraction SBRT compared to fractionated SBRT because of the impossibility of reoxigenation.[1-3] A clinical verification of this modelling is necessary. Lastly, from a clinical point of view, there are not enough data to support extensively the use of single fraction SBRT. Most of the available results come from brain and bone metastases. In both these scenarios, however, there is a trend towards a coming back of fractionated SRT, to reduce complication rates (radionecrosis for brain and vertebral body fracture for bone).[4,5] For lung SBRT, two published trials evaluated favorably the role of single fraction SBRT compared to 3 or 4 fractions.[6,7] However, both were not superiority trials and presented data would require further validation in a phase III study, which is not planned however. Moreover,

for central lesions as well as for upper abdominal lesions, single fraction SBRT can be criticized due to the high rates of toxicity.[8] Considering all these technical, radiobiological and clinical points, I would conclude that single fraction SBRT cannot be regarded as a standard for oligometastatic patients. On the contrary, its use should be limited to clinical trials or clinical situations in which available data are sufficiently mature and convincing.

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ARTIFICIAL INTELLIGENCE AND OPTIMIZATION OF THE BREAST CANCER ADJUVANT TREATMENT. EVIDENCE AND BACKGROUND

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Artificial intelligence (AI) is expected to take a key role in future developments of medical specialties, including radiation oncology. It could make simpler and faster many steps of the complex workflow of breast cancer radiotherapy

Artificial intelligence demonstrated its value for automated contouring of organs at risk and target volumes. Auto-segmentation was originally used for OARs contouring. Recently, automated contouring using AI through deep learning algorithms was implemented for breast cancer target volume. Some studies showed that these algorithms significantly reduce contouring variation among physicians and the time of delineation.[1]

Recently, AI-based technology was introduced for automated treatment planning. This approach for breast cancer using automated treatment planning for intensity modulated radiation therapy (IMRT) was evaluated at the Princess Margaret Hospital.[2] The authors showed a good quality of the dose distributions and a shorter total planning treatment time. Similar results was reported in other studies focused on VMAT treatment planning of the breast combined with the nodal regions.[3]

Multi-omics data analysed using AI may also provide better models to predicting treatment response.

We aim to discuss current evidence on artificial intelligence for breast cancer patients, focusing on the contouring, the treatment planning and the clinical outcome prediction models

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INTELLIGENZA ARTIFICIALE ED OTTIMIZZAZIONE DEL TRATTAMENTO ADIUVANTE DEL CARCINOMA MAMMARIO

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Breast cancer (BC) is one of the most common malignancies in women, and its curability comes through a pathway in which radiation therapy (RT) is one of the essential steps.

Some studies have suggested that radiation induced damage to the lung and heart can even offset the benefit of loco-regional breast cancer RT: uncertainties regarding volume delineation and subsequent target and normal tissue doses may increase the complication risk.

Artificial intelligence (AI) is increasingly used for process management in radiation oncology and in the field of breast cancer radiotherapy, including simulations, image segmentations, treatment planning, and quality assurances, which have seen varying degrees of digitization and consequent automation over the years. AI can increase the standardisation of working processes, lessen radiation oncologists' efforts and improve homogeneity. Thanks to AI application, it is possible to save time, lower costs, and raise efficacy. Moreover, recent advances in AI

are addressing challenges related to the detection, classification, and monitoring large volume of data that ultimately result in improved clinical decision-making and thus better quality care for all patients. The use of automated data discovery and AI in breast cancer treatment and research has increased exponentially, and the continuous development of improved computer science and machine learning tools helps raise the efficiency of the different aspects in the breast cancer management by automating various processes that are usually either performed manually or in a suboptimal way. Further evidence is required to provide sufficient confidence for a shift towards "complete automation" and, at the same time, the ethical, legal and social implications of these developments must be also investigated. AI could provide software tools to help radiation therapists ensure accurate and safe treatment, as well as increase efficiency and patient access; however, radiation therapists will continue to have an important role in being present to monitor the performance of these automated systems and the patient.

MEDICAL OPTIONS IN IN METASTATIC RENAL CELL CARCINOMA (MRCC)

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Metastatic renal cell carcinoma (mRCC) cannot be cured and 5-year survival rate is about 12%, with a decreasing trend correlated to improvement of overall survival (OS) after the introduction of new drugs. Immunotherapy using checkpoint inhibitors (CPIs), alone or in combination, has now integrated all guidelines based on OS benefit both in first and second-line setting.

Currently, CPIs-based combinations represent the standard of care in first-line setting. With the longest follow up period (about 50 months), in the phase III randomized clinical trial (RCT) Checkmate-214, nivolumab plus ipilimumab immunotherapy combination significantly prolonged OS versus sunitinib (median OS 48 versus 26.6 months respectively; HR 0.65 [99.8% CI, 0.61 to 0.86]; p<0.001) in intermediate and poor-risk untreated patients with mRCC. The patients received CPIs combinations achieved higher response rate (ORR) 42 *vs* 27% (complete response 10% *vs* 1%). In the KEYNOTE-426 phase III RCT combination of pembrolizumab and axitinib resulted in better outcomes over sunitinib. With a median follow up of 42 months, the patients treated with experimental arm achieved longer OS (median 46 *vs* 40 months; HR 0.73 [95% CI, 0.60 to 0.88]; p<0.0001), longer PFS (median 16 *vs* 11 months; HR 0.68 [95% CI, 0.6 to 0.8]; p<0.0001) and higher ORR 60% *vs* 40% (complete response 10% *vs* 35) than sunitinib. More recently, results form phase III RCT Checkmate-9ER were also reported. With a median follow up of 18 months, nivolumab plus cabozantinib combination demonstrated superiority over sunitinib by significantly improving the progression-free survival time, the overall response rate, and overall survival. In the experimental arm reported median PFS was 16.6 months for the combination vs 8.3 months for sunitinib (HR 0.51 [95% CI, 0.41 to 0.64]), median OS was not reached for both arms (HR 0.60 [95% CI, 0.40 to 0.89]) and ORR was 56 *vs* 27% (complete response 8% *vs* 5%). Finally, CLEAR phase III RCT adding a novel option, lenvatinib plus pembrolizumab, to first-line treatment scenario. Lenvatinib plus pembrolizumab combination significantly improving PFS compared to sunitinib (median 24 *vs* 9 months; HR 0.39 [95% CI, 0.32–0.49]). Combination also improved the ORR compared to sunitinib (71.0% *vs* 36.1%) with an impressive complete response rate of 16.1% versus 4%. OS was also significantly longer with lenvatinib plus pembrolizumab than sunitinib (HR 0.66; [95% CI, 0.49 to 0.88]. Clinical benefits have been observed with multiple immune checkpoint inhibitor/tyrosine kinase inhibitor combinations in advanced renal cell carcinoma. The various combination treatments will unlikely be compared head-to-head, but several clinical considerations, such us quality of life, safety profile or available treatment sequencies may guide drug selection.

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TREATMENT ALGORITHM IN ANAL CARCINOMA: LESSON LEARNED OVER THE PAST 30 YEARS

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In the last 30 years, squamous cell carcinoma of the anus and studies related to this oncologic scenario have drawn global attention. Based on the evidence provided by several phase II and phase III trials, concomitant chemoradiotherapy remains the standard of care as definitive treatment.[1] The main objective of this analysis is to provide an overview of the treatment algorithm of patients with anal carcinoma, explore trends in research and investigate the

future directions in the clinical management. Publications published between 1990 and 2020 were retrieved from the main databases. Different aspects of anal carcinoma research, including bibliometric parameters, treatment issues and irradiation technique, were analyzed.

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TREATMENT OF SQUAMOUS CELL CARCINOMA OF THE ANUS, UNRESOLVED AREAS AND FUTURE PERSPECTIVES FOR RESEARCH. PERSPECTIVES OF RESEARCH NEEDS IN ANAL CANCER

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Anal cancer is a relatively rare, mostly HPV-related cancer. The curative treatment consists of concurrent chemoradiation delivered with modern radiotherapy techniques. The prognosis for most patients with early localized disease is very favourable; however patients with locally advanced disease and/or HPV negative tumours are at higher risk of locoregional and distant treatment failure. Tailored approaches are presently being investigated to determine the most suitable regimen in terms of radiotherapy dose prescription, target volume selection, normal tissue avoidance and combination therapy. Metastatic anal cancer is treated with chemotherapy aiming at prolonged survival. The role of immune therapy in the clinical setting is being investigated. There is little knowledge on the biology of anal cancer, and an urgent need for more clinical and translational research dedicated to this disease. The evidence-base for the current treatment will be briefly reviewed, and perspectives on future research needs are high-lighted (Figure1).

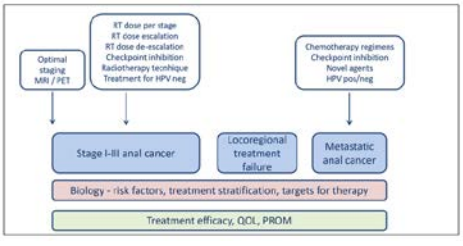

Figure 1. Ongoing and potential future research topics in anal cancer management.

USE OF AUTO SEGMENTATION IN THE DELINEATION OF ORGANS AT RISK (OARS) IN GYNAECOLOGICAL CANCER (GC), A REVIEW OF LITERATURE AND PRELIMINARY RESULTS

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Aim: The use of artificial intelligence (AI) applications in radiation oncology is emerging, however only few reports exist for GC[1-4]. Accurate segmentation of OARs and target volumes is crucial for radiation treatment planning, but manual delineation is time-consuming. One solution is atlas-based auto-segmentation (ABAS), a tool that automatically contours the OAR volumes. The purpose of this study was a literature review aimed to investigate the use of auto-segmentation in clinical routine for GC, also reporting our preliminary data.

Methods: ABAS is supposed to reduce time-consuming and inter and intra observer's variability, which may significantly affect dosimetric parameters. However, different performance was observed in some structures using ABAS. Recent developments in deep learning techniques overcame this limitation[5-6], although they are not yet so widespread in routine. We also implemented the process of ABAS function for GC patients, with a feasibility study included 23 patients selected retrospectively, treated with external beam radiation therapy (EBRT) between 2019 and 2021. Ten patients were registered in an atlas library for ABAS with OAR manual contours (MC) carefully defined by two skilled radiation oncologists. ABAS was conducted in the remaining 13 patients to generate OARs contours. The contour comparison has been performed using the Dice Index (DI) defined as the ratio between twice the intersection and the sum of manual delineation (MD) and ABAS structures (AS) and the Jaccard Index (JI) defined as the ratio between the intersection and the union of MD and AS.

Results: In our study**,** the auto-segmentation process required about 6 minutes for each CT set. DI and JI results are summarized in Table 1. The median DI and JI values for rectum, bladder, right and left femurs were respectively 0.64 [0.34-0.81] and 0.47 [0.21-0.68], 0.80 [0.36-0.87] and 0.66 [0.22-0.77], 0.88 [0.80-0.94] and 0.79 [0.67-0.88], and 0.91 [0.86-0.93] and 0.84 [0.76-0.87].

Conclusions: According to literature data, our preliminary results for ABAS-bilateral-femurs segmentation showed satisfactory performance, while ABAS-bladder and -rectum showed inferior results: the significant bone density interface could help ABAS in femur delineation. Although in some cases the auto-segmentation still required manual corrections, its implementation in daily clinical practice could change the physician workflow increasing consistency and time-saving.

Table 1. Dice Index (DI) and Jaccard Index (JI) results.

	Bladder		Rectum		Right Femur		Left Femur	
	DI	JI	DI	JI	DI	JI	DI	JI
Mean	0.72	0.58	0.63	0.47	0.88	0.79	0.90	0.82
Median	0.80	0.66	0.64	0.47	0.88	0.79	0.91	0.84
Std Dev	0.15	0.16	0.12	0.13	0.03	0.05	0.02	0.03
Max	0.87	0.77	0.81	0.68	0.94	0.88	0.93	0.87
Min	0.36	0.22	0.34	0.21	0.80	0.67	0.86	0.76

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THE MEDICAL PHYSICIST'S PERSPECTIVE ON ARTIFICIAL INTELLIGENCE (AI) IN GYNECOLOGICAL RADIATION THERAPY (GRT): NOT ONLY PLANNING

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The aim was to provide an overview of the AI integration in GRT from the medical physicist's (MP) perspective. The MP's traditional role in technology implementation is rapidly evolving, asking for managing AI tools not only in the automatic treatment planning (ATP) but in the whole radiotherapy (RT) workflow.

The GRT workflow was analysed to identify the major AI applications, as synthetic computed tomography generation, image auto-segmentation, and radiomics[1-4]. Traditionally, the main MP's role is treatment planning (TP), one of the most time-consuming and operator-dependent steps. In clinical practice, three ATP paradigms have been proposed[5]. The automated rule implementation and reasoning (ARIR) mimics the human manual and iterative planning process. Knowledge-based planning (KBP) builds statistical models to extract features from priori good plans. KBP-extracted information is used as TP inputs to assist human planners in the initial TP setting. Finally, the multi-criteria optimisation (MCO) allows to browse the optimal plans Pareto surface: without recalculations, clinical plans can be chosen sliding bars to adjust the dosimetric criteria combination.

Literature research on GRT led to KBP and deep learning (DL) application in external beam GRT and gynaecological brachytherapy (GBT). KBP can generate high-quality and clinically acceptable cervical plans[6-8], even as a multi-institutional clinical trial QC system[9]. DL has instead been applied in GBT to achieve dose distributions comparable to the Monte Carlo methods with significantly lower calculation time[10].

Last but not least, AI could help in patient-specific QA to individuate the most challenging plans to be checked or to predict the gamma passing rate.

A research project delineation followed the literature research. Recently, prostate RT plans were manually analysed to determine customized constraints achievable for a given patient's anatomy before optimization, focusing on rectum and bladder proximity to the target. The highlighted relationships suggested institution-specific criteria to standardize plan quality and consistency. The new-born project aims to develop an independent DVH-prediction AI tool to detect and eventually re-plan outlier plans in GRT.

The literature research stimulated interest in AI applications in RT, leading to the definition of a research project on a DVH prediction tool broadening one of the last projects at our Institution.

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RADIOTHERAPY (IORT) IN ABDOMEN AND PELVIS MALIGNANCIES

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Aims: Since its introduction in the 1960s, intraoperative radiotherapy (IORT) has been used, alone or combined with external beam radiotherapy (EBRT) in the treatment of abdominal and pelvic tumors. IORT allows the delivery of a higher radiation dose to the tumor bed /primary tumor during surgery thus sparing the surrounding dose-limiting healthy tissues with a consequent toxicity benefit to abdominal organs. Many experiences reported that, within a multidisciplinary approach, IORT could obtain an escalation dose which could improve local control. The aim of this review is to evaluate the rationale and oncologic outcomes of IORT in retroperitoneal soft tissue sarcomas (RPS) and rectal/ gastric/ pancreatic cancers.

Methods: A review of literature in MEDLINE/PubMed database was carried out to identify relevant articles about the use of IORT in abdominopelvic tumors.

Results: The evidence currently available suggests that IORT, within a multimodality therapy approach, in selected patients (pts) with local advanced rectal cancer (LARC) and local recurrent rectal cancer (LRRC) can improve local control and survival and its use is now well established. In pts with RPS and gastric cancer IORT integrated with EBRT +/- chemotherapy has demostrated a positive impact on local control, although there is a lack a evidence on survival benefit. In resectable pancreatic cancer IORT, as anticipated boost, has showed a possible role in improvement of local control after surgery with a positive survival benefit in some series, and it represents an emerging field of interest in pts with borderline resectable disease, in a dose escalation program

Conclusions: IORT as a dose escalation technique allows to improve local control in several abdominopelvic malignancies with a consequent positive impact on survival . Pts selection is needed to define a subset of pts who can benefit most from this treatment modality. Prospective clinical trials should be effort .

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INTRAOPERATIVE RADIATION THERAPY FOR MALIGNANCIES OF ABDOMEN AND PELVIS

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Intraoperative Radiation Therapy (IORT) has a long history in cancer treatment and became part of the armamentarium of radiation oncologists more than a century ago. IORT is the delivery of a single large radiation dose to the tumour mass/tumour bed during the surgical operation, with the direct visualization of the target volume and the possibility to displace or shield normal tissues. Increasing treatment accuracy, IORT may reduce toxicity to OARs. Furthermore, the biologic effect of the large single dose delivered during surgery is considered to be 2–3 times higher than the same dose delivered with a standard dose/fraction treatment,[1] thus, facilitating dose escalation with the aim of improving local control, partic-

ularly if IORT is associated with external beam radiotherapy. Breast cancer, intra-abdominal cancers, soft tissue sarcomas and many other cancer sites can be treated with IORT.

Over recent decades, the development of mobile radiation generating machines, located in shielded operating rooms, has made this procedure much easier to perform, obviating the need for patient transferal from surgery to radiotherapy department, particularly difficult for patients with abdominal surgery.

IORT has been used in the primary management as well as in the salvage setting for many solid abdominal/pelvic tumours. Borderline resectable or locally advanced pancreatic cancer, locally advanced or relapsed rectal cancer, retroperitoneal sarcomas, locally advanced or recurrent gynecologic and prostate cancers were treated with IORT.[2-6] The possibility to mechanically retract, for temporary displacement, dose-sensitive organs at risk - in particular stomach, duodenum, bowel and liver – out of the target volume is particularly useful in the attempt to obtain dose escalation.

In general, IORT alone may provide better local control, with an acceptable toxicity profile, in patients with close surgical margins or with minimal residual disease. The association of surgery with both IORT and EBRT, performed in a pre or post-operative setting, is advisable and allows better results also in patients with gross residual disease.

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CURRENT APPLICATIONS OF ARTIFICIAL INTELLIGENCE IN HEAD AND NECK RADIOTHERAPY

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In the last decade the huge quantity of digital data and advances in computational power have boosted the application of Artificial intelligence in medicine, especially in Radiotherapy, discipline largely based on computer science and imaging. Artificial intelligence methods have several applications both in clinical decision and in each step of radiotherapy workflow for head and neck cancers.

In the field of personalized medicine, Machine Learning algorithms can be used to analyse a large amount of radiomics features, alone or in association with other data, with the aim to predict outcomes, toxicity or pathological findings and to create decision-making tools to personalize the treatment. Artificial intelligence may also have a role along the whole treatment planning process, from autosegmentation to dose optimization. Various solutions, as AI-based segmentation and treatment planning, are already available for clinical use.

The OARs and target volumes delineation of is the most vulnerable area and the largest source of uncertainty in radiotherapy workflow. H&N OARs have complex anatomical shape, variable size, low contrast in simulation CT. The manual delineation is very time consuming and is burdened by large intra and inter-observer variability. The initial approach for automatic delineation was mainly atlas-based, using an hybrid registration to deform structures from an atlas. Atlas based method provides little improvement to the workflow since the result usually needs to be manually edited. In OAR segmentation, several deep-learning based methods have been developed and are commercially available. Expert reviewers assumed that CNN-based contours require less correction than atlas-based segmentation, with improvement of consistence and time decrease. ML algorithms have a role also in treatment planning. IMRT is the gold standard technique in HNC treatment due to the big volume and the concave shape of targets, the large number of OAR, the overlap between targets and OARs and the high dose levels. ML-based autoplanning aims to improve IMRT and VMAT efficiency and consistency. All autoplanning approachs mimic the process of iterative evaluations and adjustments made by experienced operators. Knowledge-based planning (KBP) is the most common and early commercialized approach, based on prediction of the best achievable DVHs to guide the plan optimisation, saving time and maintaining quality. Artificial intelligence may optimize the adaptive radiation therapy process (ART). ART is a replanning process frequently required in head and neck cancer treatment, both for anatomical changes and tumor shrinkage.

This process needs to repeat the workflow, from new scan to new plan, and is usually done in offline set. This operation is time and resources consuming and prone to errors or treatment delay. With the increase computational speed, ML algorithms may assure target and OAR propa-

gation on current anatomy and planning recalculation while the patient is on the treatment table, with the possibility of "online" ART. Today there are few commercial online image-guided adaptive therapy solutions, which contains deep-learning AI that provide online plan adaptation on daily CBCT.

Conclusion: Artificial intelligence has a role in several aspects HNC radiation treatment, enhancing clinical decisions and treatment quality, although the clinical use is still limited.

CURRENT EVIDENCE AND APPROACHES: UPDATE ON RADIUM-223

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Currenly, Radium-223(223-Ra)chloride is the only alpha-emitter radionuclide approved for the treatment of osteoblastic metastases in castrated-resistant prostate cancer (mCRPC) patients, able to prolong not only the time to first symptomatic skeletal-related event but also survival, as observed in the ALSYMPCA phase 3 trial.[1]

223-Ra causes an intense, local cytotoxic effect through the induction of double-stranded DNA breaks and at the same time, the short range of alpha particle has the potential to minimize damage in non-targeted cells, reducing toxicity to normal tissue. This latter characteristic, in association with a rapid blood clearance, confers on 223-Ra a good safety and tollerability; REASSURE, a single-arm observational study about the long-term safety of 223-Ra, is ongoing.[2]

On the basis of these outcomes, many prospective trials have arisen to testing the use of 223-Ra in combination with other mCRPC pharmaceutical agents. Unfortunately, in the ERA-223 trial,[3] evaluating the concomitant use of 223-Ra and Abiraterone with prednisone/prednisolone, an unexpected increased incidence of bone fractures in the 223-Ra arm was noted. That induced EMA in 2018 to controindicate the use of 223-Ra as combined therapy and also to restrict the indication of 223-Ra in monotherapy to bone symptomatic CRPC patients, progressing after at least 2 previous lines of systemic therapy or not eligible for other therapy. ERA-223 findings could be explained assuming that the risk of fractures in the 223-Ra arm is increased by the concurrent steroid use, supported by the fact that the concomitant use of bone-health agents is associated with a lower incidence of fracture both in ERA-223 and ALSYMPCA trials and also in the PEACE phase 3 study that is evaluating the association between 223-Ra and Enzalutamide.[4]

Addictional prospective trials are ongoing to tested the combination of 223-Ra and Docetaxel or with novel agents, such as immune-checkpoint inhibitors.[5] Outside the trials, an increasing number of real-life studies are providing data about 223-Ra safety/effectiveness, hightlighting the importance of a multidisciplinary management for the timing of therapy and patient selection. According to literature, the real-life experience of our Radiation Oncology Center in Bologna,[6] shows, in contrast with the latest EMA recommendations, that an earlier use of Ra-223 seems to be more tollerate on toxicity profile and better effective on tumor control and survival.

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RECENT ACQUISITIONS AND FUTURE PERSPECTIVES: LU177 PSMA THERAPY IN PROSTATE CANCER

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Despite advances in the treatment of prostate cancer, 10-20% patients develop a metastatic castration-resistant disease (mCRPC). In this scenario, survival is limited with a median overall survival (OS) of 13-32 months and 5-years survival rate of 15%. Additionally, morbidity in these patients increases significantly. Therefore, novel therapeutic agents for mCRPC represent a clinical need.

Prostate specific membrane antigen (PSMA) is a transmembrane glycoprotein over-expressed in prostate cancer cells and has been recognized as ideal target for a theranostic approach. Ligands for this receptor are now available. Lutetium-177 (Lu-177) therapeutic action is due to the emission of beta minus particles that have a maximum range of 1.7mm in soft tissue with maximum energy of about 0.5MeV and produce single strand breaks in the DNA of targeted cancer cells. Labelling PSMA ligands with Lu-177, Lu177PSMA is obtained and employed for therapy in those patients who express PSMA. Initial proofs of efficacy and safety of Lu177PSMA in mCRPC were collected from retrospective observational reports made on patients receiving

Lu177PSMA on compassionate basis when all traditional therapies were exhausted. Few years ago, Hofman et al published a single-arm phase-2 trial on 30 patients with progressive mCPRC after extensive prior regimens showing a PSA decline of more than 50% in 57% of patients of whom 82% experienced an objective response (OR). In a subsequent extended analysis by the same research group, 64% out of 50 patients experienced PSA decline>50% and 56% of OR. Lu177PSM has been also investigated in randomized controlled trials. The TheraP trial is a phase-2 trial that randomizes 200 patients to either Lu177PSMA or cabazitaxel. TheraP trial showed 65% PSA responses in the Lu177PSMA arm compared to 37% in cabazitaxel arm as well as a lower rate of G3-4 adverse events in the experimental arm. The VISION trial is a phase-3 trial randomizing 750 patients (2:1) to receive standard of care (SOC) or SOC+Lu177PSMA. Patients receiving SOC+Lu177PSMA experienced a prolonged median both progression free survival (8.7 months vs 3.4 months in SOC arm) and OS (15.3 *vs* 11.3 months). Grade 3-4 toxicity was higher in the experimental arm although quality of life comparable. These results are encouraging and Lu177PSMA is a promising candidate to change the treatment paradigms in mCRPC. Additionally, Lu177PSMA is also under evaluation in the hormone sensitive oligometastatic setting.

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Selected Oral Communications

B01

HIGH RADIATION DOSE DELIVERY BY LATTICE APPROACH TO HYPOXIC AREAS IN VOLUMINOUS SOLID TUMOURS UNSUITABLE TO SURGERY OR ABLATIVE RADIOTHERAPY (LATTICE_01): A MULTICENTRIC STUDY

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Aims: To evaluate feasibility, toxicities and clinical response (CR) in patients with a voluminous solid tumour, unsuitable to surgery or ablative radiotherapy, treated with LATTICE technique. The novel course provided to deliver inhomogeneous high doses of radiation to different areas within the gross tumour volumes (GTV).

Methods: From June 2020 to June 2021 we enrolled all metastatic patients with a diagnosis of voluminous solid tumour unresectable and unsuitable to ablative radiotherapy in the experimental centres. Among these, we selected the patients who had a potential life expectancy major of six months.

Results: In the period of enrolment, ten patients, with histological diagnosis of tumour and radiological images suggestive of systemic disease were recruited. All patients presented a Karnofsky Performance Status ≥70 and the median age was 62 years (range 59-81). The high doses of radiation, included in the GTV, is called VERTEX. These represented, into the treatment plan, hypoxic tissue areas and median cc-volume of VERTEX was 1.89cc. To these the median total dose delivered was 21Gy (range 10-50Gy) in 1-5 fraction. Instead, to GTV the median total dose of 30Gy (range 18 – 50Gy) have been delivered with a median cc-volume of 550,15cc. The toxicities data registered for our patients were poor: 44% of the patients presented erythema G1, while the incidence of diarrhoea G1 was 11%. Besides, these toxicities data have been proved same as literature records. In the period of observation after the treatment, the clinical response (CR) has been evaluated with the 55% of CR registered. 22% of the patients had stable disease (SD) and 11% showed local progression (LP).

Conclusions: The LATTICE_01 approach was feasible and well tolerated with encouraging results in terms of toxicities and CR. These preliminary results seem to indicate that this kind of therapy could emerge as a therapeutic option in this setting of patients.

B02

UTERUS MOVEMENT ANALYSIS BASED ON THE CONTRIBUTION OF ON-BOARD HYBRID MRI

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Aims: Organ motion (OM) and volumetric changes of the target represent a significant issue during radiotherapy (RT) delivery. This problem also concerns patients

affected by locally advanced cervical cancer (LACC) undergoing chemoradiotherapy (CHT) due to its peculiar anatomical site. Magnetic Resonance-guided Radiotherapy (MRgRT) combines the benefits of the improved contrast offered by Magnetic Resonance Imaging (MRI) with the possibility to deliver RT plans based on daily anatomical displacements and represents an improvement to the current standard. We sought to analyse the volumetric and position changes of the cervico-uterine structure (CUS) during RT, based on which treatment plan adaptation strategies could be developed to successfully manage OM.

Methods: LACC patients undergoing CRT were considered for the analysis. Each patient received a dose of 44.2-51.9 Gy (tumor BED10) in 22-25 RT daily fractions using the MRIdian system (ViewRay, Mountain View, California, US). All daily positioning 0.35 T 25-second MR-scans were co-registered with the planning MR-scan (pMR) by rigidly aligning the bony anatomy. The CUS were delineated, and the inter-fraction volume changes were assessed in each scan (Figure 1). Interfractional CUS displacements were evaluated by comparing its geometric centroid (GC) of each daily fraction with the ones of the pMR (ΔGC-pMR) and the ones of previous fraction (ΔGC-Fx). Different PTVs were obtained adding different isotropic margins to the pMR-CUS and a margin including 95% of the CUS of all fractions were considered adequate.

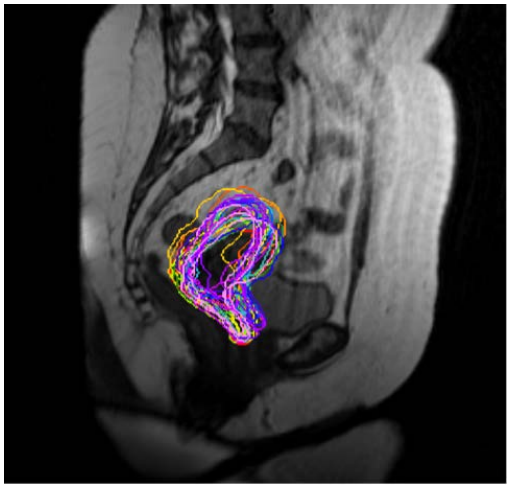

Figure 1.

Results: We collected data of 10 LACC patients. A total of 232 pre-treatment MR scans were reviewed and contoured. The median volume reduction was 32.4% (26.2%-53.6%). A significant displacement between the CUS position of every single fraction and the planning position was found (ΔGC-Plan mean = 0.93±0.21 cm), mostly located in the cranio-caudal (0.48±0.17 cm) and antero-posterior (0.53±0.13 cm) direction. Analysing the CUS position in relation to previous fractions, we noted larger mobility in the first 5 fractions (ΔGC-Fx mean= 0.96±0.09 cm). A correlation between the reduction of the CUS volume (ΔV) and its mobility (ΔGC-Fx) was also found (R= 0.71).

Conclusion: CTV-PTV margins of 15 mm are required to achieve adequate dose coverage. CUS mobility is not uniform during RT: adaptive strategies and customization of RT margins can offer potential solutions to maximize CTV coverage and minimize OAR dose.

B03

DEFINITION OF LOCAL RECURRENCE SITE IN RESECTED PANCREATIC CANCER: A MULTICENTER STUDY (DOLORES-1)

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Aims: To generate a local failures (LF) risk map in resected pancreatic cancer (PC) patients and validate the results of previous studies on this topic. We also aimed to propose new guidelines for postoperative target delineation in PC patients.

Methods: A retrospective, multicenter, observational study, on behalf of AIRO (Italian Association of Radiation and Clinical Oncology) was conducted collecting data and imaging (contrast enhanced Computed Tomography, [CT]) of resected PC patients with LF from six Italian centers. A radiologist specialized in gastrointestinal tumors delineated the LF on the follow-up contrast enhanced CT and reported the recurrence areas on

the CT images of a representative patient (Figure 1A-B). The 70% of LF points were randomly extracted from the clinical target volume (CTV) based on the RTOG guidelines and combined to the 30% of points randomly obtained from the LF database. Based on a Kernel density estimation, the 3D distribution map of LF points was generated and compared with the results of two previously published studies using the Dice index.

Results: Sixty-four patients were included in this analysis. Most patients (59.4%) underwent adjuvant treatment after surgery. Twenty-one (32.8%) patients experienced LF closer to the root of the celiac axis (CA) and forty-three patients (67.2%) experienced LF closer to the root of the superior mesenteric artery (SMA). The mean (± standard deviation) distance of LF points to CA and SMA was 21.5±17.9 mm and 21.6±12.1 mm, respectively. The Dice values comparing the isolevel of risk map corresponding to the 80% and 90% probabilistic density and the CTV80s and CTV90s proposed in the previous publications were 0.45-0.53 and 0.58-0.60, respectively.

Conclusions: According to both PC pattern of failure and RTOG guidelines, a new postoperative CTV was proposed and modelled on our validated LF risk map. The adoption of the Kernel density approach resulted feasible and automatic in our study, and might represent a robust tool for a probabilistic PC postoperative CTV definition.

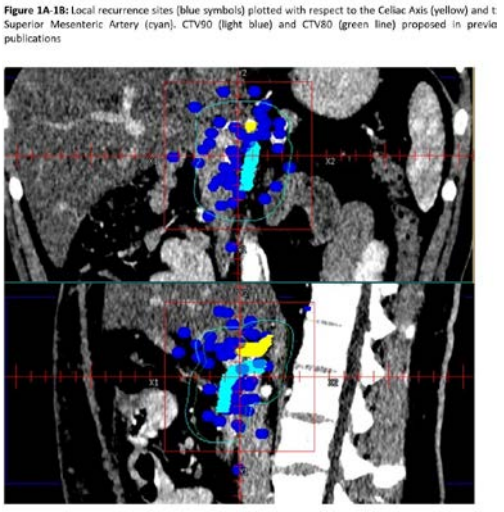

Figure 1.

B04

REAL-WORLD EXPERIENCE OF ABIRATERONE ACETATE PLUS PREDNISONE IN CHEMOTHERAPY NAIVE PATIENTS WITH METASTATIC CASTRATION RESISTANT PROSTATE CANCER: LONG-TERM RESULTS OF THE PROSPECTIVE ABITUDE STUDY

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Aims: Limited real-world data exist on the effectiveness and safety of abiraterone acetate plus prednisone in the treatment of patients with metastatic castration resistant prostate cancer (mCRPC) naïve to chemotherapy. Most of the few available studies had a retrospective design and included a small number of patients. In the interim analysis of the prospective ABItude study, abiraterone showed good clinical effectiveness and safety profile in the chemotherapy naive setting over a median follow-up of 18 months.

Methods: We evaluated clinical and patients reported outcomes (PROs) of chemotherapy-naïve mCRPC patients treated with abiraterone acetate plus prednisone as for clinical practice in the Italian, observational, prospective, multicentric ABItude study. mCRPC patients were enrolled at abiraterone start (February 2016-June 2017) and followed for 3 years, clinical endpoints and PRO, including quality of life and perceived pain, were prospectively collected. OS and rPFS were evaluated using Kaplan-Meier curves. Quality of life were assessed by FACT-P, EQ-5D-3L and EQ VAS.

Results: Of the 481 patients enrolled, 454 were evaluable for final study analyses. At abiraterone acetate plus prednisone start, the median age was 77 years, with 58.6% elderly patients (≥75 years) and 69% having at least one comorbidity (57.5% cardiovascular diseases). Visceral metastases were present in 8.4% of patients. Over a median follow-up of 24.8 months, median PFS (any progression reported by the investigators), time to abiraterone discontinuation and overall survival were, respectively, 17.3 months (95% CI, 14.1-19.4), 16.0

months (95% CI, 13.1-18.2), and 37.3 months (95% CI, 36.5-not estimable). Prostate-specific antigen reduction ≥50% was achieved by 64.2% of patients. Quality of life remained stable during treatment. Median time to pain progression according to Brief Pain Inventory data was 31.1 months (95% CI, 24.8 – not estimable). 62 patients (13.1%) had at least one adverse drug reaction (ADR) and 8 (1.7%) one serious ADR. Benefit of Abiraterone acetate plus prednisone was particularly noticeable in patients starting treatment without symptoms and with PSA<80 ng/ml, with a median PFS of 27.6 months.

Conclusion: With longer follow up, abiraterone acetate plus prednisone therapy remains safe, well tolerated and active in a large unselected population. Early start of treatment in asymptomatic patients and with lower PSA values could further improve outcomes if compared to general population of mCRPC patients.

B05

A MULTICENTER LARGE RETROSPECTIVE DATABASE ON THE PERSONALIZATION OF STEREOTACTIC ABLATIVE RADIOTHERAPY FOR LUNG METASTASES FROM COLON-RECTAL CANCER: THE LAIT-SABR STUDY

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Introduction: Stereotactic ablative radiotherapy (SABR) has been shown to increase survival rates in oligometastatic disease (OMD), but local control of colorectal metastases still remains poor. We aimed to identify potential predictive factors of SBRT response through a multicenter large retrospective database and to investigate how lung SBRT can impact on the progression to the polymetastatic disease (PMD).

Material and Methods: The study involved 23 centers, and was approved by the Ethical Committee (Prot. Negrar 2019-ZT). 1033 lung metastases were reported. Lesion diameter, dose, fractionation, and site of primary tumor were evaluated as potential predictive marker for SBRT response for the primary end-point local progression-free survival (LPFS). EGFR, KRAS, NRAS, BRAF, and MSI were also evaluated. Secondary end-point was the time to the polymetastatic conversion (tPMC).

Results: The median follow-up was 26 months. The median lesion diameter was 13 mm (range 5-58 mm). The 1- and 2-year LPFS were 86.1%, and 75.4%, respectively. At the univariate analysis, the 2-year LPFS for lesions treated with a BED <100 Gy, 100-124 Gy, and ≥125 Gy was 76.1%, 70.6%, and 94%, respectively (p=0.000). The 2-year LPFS for lesion measuring ≤10 mm, 10-20 mm, and >20 mm was 79.7%, 77.1%, and 66.6% (p=0.027). The 2-year LPFS of lung metastases treated with a single or a multifraction SBRT was 80.7%, and 73.5%, respectively (p=0.048). At the multivariate analysis a BED ≥125 Gy significantly reduced the risk of local progression (HR 0.24, 95%CI 0.11-0.51; p=0.000), while a lesion diameter >20 mm significantly correlated with increased risk of local progression (HR 1.49, 95%CI 1.03-2.17; p=0.034). The median tPMC was 26.8 months, and the 2-year tPMC was 54.5%. The 2-year tPMC for lesions treated with a BED <100 Gy, 100-124 Gy, and ≥125 Gy was 12.6, 27.7, 36.9 months, and 40%, 54%, and 73.8%,

respectively. The median tPMC for patients treated to 1, 2-3 or 4-5 simultaneous oligometastases was 28.5, 25.4, and 9.8 months, with a 2-year tPMC of 58.2%, 50%, and 37.6%, respectively (p=0.035).

Conclusions: The present is the largest series of lung colorectal metastases treated with SABR. The results support the use of SBRT in lung oligometastatic colorectal cancer patients as it might delay the transition to PMD or offer relatively long disease-free period in selected cases. Several biological and clinical predictive factors were identified to assure the highest local control.

B06

INTRAOPERATIVE ELECTRON RADIATION THERAPY (IOERT) BOOST IN BREAST CANCER TREATMENT: ITALIAN MULTICENTRE EXPERIENCE

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Aim: To evaluate the safety and effectiveness of intraoperative electron radiotherapy (IOERT)-boost in patients with early-stage breast cancer, undergoing conservative surgery and postoperative whole breast irradiation (WBI).

Method: Retrospective multicentre data were collected from January 2011 to March 2018 in 8 Italian Radiation Oncology Department. The follow-up visits were performed at 6-8 weeks after IOERT and according to the established timing schedule after WBI. Acute and late toxicity were assessed according to the Common Terminology Criteria for adverse events (CTCAE) during follow up. The objective (obj) and subjective (subj) cosmetic outcome were evaluated, according to the Harvard scale, at 1 year after the end of treatment. In-field local recurrence (LR), out-field LR, disease free survival (DFS) and overall survival (OS) were calculated.

Result: 797 patients were enrolled (Table 1). IOERT-boost was performed in all patients during surgery. The prescribed dose was between 9-12 Gy, at the reference isodose. WBI was administered for a total dose of 50Gy in 25 fractions (fx) in 602 (76.2%) cases and hypofractionated (40.5Gy/15fx-42.56Gy/16fx) in 188 (23.8%) patients. Acute toxicity occurred in 558 cases (70%): 378 patients showed mild erythema and/or spontaneously regressed seroma within 30 days (G1); 179 patients developed seroma requiring drainage (G2); one patient developed surgical wound infection (G3). No late side effects were reported. The obj-cosmetic result was excellent in 45%, good in 35%, fair in 19% and poor in 1% of cases. The subj-cosmetic result was excellent in 10%, good in 20%, fair in 68% and poor in 2% of cases. After a median follow-up of 57 months (range: 12-109 months), 785 patients are alive, and 12 patients died (10 for cancer and 2 for other causes). Overall, 13 patients (1.63%) presented a local recurrence: 6 patients a "true recurrence" in the IOERT irradiation field and 7 patients a recurrence outside the treatment field. 25 patients developed distant metastases (3.14%). At 5 years, in-field LR was 99.2% (95%CI: 98-99.7); out-field LR was 98.9% (95%CI :97.4-99.6); DFS was 96.2% (95%CI: 94.2-97.6); OS was 98.6% (95%CI: 97.2-99.3).

Conclusion: IEORT-boost appears to be safe, providing an excellent local control for patients with early-stage breast cancer. Safety and long-term effectiveness of IOERT-boost should encourage this modality of treatment, with potential to reduce cancer recurrence.

Table 1. Summary of patients' and disease characteristics.

Total: 797 patients	**N (%)**
Median age in years (range)	58 (21-84)
PS ECOG	
0	754 (94.60)
1	41(5.14)
2	2 (0.26)
Laterality	
Right	389 (48.81)
Left	408 (51.19)
Histology	
CDI	713 (89.46)
CDis	2 (0.25)
CLI	82 (10.29)
T stage	
Tis	2 (0.225)
T1	721 (90.46)
T2	72 (9.09)
T3	2 (0.225)
N stage	
N0	642 (80.55)
N1	134 (16.81)
N2	12 (1.51)
N3	9 (1.13)
Grading	
G1	159 (19.95)
G2	443 (55.58)
G3	195 (24.47)
ER	
Positive	710 (89.08)

B07

STEREOTACTIC RADIOSURGERY FOR KOOS GRADE III AND IV VESTIBULAR SCHWANNOMAS. LONG-TERM FOLLOW-UP BASED ON A CASE SERIES OF 91 PATIENTS

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Aims: For Koos grade (KG) III (*i.e.* extended to cerebellopontine cistern without brainstem displacement) and IV (*i.e.* compressing the brainstem and displacing cranial nerves) vestibular schwannoma (VS) microsurgery or combined microsurgery-stereotactic radiotherapy (SRT) are mostly recommended. Recently, stereotactic radiosurgery (SRS) or fractionated SRT (FSRT) have been investigated as treatment upfront. Patients with KG III and IV *vs* submitted to exclusive stereotactic radiotherapy (SRT) or after microsurgery in two Italian Radiotherapy Oncology Centres were retrospectively analyzed.

Methods: Patients received SRS or FSRT. Hearing capacity was classified according to Gardner–Robertson scale, where class I-II patients had "serviceable hearing" function. Trigeminal and facial nerve functions were assessed before and after treatment. Local control (LC), hearing function (HF), trigeminal and facial nerve function and toxicity were assessed.

Results: 91 patients were evaluable for clinical and magnetic resonance imaging (MRI) response, and late toxicity. 65(71%) and 26(29%) had KG III and IV VS, respectively. 67(74%) patients received SRS with a median dose of 14 Gy (range, 12-20) and 24 (26%) a FSRT (18-50 Gy in 3-25 fractions). Median tumor diameter was 17 mm. 58(64%) patients received exclusive SRT, in 33 (36%) SRT was performed as salvage therapy for recurrent or progressive tumors after microsurgery. All patients submitted to previous microsurgery had a "non-serviceable" HF; 14/33 (42%) had a severe dysfunction or total facial nerve palsy and 3/33 (9%) had moderate trigeminal dysfunction. 30/58 (52%) patients submitted to exclusive SRT had a "serviceable" HF; 2/58 (3%) a moderate and severe facial dysfunction and 5/58 (9%) had moderate trigeminal dysfunction. At a median follow-up of 6 years (range, 3-16), MRI LC was 100%. No patients receiving previous surgery improved their symptoms after SRT and no late toxicity was recorded. Regarding patients submitted to exclusive SRS and FSRT, hearing preservation in "serviceable hearing" patients was 83%. 2 (3%) patients developed incomplete and transient ipsilateral facial nerve palsy, which regressed in a median time of 6 months; moderate trigeminal dysfunction proved reversible in 5 (9%) and permanent in only 2 (3%) patients.

Conclusions: On the basis of this large series, exclusive SRT appears to be safe and effective treatment option for KG III-IV *vs* and could be considered as an alternative to combined approaches in this selected population.

B08

ONCOGERIATRIC ASSESSMENT IN ELDERLY BREAST CANCER PATIENTS: A MONOISTITUTIONAL EXPERIENCE

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Aims: Despite breast cancer (BC) is increasingly prevalent in older patients, very often these patients are considered frail and not included in clinical trial due to the incidence of age–related concomitant pathologies. The recent updated paper from the European Society of Breast Cancer Specialists (EUSOMA) and the International Society of Geriatric Oncology (SIOG) recommends that decision making should not be driven by age alone but should involve geriatric assessments plus careful consideration of life expectancy, competing risks of mortality, and patient preferences. Regarding adjuvant radiotherapy (RT), they suggested not to undertreat these patients except older patients with low-grade, hormone receptor-positive disease where the absolute benefit could be modest. The aim of the study was to identificate frail patients with BC, candidate for RT, and to measure through an Oncogeriatric multidisciplinary and multidimensional evaluation the impact of frailty on toxicities and outcomes.

Methods: A prospective observational study was designed in our Center (EUSOMA certified) for all patients with ≥75 years, candidate for RT. Frail patients were identified from Geriatric8 questionnaire (G8q) before RT. Patients resulted frail (score≤14) were evaluated by a multidimensional geriatric assessment, investigating cognitive (MMSE, GDS), functional (ADL, IADL, Tinetti), nutritional (MNA short) domains, to define the frailty phenotype. G8q was repeated at the end of RT.

Results: We screened a total of 210 oncologic patients. In our current analysis, we considered 26 breast cancer patients (median age: 78; range: 75-86). All the patients underwent G8q before and after RT. Twelve patients (46.2%) were baseline identified as frail (G8q range 8-14) and 10 of them agreed to underwent a multidimensional geriatric assessment. Five (50.0%) of the 10 patients resulted vulnerable. One frail patient refused RT while the remaining were carefully monitored during treatment, according to geriatric prescriptions. All frail patients completed treatment without acute toxicity >grade2 (RTOG). The G8q at the end of RT did not show a significant deterioration.

Conclusions: Although this study is still ongoing,

preliminary results confirmed that G8q represents a simple tool to identify frail patients in daily practice. Moreover, the support of a multidisciplinary approach in vulnerable patients resulted useful in order to obtain their compliance to the treatment without increased toxicity.

B09

EWING SARCOMA: PROGNOSTIC ROLE OF 22Q12 TRANSLOCATION

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Aims: Ewing sarcoma (EWS) is a rare malignancy and it has a high metastatic potential. In 90% of EWS the most common genetic abnormality is 22q12 translocation. Nevertheless, the prognostic role of EWS chromosomal abnormalities is still investigational.This report is a retrospective analysis investigating the correlation between chromosomal abnormalities and clinical outcome of non-metastatic EWS patients treated with neoadjuvant chemotherapy followed by local treatment.

Methods: A retrospective review of EWS cases treated in our institution from April 2002 to July 2019 was obtained. Fluorescent in situ hybridization technique (FISH) has been used to detect 22q11 rearrangement. We performed a statistical analysis to assess the predictive correlation of genetical and clinical features on Overall Survival (OS) and Distant Metastasis-Free Survival (DMFS).

Results: Data from 27 non-metastatic EWS patients were collected. Primary tumor location was the trunk in 48% of cases (n=13) and limbs in 52% of cases (n=14). Skeletal and extraskeletal disease was observed in 20 (74%) and 7 (26%) patients, respectively; 22q12 translocation was found in 22 cases (81%), however 5 cases (19%) had lack of translocation. All patients received induction chemotherapy according to the ISG/SSGIII in 18 (66%) cases and the ISG/AIEOP-EWS1 protocol in 9 (34%). Surgery was performed in 24 patients (88%), with a 87% R0 resection rate (n=21). Preoperative or postoperative irradiation was delivered in 5 (19%) and 7 (26%) cases, respectively, while 3 (11%) patients received definitive radiotherapy up to 54 Gy in 36 fractions. After a median follow-up of 23 months (range 9-73 months), 4 patients died of disease and metastatic relapse occurred in 9 patients. OS was 96% at 1 and 2 years. DMFS was 96% at 1 year and 73% at 2 years. Absence of 22q12 translocation was the only feature significantly associated with impaired DMFS (median 18 months versus not reached, p=0.005) and OS (median not reached, p=0.038).

Conclusion: In our report lack of 22q12 translocation showed a correlation with OS and DMFS in non-metastatic EWS. Giving its potentially prognostic role, assessment of 22q11 rearrangement could be useful for customized treatment. Anyhow, further prospective studies are needed.

B10

PREOPERATIVE RADIATION THERAPY IN EARLY BREAST CANCER: RESULTS FROM ROCK TRIAL (NCT03520894)

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Aims: Breast-conserving surgery (BCS) followed by postoperative radiation therapy (RT) to the ipsilateral breast is the current standard of care in women with early breast cancer (eBC). However, standard RT regimens are characterized by long treatment time with socioeconomic consequences and possible acute and late locoregional toxicities. Several studies suggest that BC can be more sensitive to high doses administered in short intervals. Preoperative robotic stereotactic radiosurgery (prRS) with a single fraction at the total dose of 21 Gy may yield potential advantages if compared with standard BCS followed by adjuvant RT. Our institution is currently conducting an exploratory trial on eBC patients undergoing prRS.

Methods: We recruited women with histologically proven invasive hormonal receptor positive, HER2 negative eBC, with tumour diameter up to 25 mm, negative clinical nodal status, aged 50 or older and eligible for BCS. Fiducial markers (3-5) were introduced in peri/intralesional position one week before planning CT. Magnetic resonance imaging (MRI) was used in conjunction with standard computed tomography (CT)-based planning to identify contrast enhancing tumors. Patients received 21 Gy in single fraction with CyberKnife® followed by definitive surgery two weeks later. The objec-

tives of this preliminary analysis were incidence of acute skin toxicity after treatment (evaluated according to EORTC/RTOG scale) and efficacy.

Results: Of 49 patients screened on mammography, 18 were eligible for histology. Of those, 7 were excluded at the time of MRI due to multifocal disease and 12 patients were successfully treated. All required dosimetric parameters were met in all patients. The median follow-up was 18 months. All treated patients underwent BCS within 14 day from prRS without any delay or complication. No patients showed erythema, pain or wound dehiscence at the time of BCS. No patients experienced acute skin toxicity of grade 2 or higher. According to Chevallier's classification, 1 patient had a pathological complete response (pCR).

Conclusions: Preliminary results from ROCK trial showed that single dose preoperative prRS is a feasible technique in selected eBC with a good safety profile and a promising rate of response. This new approach in eBC management is currently based on limited data but warrants further investigation.

B11

SEQUENTIAL MIXED BEAM APPROACH (INTENSITY MODULATED RADIOTHERAPY FOLLOWED BY PROTONTHERAPY BOOST) FOR LOCALLY ADVANCED NASOPHARYNGEAL CANCER: INTERIM ANALYSIS ON 41 PATIENTS

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Aims: To evaluate the toxicity profile and clinical outcomes of patients (pts) treated with a Mixed Beam (MB) approach (Intensity Modulated Radiotherapy-IMRT followed by a proton therapy boost) in patients with locally advanced nasopharyngeal cancers (NC). Methods We reviewed all pts treated between June 2012 and May 2020. Inclusion criteria were: clinical stage T3-T4 (any N) NC, curative-intent treatment and minimum follow-up time of 6 months. Patients with early stage (cT1-cT2) NC and/or tumors from head and neck subsites other than the nasopharynx and/or with metastatic disease were excluded. Radiation treatment was performed as follows: IMRT on macroscopic disease and on the whole neck up to a total dose of 54 Gy (2Gy/day, 5 days/week) followed by a proton therapy boost on of the macroscopic disease only up to a total dose of 70-74 Gy Relative Biological Effectiveness (RBE) (2Gy RBE/day, 5 days/week). The irradiation of the intermediate high-risk volume (from 54 to 60 Gy RBE) was performed with either IMRT (simultaneous integrated boost) or protons (sequential boost) in all pts. Toxicity profile was assessed according to the Common Terminology Criteria Adverse Events V 4.03. Results Forty-one pts (median age 49 years–29 male) were analyzed. Induction chemotherapy was performed in 63% of pts while all patients received platinum-based concurrent chemoradiation. The median RT total dose was 70 Gy(RBE) with 24% of pts treated with total dose > 70 Gy(RBE). The high-risk volume was treated with IMRT and protons in 12 and 29 cases, respectively. The overall treatment time was 57 (range 49-75) days. The toxicity profile was reported in Table 1. Moreover Temporal lobe necrosis (grade 1), visus impairments and endocrine disorders were reported in 14%, 17% and 14% cases, respectively. After a median follow up of 34 months (range 5-101), 27 (66%) pts were alive without disease, 4 (10%) were alive with disease, and 8 pts died (of these, 6 for disease progression). Four pts had a local tumor recurrence while 3 developed distant metastases. The OS at 2 and 5-years and LRFS at 2 and 5 years were 90% and 73% and 92% and 88%, respectively. Conclusions A sequential MB approach is feasible and safe for locally advanced NC. A larger cohort and a longer follow up are required to confirm these promising preliminary results both in terms of toxicity profile and oncologic outcomes.

Table 1. Acute and late toxicity.

Acute toxicity	% of patients	Late toxicity	% of patients
Skin	G2 = 63% G3 = 2%	Skin	G1 = 19%
Mucositis	G2 = 63% G3 = 12%	Dysphagia	G1= 19%
Dysphagia	G2= 41% G3= 10%	Xerostomia	G1 = 69% G2 = 19%
Weight loss	G2 = 15% G3 = 0%	Soft tissue fibrosis	G1 = 15% G2 = 3%
Enteral nutrition	Yes = 12% No = 88%	Hearing impairment	G1 = 31% G2 = 11% G3 = 10%

B12

PALLIATIVE RADIOTHERAPY (PRT) IN METASTATIC OR LOCALLY ADVANCED END-STAGE CANCER PATIENTS (PT): IMPORTANCE OF AN ADEQUATE PROGNOSTIC EVALUATION IN DECISON-MAKING PROCESS

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Aims: PRT can improve quality of life in end-stage cancer pt. An accurate prognostic evaluation of life-expectancy is essential to avoid choise of aggressive fractionation regimens near the end of life. We investigated the use of PRT in our Institute, before and after the introduction of validated prognostic scores (PS), to evaluate if our clinical practice was really changed and results improved.

Methods: we retrospectively reviewed medical charts of 2247 pt (Historical Group–HG) who received PRT from January 2010 to December 2017. Fractionation regimens, treatment modalities, cancer characteristics were evaluated respect to death date. Results were analysed at a physicians's meeting (May 2020) and introduction of validated PS (ECOG-PS-based Palliative Prognostic Index, TEACHH MODEL-Number of Risk Factors Method, GPA Index) to improve our ability to predict prognosis at the first visit was proposed. The use of PS was in any case at the discretion of the referring physician for each pt. We estabilished to re-evaluate three outcomes after 12 months (May 2021), analyzing pt treated with PRT from June to December 2020: number of pt interrupting PRT for worsening clinical conditions, number of fractions prescrived in pt died within 4 weeks after the end of PRT (1 *vs* > 1) and number of fractions prescrived in pt died after 5-12 weeks after the end of PRT (5 *vs* > 5).

Results: From June to December 2020, we performed 179 treatment of PRT. PS were utilized or not respectively in 82 (46%) (Scale Positive Group–SPG) and 97 (54%) (Scale Negative Group–SNG) cases. Pt interrupting treatment for worsening clinical conditions were respectively 7%, 7% and 0% respectively in the HG, SNG and SPG (p=0.001). Among pt died within 4 weeks after the end of PRT, prescription of single fraction was 25%, 16% and 89% respectively in the HG, SNG and SPG (p=0.0001). No pt of SPG received prolungated schedule (≥10) opposite to 36% and 24% in the HG and SNG. Among pt died after 5-12 weeks after the end of PRT, short schedule (≤5) was prescribed in 64%, 72% and 83% respectively in the HG, SNG and SPG, showing a trend in favor of SPG (NS).

Conclusions: Physicians tend to overestimate life expectancy at the end of life prescribing inappropriate prolungated regimens. The use of validated PS at the first visit improve physicians's decision-making.

B13

DNA METHYLTRANSFERASE GENE POLYMORPHISMS TO PREDICT RADIATION-INDUCED SKIN FIBROSIS IN BREAST CANCER PATIENTS: A MULTIFACTORIAL GENETIC APPROACH

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Aims: To investigate the role of four polymorphic variants of DNA methyltransferase genes as potential risk factors for radiation-induced fibrosis in breast cancer patients. We also assessed their ability to improve prediction accuracy when combined with mitochondrial haplogroup H, which was previously found to be independently associated with a lower hazard of radiation-induced fibrosis.

Methods: DNMT1 rs2228611, DNMT3A rs1550117, DNMT3A rs7581217, and DNMT3B rs2424908 were genotyped by real-time polymerase chain reaction in 286 Italian breast cancer patients who received radiotherapy after breast conserving surgery. Subcutaneous fibrosis was scored according to the Late Effects of Normal Tissue–Subjective Objective Management Analytical (LENT-SOMA) scale. The discriminative accuracy of genetic models was assessed by the area under the receiver operating characteristic curves (AUC).

Results: Significant differences among DNMT1 rs2228611 genotypes in the cumulative incidence of grade ≥2 subcutaneous fibrosis were found by log-rank test (p=0.018) in the Kaplan-Meier curves. Multivariate Cox regression analysis revealed DNMT1 rs2228611 as an independent protective factor for moderate to severe radiation-induced fibrosis (GG *vs.* AA; hazard ratio, 0.26; 95% confidence interval [CI], 0.10 to 0.71; p=0.009). Adding DNMT1 rs2228611 to haplogroup H increased the discrimination accuracy (AUC) of the model from 0.595 (95% CI, 0.536 to 0.653) to 0.655 (95% CI, 0.597 to 0.710).

Conclusions: DNMT1 rs2228611 may represent a determinant of radiation-induced fibrosis in breast cancer patients in genetic-based predictive.

B14

IMPACT OF POSTOPERATIVE RADIOTHERAPY ON BIOCHEMICAL RECURRENCE IN PN1 PROSTATE CANCER PATIENTS: ESTABLISHING THE MOST APPROPRIATE TIMING FOR RADIOTHERAPY ADMINISTRATION

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Aims: The optimal management strategy for pN1 prostate cancer (PCa) patients after primary surgery is

still debated. To address these voids, we compared long-term biochemical recurrence rates (BCR) in pN1 patients that underwent adjuvant radiotherapy (aRT) *vs.* observation + /- salvage RT (sRT) after robot-assisted radical prostatectomy (RARP).

Methods: We retrospectively identified 500 pN1 PCa patients without distant metastases, treated with RARP and extended pelvic lymphadenectomy at a single centre between 2010 and 2020. We excluded all patients with an inadequate number of lymph nodes removed (less than 10) or with high burden nodal disease (more than 10 positive lymph nodes). Moreover, patients with persistently detectable PSA after RARP and patients with missing data were also excluded. Eventually, 220 patients were included. All patients that underwent aRT or sRT received androgen deprivation therapy for 9-12 months. First, Kaplan-Meier plots depicted BCR rates and univariable and multivariable Cox regression models focused on predictors of BCR. Second, univariable and multivariable Cox regression models were refitted after propensity score (PS) matching.

Results: Overall, 133 (60.4%) *vs.* 87 (39.6%) patients were treated with aRT *vs.* noRT/sRT respectively. Specifically, 26 (11.8%) patients initially managed with observation after RARP developed BCR and were subsequently treated with sRT. Median time from RARP to sRT was 40 months (IQR: 17-62). The aRT patients were older (67 *vs.* 63 yrs, p<0.001). Higher rates of postoperative pathological ISUP grade group 4-5 pCa were observed in aRT patients (51.2 *vs.* 25.2%; p<0.001). A statistically significant difference was recorded in aRT and noRT/sRT regarding pT stage (5 *vs.* 14 patients in stage pT2; 43 *vs.* 40 in stage pT3a and 85 *vs.* 33 in stage pT3b, p <0.001). Median time to BCR was 62 *vs.* 38 months in aRT *vs.* noRT/sRT patients (p=0.001). In multivariable Cox regression models, noRT/sRT patients were associated with higher BCR rates (hazard ratio [HR]: 3.27, p<0.001), relative to aRT group. After PS matching (ratio 1:1; aRT = 57 *vs.* noRT/ sRT= 57) a 5-year BCR rate significant difference was observed (respectively, 40.4 (aRT) *vs.* 76.4% (noRT/sRT); p<0.01).

Conclusions: Adjuvant radiotherapy should be considered in treatment of pN1 patients. Specifically, patients managed with observation/sRT experienced BCR approximately two years before their aRT counterparts.

B15

A MULTICENTER STUDY ON INTENSITY MODULATED RADIOTHERAPY TECHNIQUES FOR ANAL CARCINOMA (RAINSTORM) ON BEHALF OF AIRO GASTROINTESTINAL STUDY GROUP

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Aims: To evaluate the pattern of care, clinical results and the impact of treatment parameters on oncological outcomes in anal cancer (AC) patients treated with Intensity-modulated radiotherapy (IMRT) techniques.

Methods: A multicenter retrospective observation study was designed on behalf of AIRO (Italian Association of Radiotherapy and Clinical Oncology) gastrointestinal study group.

Table 1. Patient, tumor and treatment characteristics.

Patient and tumor characteristics		N=987	%	Treatment details		N=987	%
Age = 62.00 years (range: 54.00-80.00)							
Gender	M	281	28.42	median Total Dose 55 Gy (range: 45-75)			
	F	706	71.53				
ECOG Performance Status	0	775	78.52	IMRT modalities	static or dynamic IMRT	302	30.60
	1	197	19.95		VMAT	470	47.62
	2	15	1.53		HT	215	21.78
HPV	Negative	210	21.27				
	Positive	229	23.20	Boost modalities	Sequential	252	25.54
	NR	548	55.53		SIB	568	57.54
HIV	Negative	747	75.68		SIB+ Sequential	122	12.36
	Positive	90	9.12		SIB+ Sequential BRT	45	4.56
	NR	150	15.20				
Tumor site	Anal Canal	879	89.06	Concomitant chemotherapy	MMC + 5FU	634	64.23
	Anal Margin	108	10.94		MMC + Cap	145	14.69
Histology	Squamous	880	89.15		Cisplatin + 5FU	21	2.13
	Basalioid	84	8.51		Cisplatin + Cap	67	6.79
	Other	23	2.34		MMC	2	0.20
Grading	G1	68	6.88		5FU	8	0.81
	G2	328	33.23		Cisplatin	3	0.30
	G3	233	23.60		Cap	29	2.94
	NR	358	36.29		Other	21	2.13
TNM Stage	T1-T2 N0	330	33.43		NR	4	0.41
	T3-T4 N0	106	10.74		Any	53	5.37
	N+	551	55.83				
Disease extension	Early	330	33.43	RT interruption		67	6.78
	LAD	633	64.13	RT break >5 days		186	18.84
	ED	24	2.44	median OTT = 44 days (range: 25-115)			

Legend: ECOG=Eastern Cooperative Oncology Group; HPV=Human Papilloma Virus; HIV=Human immunodeficiency virus; NR=non-reported; Early Disease: T1-T2 tumors; LAD=locally advanced disease (T3-T4 or N+= node positive tumors); ED=Extended Disease (lumbo-aortic and/ or common iliac lymph nodes). IMRT=; Intensity Modulated Radiation Therapy; VMAT= Volumetric Modulated Arc Therapy; HT= Helical Tomotherapy; SIB=Simultaneous Integrated Boost; 5-FU=fluorouracil; MMC= mitomycin C; Cap=Capecitabine; RT=radiotherapy; OTT= Overall treatment time.

Results: 987 patients from 25 different Italian centers and treated between 2007-2019 were analyzed. Clinical and treatment characteristics are shown in Table 1. A SIB strategy was used in 568 patients (57.5%). An additional sequential boost was administered in 167 patients (16.9%) using external beam RT (EBRT) or Brachytherapy (BRT) in 122 (12.4%) and 45 patients (4.6%), respectively. The median Total Dose was 55 Gy (range: 45-75). Concomitant chemotherapy was administered in 934 patients (94.6%). Grade 3 acute skin, gastrointestinal and urogenital toxicity were reported in 251 patients (25.4%), 61 (6.2%) and 5 patients (0.5%), respectively. The median overall treatment time (OTT) was 45 days (range: 25-115). A treatment interruption >5 days occurred in 186 patients (18.8%). RT was not completed in 67 patients (6.8%). The overall clinical complete response (CR) rate (beyond 6 months) was 90.6%. The 3-year local control rate (LC) was 85.8% (95%CI:84.4-87.2) and the 3-year colostomy-free survival (CFS) was 77.9% (95%CI:76.1-79.8). Three-year progression free survival (PFS) and overall survival (OS) rates were 80.2% (95%CI:78.5-81.9) and 88.1% (95%CI:78.8-89.4), respectively. Histological grade 3 and nodal involvement were associated with lower CR rate (p=0.030 and p=0.004, respectively). A statistically significant association was found between advanced stage, nodal involvement, and LC, CFS, PFS and OS. Age> 68.5 and OTT ≥45 days were significantly correlated with a lower PFS (p=0.052 and p=0.050, respectively) and histological grade 3 with a lower LC (p=0.025). No statistically significant association was found between total dose, dose/fraction and/or boost modality, and clinical outcomes.

Conclusion: Excellent clinical results and a mild toxicity profile were reported in this large cohort of patients, confirming IMRT techniques as standard of care for the curative treatment of anal cancer patients. Lymph node involvement and high histological grade were confirmed as the most impactful negative prognostic factors on complete clinical response, LC, CFS, OS and PFS.

B16

A PROSPECTIVE COHORT STUDY EXPLORING EARLY CARDIAC TOXICITY IN RADIOTHERAPY FOR STAGE III NON-SMALL LUNG CANCER: PRELIMINARY ANALYSIS

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Aims: To evaluate early cardiac function variation after chemoradiotherapy (CRT) in LA-NSCLC through the multimodal use of advanced imaging methods to explore the associations between early cardiac risk factors and late adverse events.

Methods: This trial is a prospective, observational cohort study. At the beginning of the treatment, all patients undergone screening tests with clinical history, physical examination, blood chemistry (including lipid dosage, cardiac markers as TnI, NTproBNP, CKMB and PCR), 12-leads ECG and echocardiographic examination. A weekly evaluation was detected during treatment with ECG and cardiac marker assays. ECG, echocardiographic examination and strain evaluation was performed at month 1 (M1) and months 3 (M3) after the end of CRT.

Results: This preliminary analysis included thirty-four patients. The median age was 69.5 years (range, 43-87). The median follow-up was 27.8 months. 62% of patients were in stage IIIA. Radiotherapy was delivered with a median total dose of 60 Gy with conventional fractionation. All patients were treated with concurrent CRT and in 65% used a platinum-based regimen. None of the bio-humoral markers changed during CRT. No change of normal values of QTcB and QTcF were found during the treatment. No difference was recorded between normal baseline values and at M3 for mean end-diastolic Volume (EDV; 109.5 *vs.* 102.4, p=0.099) and mean End-Systolic Volume (ESV; 48.5 *vs.* 48.4, p=0.967). Echocardiography Global Longitudinal Strain (GLS) and Ejection Fraction (EF) progressively decreased from baseline to M1 and M3. There was a strict correlation between GLS and FE reductions (at M1: p=0.034; at M3: p=0.018). No correlations emerged between GLS or EF and bio-humoral markers, QTcB and QTcF, the total EQD2 dose, the use of concurrent platinum-based chemotherapy, all cardiovascular (CV) risk factors, all drug therapies intake and ASCVD score. No patients died of CV complications. Eight patients (23.5%) had a CV event at a median fol-

low-up of 15.8 months after CRT and in all but one patient heart rhythm problems were recorded. Hearth failure aùffected one patient.

Conclusions: This preliminary data shown that a reduction in GLS was the only variation observed at M1 and M3 after CRT in these patients. These results encourage us to continue the study in order to estimate the overall and individual incidence of any early cardiac event and to identify any variables that cause an increased risk of acute cardiac events.

B17

ATLAS BASED AUTO-SEGMENTATION (ABAS) IN THE DELINEATION OF RECTUM AND BLADDER IN CERVICAL CANCER PATIENTS DURING INTRAUTERINE BRACHYTHERAPY PLANNING

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Aim: Artificial intelligence (AI) has been applied into several aspects of radiation oncology practice but its role in brachytherapy is scarcely discussed. On the other hand, there has been an interest renewal in brachytherapy as a crucial part of curative radiation therapy for cervix cancer. The contouring in brachytherapy is critical and time consuming due to a new implant for each fraction of its schedule treatment, generally once a week for 4-5 weeks. This study evaluated the feasibility of atlas based auto-segmentation (ABAS) in the delineation of rectum and bladder in cervical cancer patients during intrauterine brachytherapy (IB) planning.

Methods: In our Department, IB procedure requires empty rectum and bladder filled with 100 ml of saline solution through a urethral catheter before each CT scan and treatment fraction. Ten different patients treated with IB in 2020 have been retrospectively selected. Organs at risk (OARs) volumes previously defined by two skilled radiation oncologists were used to create an atlas library in ABAS. Automatic-segmentation has been used to generate OARs contours on a total of 16 planning CTs of 4 patients treated with intrauterine brachytherapy from January 2021 to April 2021. The following contour comparison has been performed using the Dice similarity coefficient (DC) defined as the ratio between the intersection and the union of manually contoured and ABAS structures.

Results: The auto-segmentation process requested about 4 minutes for each CT set. DC results are summarized in Table 1. The median DC rectum value was 0.45 [0.17-0.66], while the median DC bladder value was 0.82 [0.65-0.89]. The mean standard deviation of DC values for a single patient was 0.08 and 0.03 for rectum and bladder, respectively.

Conclusions: In these preliminary results, bladder segmentation showed a higher accuracy compared to the rectum segmentation with smaller inter-fractions variation for a single patient. The suboptimal results for rectum could partially be explained by different organ preparation: the emptying of the rectum was self-regulated by patients at home, while the bladder was filled by a standard procedure in the Department. Ongoing studies are evaluating the impact of a stricter rectum preparation. The implementation of ABAS with manual adjustments in daily clinical practice could change the workflow of physicians to reduce time consumption, however further implementations and investigations of AI are needed.

Table 1. Dice similarity coefficient (DC) results.

Bladder					
Patient	Fx 1	Fx 2	Fx 3	Fx 4	σ
1	0.82	0.82	0.82	0.86	0.02
2	0.69	0.72	0.65	0.73	0.03
3	0.82	0.78	0.89	0.87	0.04
4	0.83	0.79	0.77	0.83	0.02
Rectum					
Patient	Fx 1	Fx 2	Fx 3	Fx 4	σ
1	0.39	0.22	0.23	0.17	0.08
2	0.40	0.44	0.45	0.56	0.06
3	0.42	0.49	0.60	0.59	0.07
4	0.47	0.59	0.66	0.45	0.09

Abbreviations: Fx = fraction, σ = standard deviation

B18

EROS 2.0 STUDY: LATE VAGINAL TOXICITY COMPARISON BETWEEN TWO INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY) SCHEDULES IN ADJUVANT TREATMENT OF ENDOMETRIAL CANCER

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Aims: To evaluate the incidences of late toxicity after two different high dose rate (HDR) vaginal interventional radiotherapy (IRT, brachytherapy) dose schedules in Stage I-II endometrial cancer.

Methods: Between 2014 and 2020, FIGO 2009 Stage I-II endometrial cancer patients who had undergone Total Abdominal Hysterectomy with Bilateral Salpingo-Oophorectomy (TAH-BSO) with/without pelvic/paraaortic lymph node dissection and treated by adjuvant vaginal HDR-IRT were included, non-endometrioid histologies were excluded. A median follow-up larger than 6 months was required. OncentraBrachy treatment planning system (TPS) and MicroSelectron device with a 192Ir source were used to treat the first cohort of patients (cohort 1 – C1). The proximal third of the vagina was irradiated by a HDR-IRT schedule of 7 Gy per fraction/weekly (total dose 21 Gy), prescribed 0.5 cm from the applicator surface. OncentraBrachy treatment planning system (TPS) and a Flexitron device with an 192Ir source were used to treat the second cohort of patients (cohort 2 – C2). The upper 3 cm of the vagina was irradiated by an HDR-IRT schedule of 6 Gy per fraction/weekly (total dose 24 Gy) prescribed 0.5 cm from the applicator surface. Vaginal toxicity was scored according to CTCAE 5.0 scale. Presence *vs* absence of any toxicity grade was compared. Toxicity was evaluated against clinical covariates (age, lymphadenectomy, fractionation, stage) by Pearson correlation test and in multivariate fashion by logistic regression.

Results: 114 Stage I and 3 Stage II patients, median age 62 (32-85) years have been included in the study. The mean follow-up of the series was 57 months in C 1 (40-76) and 17 months in C 2 (8-42). Vaginal late toxicity was found in 40 patients of the group 1 and 15 patients of the group 2. No severe late toxicity was observed except for one Grade 3 vaginal stricture in C1. Univariate analysis showed that lymphadenectomy (p=0.006), and radiotherapy fractionation (p=0.002) were significantly associated with a higher probability to develop late vaginal toxicity. After stepwise logistic regression among other covariates age (p=0.02) and fractionation (p=0.001) were found significantly correlated. The AUC of logistic regression was 0.705. The 3-year probability of local-relapse free, distant metastasis-free and cause-specific survivals for all patients were 96.6%, 94.8% and 99.1%.

Conclusions: The analysis showed a lower late vaginal toxicity in C2 compared to C1. Specific large studies involving cost efficacy measures are needed to confirm the presented results.

B19

ABSTRACT WITHDRAWN

B20

UNUSUAL 131-I LIVER UPTAKE ON RXWBS AFTER RAI: A SHORT CASE SERIES

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Aims: The treatment of choice in well-differentiated thyroid carcinomas (DTCs) is surgery, often followed by radioiodine therapy (RAI) when total thyroidectomy has been performed. Post-RAI, Iodine-131 whole body scan (Rx-WBS) has the highest sensitivity to detect radioiodine body uptake, both in case of normal thyroid remnant as well as in case of metastatic foci. However, unexpected false positive radioiodine uptake could be reported. Here we present a case series with unusual false positive radioiodine liver uptake on Rx-WBS that could have changed therapeutic management.

Methods: We report a series of five patients (four female and one male; mean age: 48y) at early stage DTC and low serum thyroglobulin levels after surgery; according to TMN thyroid cancer classification (AJCC8), 3 pts with pT1a and two pts with pT2, 3 pts with pN1 and two pts with pN0. All pts were treated in our Center from 2018 to 2020, with ablative/adjuvant RAI. After the detection of the unusual liver uptake, pts underwent to magnetic resonance (MR) with epatospecific contrast enhancement and a CEUS in order to biopsy the suspicious lesions.

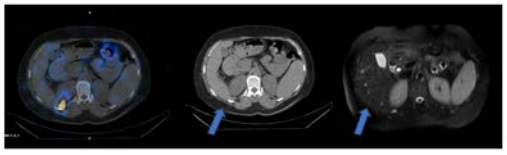

Figure1. On the left RxWBS scan showing iodine-avid focus in the liver; in the middle and on the right, CT scan of the SPECT and RM respectively, in which no lesions were found (see blue arrows).

Figure 1.

Results: In the first case the hepatic findings at RxWBS were considered as false positive because no correspondence has been found during the subsequent diagnostic exams, likely caused by a transient inflammatory

condition (Figure 1). In the second case no lesion was detected neither by resonance and ultrasound. In the third case the lesion was classified at the CEUS as an angioma in reason of an increate permeability of the vessels and a greater radioiodine uptake in that site. In the last case patient underwent only MR that showed a benign lesion as focal nodular hyperplasia (FNH). In all cases biopsy was not performed: for the first three patients lesion was not found at CEUS and for the last two patients biopsy was not necessary. At last follow-up data, one patient had a locoregional disease recurrence in the neck and underwent surgery with complete remission while the other patients have an excellent response of disease, according to ATA 2015 response assessment.

Conclusions: In literature, very few cases of unusual Rx-WBS uptakes are described and, when reported, the mechanism or radioiodine uptake is often debated. As physicians, we must evaluate carefully these false-positive findings in order to avoid misdiagnosis and inadequate treatments.

AIRO GIOVANI
Oral Communications

C01

HYPOFRACTIONATED-ACCELERATED RADIOTHERAPY DURING COVID 19 PANDEMIC: EXPERIENCE AT UNIVERSITY OF CATANIA AND POTENTIALS FOR A PRACTICE-CHANGING APPROACH

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Aims: Hypofractionated-accelerated Radiotherapy (HF-RT) is an advanced treatment modality that allows patients to complete their course of radiotherapy faster than conventional treatment by delivering more doses of radiation per fraction. To date at University of Catania it is applied as a standard of care for prostate and breast cancer, but thanks to its ability to optimise treatment schedules, it has been widely used during COVID-19 pandemic in many other types of cancer. Our aim is to evaluate the efficacy and the safety of HF-RT in different kinds of cancer.

Methods: Following several recommendations from international scientific societies, we enrolled 195 patients who received HF-RT from February 2020 to May 2021 and 246 patients who received conventionally fractionated RT (CF-RT) in the same period. Then, we compared the outcomes in terms of efficacy (tumor control and quality of life) and safety (acute and late toxicity) between these two groups of patients. The patients enrolled were affected by different types of cancer such as breast, prostate, lung, rectal, brain, gynecological, gastro-esophageal, bladder, H&N, hematologic and skin tumors. Table 1 summarizes HF-RT schedules applied.

Table 1.

	RECTUM	LUNG	BRAIN	BREAST	PROSTATE	BLADDER	H&N	GYNEC.	OTHERS
2,25 GY X 20-23 FX	2,75%	1,1%	---	---	---	---	---	---	1,65%
2,65 GY X 16 FX	---	---	---	41,8%	---	---	---	---	---
2,5 GY X 16-18 FX	0,55%	1,65%	1,1%	---	---	---	---	1,1%	0,55%
2,5 GY X 20-23 FX	---	1,1%	4,4%	---	---	---	2,75%	0,55%	4,4%
2,5 GY X 28-29 FX	---	---	---	---	9,35%	---	---	---	---
2,67 GY X 15 FX	---	---	2,75%	---	---	---	---	---	---
2,75 GY X 22-24 FX	---	---	---	---	1,65%	---	---	---	---
3 GY X 10-13 FX	---	---	1,1%	---	---	---	---	---	3,3%
3 GY X 14-17 FX	---	1,65%	---	---	0,55%	---	---	---	---
4 GY X 5-6 FX	---	---	---	---	---	---	---	---	3,85%
4 GY X 8-10 FX	---	---	---	---	---	---	---	---	2,75%
5 GY X 3-4 FX	---	---	---	---	---	1,1%	---	---	---
5 GY X 5-6 FX	1,65%	---	0,55%	---	---	1,1%	---	0,55%	2,75%

Results: HF-RT in breast cancer resulted in less acute toxicity than CF-RT (skin and breast side effects) and improved the quality of life; in prostate cancer we achieved high rates of biochemical control with low rates of GI and GU toxicity; in lung cancer, the most common acute toxicities observed was radiation pneumonitis and esophagitis. In rectal and gynecological cancers the only radiotoxicity reported was a G2 diarrhea with a similar rate of local control and disease free survival; in brain cancer HF-RT maintains rates of disease control, time to recurrence, without increasing acute/late toxicity. Skin tumors (BCCs/SCCs) obtained good cosmesis and local control

Conclusions: HF-RT, widely used during COVID-19 pandemic at University of Catania, has been shown to keep therapeutic results unchanged, sometimes improving them, with a good tolerance profile, demonstrating that we

can take advantage of its ability to streamline the department organization, simultaneously maintaining an adequate general safety. HF-RT could change pattern of practice in many cancer types, but more evidence is needed.

C02

ACTIVITY OF A COMPLEX RADIANT THERAPY AND ONCOLOGY CENTER DURING COVID-19 PANDEMIC. EVALUETING THE IMPACT OF COVID IN DOCTOR-PATIENT INTERACTION

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Aims: In the last year, Italy faced a COVID-19 emergency and implemented preventive measures in order to protect patients and healthcare providers from a disease outbreak. The pandemic control strategies impacted patient experience directly. Questionnaires evaluating patients reported measures (PREMs) may assess critical issues and represent a helpful tool to measure the patient perception of healthcare service. Our purpose was to prospectively assess patient satisfaction about doctor-patient interaction in a complex radiation therapy and oncology facility during the COVID-19 pandemic.

Methods: Two validated questionnaires (EORTC QLQ-C30, FACIT-TS-G version 1) and 14 specific questions evaluating patients' perception of COVID-19 measures were administered to cancer patients receiving either systemic and/or radiation treatment.

Results: One hundred twenty-five patients admitted to our department from 1-30 April 2020 underwent the survey. The majority (66.4%) of patients were women and the most common disease was breast cancer (40%). The average Global Health Status (GHS) of EORTC QLQ-C30 was 61.67. Emotional functioning, social, and cognitive domains obtained scores of 75.48, 80.13, and 84.67, respectively. FACIT-TS-G results revealed 120 patients rated the treatments effective and 108 patients thought the side effects were the same as expected or better. Most (89.6%) rated their treatment good, very good, or excellent. Concerning COVID-19-related questions, patients reported overall very good level of information.

Conclusions: Despite the introduction of strict COVID-19 control measures, there was a high level of cancer outpatient satisfaction. The satisfaction levels may influence compliance, continuity of treatments, and patient-doctor communication, impacting the quality of clinical care in the next phases of the pandemic.

Table 1. Patients' Characteristics.

	n		%
Sex	41	males	32,8
	83	females	66,4
	1	unknown	0,8
Age (years)	2	18-30	1,6
	20	31-45	16
	39	46-60	31,2
	48	61-75	38,4
	14	76-90	11,2
	1	>90	0,8
	1	unknown	0,8
Median Age (range)		61-75 years	
Level of Education	15	Elementary School	12
	37	Middle School	29,6
	46	High School	36,8
	26	Graduate – Post Graduate	20,8
	1	unknown	0,8
Primary malignancy	50	Breast	40
	17	Lung	13,6
	8	Genito-Urinary	6,4
	3	Gastro-Intestinal	2,4
	7	Gynaecological	5,6
	10	Head and Neck	8
	10	Brain	8
	4	Haematologic/	3,2
	16	Other	12,8

Table 2. FACIT-TS-G Results.

	A lot worse	A little worse	About the same	A little better	A lot better
TS1: Compared to what you expected, how do you rate the effectiveness of the treatment so far?	2 (1.6%)	2 (1.6%)	53 (42.4%)	38 (30.4%)	30 (24%)
TS2: Compared to what you expected, how do you rate the side effects of treatment so far?	3 (2.4%)	14 (11.2%)	41 (32.8%)	42 (33.6%)	25 (20%)
	No, not at all	Yes, to some extent	Yes, for the most part	Yes, Completely	
TS3: Did your doctor(s) help you evaluate the effects of your treatment so far?	9 (7.2%)	32 (25.6%)	56 (44.8%)	28 (22.4%)	
TS4: Do you feel you received the treatment that was right for you?	1 (0.8%)	22 (17.6%)	69 (48%)	42 (33.6%)	
TS5: Are you satisfied with the effects of this treatment so far?	2 (1.6%)	36 (28.8%)	52 (41.6%)	35 (28%)	
	No	Maybe	Yes		
TS6: Would you recommend this treatment to others with your illness?	3 (2.4%)	25 (20%)	97 (77.6%)		
TS7: Would you choose this treatment again?	3 (2.4%)	25 (20%)	97 (77.6%)		
	Poor	Fair	Good	Very Good	Excellent
TS8: How do you rate this treatment overall?	1 (0.8%)	12 (9.6%)	44 (35.2%)	40 (32%)	28 (22.4%)

Table 3. Covid-focused questionnaire results.

	Category of response (n, %)			
	Strongly disagree	Disagree	Agree	Strongly agree
General information about COVID-19 pandemy				
Q1: I have heard about COVID-19 epidemy.	2 (1.6%)	7 (5.6%)	75 (60%)	41 (32.8%)
Q2: I have heard about recommended sanitation precautions to prevent the spread of COVID-19 epidemy.	3 (2.4%)	1 (0.8%)	40 (32%)	81 (64.8%)
Q3: I have heard about the behaviors and limitations that must be followed in case of flu symptoms (fever, cough, dyspnea...) or positive/ result in progress swab.	1 (0.8%)	4 (3.2%)	41 (32.8%)	79 (62.2%)
Q4: I have heard about precautions that AOU Careggi plays out to prevent the spread of COVID-19 epidemy.	4 (3.2%)	11 (8.8%)	58 (46.4%)	52 (41.6%)
Q5: Actually, I believe that exist an effective communication with local services (general practitioner, local health company, continuity health care service, pharmacy...) about COVID-19 epidemy management.	4 (3.2%)	24 (19.2%)	64 (51.2%)	33 (26.4%)
Satisfaction with precautions against COVID-19 epidemy adopted in Radiotherapy Centre				
Q6: I am satisfied about triage measures applied at the checkpoint at the entrance of the Radiotherapy Centre (body temperature check, hand sanitation, mask supply).	1 (0.8%)	1 (0.8%)	40 (32%)	83 (66.4%)

Q7: I am satisfied about wearing a mask in the Radiotherapy Centre.	0	1 (0.8%)	33 (26.4%)	91 (72.8%)
Q8: I am satisfied that there are restrictions on carers entering the Radiotherapy Centre with me.	4 (3.2%)	5 (4%)	33 (26.4%)	83 (66.4%)
Q9: I am satisfied about the doctor wearing personal protective equipment (PPE) when visiting me in the Radiotherapy Centre.	0	4 (3.2%)	34 (27.2%)	87 (69.6%)
Q10: I am satisfied about the healthcare personnel (nurses, technicians, social health operators) wearing personal protective equipment (PPE) when attending me during my stay in the Radiotherapy Center.	0	3 (2.4%)	35 (28%)	87 (69.6%)
Q11: I believe that the COVID-19 precautions being taken by the Radiotherapy Centre are adequate and necessary.	1 (0.8%)	0	38 (30.4%)	86 (68.8%)
Q12: I am aware that there may be delays in clinical visits because of the precautions taken during COVID-19 epidemy.	4 (3.2%)	6 (4.8%)	48 (38.4%)	67 (53.6%)
Q13: I am aware that there may be delays in my treatment because of the precautions taken during COVID-19 epidemy.	3 (2.4%)	13 (10.4%)	46 (36.8%)	63 (50.4%)
Q14: I am satisfied about the doctor-patient relationship despite the precautions taken by the Radiotherapy Centre during COVID-19 epidemy.	3 (2.4%)	7 (5.6%)	44 (35.2%)	71 (56.8%)

Results: One hundred twenty-five patients admitted to our department from 1-30 April 2020 underwent the survey. The majority (66.4%) of patients were women and the most common disease was breast cancer (40%). The average Global Health Status (GHS) of EORTC QLQ-C30 was 61.67. Emotional functioning, social, and cognitive domains obtained scores of 75.48, 80.13, and 84.67, respectively. FACIT-TS-G results revealed 120 patients rated the treatments effective and 108 patients thought the side effects were the same as expected or better. Most (89.6%) rated their treatment good, very good, or excellent. Concerning COVID-19-related questions, patients reported overall very good level of information.

Conclusions: Despite the introduction of strict COVID-19 control measures, there was a high level of cancer outpatient satisfaction. The satisfaction levels may influence compliance, continuity of treatments, and patient-doctor communication, impacting the quality of clinical care in the next phases of the pandemic.

C03

NEEDS OF PATIENTS WITH NEURO-ONCOLOGICAL DISEASES DURING A COVID PANDEMIC: EXPERIENCE OF A SINGLE INSTITUTION.

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Aims: The COVID-19 pandemic has complicated a very delicate moment in the doctor-patient relationship: communication. It is essential not to neglect the emotional state of patients (pts), their perspectives and experiences related to the disease to promote compliance with treatment.This is very important in the neuro-oncology field where therapeutic choices are often complex and the prognosis not favorable. The assessment of the needs of the PTS and their caregivers is a priority to ensure an adequate standard in taking charge in a moment of collective difficulty. The aim of this study is to better understand how COVID-19 affects the emotional state and medical relationship in the neuro-oncology population.

Methods: A survey of 41 questions and another one of 16 questions were submitted respectively to the pts with brain neoplasia belonging to the neuro-oncology departments of our institute and their caregivers. The pts were enrolled within the Neo-Co protocol, after approval by the ethics committee. The multiple choice answers were collected from April 20 to May 21. For the pts the topics of analysis concerned the diagnosis of the disease and the treatments received, the quality of life, the perception of anxiety and personal resources. The care burden, anxiety and quality of life were analyzed for caregivers.

Results: 131 pts and 57 caregivers between 18 and 70 years completed the questionnaire. The most common diagnoses were gliomas (47%) and meningiomas (29%). 5% of pts contracted COVID infection. Overall, 94% of pts were satisfied with the treatments received and 79% of pts experienced no changes in treatment timing due to covid. 61% of pts rated their quality of life as good. 65% of pts declared to have sufficient resources to deal with the situation. There was a correlation between QoL and resources (p=0.003). 78% of caregivers defined their care burden increased during the pandemic and 63% defined their quality of life as good. There was a correlation between pts and caregiver QoL (Fisher's exact = 0.160). We also found in the pts population a correlation between Covid anxiety and anxiety for the diagnosis of brain tumor (54% p=0.0000).

Conclusions: We must continue to provide high quality assistance, information and support in the era of COVID, trying to satisfy the request for consistency in methods and information.

C04

CANCER PATIENT MANAGEMENT DURING THE THIRD WAVE OF THE COVID 19 PANDEMIC

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Aims: The SARSCoV-2 caused coronavirus disease 2019 (COVID19), an epidemic which originated in China and spread around the world rapidly becoming a pandemic.A prompt identification of infected patients,together with all the prevention measures, is fundamental to manage the risk of Covid19 in our Radiotherapy department and to manage Covid19 patients.

Methods: Between November 2020 and June 2021, all patients who accessed Radiotherapy department

received a telephone triage 72 hours before entering our ward, questioning about Covid19 symptoms and an interview on possible contacts with positive patients. The same questionnaire was administered before the patients entered the ward, confirming the information provided by telephone. Despite the measures taken, during the third wave our Region and consequently our department was called upon to handle a large number of cases.For this reason, asymptomatic positive patients undergoing treatment were identified and the treatment was carried out, preferring hypofractionation therapies. Our department closed to the public at set times, after guaranteeing treatment to patients not affected by Covid19. Positive patients accessed through a dedicated path on a bio-containing stretcher. The treatment was performed by health staff equipped with appropriate PPE and daily disinfection of the rooms was performed.

Results: 2465 patients received the telephone triage.Seven patient reported contact with a swab positive patient. Despite being asymptomatic, two negative nasopharyngeal swabs were performed. Four patient reported contact with positive cohabitants and started treatment to negativize family members. Four patients were found to be positive during treatment and two patients admitted to the COVID ward required non-postponable radiotherapy. No patient was infected in the ward.Two patients withdrew the treatment as positive and symptomatic and one positive and symptomatic patient, suffering from head and neck cancer, refused to continue the treatment.Furthermore, no health professionals tested positive during the third wave.

Conclusions: The measures adopted in terms of management of Covid19 positive patients who need radiotherapy has made it possible to guarantee treatment to all cancer patients who entered the ward, whether Covid19 positive or not; the prevention of contagion between patients and health workers was also guaranteed.

C05

THE IMPACT OF THE COVID-19 PANDEMIC ON RADIOTHERAPY ACTIVITIES: ANALYSIS OF A MONO-INSTITUTIONAL INTERNAL PROCEDURE PROTOCOL DURING THE SECOND WAVE

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Aims: Italy was one of the most affected countries in Europe by COVID-19 pandemic. During the national lockdown we ensured Radiotherapy (RT) activities with a reorganization of our Unit according to a specific internal procedure protocol, as reported in a previous publication. This protocol was adapted for the second wave and specific national and international guidelines were also adopted for a wider use of hypofractionated RT.

Methods: RT activity during the second wave was analyzed according to a specific internal procedure protocol and Ministry of Health recommendation concerning a reorganization of visits workloads and RT planning, definition of dedicated routes and triage areas, management of suspected and positive COVID-19 cases, use of personal protective equipment, management of environments and management of intra-institutional meetings and tumor boards. A comparison of activity volumes of RT Unit in the period October 2020–February 2021, with the same period COVID-free (October 2019–February 2020).

Results: In October 2020-February 2021, 297 first RT visits were performed, 205 new patients were prepared for Simulation Computed Tomography (Simul CT) and 237 patients were treated on one LINAC. In the same period of 2019-2020, 370 patients underwent first RT visits, 166 new patients were prepared for Simul CT and 195 patients were treated on one LINAC (Table 1). No positive cases of COVID-19 positivity in healthcare professionals were recorded. There were 3 cases of COVID-19 positivity between treated patients, with a median RT interruption of 11 days (range: 1-21). Finally, 3 new protocols for clinical trials using high conformal and short course RT was proposed and approved by institutional tumor board and ethics committee for accelerated partial breast RT, dose-intensification in short course RT for rectal cancer and ultra-hypofractionated stereotactic RT for prostate cancer and are currently on-going.

Conclusions: Although the number of first visits was slightly lower during the second wave, the number of planned and treated patients did not decrease, according to the workload of the center. These data confirmed the efficacy of our organizational model planned to guarantee an optimal continuity of RT courses without workload reduction nor treatments interruption and ensuring safety of cancer patients, environments and radiation oncology staff, as reported in the previous experience during the first wave of pandemic.

Table 1. Comparison of activity volumes of our Radiotherapy Unit in the period October 2020 – February 2021, with the same period COVID-free (October 2019 – February 2020).

	Time: October 2020 – February 2021	Time: October 2019 – February 2020
First Radiotherapy visit	297	370
New patients prepared for Simul CT	205	166
Patients treated on LINAC	237	195

C06

COVID-19 PANDEMIC IMPACT ON PSYCHOLOGICAL STATE AND CARE OF CANCER PATIENTS UNDERWENT RADIOTHERAPY

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Aims: During COVID-19 pandemic, oncologic patients have been recognized at risk of serious complications. The infection dangerousness and the restrictive measures could both have been cause for stress among population, with greater impact on cancer patients. To investigate the psychological state of patients during radiotherapy (RT), a study was conducted in our Institute.

Methods: A self-administered and anonymous questionnaire was proposed to all patients treated in our Unit, as promoted by AIOM, from April 15th to May 30th 2020. The questionnaire investigated 5 domains by 53 questions, to assess risk perception and psychological status. Descriptive analysis was performed, in collaboration with psycho-oncologist. A subgroup analysis was conducted for lockdown phase1 *vs* phase2 (50 *vs* 50 patients).

Table 1.

Table 1: Demographic patients' characteristics (n:100), divided for lockdown phase 1 and phase 2 of COVID-19 pandemic.

PATIENTS N: 100		PHASE 1 N:50 (%)	PHASE 2 N: 50 (%)
Age (mean)		62.5	67.2
Gender	Male	24 (48%)	18 (36%)
	Female	26 (52%)	32 (64%)
Civil status	Married/partner	33 (66%)	35 (70%)
	Single	8 (16%)	2 (4%)
	Divorced/ widowed	9 (18%)	3 (6%)
Sons	Yes	39 (78%)	45 (90%)
	No	11 (22%)	5 (10%)
School grade	Primary	13 (26%)	14 (28%)
	Middle or high	16 (32%)	28 (56%)
	University	11 (22%)	8 (16%)
Job status	Employed	14 (28%)	10 (20%)
	Unemployed	11 (22%)	11 (22%)
	Retired	25 (50%)	29 (58%)
Family network	Alone	4 (8%)	5 (10%)
	Cohabitation family	46 (92%)	45 (90%)
	First RT visit	3 (6%)	2 (4%)
Treatment intent	Curative	45 (90%)	46 (92%)
	Palliative	2 (4%)	2 (4%)

Results: An overall of 100 patients joined the study. Provided COVID information: 42% of patients stated to receive satisfactory information from traditional/social media and, in addition, from family doctor (37%) and/or radiation oncologist (14%). Mood: anxiety and concern have been declared by 53% of patients; sadness, sense of impotence or vulnerability by 20% of patients; 26% felt calm or indifferent; 8% was angry for government management. Family members and/or themselves risk of infection (34%), future economic situation (10%), oncologic cares interruption (4%) were the main concerns. Social relations: a daily life modification was perceived by 31%, due to restrictive measures for familiar contacts. Nevertheless, despite the distance, interpersonal relationships did not modify in 75% of cases. The 60% of patients was satisfied of quality of life, and the 54% enjoyed daily activity. Medical history: previous psychological disorders were found in 9 patients: 1 needed drugs adjustment, nobody considered suicide. The 3% of patients increased smoke, food and alcohol habits. Safety: 56% of patients considered the RT Unit a safe place and 80% did not postpone visits or exams during this period. No patient stopped treatment for fear of infection. Demographic patients' characteristics are shown in Table 1. No significant differences in answers were found between the 2 subgroups.

Conclusions: Our analysis showed that oncologic patients were quite worried about COVID-19, but safety measures and specific published protocol adopted by our Institute probably resulted adequate to guarantee care continuity, limiting psychological distress and keeping a good quality of life.

C07

TREATMENT WITH RADIOTHERAPY OF COVID POSITIVE PATIENTS DURING THE PANDEMIC: OUR EXPERIENCE

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Aims: During the 2020 Covid pandemic our Hospital was designated as a Covid Hub center. According to the directions provided by the regional health authorities all non-essential clinical activities were stopped. The management of cancer patients (pts) was included among essential activities. Aim of this report is to describe the essential features of our clinical activity in relation to the pandemic context.

Methods: We reviewed the data of our overall clinical activity comparing data of the pandemic period with data from a similar period in the previous year. We also reviewed the clinical charts of pts treated with RT while they were positive to Covid infection.

Results: During the covid pandemic we did not record a significant decrease in the number of pts treated. From 3/2019 to 12/2019 we treated 847 pts. In the same period of 2020 we treated 798 pts (-5.7%). From 11/2020 to 5/2021, 10 C+ pts were treated with RT. 5 pts were already being treated in our hospital: 3 pts were hospitalized for covid-related symptoms and received palliative RT for metastasis; 1 pt was diagnosed C+ during preoperative CRT for a rectal cancer and continued the treat-

ment with exclusive RT; 1 pt received adjuvant RT to the breast. 5 pts were referred from other hospitals designated as regional oncological Hub centers, therefore they were not allowed to treat C+ pts according to regional rules. 3 pts were found C+ when RT was already started at the oncological hub and continued the treatment at our center. 2 pts were referred to us before the start of RT. All pts received a nasopharingeal swab in the day of simulation and weekly afterwards until they became negative. Internal guidelines have been defined to optimize the pathways of C+ pts within the hospital for outpatient treatments: each pt reached the RT building with his own car and a doctor or a nurse dressed with personal protective equipment accompanied the pt to the RT ward through a secondary entrance. The pathway followed by C+ pt was not shared with other pts. In-pt treatments followed similar criteria to avoid contamination. C+ pts were treated in the last treatment slots of the day and all the rooms involved were sanitized after each procedure. No epidemic outbreaks occurred among pts or clinical staff during the pandemic period.

Conclusions: Due to favorable conditions and to the respect of specific procedures we were able to maintain clinical activity during the Covid pandemic without relevant epidemic events.

C08

LOW DOSE LUNG RADIOTHERAPY FOR THE TREATMENT OF COVID-19 PNEUMONIA: PRELIMINARY RESULTS OF AN ITALIAN MONO-INSTITUTIONAL TRIAL (XXX)

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Aim: To assess the feasibility of low-dose radiotherapy (LDRT) erogated to both lungs for the treatment of symptomatic SARS-CoV-2 pneumonia.

Methods: Three patients underwent LDRT for the treatment of COVID-19 pneumonia from May 2020 to April 2021 at XXX University Radiation Oncology Department. All the patients, enrolled in the XXX protocol (XXX), were treated with a single fraction; average prescription dose was 0.7 Gy delivered to both lungs. Main inclusion criteria included: age ≥ 50 years, diagnosis of SARS-CoV-2 infection confirmed by RT-PCR, a XXX Covid Respiratory Scale (XXX) score 2-3, a radiological finding of SARS-CoV2 induced-pneumonia and at least 3 of the following laboratory criteria: CRP > 5 times/LDH > 2 times/D-dimer > 3 times/AST > 2 times the maximum limit of the normal value and/or total lymphocytes < 1000/ml and/or ferritin > 500 ng/ml. Primary outcomes measures were length of hospital stay and number of intensive-care unit (ICU) admission; secondary outcomes were variation of the XXX score and of the radiological findings of pneumonia and occurrence of any adverse event.

Results: Three patients were enrolled and underwent LDRT. LDRT was safely performed without significant side effects, nonetheless two patients deceased, one (an 81 years old male) due to E. coli infection leading to septic shock and the other (a 79 year old male, on radiotherapy treatment for esophageal cancer and in already poor conditions) due to worsening of COVID-19. One 61 years old female patient underwent LDRT for less severe COVID-19 pneumonia: after LDRT her chest X-rays improved, as well as her clinical conditions with complete resolution of the symptoms. Blood levels of CRP and ferritin generally decreased in all patients after LDRT.

Conclusions: Early results of our mono-institutional study seem to demonstrate feasibility of LDRT for the treatment of COVID-19 pneumonia; larger cohorts are required to reach conclusion regarding the effectiveness of the treatment for COVID-19 pneumonia.

C09

COVID-19 AND RADIATION ONCOLOGY: THE EXPERIENCE OF OUR RADIOTHERAPY CENTER

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Aim: The coronavirus disease 19 (COVID19) pandemic has led to a reorganization of health care worldwide to guarantee appropriate patients' (pts) assistance, especially to those with cancer. Our radiotherapy center (RT-C) is located in Sardinia where, likely due the insularity and low population density, the spread of the virus has been relatively limited compared to the rest of Italy. The maximum spread of the virus took place from the second half of 2020 until April 2021. In this abstract we illustrate the pts's anti-COVID19 flow and report the comparison between the radiation activities carried out during the year preceding the pandemic (February 2019-February 2020) and during the pandemic (March 2020-April 2021).

Materials and Methods: All necessary measures have been put in place to minimize the spread of the virus among pts and dedicated staff. For all staff members, individual protective devices (face masks, gloves, protective goggles) were made available in accordance with the provisions of the Istituto Superiore di Sanità. From March

to October 2020 the pts's access to our RT-C was granted after telephone screening to identify any respiratory symptoms, fever, social contact with covid-19 suspected or positive, followed by a second triage at the center admittance. Pts considered as suspected positive were sent to perform molecular swabs. From November 2020 following the greater spread of the virus in Sardinia we applied a more restrictive anti-COVID19 flow, performing molecular swabs before every RT activities.

Results: From March 2020 until today among the staff (comprising 57 units including all health care professionals) we had 3 positive subjects; 5 pts contracted the infection during RT treatment and 5 were identified positive before entering the center. By comparing the RT activity within the period February 2019 - February 2020 and March 2020 - April 2021 we observed no changes in the number of services provided. In the years before pandemic, first RT consults, simulation TC scan and RT treatments amounted to 2907, 2171 and 1655, respectively, compared with 3021, 2442 and 1761 during the pandemic year (Figure 1). We applied dose hypofractionation especially for breast cancer and palliative treatments according to AIRO and ASTRO guidelines.

Conclusions: The anti-covid flow implemented in our RT-center allowed us to continue performing radiation treatments with no interruptions, guaranteeing safety for pts and staff.

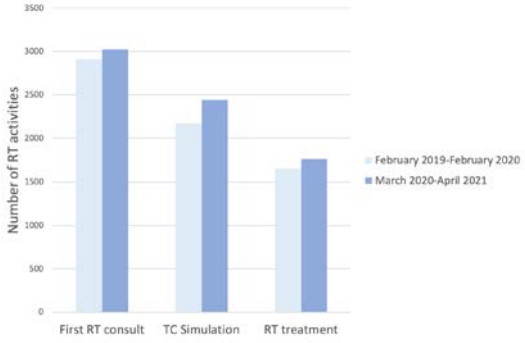

Figure 1.

C10

SIMULATION CT SCAN AS A TOOL FOR EARLY IDENTIFICATION OF ASYMPTOMATIC COVID 19 PATIENTS

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Introduction: SARS-Cov2 pandemic dramatically changed our lifestyle. In the setting of "frail" oncological patients, the right balance between not postponable treatments and the risk of disease spread in this category of patients was difficult to find. The aim of this study was to investigate whether a routine thorax CT scan during simulation procedures would be able to detect asymptomatic COVID19 patients.

Materials and Methods: In our institution, generic prevention measures were set up across the whole hospital (temperature detection, supply of PPE and sanitizing gel). Upon approval of our institutional board and after patient's signature of the informed consent, we performed a thorax CT scan during the radiotherapy simulation phase, independently from the tumor location. If the pulmonary imaging was suspicious for coronavirus infection, the workflow included radiologists consultation, molecular buffer, patient's isolation at home until results were available and CT scan sterilization. In case of positivity, postponable treatments were deferred, while for more urgent situations patients were treated on a single LINAC as the first treatment of the day. Operators wore isolation gown, face shield and goggles as recommended for COVID+ patients management.

Results: 2070 CT scan were performed from 27/03/2020 to 30/04/2021. Suspicious imaging was detected in 27 patients, with the following results: 8 patients turned out positive to the molecular buffer, 2 patients had a radiological diagnosis of non-Covid pneumonia and started antibiotic therapy, 2 patients had coronavirus pneumonia outcomes with negative buffer. The remaining 13 were considered negative by our Radiologist, so they did not perform other diagnostic investigations. However, among all the radiologically-negative group (2043 patients), 11 patients turned out positive during treatment: 4 of them executed the buffer because of flu symptoms, the remaining ones casually discovered the positivity. Patients' characteristics and outcome are summarized in Table 1.

Conclusions: Simulation CT scan was an easy and rapid way to early individuate asymptomatic COVID pneumonia and help the management of this critical patients. It also avoids infection outbreak among both patients and healthcare personnel.

Table 1.

SUSPECT IMAGING WITH NEGATIVE BUFFER								
SEX	AGE	PRIMARY TUMOR	TREATMENT SITE	RADIOLOGY	MOLECULAR SWAP	RT POSTPONED	RT SUSPENDED	RT WHILE POSITIVE
M	64	Head and Neck	Head and Neck	Negative	Not executed	NO	NO	NO
M	70	Head and Neck	Head and Neck	Negative	Not executed	NO	NO	NO
M	60	Lung	Adrenal gland, Bone	Negative	Not executed	NO	NO	NO
M	68	Head and Neck	Head and Neck	Negative	Not executed	NO	NO	NO
M	71	Brain	Brain	Previous Covid	Negative	NO	NO	NO
F	53	Brain	Brain	Negative	Negative	NO	NO	NO
M	78	Melanoma	Brain, Soft tissue, Adrenal gland	Negative	Not executed	NO	NO	NO
F	71	Breast	Breast	Positive	Negative	NO	NO	NO
F	64	Breast	Breast	Negative	Not executed	NO	NO	NO
M	83	Biliary tree	Liver, Lymphnodes	Non-Covid Pneumonia	Not executed	NO	NO	NO
F	72	Head and Neck	Head and Neck	Negative	Not executed	NO	NO	NO
F	61	Breast	Breast	Negative	Not executed	NO	NO	NO
M	76	Stomach	Lymphnodes	Negative	Not executed	NO	NO	NO
M	61	Sarcoma	Bone	Negative	Negative	NO	NO	NO
M	83	Bladder	Lymphnodes	Positive	Negative	NO	NO	NO
M	70	Lung	Bone	Non-Covid Pneumonia	Not executed	NO	NO	NO
M	74	Merkel	Soft tissue	Negative	Not executed	NO	NO	NO
M	68	Head and Neck	Head and Neck	Previous Covid	Negative	NO	NO	NO
F	70	Thyroid	Brain	Positive	Negative	NO	NO	NO
POSITIVE AFTER SIMULATION CT								
SEX	AGE	PRIMARY TUMOR	TREATMENT SITE	RADIOLOGY	MOLECULAR SWAP	RT POSTPONED	RT SUSPENDED	RT WHILE POSITIVE
F	82	Rectum	Liver	Positive	Positive	YES	NO	NO
M	45	Brain	Brain	Positive	Positive	YES	NO	NO
M	67	Brain	Brain	Positive	Positive	YES	NO	YES
M	78	Lung	Lung	Positive	Positive	Death before start		
F	45	Breast	Bone	Positive	Positive	YES	NO	NO

C11

AUTOMATIC LOWER DOSE OBJECTIVE(ALDO) *VS* MANUAL TREATMENT PLANNING (MTP) FOR MULTIPLE BRAIN METASTASES RADIOSURGERY WITH SINGLE ISOCENTER

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Aims: To compare two different approaches in terms of optimization, regarding isodose prescription, target coverage and organs at risk (OARs)dose sparing for multiple brain metastases (BMs) radiosurgery (SRS) with single isocenter.

Methods: From 08/2019 to 04/2021, 321 BMs (mean 8, range 3-21) have been treated by a Single iscocenter SRS in 38 patients. The prescribed dose (Dp) was 27Gy in 3 fractions. PTV was defined by 1mm isotropic margin from each lesion. None of PTVs was overlooking to chiasm or brainstem. Mono-isocenter VMAT plans with 5non-coplanar arcs (couch0°,±45°,±90°) were generated for all patients, 2 different modalities of optimization –one based on mono-isocenter SRS dedicated optimization tool and the other on human experience– were compared: ALDO *vs* MTP. A dose normalization of 100%Dp at 98%PTV was adopted, while D2%(PTV)<150%Dp was accepted. OARs were defined as chiasm, brainstem and heathy brain minus PTVs. Plan-optimizations were compared by the isodose prescription, D100% and D2% for PTVs, maximum dose for chiasm and brainstem, V18Gy for the healthy brain, number of monitor units (MU) and OTT.

Results: PTVs sum PTVs, calculated for each patient as an index of intracranial disease, had mean dimension of 6.2cc (range 3.71-11.6cc). Isodose prescription for ALDO was included between 60-65%, while for MTP between 75-80%. For both optimizations, D100% ranged between 25,05-27, 3Gy, while the D2% was higher for ALDO than MTP: 38-39 Gy for ALDO and 33-34Gy for MTP. All plans had to respect the constraints and no difference was highlighted by comparing ALDO-MTP. The mean of the maximum dose to chiasm was 4.8Gy and 4.4Gy for ALDO and MTP, respectively. The mean of the maximum dose to brainstem was 9.7Gy and 9.3Gy for ALDO and MTP, respectively. For all cases, V18Gy<30cc, as prognostic factor for radionecrosis, was respected (range 5.4-15cc for ALDO and6.2-20cc for MTP). Mean MU and OTT for ALDO were 4454 and 3 minutes, respectively; while for MTP mean of MU was 2325 and mean of OTT was 1.7 minutes.

Conclusions: Both ALDO and MTP showed good results regarding target coverage, OAR savings, and low-dose healthy brain. ALDO uses lower prescription isodoses to achieve similar results to MTP, leading to a D2%> 150% Dp, which may be related to a higher risk of radionecrosis. The expert physician and physicist could choose between ALDO-MTP to personalize treatments based on histology, size and number of BMs, proximity to OARs, optimizing the patient-tailored treatment plan.

C12

PSYCO-ONCOLOGIST'S KEY ROLE IN THE RADIOTHERAPY CARE PATHWAY

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Aim: Receiving cancer diagnosis leads the establishment of several psychological dynamics that represents a "baggage" during cancer treatments, making the care pathway more stressful. Moreover, the idea to be exposed to "radiation" generates an important concern in the oncological patient. Based on this background, the aim of this analysis was to investigate the role of psycho-oncologist during radiotherapy (RT).

Method: According to the own care management policy of our Department, all patients during RT were welcome to receive freely and charge-free an assessment regarding their cognitive, emotional and physical state and related psycho-oncological support during treatment. A set of screening tests that investigate emotional distress and patient's mood is administered, including: Hospital Anxiety Depression Scale (HADS), Distress Thermometer, Brief Cope, Impact of Event Scale-Revised. During RT, easy tools, such as Mindfulness-based stress reduction techniques, were performed to manage stress, reducing physical symptoms, mood and sleep disturbances. These psycho-therapeutic approaches were developed in individual sessions and/or in small group sessions.

Result: Between 2020-2021, 1017 patients underwent to RT. Of these, 856 (84%) accepted to participate in psycho-oncological support program receiving at least a first evaluation. Excluding patients treated with short RT course (1-5 fractions), the remaining 428 cases(50%) were followed during RT course with structured psycho-oncological interviews for a median of 3 sessions (range 2-5). In this subgroup, the median RT fractions were 25 (range 15-33). The median age was 60 years (range 20-78). Female were 314 (73%) and male 114 (27%). The most represented cancer type was breast with 219 cases (51%), followed by prostate(86-20%), gynecology/GI (49-12%), H&N/lung (44-10%) and brain (30-7%). Of the patients followed, 33 cases were followed for psychological disorders by external specialists. All patients completed their treatment without delay reporting a reduction in RT anxiety during the interviews and a "feeling of welcome".

Conclusion: The approach to the patient in a RT center should be multidisciplinary and the result of a growing collaboration between physicians, physicists, technicians, nurses and administrators, with the coordination of the psycho-oncologist, whose role cannot be omitted, as long as a cure can be offered that takes into consideration not only the patient(who is affected by cancer)but the person.

Oral Communications

CO01

1.5T MR-GUIDED DAILY ADAPTIVE RADIOTHERAPY: PRELIMINARY CLINICAL REPORT OF THE FIRST 2000 FRACTIONS DELIVERED AT ADVANCED RADIATION ONCOLOGY DEPARTMENT (ARO) IN NEGRAR (VR)

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Aims: 1.5T MR-linac improves target volume and adjacent OARs visualization, ensuring high precision in radiation treatment delivery. Daily MR-imaging allows on-table adapted planning and real-time intra-fraction imaging without additional exposure to radiation. Herein we present the preliminary report of the first 2000 fractions delivered at our department. We aim to describe the clinical workflow, feasibility and patient-reported tolerability (PROMs) by means questionnaires prospectively assigned at baseline and after daily-adapted RT.

Methods: Since October 2019, Elekta Unity MR-linac has been available in our department. Two different workflow were used depending on the OARs daily anatomy: Adapt To Position (ATP) where the reference plan position is adjusted rigidly to match the position of the targets and OARs, and Adapt To Shape (ATS) where a new plan is created to better match the anatomy of the day. Both workflows include an initial 3D MRI scan for plan adaptation, another one for verification after planning and before beam on, a real-time intra-fraction MR imaging on sagittal and coronal axis, and a last 3D MRI scan to check intra-fraction movements and OARs deformations. Toxicity and quality of life were assessed at baseline and after treatment using the CTCAE v5.0, IPSS, ICIQ-SF, IIEF-5, EPIC-26, EORTC-QLQ-C30 and PR-25 questionnaires.

Results: Between October 2019 and February 2021, 263 patients with 308 target sites were treated with MR-guided radiation therapy in 2000 total fractions. Median patient age was 70 years (39–86). Among 308 tumor sites, the most frequently treated region was pelvis (n=225, 73%). The most common diagnosis was prostate cancer (n=207). On–table adaptive radiation therapy was used at every treatment session: ATP workflow in 57 fractions (3%) and ATS workflow in 1943 fractions (97%), respectively. Median prescribed dose was 35Gy (20–67.5Gy) in median 5 fractions (5–30). Mean total treatment time was 43 minutes (20–56). Treatments were well-tolerated and no acute G>2 toxicities were reported. Concerning the PROMS, all questionnaires showed no relevant deterioration between the pre-, post-RT and follow-up evaluations.

Conclusions: MR-guided radiation treatment using 1.5T MR-linac has been successfully implemented into clinical routine at our department. The data reported support an optimal profile of tolerability of daily on-table adaptive radiation therapy in acceptable time slots. These results are confirmed by PROMs.

CO02

MITIGATION ON BOWEL LOOPS DAILY VARIATIONS BY 1.5-T MR-GUIDED DAILY-ADAPTIVE SBRT FOR ABDOMINO-PELVIC LYMPH-NODAL OLIGOMETASTASES

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Purpose: We report preliminary dosimetric data concerning the use of 1.5-T MR-guided daily-adaptive radiotherapy for abdomino-pelvic lymph-nodal oligometastases. We aimed to assess the impact of this technology on mitigating daily variations for target coverage and organs-at-risk (OARs) sparing.

Methods: 150 sessions for 30 oligometastases in 23 patients were analyzed. All patients were treated with MR-guided stereotactic body radiotherapy (SBRT) for a total dose of 35Gy in 5 fractions. For each fraction, a quantitative analysis was performed for PTV volume, V35Gy and Dmean. For OARs we assessed daily variations of volume, Dmean, Dmax. Any potential statistically significant change between baseline planning and daily-adaptive sessions was assessed using the Wilcoxon signed-rank test, assuming a $p<0.05$ as significant.

Results: Average baseline PTV, bowel, bladder and single intestinal loop volumes were respectively 8.9cc(range,0.7-41.2cc), 1176cc(119-3654cc), 95cc(39.7-202.9cc), 18.3cc(9.1-37.7cc). No significant volume variations were detected for PTV (p=0.21) bowel (p=0.36), bladder (p=0.47), except for single intestinal loops, which resulted smaller (p=0.026). Average baseline V35Gy and Dmean for PTV were respectively 85.6%(72-98.8%) and 35.6Gy(34.6-36.1Gy). We recorded an improved target coverage in favor of daily-adaptive strategy *vs* baseline planning for, although not reaching statistical significance. (p=0.11 and p=0.18 for PTV-V35Gy and PTV-Dmean). Concerning OARs, a significant difference was observed in favor of daily-adapted treatments for single intestinal loop Dmax [23.05Gy(13.2-26.9Gy) at baseline *vs* 20.5Gy(12.1-24Gy); p-value=0.0377] and Dmean [14.4Gy(6.5-18Gy) *vs* 13.0Gy(6.7-17.6Gy); p=0.0003]. For bladder, average Dmax was 18.6Gy(0.4-34.3Gy) *vs* 18.3Gy(0.7-34.3Gy) for a p=0.28; average Dmean was 7.0Gy(0.2-16.6Gy) *vs* 6.98Gy(0.2-16.4Gy) for a p=0.66. For bowel, no differences in terms of Dmean [4.78Gy(1.3-10.9Gy) *vs* 5.6Gy(1.4-10.5Gy); p=0.23] were observed after daily-adapted sessions. A statistically significant difference was observed for bowel Dmax [26.4Gy(7.7-34Gy) *vs* 25.8Gy(7.8-33.1Gy); p=0.0086].

Conclusions: Daily-adaptive MR-guided SBRT reported a significantly improved single intestinal loop sparing for lymph-nodal oligometastases. Also bowel Dmax was significantly reduced by daily-adaptive strategy. A minor advantage was also reported in terms of PTV coverage, although not statistically significant.

CO03

LINAC-BASED STEREOTACTIC ARRHYTHMIA RADIOABLATION (STAR) FOR ATRIAL FIBRILLATION: PRELIMINARY EVALUATIONS

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Aim: Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia. Current European guidelines recommend catheter ablation of AF in symptomatic patients, refractory to antiarrhythmic therapy. Pulmonary veins (PVs) isolation is the cornerstone of any ablation procedure. Stereotactic arrhythmia radioablation (STAR) was used to treat, safely and effectively, ventricular arrhythmias. Based on the latter background, the aim of this prospective phase II study (NCT04575662) will be to investigate the feasibility of STAR for the treatment of paroxysmal AF in elderly patients.

Method: The inclusion criteria are age>70 years, symptomatic AF, antiarrhythmic drugs intolerance/non-response to antiarrhythmic drugs. A sample size of 20 patients is planned to complete trial. Patients undergo to treatment simulation 4DCT (1mm slice thickness). The target volume is identified in the area around PVs and named as clinical target volume (CTV). Main Organs at Risks (OaRs) are esophagus and main bronchus. Internal target volume (ITV) and OaRs planning risk volume (PRV) are created to compensate heart and respiratory movement. Considering OaRs constraints and target motion, the planning target volume (PTV) is defined adding 0-3 mm to ITV in all directions, excluding the overlap area with OaRs PRV, where PTV is cropped. STAR treatment is performed in order to obtain PVs electrical isolation with FFF-VMAT technique in free-breathing for a dose of 25Gy prescribed to the PTV. A “cold boost” is realized to the interface between PTV-OaRs PRV.

Result: In May 2021, 3 patients were enrolled and planned in the trial, 1 underwent to STAR treatment. The median CTV, ITV-PTV volumes were, respectively, 12.4cc, 21.9cc and 38.3cc. A median of 3mm isotropic margin was applied between ITV-PTV. To obtain a PRV for esophagus a median of 4mm anisotropic margin was applied; for main bronchus, a median of 4mm isotropic margin was used. The prescription dose was 25Gy/1fx at

isodose of 80%, with D98% 20Gy and D2% 33Gy. The treatment was delivered using 10X-FFF VMAT 3 coplanar arcs in 3 minutes. The maximum dose to the esophagus, left and right bronchus PRV were, respectively, 14.4, 15.4 and 7.2 Gy. The mean dose to heart minus PTV was 5.8 Gy. No acute side effects were reported.

Conclusion: STAR is an advanced form of radiation therapy tailored to treat heart arrythmia that delivers non-invasive, precise high-dose of radiation, whose role in AF treatment will be evaluated in the present ongoing trial.

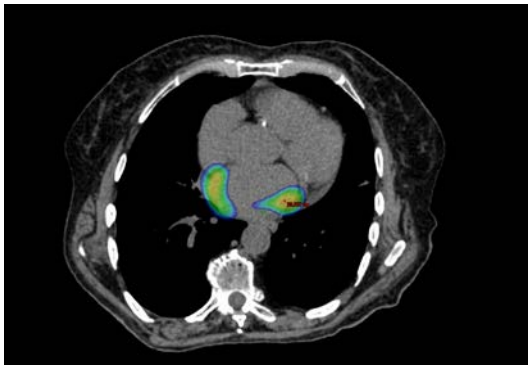

Figure 1.

CO04

CONFRONTO FRA VMAT E IMPT NEI PAZIENTI CON CARCINOMA DEL RINOFARINGE: RISULTATI DOSIMETRICI E MODELLI NTCP

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Aims: The aim of this study is to evaluate the potential benefits of intensity-modulated proton therapy (IMPT) compared to volumetric modulated arc therapy (VMAT) techniques in patients with nasopharyngeal cancer (NPC).

Methods: We performed a retrospective comparative study on a cohort of 50 consecutive locally advanced NPC treated between 2016 and 2019 with definitive VMAT and chemotherapy. Each photon plan was compared to proton dose distribution optimized with the current beamline and simulating a gantry geometry. A Simultaneous integrated boost regimen was given in 33 fractions with a total dose of 69.96 Gy. Dose-volume points (PTV D99, D50, D1) for both target and OAR, conformity (CI) and homogeneity index (HI) and integral dose to the patient were extracted for comparison. 16 validated NTCP models from literature for various toxicities were applied and ΔNTCPx-p differences calculated between photons and protons for each model. Patients were considered eligible for proton therapy in case the ΔNTCPx-p was larger than 10% threshold for at least one model, selected by clinical relevance into a subgroup of 7, or the summed ΔNTCPx-p was larger than 35%. The analysis was repeated splitting the patients in subgroups according to tumor staging T1T2 (27pts,54%) , T3T4 (23pts,46%); nodal involvement N0 (7pts,14%),N1 (29pts,58%), N2N3 (14pts,28%).

Results: A target coverage of PTVD99 higher than 67.5 GyE for proton plans was guaranteed. Proton showed comparable homogeneity and improved conformity (ΔCIx-p= -9.4%) with respect to photon plans and a reduction of 45.0% in integral dose. For OARS, average ΔDAvgx-p and ΔD1x-p were respectively -8.0±6.7 GyE (-30.4%± 25.0%) and -2.1±4.9 GyE (4.4%±13.6%) with largest differences for cord, brain and oesophagus. A reduction in NTCP was observed for xerostomia (-12.5%), brain necrosis (-2.3%) mucositis (3.2%), tinnitus (-8.6%), hypothyroidism (-9.3%), trismus (-5.4%), while was negligible for dysphagia and toxicities in optical pathways (<2%). According to our selection criteria 40% of the analyzed patients were eligible for proton therapy with an improved benefit in terms of better toxicity profile for T3/T4 tumors (54%).

Conclusions: NTCP-model approach can be potentially useful in clinical practice for selecting NPC patients who can mostly benefit by proton therapy with respect photons in terms of toxicity profile.

CO05

IS THE ITALIAN RADIOTHERAPY "WOMAN"?

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Aims: In 2018th, ESTRO launched a campaign for Marie Curie legacy, highlighting that Marie Curie is the mother of radiotherapy. Nevertheless, women are usually underrepresented in medical leader positions. The questions are: Today, does Italian radiotherapy remain "woman" in coherence with its own legacy? How representative is in Italy the female gender among the leadership positions of radiation oncology (RO) compared with other oncological disciplines such as medical oncology (MO), surgical oncology (SO) and Medical Physics (Mph)?

Methods: Data about the number of female members and leaders are derived from Websites of the scientific societies of AIRO (RO), AIOM (MO), SIC (SO) and AIFM (MPh), searching comparable data such as numbers of female member out of the total, numbers of the female head of medical centres, numbers of female presidents of the executive council. The respective rates of each discipline were compared.

Results: The number of female members and head of Italian medical centres was obtainable only from the Airo website. They were 867 women out of 1438 total AIRO members (60%) and 47 (27,3%) women out of 172 head of the registered Italian radiation oncology centres. The other societies did not report the correspondent data on their own website. Regarding the percentage of women among the in-charge executive council as obtained from AIRO, AIOM, SIC and AIFM websites, they were respectively: 4/13 (30.7%), 3/12 (25%), 1/15 (6.6%%) and 5/17 (29.4%). No woman is currently president in any society. The number of female past presidents has respectively been 2/16 (12.5%) (AIRO), 1/20 (5%) (AIOM), 0/33 (0%) (SIC) and 2/5 (40%) (AIFM). Finally, the number of past female members elected in the executive councils has been: 23/150 (15,3%) for AIRO, no data from AIOM, 4/232 (1,7%) for SIC and 20/65 (30,7%) for AIFM.

Conclusions: Even though the mother of radiotherapy was a female, and most radiation oncologists are female, a gender disparity exists in the radiation medical community, especially in responsibility positions. However, the female gender fares better in physicist's society. Female radiation oncologists fare better than medical oncologists and much better than surgical oncologists.

Sadly, it must be said that the female gender is completely neglected in the surgical society.

CO06

COMPARISON OF AUTOMATED SEGMENTATION TECHNIQUES FOR T2-WEIGHTED MAGNETIC RESONANCE IMAGES OF THE PROSTATE

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Aims: The contouring of regions of interest (ROIs) is a crucial step in the radiomic workflow. This study aims at comparing different strategies for automatically segmenting the prostate in magnetic resonance images (MRIs) of the male pelvis.

Methods: One hundred prostate cancer patients who had undergone pre-surgical multi-parametric MRI and prostatectomy in our Institution between 2014 and 2018 were considered. The prostate was manually contoured on the axial T2-weighted images by a junior radiologist (ZH) and subsequently checked by three expert radiologists (PP, SA, GP) to define a ground truth. The prostate was then auto-contoured using six different *Methods:* (1) a commercial package (SyngoVia, Siemens Healthcare), (2) a multi atlas-based algorithm (Raystation 9B, RaySearch Laboratories) and (3-6) four U-net based deep learning (DL) networks (U-net, Transfer Learning (TL), Generative Adversarial Network (GAN), and EfficientDet3D (ED3D)). The resulting contours were then compared against the ground truth in terms of Dice similarity coefficient (DSC), mean surface distance (MSD) and other metrics, considering two different training/testing splits (70:30 and 50:50).

Results: The mean DSC of the different methods were: 0.914 (DL, average), 0.872 (Siemens software), and 0.887 (atlas) for the 70:30 split. Similar results were obtained considering the 50:50 split. Additionally, DL models were proven to be more reliable in terms of worst performance (0.854 minimum DSC and 3.91 maximum MSD). Overall, the method with the best median for each index resulted to be Efficient3D (Table 1).

Conclusions: The present study demonstrates that automated segmentation techniques can provide excellent results and can henceforth be considered mature to be implemented in the medical workflow and research. However, further studies are warranted to evaluate the consequences of automatic contouring in terms of end-user results and robustness.

Table 1. Best method for each metric and splitting.

Metrics	70-30 splitting		50-50 splitting	
	Best median	Distributions not statistically different	Best median	Distributions not statistically different
DSC	Efficient3D	TL	Efficient3D	TL
MSD	Efficient3D	TL Atlas	Efficient3D	Unet
HD95	Efficient3D	TL	Efficient3D	GAN
Relative Difference Volume	GAN	Unet Efficient3D Atlas TL Siemens	Efficient3D	GAN Unet TL Atlas

Abbreviations: DSC: Dice Similarity Coefficient; **GAN:** Generative Adversarial Network; **HD95:** Hausdorff Distance; **MSD:** Mean Surface Distance; **TL:** Transfer Learning

CO07

IN SILICO FEASIBILITY STUDY OF SIMULTANEOUS INTEGRATED BOOST IN CARBON ION RADIOTHERAPY FOR ADENOID CYSTIC CARCINOMA OF THE HEAD AND NECK

B. Vischioni[1], E. Mastella[1], M. Bonora[1], S. Ronchi[1], R. Ingargiola[1], F. Patti[1*], A.M. Camarda[1,2], L. Goanta[1,3], D. Maestri[1], E. Rossi[1], G. Magro[1], A. Vai[1], A. Mirandola[1], S. Russo[1], M. Ciocca[1], S. Molinelli[1], E. Orlandi[1]

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Aims: Simultaneous integrated boost (SIB)-intensity modulated radiotherapy (IMRT) is one of the major technical photon-based RT advances in the last 20 years, while in carbon ion RT (CIRT) the optimal strategy of SIB treatments is still unknown. In this work, we investigated the feasibility of a SIB strategy for adenoid cystic carcinoma (ACC) of the head and neck (H&N) with the aim of a better dose conformation using the SIB.

Methods: CIRT plans of 10 ACC H&N patients previously treated at our Center were re-planned according to a SIB approach. For our standard sequential boost irradiation (SEQ), the prescribed dose to the median volume (D50%) was 41.0 Gy(RBE)/10 fractions to the CTV-low risk (LR), plus 24.6. Gy(RBE)/6 fractions to the CTV-high risk (HR). Two SIB fractionation schemes were investigated maintaining the high dose level of 65.6 Gy(RBE)/16 fractions to the CTV-HR, and different low dose levels to the CTV-LR D50%: 48.0 Gy(RBE) (SIB48.0) and 54.4 Gy(RBE) (SIB54.4). The same beam arrangements of the SEQ plans were used. In the SIB plans, priority was given to the CTV-HR coverage, keeping the same organs at risk dose constraints fixed. The D98%, D50%, D2%, and the homogeneity index (HI) were chosen for target coverage comparison. For the CTV-LR, the biological effective dose (BED) was calculated to compare the different fractionation schemes. Ring-shaped structures were created with margins of 2 cm from the CTV-LR to compare the dose to normal tissues.

Results: Comparable CTV-HR coverage was obtained with the 3 treatment approaches. With the SEQ, SIB48.0 and SIB54.4 the CTV-LR D50% were 50.3%, 11.9% and 6.0% higher than the prescription, while the HI were (66.3±7.8)%, (44.4±2.3)% and (29.5±3.3)%. A comparable BED(D98%) was obtained with the SEQ and SIB48.0 protocol, while with the SIB54.4, the BED(D98%) was 9 Gy higher. The BED(50%) and BED(D2%) were significantly reduced with both the SIB dose levels. A comparable BED to the healthy tissues was obtained with the 3 protocols.

Conclusions: An improved dose conformation was obtained in the CTV-LR with both two SIB dose levels, together with a significant reduction in the median and maximum doses, showing the ability of the SIB to reduce undue dose to the LR volume when treating H&N ACC. A future clinical trial will be designed to evaluate the efficacy and safety of the optimal SIB protocol for H&N ACC compared to the standard sequential approach used so far.

CO08

IS THERE A ROLE FOR A MULTIDISCIPLINARY TUMOR BOARD SMART VIRTUAL ASSISTANT IN LOCALLY ADVANCED CERVICAL CARCINOMA? A PROOF OF CONCEPT

G. Macchia[1], G. Ferrandina[2], S. Patarnello[3], R. Autorino[4], C. Masciocchi[3], V. Pisapia[3], C. Calvani[3], C. Iacomini[3], A. Cesario[5], B. Gui[6], V. Rufini[7], L. Boldrini[4], M.A. Gambacorta[4], G. Scambia[2], V. Valentini[4]

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Aims: The first prototype of the "Multidisciplinary Tumor Board Smart Virtual Assistant" is presented, aimed to (i) Automated classification of clinical stage starting from different free-text diagnostic reports; (ii) Resolution of inconsistencies by identifying controversial cases drawing the clinician's attention to particular cases worthy for multi-disciplinary discussion; (iii) Support environment for education and knowledge transfer to junior staff; (iv) Integrated data-driven decision making and standardized language and interpretation.

Material/Methods: Data from patients affected by invasive carcinoma of the cervix (LACC), FIGO stage IB2-IVa, treated between 2015 and 2018 were extracted. Magnetic Resonance (MR), Gynecologic examination under general anesthesia (EAU), and Positron Emission Tomography–Computed Tomography (PET-CT) performed at the time of diagnosis were the items from the Electronic Health Records (eHRs) considered for analysis. An automated extraction of eHR that captures the

patient's data before the diagnosis and then, through Natural Language Processing (NLP), analysis and categorization of all data to transform source information into structured data has been performed. Thereafter, an Artificial Intelligence method was developed to support the clinical staff in their decision with regards to tumor staging and to help them identify the most complex cases where deeper analysis and discussion were required (e. g. conflicting information from different exams).

Results: In the first round, the system has been used to retrieve all the eHR for the 96 patients with LACC. This was the training set of the study, with validated 2009 FIGO staging classification ranging from I B2 to IV A as output. For these patients, available eHR included MR, EUA, and PET-CT diagnostic reports. The system has been able to classify all patients belonging to the training set and - through the NLP procedures - the clinical features were analyzed and classified for each patient. A second important result was the setup of a predictive model to evaluate the patient's staging. Our approach has led to predict patient's staging with an accuracy of 94%. Lastly, we created a user-oriented operational tool targeting the MTB who are confronted with the challenge of large volumes of patients to be diagnosed in the most accurate way. The resulting decision support system is summarized in Figure 1. Furthermore, the MTB Smart DA was tested in a 13 LACC patients validation cohort showing an accuracy of 93%, in line with the training set performances.

Conclusion: This is the first proof of concept concerning the possibility of creating a smart virtual assistant for the MTB. A significant benefit could come from the integration of these automated methods in the collaborative, crucial decision stages.

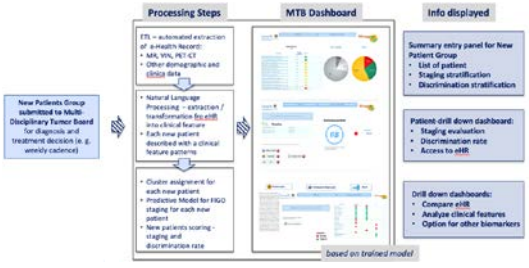

Figure 1.

CO09

LOCALLY ADVANCED PANCREATIC CANCER TREATED WITH RISK ADAPTED ABLATIVE RADIATION THERAPY: MAY COMPUTED TOMOGRAPHY RADIOMIC PARAMETERS PREDICT RESECTABILITY?

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Aims: To assess if radiomic features may predict surgical resection in LAPC treated with neoadjuvant therapy.

Methods: We retrospectively reviewed patients with LAPC treated with intensive chemotherapy followed by a Risk Adapted Ablative Radiotherapy (RAdAR) approach. Patients were divided into training and validation set. Analysing the Gross Tumor Volume (GTV) in planning CT, 1655 radiomic features were extracted. Both extracted features and clinical data contribute to create and validate the predictive model of resectability status. The discriminating performance of each model, obtained applying a LASSO regression analysis, was assessed with the area under the receiver operating characteristic curve (AUC). The validated model was applied to the entire dataset to obtain the most significant features.

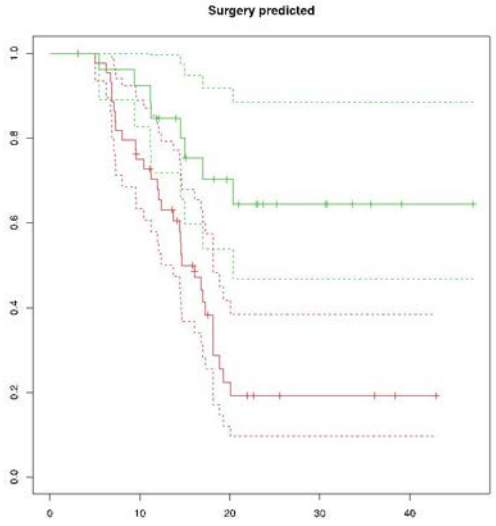

Figure 1.

Results: A total of 71 patients were included, with a median age of 65 y.o. The 57.8% of patients were male. The median period of induction chemotherapy was 6 months. RAdAR was delivered with stereotactic ablative radiation therapy (SAbR), administering 30 Gy in 5 fractions to the tumor volume (PTVt) and 50 Gy dose-painted boost to the vascular involvement, or with (hypo-)fractionated ablative radiotherapy (HART) prescribing 50.4 Gy in 28 fractions to the PTVt, with a vascular boost of 78.4 Gy. Thirty-two patients (45.1%) underwent exploratory laparotomy after RT, and 19 (26.8%) ultimately received surgical resection. After the first step of variable selections, a predictive model was developed

with a median AUC for training and validation sets of 0.862 (95%CI: 0.792-0.921) and 0.853 (95%CI: 0.706-0.960) respectively. The validated model was applied to the entire dataset and 4 features were selected to build the model with predictive performance as measured using AUC of 0.943 (95%CI 0.890-0.997). Overall Survival (OS) curves and their confidence intervals, estimated by Kaplan–Meier method as a function of surgical resection (resected versus non-resected patients) as predicted by the model, are shown in Figure 1. The figure shows the "predicted" OS curves from radiotherapy for resected (green line) versus non-resected (red line) patients and their confidence intervals (dotted lines) . The two curves are significantly different ($p<0.001$).

Conclusions: We built a radiomic model that could help predict resectability in LAPC treated with neoadjuvant therapy. In the context of a complex long-course downstaging and challenging indication to surgery, radiomic showed a promising decision-making role.

CO10

DELTA RADIOMICS CAN PREDICT PATHOLOGICAL COMPLETE RESPONSE IN LOCALLY ADVANCED RECTAL CANCER PATIENTS UNDERGOING NEOADJUVANT RADIOTHERAPY

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Aim: The present tudy was designed to evaluate MRI delta texture analysis (D-TA) in predicting the outcome in terms of complete pathological response, of patients with locally advanced rectal cancer undergoing neoadjuvant chemoradiotherapy (C-RT) followed by surgery.

Methods: We performed a retrospective analysis on 100 patients with locally advanced rectal adenocarcinoma undergoing C-RT and radical surgery between January 2013 and December 2019 in three different centers. The gross tumor volume (GTV) was evaluated at both baseline and after C-RT MRI and contoured on T2, DWI, and ADC sequences. Multiple texture parameters were extracted with LifeX Software and D-TA was calculated as the percentage variations in the two time points. By performing univariate analysis and multivariate analysis (logistic regression), these TA parameters were then correlated with patients' pathological outcomes. Complete pathological response (pCR, with no viable cancer cells: TRG 0) was chosen as the statistical endpoint. ROC Curves were calculated on the three different datasets.

Results: In the whole cohort, 21 patients (21%) showed a pCR. At univariate analysis and binary logistic analysis, the only parameter that resulted significantly correlated with pCR in the Training dataset was ADC GLCM-Entropy. The binary logistic regression was repeated in the two Validation Dataset. AUC for pCR was 0.87 in the Training Dataset and respectively 0.92 and 0.88 in the two Validation Datasets.

Conclusions: Our results suggest that D-TA has a significant role in the prediction of pCR, thus this method may lead to select patients who may potentially avoid surgery. Further analysis with prospective and multicenter trials is warranted.

CO11

PREDICTION OF TUMOR RESPONSE USING MRI-BASED CLINICAL RADIOMICS MODEL IN LOCALLY ADVANCED RECTAL CANCER PATIENTS

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Aims: Neoadjuvant chemoradiotherapy (CRT) followed by total mesorectal excision (TME) is a standard treatment for locally advanced rectal cancer (LARC) patients. Local staging and treatment response are evaluable with Magnetic Resonance Imaging (MRI). Data from clinical images, based on automatic extraction of features from radiological images (radiomic features) and machine learning approaches, showed encouraging results for morphologic and clinical assessment. A new approach investigates pre-CRT MRI-based biomarkers for response prediction. We present a machine learning model combining pre-CRT MRI-based clinical and radiomic features for early prediction of treatment response in LARC patients.

Methods: Inclusion criteria were: non-mucinous LARC, 3.0T MRI, availability of clinical outcome, long-course CRT. Seventy-two MRI, with T2-weighted and DWI sequences, were analyzed. Two readers independently delineated each tumor. Radiomic features were extracted from the "tumor core" (TC) and the "tumor border" (TB). Partial least square (PLS) regression was used as the multivariate, machine learning, algorithm of choice and leave-one-out nested cross-validation was used to optimize hyperparameters of the PLS. We obtained 9 "clinical" MRI-based features: tumor location (high, middle, low rectum), whole tumor volume, cranio-caudal extension, distance from the internal anal sphincter, mesorectal fascia infiltration, extramural vascular inva-

sion, extramural depth invasion, T and N-stage. Radiomic features extraction was performed using PyRadiomics. The classification performances were assessed through Receiver Operating Characteristic (ROC) analyses. The Statistical Analysis was performed in Matlab.

Results: Table 1 reported patients characteristics. 1405 radiomic features extracted were used for analysis. Combining clinical with radiomic features, the MRI-Based "clinical-radiomic" machine learning model properly predicted treatment response (AUC=0.793, p=5.6*10-5). The AUC were 0.689 using the 9 clinical and 790 radiomic features extracted from the TC and 0.541 using the 9 clinical and 626 radiomic features extracted from the TB. A highly synergistic effects was obtained combining TB and TC features, replicating the results previously found with an AUC=0.793.

Conclusions: Tumor prediction improved combining MRI-based clinical and radiomic features, the latter extracted from both TC and TB. Prospective validation studies in randomized clinical trials are warranted.

Table 1. Descriptive baseline characteristics of included patients (n = 72).

Variable Value	Value	
Gender		
Male	48 (67%)	
Female	24 (33%)	
Mean age (IQR*)	65 (57.5–73.8)	
MRI exam	72	
Clinical MRI assessment		
Mean cancer volume (Mean±SD)	21,885±20,539 mmq	
Location		
High	7 (10%)	
Middle	33 (46%)	
Low	32 (44%)	
Craniocaudal extension (Mean±SD)	55±22 mm	
Distance from IAS (Mean±SD)	31±27 mm	
Depth of extramural invasion (Mean±SD)	7±7 mm	
Presence of mesorectal fascia infiltration	44 (61%)	
Presence of EMVI	50 (69%)	
Primary cT stage**		
T1-T2	14 (19.4%)	
T3	55 (76.4%)	
T4	3 (4.2%)	
Primary cN stage**		
N0	2 (2.7%)	
N1	22 (30.6%)	
N2	48 (66.7%)	
Treatment response***		
MR	48 (67%)	34 TRG1 (71%)
		14 TRG2 (29%)
nMR	24 (33%)	17 TRG3 (71%)
		7 TRG4 (29%)

*IQR Inter-Quartile Range; SD Standard Deviation; IAS Internal Anal Sphincter; EMVI Extramural Vascular Invasion; MR Major Pathological Response; nMR non-Major Pathological Response.
**Assessed with MRI and derived from clinical MRI reports in the hospital's patient database. ***Assessed according to Mandard Tumor Regression Grade (TRG) system on surgical specimen after neoadjuvant treatment in 69/72 patients. In three patients, a sustained complete clinical response (with repeated negative MRI examinations and endoscopy with or without biopsy) was considered surrogate for a complete response; the follow-up (mean ± SD) was 47 ± 11 months.

CO12

EVALUATION OF ERI AS RESPONSE PREDICTOR IN CERVICAL CANCER: A RETROSPECTIVE STUDY ON T2 AND DWI MR IMAGES

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Aims: Early Regression Index (ERI) is a image-based biomarker that has recently reported interesting results in predicting pathological complete response (pCR) after neoadjuvant chemoradiotherapy (nCRT) in case of rectal cancer. Such parameter is generally calculated on T2-weighted MR images and consists in modelling the early tumour regression combining the GTV volume measured during treatment simulation (Vpre) and at mid therapy (V_{mid}): ERI= $-\ln[(1-(V_{mid}/V_{pre}))^{(Vpre)}]$. This study aims to evaluate the feasibility of using this parameter in the context of Locally Advanced Cervical Cancer (LACC), evaluating its ability in predicting pCR starting from T2 and diffusion weighted images (DWI).

Methods: 88 patients affected by LACC (FIGO IB2-IVA) were enrolled in this study. All the patients underwent nCRT, combining weekly 40 mg/m^2 of cisplatin with concurrent RT, administered using a simultaneous integrated boost (SIB) technique delivered in 22 fractions and prescribing 50.6 Gy to PTV1 (CTV1+5 mm) and 39.6 Gy to PTV2 (CTV2+5 mm). CTV1 coincided to GTV, which was identified on the staging MRI and CTV2 was delineated as the union of the entire cervix, the uterus, parametria, vagina and the corresponding drainage nodal according to the disease stage. An MRI protocol consisting in two acquisitions (T2-w and DWI) in two times (before treatment and at mid therapy) was applied. GTV was delineated and ERI was calculated for both imaging modalities. A radical hysterectomy was performed for each patient within 8 weeks after nCRT: pCR was considered in case of absence of any residual tumour cells at any site (pR0). The ERI performance in identifying pCR patients was quantified calculating the area (AUC) under the Receiver Operating Characteristic (ROC) curve and measuring sensitivity, specificity at the best threshold value.

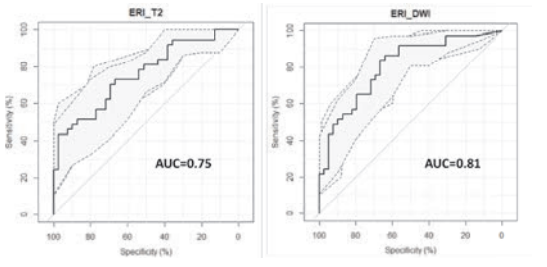

Figure 1.

Results: The ROC curves obtained for ERI calculated on T2 (ERI_T2) and DWI (ERI_DWI) are reported in Figure 1. The performance of ERI_DWI (AUC=0.81 with 95% CI ranging from 0.70 to 0.91) are superior to those reported by ERI_T2 (AUC=0.76 with 95% CI ranging from 0.65 to 0.87). At the best cut-off threshold, ERI_T2 shows high specificity (97,4%) with low sensitivity (43%), while ERI_DWI high sensitivity (86.5%) and limited specificity (64.1%)

Conclusion: This study confirmed ERITCP as a good biomarker also in case of LACC, especially if calculated considering DWI. Using this indicator, it is possible to early identify not responders and modifying the treatment accordingly.

CO13

MACHINE LEARNING FOR THE EVALUATION OF ACOUSTIC NEUROMA RESPONSE TO CYBERKNIFE TREATMENT

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Aim: To use machine learning (ML) methods applied on pre-treatment MR images in order to predict acoustic neuroma response to Cyberknife® radiotherapy and to promptly adopt a personalized treatment on the patient.

Materials: Patients (pts) affected by acoustic neuroma from 2004 to 2016 were retrieved and retrospectively revaluated. All pts treated with Cyberknife® who had a follow up with contrast-enhanced MRI at both 24 and 36 months were included in the study. We collected clinical, audiometric and treatment data and MRI scans acquired before and after the treatment. All analysed images were acquired on 1.5T – 3T machines, using axial contrast enhanced T1-weighted sequences. Comparing the pre and post radiotherapy MRI and according to the volumetric treatment outcome, the radiotherapist assigned each patient to one of the following categories: stability, reduction and increasement. This classification was used by the ML algorithm as a reference value to identify any characteristic features of increased lesions. Three different time points (24, 36 months and the last one available) were considered. A fourth label was extracted from the pts response at 24 and 36 months to determine the possible pseudo-progression of the neuroma. The radiomic features were extracted only on the pre-treatment MRI and semi-automatic tumour segmentations were carried out by a radiotherapist using the level tracing effect of the 3DSlicer image analysis software. These features, combined with clinical data, were analysed using 3 ML

Methods: Support vector machine (SVM), logistic regression (LR) and random forest (RF). The oversample algorithm SMOTE was used to address the imbalanced dataset. Models were validated with 10-fold cross validation repeated 20 times.

Results: 103 pts presenting an acoustic neuroma treated with Cyberknife® at our institutes were selected. Considering all experiments, the best results for the 4 labels were obtained using the SMOTE algorithm. The obtained accuracies were 0.857±0.126 at 24 months, 0.846±0.113 at 36 months, 0.843±0.108 at the oldest follow-up using LR classifier while 0.852±0.119 of accuracy was found for the pseudoprogression investigation using SVM.

Conclusions: These preliminary results showed a great potential in distinguishing, before radiosurgery, pts with volume increasement from pts without, with particular regard to the pseudoprogression. Subsequent studies are ongoing to increase the stability and reproducibility of these results.

CO14

MRI-BASED RADIOTHERAPY (RT) PLANNING FOR HEAD AND NECK TUMORS

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Aims: Diagnostic Magnetic Resonance Imaging (MRI) is currently widely used as a support for the radiation oncologist (RO) in the contouring of the GTV of head and neck (H&N) tumors. However difficulties and limitations in co-registration between the CT simulation images and diagnostic MRI are relevant, mainly due to the different patient (pt) positioning between the two procedures. Planning RT treatments directly on MRI could allow to overcome this problem and to minimize the artifacts due to dental prostheses. This preliminary study aims to evaluate the feasibility of MRI-only planning in the treatment of H&N tumors.

Methods: 6 pts with H&N cancer were initially scanned with a big bore Brilliance CT scanner (Philips Medical System). Afterwards a MRI study was performed using a T1Dixon-Vibe sequence on a 1.5T Aera scanner (Siemens Healthcare). The pts were imaged in the same setup of CT simulation, using their customized thermo-

plastic mask fixed on a rigid table and MRI compatible markers (Suremark® LiquiMark). A 18-channel body coil placed above the pts' head and shoulders was used, in addition to a spine coil under the pt. Synthetic CT (sCT) images were generated from MR data using a combination of bulk electron densities (ED) and a multi atlas-based approach. Also, air-cavities and bone structures were contoured and assigned an average ED value. MR and CT images were auto-contoured using ADMIRE software (research version 3.18, Elekta AB). All contours of OARs were verified by RO who also contoured the target volumes. A medical physicist performed two treatment plans: a first plan on the simulation CT and a second plan using the sCT. The optimized plan calculated on the CT was initially copied and recalculated on the sCT using the same field arrangements, finally it was optimized again using the same planning constraints defined for the CT planning.

Results: Mean differences (n=6) in dose distributions for DVH parameters between CT and sCT-based plans were as follows: -0.1% for PTV Dmean,-0.6% for PTV D95%,+0.9% PTV D2%,+0.9% for spinal cord D2%,-1.0% for brainstem D2%, -0.9% for mandible D2%. These differences were considered acceptable even with Monte Carlo based TPS, confirming literature data related to the same treatments with MR-Linacs.

Conclusions: Our data show that sCT images generated with a combination of bulk ED and a multi atlas-based approach allow for accurate dosimetric calculations in an MRI-based treatment planning workflow for H&N cancer RT.

CO15

DUAL ENERGY COMPUTED TOMOGRAPHY (DECT) APPLICATIONS FOR PROSTATE RADIOTHERAPY: ADVANTAGES IN TARGET AND ORGANS AT RISK CONTOURING

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Aim: Dual Energy Computed Tomography (DECT) captures images in different voltages, potentially allowing a better definition of organs due to different tissues densities. The aim of this work is to evaluate the impact of DECT simulation in inter-observer variability (IOV) for prostate gland (PG) and organs at-risk (OARs) contouring.

Methods: Five radiation oncologists, with different expertise in prostate cancer (PC) treatment, performed the contouring of PG and OARs of 10 patients who underwent DECT simulation. The contouring was carried out on basal CT scan and also on 80 kV, 140 kV, mixed and 55 KeV mono-energetic reconstructions. Consistency in target volume delineation was expressed by the IOV. Dice Similarity Index (DSI), center of mass distance (dCOM) and volumes were then calculated. Median values and accompanying ranges were used to describe the data, since not all variables were normally distributed. A Wilcoxon signed-rank test was performed to compare paired variables using R Core Team (2021), with a significance level of $\alpha = 0.05$.

Results: A total of 750 structures were collected: 250 clinical target volumes (CTV), 250 rectum and bladder volumes were included in the study. Preliminar analysis did not reach statistically significant differences in the variability between the different CT reconstructions. For CTVs the median DSI values were 0.89, 0.89, 0.88, 0.89, 0.89 for basal CT, 80 kV, 140 kV, 55 KeV and mixed reconstruction, respectively. For rectum the same values were 0.84, 0.85, 0.83, 0.84, 0.86. No differences for bladder were reported. The median percentage differences of the CTV volumes were 7.5%, 6.2%, 5.5%, 5.3%, 5.7% for basal CT, 80 kV, 140 kV, 55 KeV and mixed, respectively. Rectum differences accounted to 6.4%, 6.8%, 7.4%, 5.6%, 7.4%, whereas bladder variability were 1.6%, 1.3%, 2.1%, 1.7% and 1.6%.

Conclusion: Our data show that reconstruction at 55 KeV is the sequence that provides a lower IOV in the contouring of PG and OARs, although the difference is not statistically significant. To our knowledge, this is the first study evaluating the role of DETC in IOV for PC and highlights the potentialities of DECT in improving the contouring of the PG and OARs. Further analysis are needed and are currently in progress.

CO16

AGATSTON SCORE IN PATIENTS WITH NSCLC REQUIRING THORACIC RADIOTHERAPY

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Aims: Dosimetric evaluation of heart represents a hot topic in thoracic radiotherapy, especially in the treatment of non small cell lung cancer (NSCLC). Agatston score is a semi-automated tool to calculate a score based on the extent of coronary artery calcification detected by an unenhanced low-dose CT scan. Aim of the current study is the evaluation of Agatston score in patients undergoing

radiotherapy for NSCLC.

Methods: Patients with a recent diagnosis of NSCLC requiring radiotherapy were restrospectively collected in the database of NSCLC tumor board. Pre-radiotherapy CT scan of the thorax was evaluated and the left artery descending coronary arteries (LAD) were contoured. The calcifications were quantified with automatic threshold method (range 130/500 HU) and Agatston score was calculated on the weighted density score given to the highest attenuation value (HU) multiplied by the area of the calcification speck.

Results: Sixteen patients were included for the present analysis (25% females, 75% males), with a median age of 65 years (mean age 65 +/- 1.4 years, range 46-86 years). Calcifications median value was 0,003 cc (mean value 0,081 cc, range 0-0,5 cc), whereas the Agatston score was negative in 4 patients (25%), mild in 2 patients (12,5%), moderate in 2 patients (12,5%) and severe in 8 patients (50%).

Conclusions: Patients requiring radiotherapy for NSCLC show an increased risk for a major adverse cardiac event, even not considering the radiation-induced toxicity of RT. A prospective evaluation of these patients is pivotal to design a dedicated follow up program, including a Cardiologist evaluation.

CO17

IMPACT OF SARCOPENIA IN OROPHARYNGEAL CANCER PATIENTS TREATED WITH RADIOTHERAPY AND CHEMOTHERAPY WIH RADICAL INTENT: A MONOINSTITUTIONAL EXPERIENCE

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Aims: Sarcopenia (SP), defined as loss of muscle mass and functions, recently emerged as an independent prognostic factor in oncological patients (pts), connected with poor survival and sometimes with a higher treatment toxicity profile. This study aims to determine the possible impact of SP on survival and acute toxicity in our oropharyngeal pts.

Methods: 76 pts with locally advanced oropharyngeal squamous cell carcinoma, stage III-IVC, were treated in our Center with Helical TomoTherapy (HT) between 2005 and 2021. HT was delivered with a Simultaneous Integrated Boost (SIB) technique: 66 Gy (2.2 Gy/day) or 69 Gy (2.3 Gy/day) to the tumor and positive nodal regions based on 18FDG CT/PET imaging, and 54 Gy (1.8 Gy/day) to the clinically negative neck region. All pts received concomitant platinum-based CT (at least 200 mg/m^2). SP is generally determined on single-slice CT measurement of the cross sectional muscle area (CSA) at the level of the third lumbar vertebra (L3). Swartz *et al.* (2016) proposed and validated an algorithm that correlated CSA at L3 with CSA at C3, easier to obtain in head and neck pts, and then CSA at C3 with lumbar skeletal muscle index (SMI). Twenty pts (26%) presented SP at the beginning of treatment, according to Prado (2008) that defined SP if SMI was <55.4 cm^2/m^2 in males and < 39 cm^2/m^2 in females.

Results: All pts concluded the treatment. The acute toxicity profile was analyzed as "less than" versus "more or equal to" grade 3 CTCAE 4.0. 13 pts (65%) in SP group and 22 pts (39%) in non-SP group presented a toxicity more or equal to grade 3, but this difference was not statistically significant (p-value 0.25). Overall survival was analyzed in 65 pts (47 NS and 18 S), excluding pts who finished CT RT less than 6 months ago (median follow up 41, range 3.4-126.1). Overall survival was significantly different in non-SP versus SP group (Figure 1, p value 0.035). The same difference was notable in N0-N2a pts, suggesting an important role of SP also in pts with a lower nodal burden and theoretically better prognosis.

Conclusions: Although the results are preliminary and limited to a small population, our case series has the advantage to be very homogeneous in pts and type of treatment characteristics. In our setting, SP seems to have a crucial impact on overall survival. Further investigation is necessary to confirm our data and whether SP is a potentially modifiable risk factor to improve pts outcome.

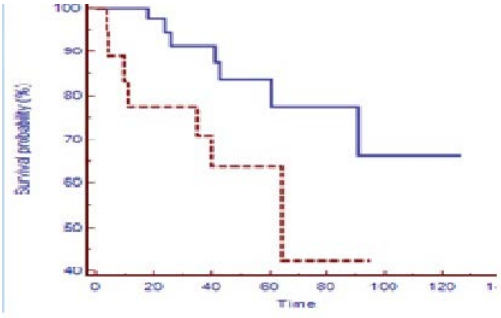

Figure 1.

CO18

THERAPEUTIC USE OF LINAC-BASED STEREOTACTIC BODY RADIOSURGERY (SRS) IN THE MANAGEMENT OF MALIGNANT SPASTICITY

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Background: Spasticity is a clinical event characterized by increased muscle contraction, sometimes painful, secondary to central nervous system damage. It leads to a high rate of nursing procedures, hospital admissions, and costs and quality of life impairment with problems in sleeping, breathing, and speaking. Standard treatment for systemic spasticity is represented by oral or intrathecal baclofen. In the case of focal spasticity, available treatment options are intramuscular botulinum toxin, alcoholic or surgical neurolysis or even selective neurotomies or rhizotomies. However, these surgical procedures are characterized by prolonged surgical sessions and may have infective, anesthetic and surgical complications. They requires an experienced team, the costs are relatively high, and the learning curve is slow. The aim of the present study is to evaluate the therapeutical effectiveness of linac-based stereotactic radiosurgery (SRS) in the treatment of malignant spasticity.

Material and Methods: Patients with spasticity to the lower limbs unresponsive to systemic therapies were treated with linac-based SRS to the spinal nerves responsible for the spasms within a prospective observational trial (n° 51262). Treatment dose was 45 Gy in a single fraction delivered with VMAT technique. The primary end-point was the reduction of the muscular resistance to passive movement measured with the Modified Ashworth Scale (MAS). Secondary end-points were toxicity, quality of life, and spinal nerves radiological features (fractional anisotropy, diffusivity).

Results: From December 2020, the first 3 patients were treated at our Institution. The first patient was treated at the bilateral nerves L4-S1 and had a complete spasms resolution the day after SRS administration that lasts 5 months after treatment. The second was treated at bilateral levels L3-L5 and had a progressive reduction up to 40% of the spasms over 4 months. The third patient was treated at the bilateral L4-5 and left S1. After 2 months, she had a MAS reduction (2 versus 3). No acute treatment-related toxicities or spasticity relapse were reported.

Conclusions: The present is the first clinical report on the use of a linac-based SRS for the treatment of malignant spasticity. These preliminary results with a short follow-up documented a clinical activity of SRS that will be explored in a larger population to better assess effectiveness, toxicity, and duration of the response.

CO19

HYPOFRACTIONATED PALLIATIVE RADIOTHERAPY IN POOR PERFORMANTS STATUS AND ELDERLY PATIENTS UNFIT OF STANDARD RADIOTHERAPY; SURVIVAL, ACUTE AND LATE TOXICITY OUTCOMES

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Purpose: Aim of this study was to evaluate survival rates, acute and late toxicity after hypofractionated palliative radiotherapy (HpRT) in patients (pts) unfit of standard RT treatment for age or low performance status. Methods and materials: From December 2010 to June 2020, 211 pts were evaluated retrospectively. Prescribed dose was 36,75 - 42 Gy (5.25 Gy fr.) in 7-8 weekly fractions. 104 pts (49,3%) were male, 107 (50,7%) female. Mean age was 79 years (range 42-100 years). Majority of pts were with 2 or more comorbidity, 88% were more than 70 years old. The primary site was head and neck (31%), lung (19%), gynecological (17%), gastrointestinal (8%), breast (7%), prostate (7%), skin (7%) sarcomas (2%) and other metastatic disease (2%). A 3DCRT technique was used in 123 pts (58,3%) and a VMAT or IMRT technique in 88 pts (41,7%). Concomitant chemotherapy was administered in 41 pts (19,4%). At the RT start median KPS was 70 (range 40-90).

Results: After a mean follow-up of 14 months, median overall survival was 11 months. Overall, 74,5% of pts completed radiotherapy at the prescribed dose and 25,5% interrupt it due to PD, clinical worsening or lost motivation. A clinical or radiological examination response was observed in 56% of patients; CR 24%, PR 32%. SD was obtained in 6%, a PD 17% of pts and in reaming 21% was not possible to evaluate (lost in follow up). In pts receiving the prescribed dose the response rate was 75%, of them 40% had a CR. Patients that completed HpRT at the prescribed (36,75 Gy-42 Gy) had a higher survival rate compared to pts which interrupt RT (median 14 mths *vs* 3 mths; p 0,0001). KPS >70, PTV <250 cc, systemic therapy during HpRT and clinical or radiological response were prognostic factors regarding OS ($p<0,05$). RT technique did not influence survival rate or local response. Pts treated with 3DCRT had higher rates of ≥G2 acute or late toxicity with a trend toward statistically significant ($p<0,067$). A G3 or higher acute toxicity was observed in only 1,8% of pts. A late toxicity ≥ G3 was observed in 8 pts (4,7%).

Conclusion: Weekly hypofractionated radiotherapy 36,75-42 Gy in 7-8 fractions appears acceptable in poor performants status and elderly pts unit of standard RT

treatment with a response rate of 75%. Total dose, KPS >70, PTV <259 cc, systemic therapy during RT resulted prognostic factors regarding overall survival. IMRT-VMAT technique is recommended to be used due to reduce G2 or higher toxicity.

CO20

ADEQUACY OF PAIN TREATMENT IN RADIOTHERAPY DEPARTMENTS: RESULTS OF A MULTICENTER STUDY ON 2104 PATIENTS (ARISE-1)

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Aim: Inadequate treatment of pain is frequent in cancer patients (pts). Furthermore, studies on the adequacy of analgesic medication during Radiotherapy (RT) are lacking. The aim of this multicenter observational prospective trial was to evaluate the analgesics prescriptions in RT Departments (Depts) using the Pain Management Index (PMI). Moreover, we analyzed the correlation of PMI with pain characteristics and other potentially predictive factors.

Methods: In this study we enrolled 2104 pts from 13 Italian RT Depts. RT aims, and characteristics of pts and pain were collected. Pain was classified as cancer pain (CP), not-cancer pain (NCP), and mixed pain (MP). The Pain Score was graded from 0 (no pain; Numeric Rating Score [NRS]: 0) to 3 (severe pain; NRS: 7-10). The Analgesic Score was graded from 0 (no pain medication) to 3 (use of strong opioids). The PMI was calculated by subtracting the pain score from the analgesic score, with negative PMI values showing inadequate analgesic prescription. This study was approved by the Ethical Committee of the participating centers (ARISE-1 study).

Results: Pts with pain were1409 and prevalence of PMI was as follows: < 0: 45.4%; ≥ 0: 54.6%. Pain was classified as follows: CP: 49.6%, NCP: 31.9%; MP: 18.5%. At univariate analysis, pts with CP and MP had more adequate analgesics prescription than NCP pts ($p<0.001$). Moreover, in pts with CP and MP a worse performance status correlated with better PMI value ($p<0.001$ and $p=0.053$, respectively) while in NCP worst performance status was correlated with negative PMI ($p=0.004$). The results of the multivariable analysis are shown in Table 1. Briefly, the parameters significantly correlated with negative PMI (inadequate pain treatment) were: curative treatment (compared to palliative treatment), better (1) PS, (compared to PS=3-4), breast cancer as primary tumor (compared to prostate, gastrointestinal, uterine, lung, and other tumors), NCP (compared to CP), and geographical location of the radiotherapy center (central-southern *vs* northern Italy).

Conclusions: Radiation Oncologists analgesics prescription was negatively influenced by more favourable pts characteristics. Educational strategies are needed in RT Depts to reduce the non-negligible percentage (45.4%) of pts with pain who receive inadequate drug therapy.

Table 1. Multivariable analysis, significant correlation of negative PMI.

		OR	S.E.	p-value
Age, years (analyzed as a continuous variable)		1.007		0.109
Aim of treatment				
	Curative	[ref]		0.000
	Palliative	0.441	0.168	
ECOG-PS				
	1	[ref]		0.107
	2	0.777	0.156	
	1	[ref]		0.010
	3	0.575	0.214	
	1	[ref]		0.030
	4	0.295	0.563	
Primary Tumor				
	Breast	[ref]		0.001
	Prostate	0.462	0.224	
	Breast	[ref]		0.000
	Gastrointestinal	0.343	0.231	
	Breast	[ref]		0.024
	Uter/Cervix	0.531	0.281	
	Breast	[ref]		0.000
	Lung	0.470	0.207	
	Breast	[ref]		0.001
	Head and Neck	0.467	0.235	
	Breast	[ref]		0.018
	Others	0.657	0.178	
Type of pain				
	Cancer Pain	[ref]		0.000
	Not-cancer Pain	2.592	0.172	
	Cancer pain	[ref]		0.405
	Mixed Pain	1.144	0.162	
Geographical location of the radiotherapy center				
	Nord of Italy	[ref]		0.000
	Center of Italy	2.244	0.225	
	Nord of Italy	[ref]		0.000
	South of Italy	1.766	0.163	

Legend: ECOG-PS: Eastern Cooperative Oncology Group Performance Status Scale; OR: odds ratio

CO21

PREDICTIVE MARKERS OF TOXICITY IN ELDERLY PATIENTS (AGED ≥ 75) TREATED WITH CURATIVE INTENT RADIOTHERAPY MANAGED BY A MULTI-DISCIPLINARY ONCOGERIATRIC MODEL

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Aims: Despite a growing number of elderly patients receiving radiation therapy (RT), little is known about side effects and outcome of irradiation in this potentially frail population. The identification of predictive factors of toxicity and frailty could offer a personalized treatment approach, thanks also to a multidisciplinary management of patients with increased risk of adverse outcomes. In this study we investigated the correlation of patient parameters with acute toxicities in elderly (≥75years) treated with curative RT.

Methods: A prospective observational study was designed in our Center for patients with ≥75years, candidate for curative RT. These patients underwent Geriatric8 questionnaire (G8q), before and at the end of RT. Patients with G8 score ≤14 were evaluated by a multidimensional geriatric assessment, investigating cognitive, functional, and nutritional domains, to define the frailty phenotype. In this setting, we retrospectively analyzed parameters like body mass index (BMI), number of comorbidities, neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and basal G8 score, as predictive factors of toxicity.

Table 1. Parameters correlated to acute toxicity.

					p value
Acute toxicity		**Overall** N=98	**No** N=27	**Yes** N=71	
	Grade 1			40	
	2			29	
	>2			2	
Age (median, [mean])		79.00 [79.7]	79.00 [80]	78.00 [79.4]	0.609
Sex (%)	female	38 (38.8)	5 (18.5)	33 (46.5)	0.021
	male	60 (61.2)	22 (81.5)	38 (53.5)	
Toxicity type (%)	none	27 (27.6)	27 (100.0)	-	
	skin	33 (33.7)	-	33 (46.4)	
	gastrointestinal	12 (12.2)	-	12 (16.9)	
	genitourinary	26 (26.5)	-	26 (36.6)	
Body Mass Index (median)		**26.30** [23.89, 28.66]	**24.62** [23.34, 27.05]	**26.81** [24.30, 29.05]	**0.031**
Basal G8 score (median)		15.00 [14.00, 16.00]	15.00 [13.50, 16.00]	15.00 [14.00, 16.00]	0.691
Number of Comorbidity (%)	0	6 (6.1)	2 (7.4)	4 (5.6)	0.938
	1	31 (31.6)	7 (25.9)	24 (33.8)	
	2	36 (36.7)	10 (37.0)	26 (36.6)	
	3	18 (18.4)	6 (22.2)	12 (16.9)	
	4	6 (6.1)	2 (7.4)	4 (5.6)	
	6	1 (1.0)	-	1 (1.4)	
White Blood Cells (median)		6.59 [5.60, 8.00]	6.67 [5.48, 8.39]	6.52 [5.72, 7.78]	0.684
Lymphocyte (median)		1.69 [1.28, 2.20]	1.60 [0.99, 2.16]	1.78 [1.40, 2.25]	0.191
Neutrophils (median)		3.70 [3.22, 4.60]	3.60 [2.96, 4.70]	3.70 [3.23, 4.30]	0.936
Platelets (median)		202.00 [177.00, 237.00]	199.00 [164.00, 243.50]	202.00 [181.75, 232.00]	0.549
Haemoglobin (median)		13.10 [12.10, 14.50]	12.90 [12.00, 14.95]	13.15 [12.10, 14.30]	0.984
Neutrophils Lymphocyte Ratio (median)		2.33 [1.67, 3.05]	2.35 [1.77, 3.65]	2.24 [1.67, 2.92]	0.306
Platelets Lymphocyte Ratio (median)		114.72 [91.18, 167.04]	137.50 [92.13, 241.89]	113.12 [91.25, 155.35]	0.229

Results: G8q was administered to 150 patients from December 2019 to April 2021. In this study we included 98 patients who started and completed RT in our Unit in this period. Of them, 38 (38.8%) had a baseline G8 score≤14 (range 4-14) and 23 agreed to underwent a multidimensional assessment. Acute toxicity grade was ≤ grade 2 in 67 patients (68.4%). We evaluated associations between BMI, number of comorbidities, NLR, PLR, G8 score and acute toxicity (Table 1). NLR, PLR and G8 score resulted not significantly correlated to toxicity. Instead, a higher BMI was associated with worse acute toxicity (p=0.031); 17 of the 31 patients reporting ≥ grade 2 toxicity were over-weighted (54.8%), 1 patient was under-weighted (3.2%). Overall, the 63.3% of population was over-weighted, with a median BMI of 26.3.

Conclusions: Our results suggested that in elderly patients ≥75years BMI correlates with worse acute toxicity, according to literature data. Although G8q considers under-weight as a possible responsible of frailty, our study suggested to pay attention to over-weight too, due to its prevalence in elderly patients and effect on toxicity. The 38.8% of patients needed a multidimensional evaluation; this approach resulted useful in order to obtain compliance to the treatment without increased toxicity and the study is still ongoing.

CO22

LASER PHOTOBIOMODULATION FOR PREVENTING ORAL MUCOSITIS AND RADIODERMATITIS IN HEAD AND NECK CANCER PATIENTS: A MULTIDISCIPLINARY PILOT CASE-CONTROL STUDY

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Aims: Oral mucositis (OM) and radiodermatitis (RD) are serious side effects of radio and/or radio-chemotherapy (RT;RT-CT) in Head and Neck Cancer (HNC) patients, which often require analgesics and sometimes enteral/parenteral nutrition to avoid suspension of therapy. Laser photobiomodulation (LPBM) is frequently used for mucosal lesions in oral medicine departments and increasing evidence exists even for treating skin affections. Our ongoing study investigates the effect of LPBM in preventing OM and RD in patients affected by HNC.

Methods: PBML is being applied 3 times a week up to the end of RT as preventive strategy in HNC patients (oropharyngeal, mouth and laryngeal cancers). Application is intraoral and/or cutaneous (neck) following the field of irradiation. Assessment of OM/RD (WHO-SCALE:Grading objective Scale, CTCAE: Common Toxicity Criteria for Adverse Events), pain (NRS:Numeric Rating Scale), functional ability, (subjec-

tive parameters), site/severity of side effect, type and posology of analgesics/opioids prescription is being regularly monitored up to 60 days after the end of RT. Pre LPBM patients in Treviso Hospital cancer are being used as controls. Quality of Life (QoL) questionnaire is being filled by all patients before,and during RT, as well as 60 days after the end of RT. Grade of satisfaction (0-10) for receiving PBM is being asked to all patients at the end of RT. Coltural exam for fungal infection is being performed the first and last days of observation.

Results: The study protocol adherence is high. Patients in the LPBM group report less severe or absence of OM/RD. The level of pain associated to OM and functional difficulties seem mitigated by the use of LPBM and reduction of analgesics/opioids intake seems practicable. None of the patients in the LPBM group have suspended RT so far. Positivity to cultural swab is being observed for the entire duration of RT despite the use of antifungal prophylaxis. QoL worsens in all patients during RT but seems to improve more quickly in PBML group after the end of RT.

Conclusions: LPBM seems a promising treatment for OM and RD prevention. Although it requires a significant effort and multidisciplinary collaboration, it appears safe and useful in terms of reduction of lesions' occurrence, related pain and drugs intake. Patient's satisfaction is high. The QoL has a key role in patient's choice and adherence to treatment so clinicians should pursue its improvement whenever possible.

CO23

AN INTERDISCIPLINARY PATHWAY OF CARE TO PREVENT FRAGILITY FRACTURES AMONG PROSTATE CANCER PATIENTS TREATED WITH RADIOTHERAPY AND LONG-TERM ANDROGEN DEPRIVATION THERAPY

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Aims: Long-term androgen deprivation therapy (ADT) and radiotherapy (RT) improve outcomes of unfavorable intermediate-risk, high-risk and locally advanced prostate cancer (PCa) patients. However, ADT is associated with accelerated bone loss[1] and high risk of osteoporosis and fragility fractures.[2] Several lines of evidence recommend assessment and initiation of antifracture treatments to counteract cancer treatment induced bone loss (CIBL). The management of CIBL remains an unsolved issue in PCa patients. Appropriate management can be provided by using interdisciplinary pathway of care (IPC).

Methods: A multidisciplinary team, that included radiation oncologists expert in PCa treatment, bone specialists with geriatric and endocrinologic background, radiologists, nurses and physicians of the hospital medical direction, was established at our University Hospital. We developed an IPC for management of CIBL that specified laboratory and x-ray (spine radiographs, DEXA) diagnostic evaluations as well as a therapeutic algorithm, according with the best available recommendations and local availability of services and staff. Our study aims to accrue in 3 years at least 100 non metastatic PCa patients aged >50 treated with RT and long-term ADT and/or with pre-existing osteoporotic fractures. Bone specialist evaluations and quality of life (QoL) assessment (EuroQoL 5D) were scheduled at the start of ADT and therefore every 6 months for 5 years. The study was approved by the Umbria Region Public Health Committee.

Results: The developed IPC meets the requirements of a Fracture Liaison Service (FLS) with regards of key indicators. The IPC addresses actions and identifies contact persons per each step from the identification to the long-term monitoring. To date, the pathway of care is in its early phase of patient enrolment and management (6 patients enrolled) and feasibility data are available.

Conclusions: Global costs for fragility fractures are very high in Italy and it has been shown that pharmacologic fracture prevention is cost-effective.[3] PCa patients are at high risk of osteoporosis and fragility fractures. In this scenario, we add evidence about the opportunity to develop an IPC integrated within FLS in hospital-based clinical management of PCa patients.

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CO24

HYPOFRACTIONATED RADIOTHERAPY IN CLINICAL PRACTICE: RESULTS OF A REGIONAL SURVEY AMONG THE PUGLIA-BASILICATA AIRO GROUP IN THE COVID-19 ERA

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Aims: Hypofractionated radiotherapy is often administered for several cancer types, for both palliative and curative treatments. Aim of this analysis was to evaluate the use of hypofractionated radiotherapy schedules in the clinical practice among the Puglia and Basilicata AIRO group before and during the COVID-19 era.

Methods: A survey, attached as "Survey ipofrazionamento Puglia&Basilicata", listing eight types of cancer (brain, brain metastases, head-and-neck, breast, lung, bladder, prostate, bone metastases), each with several hypofractionated schedules according to the literature data, was sent to all the Puglia-Basilicata RT centres, of which, 8 out of 10, replied with compiling data. The period between 2019 and 2020 was considered. Stereotactic treatments were excluded from our analysis.

Results: The data collected from the eight centres that replied to the survey show a total of 1202 patients treated with hypofractionated radiotherapy during the first six months of 2019 and 1336 patients treated during the first six months of 2020. The most commonly prescribed dose/fraction for brain was 265/266 cGy for 15 fractions. Brain metastases were mostly treated with a prescribed dose of 300 cGy/10 fractions (59.1%) or 400 cGy/5 fractions (40.9%). Very few patients with head and neck cancer (a total of 6 patients in 2019 and 8 in 2020) were treated with hypofractionated radiotherapy, primarily with 250 or 300 cGy for 10 fractions. For breast cancer two main hypofractionated RT regimens are active: 266 cGy for 16 fractions and 267 cGy for 15 fractions. For lung cancer, 5 out of 8 centres used 300 cGy for 10 fractions. The most used hypofractionated regimen for bladder cancer was 400 cGy for 5 fractions. At least seven different moderate-hypofractionation regimens were used for prostate cancer ranging from 220 cGy for 30 fractions to extreme-hypofractionation. The most used hypofractionated schedules were 250 cGy for 28 fractions (3/8 centres), 300 cGy for 20 fractions (3/8 centres) and 600cGy for 6 fractions (3/8 centres) while 3 centres did not used hypofractionated radiotherapy for prostate cancer during 2019 and 2020. Also for bone metastases there were several regimens and 87.5% of centres mainly used 400 cGy for 5 fractions or 800 cGy for 1 fraction.

Conclusions: The findings of this regional survey provided an overview of the current clinical practice of hypofractionated radiotherapy in Puglia and Basilicata and the impact of COVID-19 emergency. Significant variation was observed across curative indications for prostate cancer and bone metastases with greater concordance in other types of treatment. COVID-19 does not seem to have significantly increased the use of hypofractionated regimens. Our initiative of a multicentre collaboration has been undertaken in order to prepare the basis for prospective/observational studies in hypofractionated radiotherapy.

CO25

RE-IRRADIATION FOR RECURRENT HIGH GRADE GLIOMA (HGG) PATIENTS: RESULTS OF A SINGLE ARM PROSPECTIVE PHASE II STUDY

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Aims: A standard of care for recurrent high grade glioma (HGG) is missing. Several treatment options have been investigated including re-irradiation (re-RT). Results are promising but provided by retrospective studies. Considering the lack of prospective data, we designed a single arm prospective phase II study aiming to evaluate efficacy, and toxicity of re-RT.

Methods: Adults patients with good performance status, HGG diagnosis, and an interval time (IT) from previous RT ≥6 months were included. CT scan, T1-weighted FLAIR (fluid-attenuated inversion recovery images) and T2-weighted 3D-FLAIR followed by T1-weighted MPRAGE MRI and [11C]-Methionine-PET (11CMET-PET) were acquired for radiation therapy planning, and images were co-registered and used for target definition. The clinical target volume (CTV) was defined as the contrast-enhancing tumor on the T1-weighted and Methionine CT-PET. The planning target volume (PTV) was generated adding an isotropic margin of 3 mm from the CTV. Different total doses and fractionation were delivered in relation to target volume: ≤2 cm 25Gy/1fraction, 2.1-3cm 37.5Gy/7.5Gy/5fractions, ≥3.1 cm 49.5Gy/3.3Gy/15 fractions. Outcome was evaluated by MRI imaging at 1 months, and every 3 months thereafter. Toxicities were evaluated in terms of radionecrosis occurrence and neurocognitive status.

Results: From January 2015 to December 2019, 90 recurrent HGG patients were treated. The median age was 54 years, and the majority had KPS 90-100. The median IT before first RT and re-RT was 24 months (range 6-180 months). All patients received re-RT; re-surgery has been performed in 51 (56.7%) cases, and chemotherapy in 48 (53.3%). Twenty seven (30%) patients received re-RT as exclusive treatment. Median follow up was 64 months (range 13-110 months); median overall survival (OS) time, 1-, 2-, 3- year OS rates were 17 months (95%CI 14-19), 66.7%±4.9, 32.6%±5.0, and 22.2±4.7. Prognostic factors impacting on survival were age (p=0.005), IT firstRT-reRT (p=0.001), glioma grade (p=0.002), and IDH status (p=0.0007). Radionecrosis occurred in 9 (10%) patients; neurocognitive functions remained stable until disease progression.

Conclusions: Re-RT has proven to be a safe and feasible treatment with low toxicity. Younger patients with grade III-IDH mutated gliomas, and a longer IT had the better outcome.

CO26

PERMANENT ALOPECIA IN PEDIATRIC PATIENTS WITH MEDULLOBLASTOMA TREATED BY CRANIOSPINAL IRRADIATION: LOOKING FOR A THRESHOLD DOSE

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Aims: To identify a threshold dose constraint for permanent alopecia in patients with medulloblastoma (MB) treated with surgery followed by adjuvant chemotherapy (CT) and radiotherapy (RT).

Table 1. Characteristics by grade of alopecia (N=42).

		Total (N = 42)	No visible hair loss (N = 19)	Partial/Complete hair loss (N = 23)	p
Sex	Female	**19 (45.2)**	10 (52.6)	9 (39.1)	0.38
	Male	**23 (54.8)**	9 (47.4)	14 (60.9)	
Diagnosis age, years		**7.3 ± 3.65 6.5 (2 - 16)**	6.9 ± 3.27 7 (3 - 14)	7.5 ± 3.99 6 (2 - 16)	0.78
Age at the end of therapy		**7.7 ± 3.49 7 (2 - 16)**	7.8 ± 3.08 7 (4 - 15)	7.7 ± 3.85 6 (2 - 16)	068
Months between diagnosis and end of treatment		**5.8 ± 3.94 5 (1 - 19)**	5.9 ± 4.61 6 (1 - 19)	5.7 ± 3.40 5 (2 - 15)	0.99
Protocol	Metastatic/PNET	**24 (57.1)**	10 (52.6)	14 (60.9)	0.41
	HIT – SIOP PNET 4	**10 (23.8)**	7 (36.8)	3 (13.0)	
	AIEOP Infants	**2 (4.8)**	0 (0.0)	2 (8.7)	
	AIEOP and SNC '99	**4 (9.5)**	1 (5.3)	3 (13.0)	
	PNET 5 MB -SR	**2 (4.8)**	1 (5.3)	1 (4.3)	
Chemotherapy	HD chemotherapy	**26 (61.9)**	10 (52.6)	16 (69.6)	0.26
	CD chemotherapy,	**16 (38.1)**	9 (47.4)	7 (30.4)	
Eclipse	No	**15 (35.7)**	8 (42.1)	7 (30.4)	0.43
	Yes	**27 (64.3)**	11 (57.9)	16 (69.6)	
Technique Cranio-spinal (CSP) radiotherapy (Phase I)	3D-CRT	**30 (71.4)**	12 (63.2)	18 (78.3)	0.28
	Helical	**12 (28.6)**	7 (36.8)	5 (21.7)	
Total dose CSP (cGy) (Phase I)		**2877.1 ± 625.92 2430 (2340 - 3900)**	2532.6 ± 377.14 2340 (2340 - 3600)	3161.7 ± 653.13 3120 (2340 - 3900)	0.001*
Total fractions (Phase I)		**20 ± 8.53 15.5 (13 - 36)**	15.8 ± 5.70 13 (13 - 36)	23.4 ± 9.03 24 (13 - 36)	0.007*
Single dose/die (cGy) (Phase I)	100	**5 (11.9)**	1 (5.3)	4 (17.4)	0.07
	130	**12 (28.6)**	3 (15.8)	9 (39.1)	
	180	**25 (59.5)**	15 (78.9)	10 (43.5)	
Fraction/die (cGy) (Phase I)	1 fraction/die	**25 (59.5)**	15 (78.9)	10 (43.5)	0.020*
	2 fractions/die	**17 (40.5)**	4 (21.1)	13 (56.5)	
Technique posterior cranial fossa (PCF) radiotherapy (Phase II)	3D-CRT	**24 (57.1)**	10 (52.6)	14 (60.9)	0.59
	Helical	**18 (42.9)**	9 (47.4)	9 (39.1)	
Total dose PCF (cGy) (Phase II)		**2993.8 ± 581.64 3030 (1800 - 5580)**	3098.9 ± 274.26 3060 (2340 - 3600)	2907 ± 742.63 3000 (1800 - 5580)	0.025*
Total fractions (Phase II)		**18.4 ± 5.43 17 (6 – 32)**	18.5 ± 3.88 17 (13 - 30)	18.3 ± 6.53 17 (6 - 32)	0.63
Single dose/die (cGy) (Phase II)	100	**5 (11.9)**	1 (5.3)	4 (17.4)	0.07
	150	**12 (28.6)**	3 (15.8)	9 (39.1)	
	180	**24 (57.1)**	15 (78.9)	9 (39.1)	
	200	**1 (2.4)**	0 (0.0)	1 (4.3)	

Methods: We retrospectively analyzed 42 patients (pts) with MB treated at our Institute, from 1999 to 2019. All pts had a minimum follow up of 12 months and underwent craniospinal irradiation (CSI) followed by a boost to posterior cranial fossa (PCF) and/or to the primary tumour site. Alopecia was assessed according to CTCAE v5.0 scale. Before 2010 patients were treated with 3D CRT technique. Since 2010 IMRT by helical Tomotherapy has been used for the PCF boost, since 2015 this technique has become the standard used for CSI. In a subgroup of pts (N=27) the dose to the skin using Eclipse software (Varian Inc) was accurately assessed. The skin was fully contoured as the volume from the outer surface of the skin to a depth of approximately 3 mm. We also used the same parameters to contour only the skin of the PCF. Any relationship between presence of alopecia (partial or complete) and other characteristics was investigated by an appropriate univariate and multivariate analysis. For each significant predictor variable, a receiver operating characteristic curve was drawn for calculating the Area Under the Curve and identifying the optimal discriminatory cut-off value for prediction of alopecia. Primary endpoint was to identify a cranio-spinal dose limit that could predict the onset of alopecia.

Results: Whole brain cranio-spinal doses ranged from 23.4 to 39.0 Gy. All 42 pts were boosted with either the entire PCF or the involved field of the tumour bed, with a total dose ranging from 54.0 to 69.0 Gy. Table 1 shows characteristics of pts according to grade of toxicity (no hair loss *vs* partial/complete hair loss). The best predictor for the occurrence of alopecia was the dose of CSI (OR: 1.002; 95%CI: 1.001-1.003; p=0.003), with an optimal discriminatory cut-off value of 30.9 Gy. In Eclipse subgroup the best predictor was D median hair skin (OR: 1.216; 95%CI: 1.030-1.435; p=0.021), with an optimal discriminatory cut-off value of 28.7 Gy.

Conclusions: We tried to identify the dose threshold for permanent hair loss in pediatric patients after CSI. Our results should be confirmed in prospective protocol, but this evidence might represent an additional dosimetric reference to consider in the treatment planning in order to improve QoL of these pediatric patients.

CO27

HEMATOLOGIC PREDICTIVE FACTORS TO TEMOZOLOMIDE RESPONSE IN PATIENTS WITH HIGH-GRADE GLIOMAS: A SINGLE-CENTER RETROSPECTIVE ANALYSIS

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Aims: Gliomas account for about 60% of primary brain tumors. Among them, high grade gliomas (grade

III-IV, WHO classification 2016) show poor prognosis, with glioblastomas having a median overall survival of 14-16 months. To date, standard of treatment is radiation therapy with concomitant Temozolomide (TMZ) followed by 12 cycles of sequential TMZ (Stupp Protocol). Recent studies have demonstrated that mild hematological toxicity is associated with increased overall survival in this setting. To confirm prior results, our aim was to assess survival outcomes in high-grade gliomas that presented low platelet count (LPC) during treatment as per Stupp Protocol.

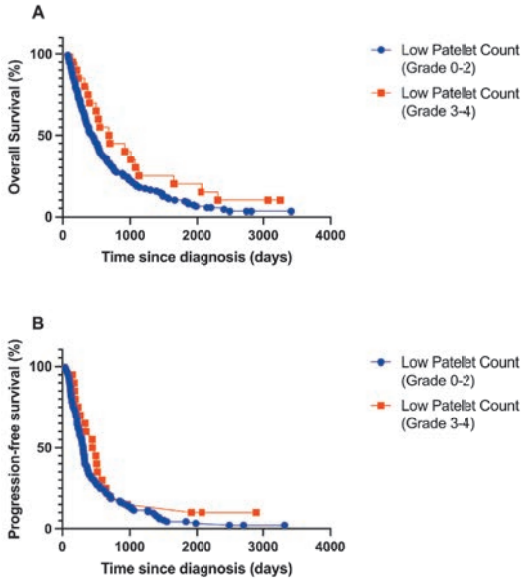

Fig. 1
(A) Kaplan-Meier estimates of overall survival; (B) Kaplan-Meier estimates of progression-free survival.

Figure 1.

Methods: This retrospective, single-institution analysis includes 149 patients with high grade gliomas treated in our center between 2012 and 2017. All patients were treated as per Stupp Protocol. Thrombocytopenia was recorded according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Primary endpoints were Progression Free Survival (PFS) and Overall Survival (OS).

Results: We retrospectively collected complete blood counts from 149 patients (86 men and 63 women). Mean age at diagnosis was 59,8 years. Eighty-eight patients (59%) underwent gross total resection; histological subtype was either glioblastoma or gliosarcoma in 129 patients (86, 6%) and MGMT gene was methylated in 50 cases (33,6%). The majority did not show LPC (n= 103, 69,1%). The LPC (grade 3-4) group showed prolonged survival, with a median OS of 22,8 months versus 14,5 months (hazard ratio 1,55; 95% CI 1,01 to 2,37; P 0.076) (Figure 1A). Median PFS was longer in the LPC (grade 3-4) group than in the LPC (grade 0-2) group (15,5 months versus 10,2 months, hazard ratio 1,47; 95% CI, 0.95 to 2,26; P 0.08) (Figure 1B). The dose of TMZ was stopped or decreased mainly because of hematologic toxicity (n=26, 17.5%); other reasons were pulmonary embolism (1,3%) and seizures (0.7%).

Conclusions: High-grade gliomas who experienced severe low platelet count (grade 3-4) during treatment showed improved OS and PFS. Although not significant, this analysis does confirm earlier reports of the association between bone marrow suppression and improved OS and PFS in glioblastoma. For better understanding of this phenomenon, further research such as a randomized controlled TMZ dose escalation trial or a two-tier dose stratification trial based on MGMT promoter methylation is needed.

CO28

TEMOZOLOMIDE PLUS 3D-CRT AFTER HIGH DOSE METHOTREXATE IN PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA: A PROSPECTIVE PHASE II STUDY

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Aims: Aim of this study is to evaluate the addition of temozolomide (TMZ) to radiotherapy in patients with primary cerebral lymphoma (PCNSL) previously treated with high dose Methotrexate (MTX-HD) in terms of overall survival (OS).

Materials and Methods: Patients with histologically proven diagnosis of PCNSL treated with high doses MTX and subsequently subjected to radiation therapy plus Temozolomide were considered for this analysis. Two clinical Target Volumes (CTVs) were defined: CTV2 was represented by Whole Brain plus leptomeninges until C2, reaching a dosage of 30 Gy in 15 daily fractions, while CTV1 comprising the initial disease location and residual mass if present. The total dose delivered on CTV1 was

related to the type of response had to treatment with HD-MTX (complete response = 6 Gy, partial response = 10 Gy, progression disease = 16 Gy). Temozolomide was administered concomitantly at the dose of 75 mg/mq/die according to our previous escalation study.[1]

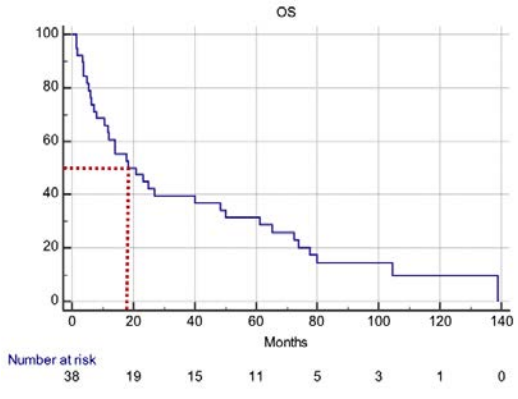

Figure 1.

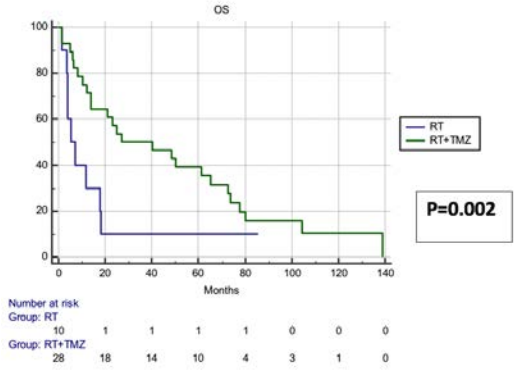

Figure 2.

Results: Thirty-eight patients were enrolled from March 2004 to December 2019: 21 male and 17 female. Median age was 66 yrs (range 23-82). Twenty-five out of 38 patients received two cycle of MTX-HD, 9 patients received only one cycle of HD-MTX because of hematological toxicity and 4 patients did not received any cycle due to poor performance status. Ten patients underwent macroscopic surgical excision, while 28 patients received biopsy. In 28 patients TMZ was associated to radiotherapy. At a median follow up of 113 months (range 21-207), 4 of 38 patients (10,5%) are alive and without disease, 32 patients died because of disease and two patients died because of other causes. Median OS for all patients was 18.3 months with at 1 yrs OS of 60% and at 3 yrs OS of 36% of patients (Figure 1). The use of concomitant TMZ significantly impact the OS (p=0.002) (Figure 2).

Conclusions: This prospective analysis shows that, despite the limit of possible patient selection, the addition of TMZ at the dose of 75 mg/mq seems to have a better outcome compared to RT alone.

Reference

1. Chiesa S, Hohaus S, Falcinelli L et al. Chemoradiotherapy with temozolomide after high-dose methotrexate for primary CNS lymphoma: a multicenter phase I study of a response-adapted strategy. Ann Hematol. 2020 Oct;99(10):2367-2375. doi: 10.1007/s00277-020-04220-1.

CO29

HYPOFRACTIONATED RADIOTHERAPY WITH SIMULTANEOUS INTEGRATED BOOST IN RADICALLY INOPERABLE CASES OF GLIOBLASTOMA

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Aim: Aim of this study was to evaluate efficacy and toxicity of hypofractionated radiotherapy (hypoRT) with simultaneous integrated boost (SIB) associated with concomitant/adjuvant temozolamide (TMZ) in radically inoperable patients affected by Glioblastoma (GBM).

Methods: Patients with a newly diagnosis of GBM not eligible for maximal safe surgical resection were evaluated in this retrospective study. If possible, a subtotal resection was performed or alternatively an open biopsy followed by hypoRT with SIB and concomitant+adjuvant TMZ. The prescription dose for hypoRT was 40.05 Gy in 15 fractions on planning target volume (PTV) with a SIB of 52.5 Gy (3.5 Gy per fraction) on residual/macroscopic disease identified as gross tumor volume (GTV). GTV was defined as the macroscopic disease detected on T1-MRI. The clinical target volume (CTV) was defined adding to GTV an isotropic margin of 1-1.5 cm, respecting the anatomical barriers and organs at risk (OaRs). The margins CTV-PTV were assigned of 3 mm. FFF-VMAT technique with 2 or more coplanar or non-coplanar arcs were generated for each treatment plan. Primary endpoints were overall survival (OS) and progression free survival (PFS). Secondary endpoint was toxicity.

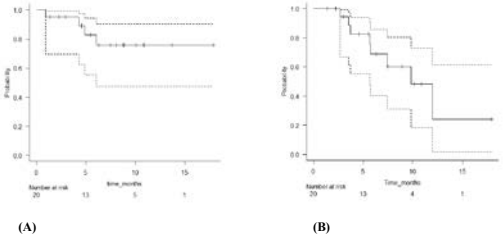

Figure 1. Kaplan- Meier curves for OS (A) and PFS (B)

Results: From September 2019 to January 2021, 20 patients (8 female and 12 male) were treated in our Department, according to study criteria. The median age was 64 years (range 37-82) and median ECOG was 2 (range 1-3). All patients have histological diagnosis of GBM IDH1 wild-type and 30% of cases showed MGMT methylation. Subtotal resection was performed in 14 patients (70%) while biopsy in 6 (30%). The median time between surgical procedure-RT was 56 days (range 15-103). The median GTV_52.5Gy was 45cc (range 13-208). The median PTV_40.05Gy was 208cc (range 84-330). At median follow-up time of 10 months (range 2-18), the median OS was not achieved (95%CI 6.06-na) and 1-year OS was 75.8% (95%CI 47.2-90.3); the median PFS was 9.8 months (95%CI 5.63-na) and 1-year PFS was 24.1% (95%CI 1.62-61.2). Regarding toxicity no acute or late neurological side effect grade ≥ 2 were reported. In all cases, prophylactic steroid therapy was administrated. Grade 3-4 hematologic toxicity occurred in 3 cases.

Conclusion: FFF-VMAT hypoRT with SIB associated with TMZ in not eligible for maximal safe surgical resection patients affected by GBM is an effective and safe treatment compared with the current literature. To confirm these results, prospective study could be warranted.

CO30

REAL-LIFE TREATMENT OF GLIOBLASTOMA RECURRENCE WITH REGORAFENIB: A SINGLE-CENTRE REVIEW

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Aims: Glioblastoma (GBM) is the most frequent and aggressive among malignant central nervous system primary tumors. Despite a multimodal treatment approach in first-line, all GBM may relapse. To date, treatment options for GBM recurrence are lacking and the management of patients remains challenging. The recent REGOMA trial suggested an overall survival (OS) benefit of regorafenib in recurrent patients. We aimed to assess the efficacy and safety of regorafenib in the treatment of recurrent GBM in our "real-life" experience.

Methods: Consecutive patients with GBM recurrence treated with regorafenib between January 2018 and May 2021 were included in a retrospective evaluation. Data collected include diagnosis, patient demographics, performance status, number of previous lines of treatment, number of treatment cycles, side effects, treatment discontinuation and survival data. Progression-free survival (PFS) and OS were estimated using the Kaplan-Meier method.

Results: We had available data for 34 patients (16 males and 18 females). Median age in the cohort was 53 years (range 26-76), and all patients had a performance status between 0-2. Thirty one (91.2%) patients received regorafenib as second-line treatment; 3 (8.2%) patients received regorafenib as third-line due to a recurrence occurred before January 2020. Surgery at the time of recurrence was done in 13 (38.2%) patients. MGMT status was methylated for 19 (55.8%), unmethylated for 12 (35.2%), while in 3 patients the data was not available. The median number of cycles received was 4 (range 1-12) with 3 (8.8%) of patients still on active treatment at the time of analysis. The most common adverse events (grade 1-2) were fatigue (88%), rash and desquamation (15%), hand-foot skin reaction (11%), hypertension (14%), hyperbilirubinemia (3%) and hypertransaminasaemia (20%). The most common grade 3 or 4 were fatigue (9%), oedema (14%), rash (6%), neutropenia (3%) and thrombocytopenia (3%). Common reasons for discontinuing regorafenib included progressive disease (70.5%) and toxicity (12%). In patients treated with regorafenib, PFS was 4 months (95% confidence interval: 3 to 7 months) and OS was 19 months (95% confidence interval: 18 to 36 months).

Conclusions: In a real-life setting, regorafenib is associated with survival similar to that reported in trials. Toxicities lead to treatment discontinuation in nearly one third of patients. Future studies should focus on identifying the patients most likely to benefit and on minimizing adverse events.

CO31

HYPOFRACTIONATED STEREOTACTIC RADIOTHERAPY OF BRAIN METASTASES: A RETROSPECTIVE POOLED ANALYSIS

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Aims: Hypofractionated stereotactic radiotherapy (HSRT) and stereotactic radiosurgery provided high tumor control in patients (pts) with brain metastases. Our

aim is to evaluate the HSRT feasibility, effectiveness and toxicity.

Methods: We retrospectively reviewed the medical records of pts with BM treated at two Radiation Oncology Centers. Between January 2015 and June 2020 a total of 78 lesions in 58 consecutive pts underwent HSRT. The median age was 60 years (35%>65 years); 50 (86%) pts had a KPS > 80. The most common primary tumor were lung (57%) and breast (20%). Forty-six (79%) pts were in the RTOG-RPA class II and 55% of cases had a DS-GPS score between 1.5 and 2.5. Forty-one (70%) pts had a single lesion and 57 (73%) of BM were telencephalic. Median lesion diameter was 1.8cm (range 0.5-5). HSRT was delivered in 3-5 fractions. Median total dose was 27 Gy (range 24-35) and median dose per fraction 8 Gy (range 6-9). We used the corresponding BED10 for each fractionation, which had a median value of 48 Gy10 (range 42.3-59.5). Twenty-five pts underwent VMAT and 33 Tomotherapy. Study end-points were OS, CSS, brain-PFS defined as the occurrence of in-field and/or out-field progression. About the 78 HSRT-treated lesions, we evaluated local control (LC), out-field progression and radionecrosis (RN) occurrence. The Kaplan-Meier method and log-rank test were used for univariate analysis.

Results: Median follow-up was 13.3 months (IQR, 4.2-21). Median OS was 16.5 months (95%CI, 10.6-22.4), the 1-year and 2-year rates were 65% and 40%, respectively. Median CSS was 19.5 months (95%CI, 13.6-25.5), the 1- and 2-year rates were 71% and 43%, respectively. One- and 2-year brain-PFS were 44% and 29%, with a median value of 9.6 months (95%CI, 4.8-14.3). At univariate analysis, OS and CSS were positively correlated with KPS ≥ 90, RPA class I and controlled primary tumor. Moreover, age (>60 years) resulted as a prognostic factor for OS (p=0.03). After HSRT, 1- and 2-year LC were 74% and 42% with corresponding values of out-field progression of 82% and 70%, respectively. No severe acute toxicity was observed. RN was reported in 4 (7%) pts; it was symptomatic in 2 cases requiring steroids.

Conclusions: HSRT appears to be feasible, effective and well tolerated. As shown, both radiotherapy centers decided to increase the total dose above 50 Gy10 (27Gy/3 or 35/5 fractions) in order to improve the outcomes as emerging from the literature data.

CO32

HYPOFRACTIONATION IN RADIOTHERAPY OF HIGH-GRADE GLIOMA: A PROPOSAL FOR FRAGILE PATIENTS

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Aims: To analyse the outcomes obtained after Hypofractionated radiotherapy (RT) fragile patients (pts) treated for High Grade Glioma (HGG).

Methods: We retrospectively analyzed 48 pts treated for HGG from March 2017 to December 2020, as shown in Table 1. We have treated fragil patients aged over 60 years or with a KPS score of less than or equal to 70 points with 50 Gy in 20 fractions (fr), 5 fr per week, while pts who showed age <60 years and KPS > 70 points underwent the standard RT schedule of 60 Gy in 30 fr, 5 fr per week. We analyzed median overall survival (OS) and progression free survival (PFS) in overall group of patients, comparing also OS and PFS data according to the different radiotherapy schedule adopted.

Table 1. Baseline characteristics (whole sample).

Sex	Female	16 (33.3)
	Male	32 (66.7)
Diagnosis age, years		61.0 ± 11.9
		64.0 (27 - 83)
Protocol	Stupp Concomitant	17 (35.4)
	Stupp Adjuvant	31 (64.6)
Karnofsky Performance Status	≤ 70	35 (72.9)
	> 70	13 (27.1)
Surgical intervention	Biopsy	10 (21.7)
	Surgery	36 (78.3)
Residual tumor mass	Yes	33 (71.8)
	No	13 (28.2)
Histological features	IDH mutation (Y/N)	4 (8.7) / 42 (91.3
	MGMT methylation (Y/N)	16 (41.0) / 23 (59.
	1p/19q region codeletion (Y/N)	2 (4.4) / 43 (95.6

Results are expressed as mean with standard deviation and median with range or as c

Results: 35 pts received 50 Gy in 20 fr and 13 pts were treated with 60 Gy in 30 fr. All 48 pts were administered Temozolomide: 31 pts in a concomitant to RT and 17 in a sequential setting. Median PFS from the end of RT was 3.73 months (range 2.37-7.50), median OS from diagnosis was of 10.6 months (range 8.37-17.1). PFS between pts who underwent hypofractionated therapy and pts who received standard treatment were compared through hazard ratio adjusted by age, resulting in a P-value of 0.93. The comparison of values of overall survival between the same pts groups gave back a P-value of 0.458 through hazard ratio adjusted by age. We observed that 47/ 48 (98%) pts had recurrence, of these 27/47 (57%) pts had residual disease, 79% of recurrences/persistence of disease were in field. Statistical analysis showed no significant differences in OS between 60Gy

standard of care schedule and for the 50Gy hypofractionated RT schedule (p=0.297).

Conclusion: The results of our analysis suggest that a moderately hypofractionated RT treatment may be a reasonable alternative to standard schedule with the same oncological outcomes; an additional investigation is being in progress to highlight clinical benefits employing multimodal imaging integrated with biomolecular and advanced imaging data, to irradiate the HGG volume in a more tailored hypofractionated way and at reduced volumes.

CO33

OUTCOME AND TOXICITY OF HEAD AND NECK ADENOID CYSTIC CARCINOMA PATIENTS TREATED WITH PROTONS AND CARBON IONS

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Aim: To analyse clinical outcomes and toxicity profiles of patients (pts) with head and neck (H/N) adenoid cystic carcinoma (ACC), treated with particle beam radiation therapy (PBRT), protons and carbon ions, in a curative setting.

Methods: Between January 2013 and January 2020, 246 patients (M/F = 112/134) with H&N ACC were treated with active scanning protons or carbon ions RT. Pts average age was 56 (range 19-89). Tumour site was minor salivary gland in 155 (63%) and major salivary gland in 91 (37%) pts. In 26 pts (11%) treatment was at disease recurrence, 220 (89%) pts were treated after first diagnosis. Before PBRT, 170 (69%) pts received surgery, of these 14 (8%) pts received radical surgery (R0), 109 (64%) pts had positive margins (R1), 25 (15%) pts had no status of margins on histological report, and 22 (13%) pts receveid debulking surgery (R2). Out of the 170 pts who received surgery, 96 (56%) had residual disease on pre-RT MRI. In carbon ion RT cases, prescribed total dose was of 65.6-68.8 Gy(RBE) in 16 fractions, 4 fractions/week. In protons cases, prescribed total dose was 59.92-72 Gy(RBE) in 28-35 fractions, 5 fractions/week. 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: 191 (78%) pts were treated with carbo ion RT and 55 (22%) pts with proton RT. Median follow-up time was 33 months (range: 3-89 months). Overall local Control (LC) at 2 years (yrs) was 85%. In R1 resected patients LC was higher than in unresected and R2 patients (p=0,009). Overall survival (OS) at 2 and 5 yrs was 89% and 71%, respectively. Overall Progression-Free Survival (PFS) at 2 yrs was 68%, with a significant difference between R0 patients and unresected patients (p=0.0165). Acute toxicity was reported as G0 in 1%, G1 in 21%, G2 in 58% and G3 in 20% (mucositis and/or erythema). In the long FU, the late maximum toxicity was G3 in 31 (13%), G4 in 3 (1%), and G5 in 1 pt.

Conclusions: Our data compares favourably with other PBRT experiences in ACC in terms of both toxicity and outcome. Selection criteria needs to be defined to address ACC to either protons or carbon ions in order to improve outcome of ACC patients.

CO34

VITAMIN D, VITAMIN B12 AND ACUTE TOXICITY IN HEAD AND NECK CANCER PATIENTS UNDERGOING RADIOTHERAPY

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Purpose: Vitamin D (VitD) has emerged as part of patients' nutritional status, and lower levels of circulating VitD have been associated with increased risk of cancer, death and treatment induced toxicity in HNCa patients. Similarly, vitamin B12 (VitB12) is considered an indicator of nutrition status, and its role during radiotherapy (RT) is unclear. This study aims to investigate whether baseline levels of serum VitD and VitB12 are associated to acute toxicity during radiotherapy.

Methods: We conducted a retrospective analysis of 102 HNCa patients treated at Centro di Riferimento Oncologico di Aviano (CRO) IRCCS between March 2019 and January 2021. Inclusion criteria included the evaluation of serum VitD and VitB12 at baseline, HNCa of all subsites, indication to radical or adjuvant RT with high-risk Planning Treatment Volume receiving 66-70 Gy, no discontinuation of the RT. Serum VitD level was defined as normal (≥30ng/mL), insufficient (10-30ng/mL) or deficient (<10 ng/mL). Serum VitB12 level was defined normal if in the range 200-900 ng/mL. During RT course, toxicity was assessed every week by the radiation oncologist to define acute mucositis and dermatitis and weight loss as well. Acute toxicity was defined as the highest grade developed during RT according to CTCAE v5.0.

Results: Eleven patients (10.8%) reported normal VitD level, whereas 68 (66.7%) and 23 (22.6%) patients had insufficient or deficient level, respectively. VitD deficiency was more frequent among current smokers (39.4% *vs.* 13.4%; p=0.013), but not among current drinkers (26.1% *vs.* 19.2%; p=0.730). G3-G4 mucositis was

reported in 41 patients (40.2%), G3-G4 dermatitis in 21 (20.6%), and weight loss>10% in 17 (16.7%). No acute toxicity was associated to baseline VitD level. All patients but 7 (6.9%) reported normal VitB12 levels. However, patients with VitB12 levels below median level (i.e., 450 ng/mL) showed higher frequency of acute G3-G4 mucositis (53% *vs.* 31.3%; p=0.037) than those with higher VitB12 level; although not statistically significant, acute dermatitis (27.9% *vs.* 13.0%) and weight loss>10% (22.2% *vs* 10.4%) were more frequent among patients with VitB12 <450ng/mL.

Conclusions: Our preliminary results suggest that baseline serum VitD levels are not associated with the risk of acute radiation-induced toxicity in our cohort, while lower levels of VitB12 might predict higher incidence of acute toxicity and mainly mucositis.

CO35

ROLE OF DEPTH OF INFILTRATION (DOI) AS AN INDEPENDENT PROGNOSTIC FACTOR IN EARLY STAGE (PT1-PT2N0M0) ORAL TONGUE SQUAMOUS CELL CARCINOMA

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Aims: The role of depth of infiltration (DOI) as an independent prognosticator in early stage (T1-T2N0) oral cavity tumors is controversial. Specifically, there is no consensus on indications to postoperative radiotherapy (PORT) in patients (pts) upstaged to pT3 in the presence of DOI> 10 mm as the sole risk factor. Starting from this unmet need, the aim of the present work is to investigate both aspects, and to contribute to optimize therapeutic management.

Methods: Data were retrospectively collected from electronical medical charts of consecutive pts treated at two Italian institutions between 2014 and 2019. Staging was defined per the AJCC TNM 7th edition; only pts treated with radical surgery +/- PORT with a minimum follow-up of 6 months were considered eligible, provided that they had signed a written informed consent. All pathological specimens were reviewed to define the DOI (>10 mm *vs* ≤ 10 mm). The following risk factors were considered for PORT indication: close/positive surgical margins, perineural and lymphovascular invasion (PNI and LVI) and high tumor grade. The role of DOI and of the other prognosticators was assessed trough uni- and multivariable analyses in terms of overall survival (OS), disease specific survival (DSS), disease-free survival (DFS) and local relapse-free survival (LRFS).

Results: Ninety-four pts with a median age of 63 and a median follow-up time of 24 months were considered. Of these, 18 received PORT, and 23 would have been upstaged to pT3 based on DOI. At 2-years, OS, DSS and LRFS were 92%, 75% and 84%, respectively. On multivariable analysis, the DOI was not an independent prognosticator for any of the considered outcomes, as well as the status of surgical margins, LVI and grade. Conversely, the presence of PNI was associated with significantly worse LRFS (p=0.03). Kaplan Meyer plots for DFS and LRFS stratified per DOI and PNI are provided in Figure 1. PORT was correlated with a significant improvement in DFS (p=0.04); and associated with a trend towards better LRFS (p=0.06).

Conclusions: Our results suggest that the DOI alone should not lead to PORT indication in T1-T2N0 oral cavity tumors upstaged to pT3 in the absence of other risk factors. The choice of performing adjuvant RT should be rather driven by the analysis of multiple prognosticators, with an emerging role of PNI as an independent prognostic factor of recurrence.

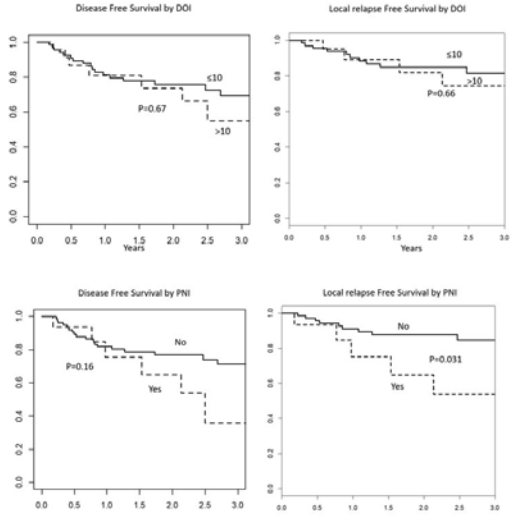

Figure 1.

CO36

ORGAN MOTION IN LINAC-BASED SBRT FOR EARLY STAGE GLOTTIC CANCER

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Aims: Aim of this study is to evaluate inter- and intra-fraction organ motion and to quantify clinical target volume (CTV) to planning target volume (PTV) margins to be adopted in the stereotactic treatment of early stage glottic cancer.

Methods: Stereotactic Body Radiotherapy (SBRT) to 36 Gy in 3 fractions was administered to 23 patients with early glottic cancer T1N0M0. Patients were treated with a volumetric intensity modulated arc technique delivered with 6MV FFF energy. Each patient underwent a pre-treatment cone beam computed tomography (CBCT) to correct the setup based on the thyroid cartilage position. Imaging was repeated if displacement exceeded 2 mm in any direction. CBCT imaging was also performed after each treatment arc and at the end of the delivery. Swallowing was allowed only during the beam-off time between arcs. CBCT images were reviewed to evaluate inter- and intra-fraction organ motion. The relationships between selected treatment characteristics (beam-on and delivery times, organ motion) were investigated.

Results: For the population systematic (Σ) and random (s) inter-fraction errors were 0.9, 1.3, 0.6 mm and 1.1, 1.3, 0.7 mm in the left-right (X), cranio-caudal (Y) and antero-posterior (Z) directions, respectively. From the analysis of CBCT images acquired after treatment, Σ and s intra-fraction errors resulted 0.7, 1.6, 0.7 mm and 1.0, 1.5, 0.6 mm in the X, Y and Z directions, respectively. Margins calculated from the intra-fraction errors were 2.4, 5.1, 2.2 mm in the X, Y and Z directions respectively. A statistically significant difference was found for the displacement in the Z direction between patients irradiated with >2 arcs versus ≤2 arcs, (MW test, p=0.038). When analyzing data from CBCT images for the whole treatment, a significant correlation was found between the time of delivery and the three dimensional displacement vector (r=0.489, p=0.055), the displacement in the Y direction (r = 0.553, p=0.026) and the margins to be adopted (r=0.626, p=0.009). Finally displacements and the subsequent margins to be adopted in Y direction were significantly greater for treatments with more than 2 arcs (MW test p=0.037 and p=0.019, respectively).

Conclusion: In the setting of controlled swallowing during treatment delivery, intra-fraction motion still needs to be taken into account when planning with estimated CTV to PTV margins of 3, 5 and 3 mm in the X, Y and Z directions, respectively. Selected treatments may require additional margins.

CO37

CORRELATION OF [^{18}F] FDG-PET/CT WITH DOSIMETRY DATA: RECURRENCE PATTERN AFTER RADIO-CHEMOTHERAPY FOR HEAD AND NECK CARCINOMA

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Aims: To analyze the pattern of failure in relation to pre-treatment [^{18}F] FDG-PET/CT uptake in head and neck squamous cell carcinoma (HNSCC) patients treated with definitive radio-chemotherapy (RT-CHT).

Methods: From 2012 to 2016, 87 HNSCC patients treated by definitive RT-CHT, with intensity modulated radiation therapy and simultaneous integrated boost, underwent pre-treatment [^{18}F] FDG-PET/CT (PETpre) and MRI/CT for radiotherapy (RT) planning purposes. Patients with local recurrence received [^{18}F] FDG-PET/CT (PETrec) at the time of the discovery of recurrence. In these patients, the metabolic target volume (MTV), MTVpre and MTVrec were segmented on PET images by an adaptive thresholding algorithm. The overlapping volume between MTVpre and MTVrec (MTVpre&rec) was generated and the dose coverage of MTVrec and MTVpre&rec was checked on the planning CT, using the D99 and D95 dose metrics. The recurrent volume was defined as "In-Field (IF)" if D95 was equal or higher than 95%, "Marginal recurrence" if D95 was between 95% and 20% or "Out-of-Field (OF)" if D95 was less than 20% of prescribed dose.

Results: We found that 10/87 patients (11.5%) had recurrence at primary site. The mean MTVpre was 12.2 cc (4.6–28.9 cc), while the mean MTVrec was 4.3 cc (1.1–12.7 cc). Two recurrences resulted 100% inside MTVpre, 4 recurrences were mostly inside (61–91%) and 4 recurrences were marginal to MTVpre (1–33%). At dosimetric analysis, 5 recurrences (50%) were IF, 4 (40%) marginal and 1 (10%) OF. The mean D99 of the overlapping volumes MTVpre&rec was 68.1 Gy (66.5–69.2 Gy), considering a prescription dose of 70 Gy to the planning target volume (PTV).

Conclusions: Our study shows that the recurrence may originate from the volume with the highest FDG-signal. Tumor relapse in the high-dose volume supports the hypothesis that an intensification of the dose on these volumes could be further assessed to prevent local relapse.

CO38

PREDICTING TOXICITY AFTER HEAD-AND-NECK CANCER RADIOTHERAPY: SYNERGIST ROLE OF BIOLOGICAL MARKERS & DOSIMETRY?

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Aims: To assess and validate the predictive ability of RADIODTECT© (RDT) (based on phosphorylated ATM protein quantification in lymphocytes) for severe acute/late toxicity (TX) after head&neck cancer (HNC) radiotherapy (RT).

Methods: 53 consecutive HNC patients (pts) treated with radical/adjuvant RT with/without chemotherapy (CHT) and prospectively and longitudinally evaluated for TX according to CTCAE v4.0 were included in a discovery cohort to test RDT ability in predicting acute TX≥grade 3 (G3). RDT was performed at least 6 months after RT end. RDT discrimination power was evaluated through AUC. ROC curve and Youden index were used to estimate the optimal RDT cutoff, using a bootstrap analysis on 10000 resamples. An analogous population of 67 consecutive HNC pts was included in the validation cohort. These pts had also late TX evaluation till 3-year follow-up (late TX≥G3). RDT and the TX scoring in the validation cohort were done blindly. RDT performance was tested using the cut-off previously established in the training cohort without any adjustment. Analysis on the validation cohort included evaluation of the possible predictive value of the RDT when added to clinical/dosimetric variables (logistic regression models).

Results: 13/53 pts (24.5%) exhibited ≥G3 acute TX in the training cohort. Optimal threshold was estimated at 46 ng/ml. Using this cutoff, 9 and 44 pts were classified as radio-resistant (RR) and radio-sensitive (RS). In the validation cohort, 47/67 pts (70%) and 10/67 (14.9%) exhibited ≥G3 acute TX and G3 late TX, respectively. 16/67 pts were labelled as RS (AUC=0.56) using the same cutoff of 46 ng/mL. A combined biological/dosimetric model (AUC=0.78) included RDT (OR=3.3 RS *vs* RR), the minimum dose to the combined parotid glands (cPG) (OR=1.14 for 1 Gy increase) and concurrent CHT (OR=4.4). Classification of pts as RS/RR was significantly associated with ≥G3 late TX (chi-squared test p-value 0.037) with OR= 4.2 (AUC=0.65). A combined biological/dosimetric model (AUC=0.76) included RDT (OR=4.5 RS *vs* RR) and the mean dose to the cPG (OR=1.04 for 1 Gy increase).

Conclusions: RDT discrimination power is probably influenced by treatment characteristics of clinical cohorts (RT setting/doses, CHT association). Therefore it is important to combine RDT with treatment/dosimetric features (AUCs largely improved for the combined models) in predicting TX. Due to our study results, implementing RTD as an easy managing test in common RT clinical practice for HNC patients is advisable.

CO39

PROGNOSTIC VALUE OF CT-DETERMINED SARCOPENIA IN PATIENTS WITH HEAD AND NECK SQUAMOUS CELL CARCINOMA TREATED WITH CHEMORADIOTHERAPY

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Aims: The aim of the study is to evaluate the impact of sarcopenia as a prognostic factor in HNSCC (Head and Neck Squamous Cell Carcinoma) patients treated with definitive or adjuvant CRT.

Methods: This single-center retrospective analysis includes 134 HNSCC patients treated with CRT from January 2015 to June 2020. Sarcopenia was evaluated by contouring skeletal muscles at level C3 on the radiation planning CT: the volume delineated was divided by the thickness of the CT-slide, in order to obtain the CSA (cross-sectional muscle area) at the level of C3. By applying the validated algorithm described by Swartz et al. in 2016, CSA at C3 was used to estimate the CSA at L3 and then adjusted for patient height (m^2) resulting in the Skeletal Muscle Index (SMI cm^2/m^2). The impact of sarcopenia on OS and DFS was evaluated using Kaplan-Meier method.

Results: Median follow-up of the cohort was 26 months (range 3-71 months) with 71 deaths, 37 local recurrences and 15 distant recurrences. Mean SMI was 32,46 cm^2/m^2, significantly higher in men than in women (35,4 cm^2/m^2 *vs* 25,56 cm^2/m). Cut-off values for sarcopenia, corresponding to the lowest gender-specific quartile, were set at 32,2 cm^2/m^2 for men and 23,15 cm^2/m^2 for women. Patients with sarcopenia (n=33) were generally older (median age 69 years *vs* 59 years). Although not statistically significant, there was a trend which suggested a worse OS in the sarcopenic patients [HR 1,654 (0,916-2,991), p=0.096]. In the univariate analysis, we found a

statistically significant association between sarcopenia and a worse DDFS (distant disease-free survival) [HR 2,732 (1,015-7,351), p=0.047].

Conclusions: Sarcopenia can be easily assessed on pre-treatment CT scans and is a promising adverse prognostic factor for OS and DDFS in HNSCC patients.

CO40

MONOINSTITUTIONAL EXPERIENCE ON THE USE OF NIVOLUMAB IN PATIENTS WITH RECURRENT OR METASTATIC HEAD AND NECK CANCER PLATINUM-REFRACTORY

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Aims: We describe and review our experience with patients affected by recurrent/metastatic tumors of the head and neck (h&n) platinum-refractory treated Nivolumab (N) in our Radiotherapy Department since 2018.

Methods: We identified 12 patients treated with N since AIFA approval. Patients characteristics are shown in Table 1. The anatomical site of primary was heterogeneus; SCC was the most common histotype. About half of them were treated after local recurrence with radiotherapy and two or more lines of chemotherapy. All patients received at least one line of platinum-chemotherapy prior to N. We started N after progression disease or local recurrence. In all cases N was administered at a dose of 3 mg/kg every 2 weeks. We analyzed safety (according to CTCAE v 4.03) and responses were evaluated by CT o MRI every 3 months. Treatment continued until tumor progression or unacceptable toxicity. Progression free survival (PFS) was defined as the time from first cycle of N to progression disease according to RECIST criteria or death and overall survival (OS) was defined as the time from first cycle to death or last follow up express on months (m).We also treated a young woman affected by metastatic sinosal undifferentiated carcinoma treated with many chemotherapy lines, after AIFA approved us the off label use.

Results: Number of cycles of N varied between 2 and 29. OS ranged between 1 and 28 months and PFS between 1 and 24 months. Nivolumab was well tolerated, even if one patient experienced hypophysitis and an other diarrhea grade 3, so the treatment was stopped. We also stopped treatment on 3 patients for progression disease. 5 patients died for worsening of clinical conditions. At the time of the current analysis there were 3 patients continuing treatment.

Conclusions: we observed in 4 patients an OS (28m, 13m, 13m and 16m) well above the median OS obtained from Ferris and coll (7,7m). The OS of these patients was also higher than Saba's post hoc analysis stratified by age (8,2m <65 years) and also higher than Ferris' stratification by prior Cetuximab use and no Cetuximab exposure (respectively 7,1m and 8,2m). Also PFS was greater than median PFS of CheckMate 141 (2m) on 3 patients (24m, 16m, 6m).The management of metastatic and recurrent h&n cancer remains complicated and prognosis poor, despite the use of multimodality therapeutical strategy. The major problems still remain the selection of patients and predictive biomarkers of immunotherapy efficacy.

Table 1. Patients characteristics.

	Sex	Age	Location of primary	Histotype	Stage	Treatment	PD LR PR	Previous lines of therapy	PD LR	Nivolumab cycles	PFS months	OS months
1	M	69	Oral cavity (lip) PO 2013	SCC	Local recurrence PO 2015	RT-CHT (weekly Cisplatin)	LR 2018	RT+ weekly Cetuximab +5FU+ Cisplatin+ Cetuximab	LR and lung metastasis 2019	20	24 m (PD 2021 weekly paclitaxel)	28 m Last follow up
2	M	76	Hypopharynx PO 2018	SCC	Local recurrence 2018	RT-CHT (weekly Carboplatin)	LR 2019	Carboplatin+ cetuximab	LR and lung metastasis 2020	29	15 m (PD 2021 palliative care)	16 m last follow up
3	F	43	Undifferentiated Sinonasal cancer PO 2015	SNUC OFF LABEL	Local recurrence 2016	Taxotere+ Cisplatin + 5FU	LR	RT+ weekly CDDP Paclitaxel+ Cisplatin capecitabine carboplatin+ vinorelbine	PD 2019	31	6 m PD 2020 weekly paclitaxel TACE for liver metastasis	13 m death
4	M	57	Oropharinx-nasopharinx 2019	SCC	Metastatic	Cisplatin + Gemcitabine			PD	1 acute hypophysitis secondary to Nivolumab	1 m Taxotere + carboplatin	5 m death
5	F	56	Hypopharynx – larynx RT 2018	SCC	Local recurrence	Cetuximab +Carboplatin+5FU			PD	2 cycles acute grade 3/4 diarrhea	1 m Taxotere (1 cycle) re-irradiation	6 m last follow up
6	M	71	Oropharinx 2017	SCC		RT-CHT (Cetuximab)	LR 2018	Carboplatin+ 5FU+Cetuximab	PD 2019	8	2 m PD capecitabine	5 m death
7	M	62	Nasopharynx	SCC	Metastatic 2019	Taxotere+ Cisplatin+ 5FU RT- CHT (Cisplatin)	PD	Gemcitabine +5FU Carboplatin	PD	3	2 m Clinical Worsening (PD 2020 palliative care)	13 m
8	M	69	Oropharinx-larinx-hypopharinx 2007 epidermoid cancer of the lip treated with surgery	SCC	Local recurrence PO 2017	RT-CHT (Cetuximab)	Partial response	Cisplatin+5FU+ Cetuximab maintenance Cetuximab Cisplatin + Taxotere	PD 2019	1	2 m Clinical Worsening	2 m death
9	M	80	Oral cavity 2007 cancer of the oral cavity treated with surgery	SCC	Local recurrence PO 2017	post operative RT	LR	Cisplatin + Cetuximab	PD 2019	4	2 m Clinical Worsening	3 m death
10	M	62	Hypopharynx: Pyriform sinus	SCC		Post operative RT-CHT (Cisplatin) 2016	PD 2020	Taxotere+ Carboplatin + Cetuximab maintenance Cetuximab	PD	4	1 m treatment still ongoing	5m
11	M	68	Larynx 2017 conservative surgery	SCC	local recurrence 2019	total laryngectomy Post operative RT-CHT (Cisplatin)	Partial response	Cisplatin+5FU +Cetuximab maintenance Cetuximab	LR	4	1 m treatment still ongoing	1 m
12	M	67	Oropharinx	SCC		Post operative RT-CHT (Cisplatin) 2020	LR 2021		LR	2	1 m treatment still ongoing	1 m

LR local recurrence
PD progression disease
PR partial response
PFS progression free survival (progression disease/death)
OS overall survival (last follow up/death)
TACE: chemoembolization
SCC: squamous cell carcinoma

CO41

THE IMPACT OF MULTIMODALITY TREATMENT IN OPERABLE MALIGNANT PLEURAL MESOTHELIOMA. A MONOCENTRIC LARGE COHORT ANALYSIS FROM THE LAST TWO DECADES

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Aim: The aim of our study is to assess the best combination of multimodality treatment of malignant pleural mesothelioma candidate to surgery. We evaluate treatment related toxicity, progression free survival (PFS) and overall

survival (OS), by surgery modality, extra pleural pneumonectomy (EPP) *vs* pleurectomy decortication (P/D).

Methods: All pts operable and treated from 2000 to 2018 and assessed within a multidisciplinary evaluation, were included. The first surgical approach used was EPP, while from 2005 the P/D surgery was also included. Continues variables were summarized with mean and standard deviation (SD); or median and inter quartile range (IQR) accordingly to their distribution. Dosimetric data, and toxicity were collected regarding RT. At last we focused on the trimodal group (n=56), treated between 2010-2018. This last defined as neoadjuvant CT, surgery with EPP or P/D and adjuvant IMRT.

Results: Patients analyzed were 109. Pts underwent S only were 15, CT+S in 38 and 56 pts underwent to the trimodal treatment. The median follow-up for all was 95.5 months. Median OS was 16.5 months (95%CI 12.9, 24.7). Median PFS was 13.4 months (95%CI 10.3, 25.1). Despite a very low median survival the multimodal treatment (S+CT) shows slightly benefit, while the greatest improvement, both in median OS and PFS have been obtained in trimodal treatment. Median D95 to PTV was 50 Gy (IQR= 47.38-51.5). A significative association was observed between higher D95 to PTV and higher PFS (HR= 0.96, 95% CI 0.91, 1.00, p=0.049). The dose appeared to be not associated to the type of progression (in field *vs* out of field HR=0.995, 95% CI 0.90, 1.10, p=0.92). Volume of PTV was not associated to esophageal toxicity or to pneumonia, but pts without dyspnea had lower median volume of PTV compared to pts with dyspnea grade 1 or 2. Lower median heart dose (<13Gy) appeared to be associated to longer OS (HR = 1.76, 95%CI 0.894, 3.45, p=0.102). Distant recurrence was the major site of progression. Patients who underwent P/D experienced a higher incidence of mild lung or esophageal toxicity but no high-grade events were recorded.

Conclusions: Unlike the literature in our series, an increase in complications was not found after EPP. The adjuvant RT has been well-tolerated, as after EPP, as after P/D, and apparently offer an outcomes improvement to S alone or to S+CT. Finally, the result on lowering median heart dose could be of major interest for a multicentric study.

CO42

ANALYSIS OF THE COMPARISON OF PREDICTIVE MODELS OF PLANNING VMAT *vs* INTENSITY MODULATED PROTON THERAPY (IMPT) FOR THE TREATMENT OF PATIENTS WITH MALIGNANT PLEURAL MESOTHELIOMA

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Aims: To evaluate the potential benefit of optimizing intensity modulated proton therapy plans (IMPT) *vs* volumetric modulated arc therapy (VMAT) plans, applied to patients with pleural mesothelioma, through a RapidPlan (RP) model.

Methods: Patients affected by malignant pleural mesothelioma and treated with VMAT-RA after lung-sparing surgery between 2012 and 2020 were included in the analysis. The dose prescription was set to 44Gy in 2Gy per fraction, and all plans, for the comparative study were normalised to the mean dose to the clinical target volume (CTV). A cohort of 82 patients was retrospectively selected; 60 were used to "train" a dose-volume histogram predictive model; the remaining 22 provided the independent validation. The performance of the RP models was benchmarked, comparing predicted versus achieved mean and near-to-maximum dose for all organs at risk (OARs) in the training set and by quantitative assessment of some dose-volume metrics in the comparison of the validation RP-based data versus the manually optimised training datasets.

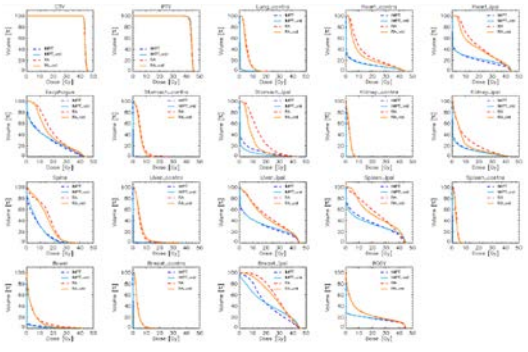

Figure 1.

Results: Treatment plans for the VMAT group and the IMPT group were found to be dosimetrically similar, regarding training and validation, and clinical planning goals were met for all facilities. The IMPT plans exceeded the VMAT plans for all OARs for contralateral regions, and allowed for a reduction in medium and low dose regions for ipsilateral OARs. Proton plans were extraordinarily better in terms of OAR savings in all cases and complete savings were achieved for contralateral structures. In particular, in the case of ipsilateral organs, the IMPT allowed a large saving in the medium-low dose ranges. Regarding target coverage, VMAT and IMPT were equivalent for CTV and PTV in both training and validation cohorts, demonstrating adequate coverage of CTV as required by the study design.

Conclusions: Two models were successfully trained and validated for VMAT and IMPT plans for pleural mesothelioma. The performance of the two models result-

ed in a high concordance between predictions and achievement. The IMPT plans outperformed the VMAT plans for all the organs at risk (with different intensity for contra- or ipsilateral structures). RP-based planning and IMPT might lead to significant dosimetric advantage and workflow simplification in managing these complex treatment indications.

CO43

A PREDICTIVE MODEL FOR OVERALL SURVIVAL IN PATIENTS TREATED WITH STEREOTACTIC RADIOTHERAPY FOR EARLY-STAGE NON-SMALL CELL LUNG CANCER

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Aim: To build and validate a predictive model of OS in patients (pts) with early stage NSCLC undergoing SBRT.

Methods: Three institutions' pts treated with SBRT (55 Gy in 5 fr or 60 Gy in 8 fr) for early-stage NSCLC were identified retrospectively to create a reference cohort (107 pts) and 2 comparative cohorts: A (32 pts) and B (38 pts). Gender, age, smoking status, Charlson Comorbidity Index (CCI), COPD GOLD classification, ECOG PS, BMI, educational qualification, history of other neoplasms (ONeo), other oncological treatments (antiblastics, surgery, RT) and number of lesions were collected. A predictive model was made using Cox regression (CR) and artificial neural networks (ANN) on reference cohort's pts. Model's efficacy was tested through Kaplan-Meier curve for survival analysis and Log Rank test for the internal comparison.

Results: All analyzed variables are shown in the table: major differences were observed in terms of age and COPD for reference cohort A, while reference cohort B diverged regarding smoking and CCI. At CR analysis, PS and ONeo were correlated to OS (PS p= 0.000, ONeo p=0.001). ANN analysis showed different degrees of importance (table). A specific model was made combining ANN findings and CR. Variables with an importance >50% or significance on CR were assigned a max. score of 2. Variables with 10-50% importance received a score of 1. So the reference cohort was divided into Group 1 (0-2 score) and Group 2 (3-9 score) to assess the variables' impact on OS. This grouping resulted to be close to statistical significance in terms of OS (p=0.081). One, 2- and 4-yrs OS resulted 93%, 85% and 65% for Group 1; 87%, 64% and 42% for Group 2. The OS analysis was performed on the comparative cohorts after the same grouping. In comparative cohort A, the model successfully assembled two groups of pts with divergent OS trends: 1- and 2 yrs OS was 100% and 100% for Group 1; 95% and 75% for Group 2. Even in comparative cohort B the model performed well with 1- and 2 yrs OS of 100% and 100% for Group 1; 74% and 42% for Group 2.

Conclusions: This predictive model, built on a cohort, interestingly performed even when applied to two different cohorts belonging to two centers. It plays as a relevant tool in the clinical practice to stratify SBRT candidates into different prognostic groups. Neural networks proved to be a valuable resource, providing useful data to build a prognostic model that certainly deserves to be validated in a prospective cohort.

Table 1.

Variable	Importance on Neural Network (%)	Cut-off	Reference cohort		Comparative cohort A		X^2	Comparative cohort B		X^2
			n	%	n	%		n	%	
Age	44,1	≤75	55	51,4	9	28,1	0,016	20	52,6	0,524
		>75	52	48,6	23	71,9		18	47,4	
		mean	75		77			74		
Pack year	35,6	≤10	24	22,4	8	25	0,465	2	5,3	0,012
		>10	83	77,6	24	75		36	94,7	
		mean	41		33			56		
Charlson Comorbidity Index	46	≤7	64	59,8	24	74	0,086	30	78,9	0,025
		>7	43	40,2	8	25		8	21,1	
		mean	7,3		6,5			6,8		
ONeo	100	No	64	59,8	18	56,3	0,436	24	63,2	0,435
		Yes	43	40,2	14	43,8		14	36,8	
Performance Status	54,4	0-1	97	90,7	31	96,9	0,23	32	84,2	0,211
		2	10	9,3	1	3,1		6	15,8	
GOLD COPD	91,4	0	30	29,4	4	12,5	0,047	2	5,3	0,005
		1-2	62	60,8	27	84,4		28	73,7	
		3-4	10	9,8	1	3,1		8	21,1	

CO44

LUNG STEREOTACTIC RADIATION THERAPY: MULTIDISCIPLINARY APPROACH TO RESPONSE ASSESSMENT

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Aim: Lung stereotactic radiation therapy (SRT) is progressively gaining ground in the treatment of both primary cancers and lung metastases. Response assessment is purely radiological and mainly CT based. Post-treatment changes in lung parenchyma can be pitfalls in evaluating the effectiveness of treatment. We reviewed post-treatment CT scans in pts undergoing lung SRT over the past 2 years, classifying radiation therapy-induced lung changes according the in four general patterns as defined by Palma *et al.*

Methods: Two radiation oncologists with extensive experience in treating lung cancers, independently reviewed CT scans of pts undergoing SRT from January 2019 to Dicember 2020. Patient's characteristics, PTV volume (expressede in "cc"), total dose, dose per fraction, biological equivalent dose reported for α/β=10 (EQD2)

were recorded and summarized in Table 1. Lung parenchyma modification patterns were reviewed and classified according to the reference radiological standards.

Results: Of 30 treated pts (32 lesions), CT scans of 20 pts (66%) for early response (<6 months) and 13 pts (43%) for late response were viewed. Early responses were: No evidence of in creased density in 4 pts, Patchy Consolidation in 6, Diffuse consolidation in 7, Patchy GGO and Diffuse GGO in 2 e 1, respectively. Late respose was available in 15 pts, wih a Modified Conventional Pattern more frequent (8 pts, 53%), followed by Mass-like fibrosis (5 pts), and 2 pts with a Scar-like fibrosis pattern. Complessively only in 2 pts it was passible to establish with sufficient certainty the response to treatment. In theese two pts the Scar-like pattern followed an early finding of No evidence of in creased density. In the other cases the absence of clear signs of progression were considered sufficient to establish disease control, still waiting to be confirmed by subsequent CT scans and/or FDG PET.

Conclusions: The exclusive morphological evaluation of the post-actinic pulmonary changes can lead to erroneous conclusions about oncological outcome in lung SRT. Lung parenchyma post-treatment changes on CT scans after SRT can be a source of misinterpretation of clinical outcome. In the absence of validated strategies for differentiation of radiation-induced lung injury versus persistent disease (radiomycs, PET, MRI, etc), it is essential to follow pts in a context of multidisciplinary discussion, where the dosimetric, clinical and radiological aspects are integrated.

Table 1. Patien's and treatment's characteristics.

	Sex	Age	Hystology	PTV volume (ml)	Dose (Gy) /Fx	Total dose (Gy)	n. of fracti ons	EQD2	Acute radiation-induced lung injury *	Late radiation-induced lung injury *
Pt 1	M	54	colon	108	7.5	60	8	87	No evidence of increased density	NE
Pt 2	F	64	lung	39	7.5	60	8	87	No evidence of increased density	Mass-like fibrosis
Pt 3	F	56	lung	38	7	56	8	79	Diffuse consolidation	Mass-like fibrosis
Pt 4	M	84	breast	55	12	48	4	88	NE	NE
Pt 5	M	77	lung	29	18	54	3	126	NE	NE
Pt 6	M	46	colon	6	18	54	3	126	No evidence of increased density	Scar-like fibrosis
Pt 7	F	68	lung	27	12	60	5	110	Patchy Consolidation	Modified Conventional
Pt 8	F	67	lung	21	9	27	3	43	Diffuse consolidation	Modified Conventional
Pt 9	F	79	lung	52	10	50	5	83	NE	Mass-like fibrosis
Pt 10	M	86	lung	82	7	56	8	79	Patchy Consolidation	NE
Pt 11	M	66	prostate	30	9	27	3	43	NE	NE
Pt 12	M	59	lung	98	8.5	34.5	4	53	Diffuse consolidation	Modified Conventional
Pt 13	M	62	H&N	42	10	30	3	50	NE	NE
Pt 14	F	79	colon	8 12	21 18	21 18	1 1	54 42	NE NE	NE NE
Pt 15	F	67	colon	20	5	50	10	62	Diffuse consolidation	Modified Conventional
Pt 16	M	72	colon	131	10	50	5	83	Diffuse consolidation	Modified Conventional
Pt 17	F	63	colon	19	5	50	10	62	Patchy Consolidation	Modified Conventional
Pt 18	F	64	lung	160	7	56	8	79	Diffuse consolidation	Modified Conventional
Pt 19	F	68	colon	15	10	50	5	83	NE	NE
Pt 20	F	72	kidney	8	8	40	5	60	Patchy Consolidation	Mass-like fibrosis
Pt 21	M	82	lung	21	7.2	50.4	7	72	NE	NE
Pt 22	F	73	lung	33	10	30	3	50	Patchy GGO	Mass-like fibrosis
Pt 23	M	58	lung	48	7	56	8	79	NE	NE
Pt 24	M	83	lung	443	8	24	3	36	Diffuse consolidation	NE
Pt 25	M	62	lung	13	15	45	3	94	No evidence of increased density	Mass-like fibrosis
Pt 26	M	74	kidney	9	10	30	3	50	Diffuse GGO	NE
Pt 27	F	51	lung	1005	8	32	4	48	No evidence of increased density	NE
Pt 28	F	70	colon	7	10	30	3	50	Patchy Consolidation	Modified Conventional
Pt 29	F	82	lung	26	12	60	5	110	Patchy consolidation	NE
Pt 30	M	83	colon	24 4	7.5 10	60 40	8 4	87 66	Patchy GGO No evidence of increased density	NE NE

*Palma DA, Radiological and Clinical pneumonitis after stereotactic lung radiotherapy: a matched analysis of three-dimensional conformal and volumetricmodulated arc therapy techniques. Int J Radiat Oncol 2011;80 506–13

CO45

EXCLUSIVE STEREOTACTIC ABLATIVE RADIOTHERAPY IN LOCALLY-ADVANCED NON-SMALL-CELL LUNG CANCER ELDERLY PATIENTS: LITTLE PALLIATION OR BIG CURE?

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Purpose: In clinical practice many elderly patients are unfit to chemotherapy (ChT) due to age and/or comorbidities and are candidates to palliative radiotherapy (RT) alone. There is a lack of prospective trials regarding the best treatment schedule in this setting of patients. We enrolled in a phase II trial unresectable locally advanced non-small cell lung cancer (LA-NSCLC) elderly patients to assess effectiveness and safety of exclusive stereotactic ablative radiotherapy (SABR).

Methods and materials: The cutoff of age ≥70 years was chosen as a commonly used definition of elderly in LA-NSCLC patients. All patients were unfit for concurrent and/or sequential ChT-RT. The tumor volume included primary tumor (T) and CT-PET positive node/s (N). A simultaneous integrated boost (SIB) was optimized to differentiate the dose for primary tumor (T) and lymph-node/s (N).

Results: 25 LA-NSCLC elderly patients unfit for concurrent and/or sequential ChT-RT were recruited. Median age was 81 years (range,72-89) and 15 (60%) were male. Histology was adenocarcinoma (ADK) and squamous cell carcinoma (SCC) in 17 (68%) and 8 (32%), respectively. The stage was IIB, IIIA and IIIB in 9(36%), 11(44%) and 5(20%) patients, respectively. All patients had ultra-central tumor with PTV overlapping the major airways. In 8 (32%) cases T and N were separately treated using SIB technique to administer a higher dose to T. Median prescribed dose was 40 Gy (range, 35-50) and 40 Gy (35-45) in 5 fractions to T and N, respectively. During a median follow-up of 18 months (range, 4-71) 6 (24%) and 7 (28%) patients had experienced isolated local recurrence and nodal regional recurrence at a median time of 9 (range, 7-17) and 9 months (range, 4-17), respectively. 5 (20%) patients developed distant metastases after a median time of 11 months (range, 4-26). At last follow-up, 19 (76%) patients were alive, 11 (44%) without radiological evidence of disease. Treatment compliance was 100% and no patients developed ≥ G3 acute and late toxicities.

Conclusions: LA-NSCLC elderly patients treated with exclusive SABR had optimal local control and promising overall survival with excellent treatment compliance and absence of ≥G3 toxicity. Our preliminary results provide an attraction to evaluate this approach in LA-NSCLC elderly patients unfit to ChT, to obtain a "big" cure beyond "little" palliation.

CO46

THE EFFICACY OF CONCURRENT NEOADJUVANT CHEMORADIOTHERAPY IN PATIENTS WITH LOCALLY ADVANCED NON-SMALL-CELL LUNG CANCER

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Aims: In LA-NSCLC concurrent neoadjuvant chemoradiotherapy followed by surgery is an established strategy of treatment. The aim of this study is to evaluate efficacy of concurrent chemoradiotherapy followed by surgery in these pts.

Methods: Pts with histologically proven NSCLC and medical/functional operability were evaluated. All pts received concurrent neoadjuvant radiochemotherapy followed by surgery. Chemotherapy drugs used included platinum compounds, taxanes, pemetrexed and gemcitabine. Some pts received induction chemotherapy before concurrent radiochemotherapy, using platinum compounds and/or taxanes. RT doses were in the range of 45-70 Gy. Primary end points were OS and DFS.

Results: 86 pts with stage IIIA-IIIB NSCLS were enrolled from January 2011 to June 2020 and classified according to histology (57 adenocarcinoma, 28 squamous, 1 carcinosarcoma), stage (7 IIB, 35 IIIA, 44 IIIB). 39 pts received induction chemotherapy (45%). After neoadjuvant approach all pts underwent surgery: 12,5% pneumonectomy, 14% bilobectomy, 68,5% lobectomy and 5% wedge resections. All pts underwent R0 surgery. In 49% downstaging was observed. 62% of pts had lymph node clearance (N0), 23% had pCR (pT0N0). Treatment was well tolerated: G2 pulmonary toxicity was observed in 10,5%. No G3-4 pulmonary toxicities were recorded. G2 oesophageal toxicities were recorded in 14% and 23% pts. No G3-4 oesophageal toxicities were observed. G2 haematological toxicity was observed in 11,6%, G3 in 8% and G4 in 10,5% of pts. With a median FUP of 30 mth, 2 and 5-year OS was 71% and 51% with median OS of 62 mth. 2 and 5-year DFS was 49% and 33% with a median DFS of 20,5 mth. Stage IIIA had a non-significant better OS than IIIB (73 *vs* 48 months). A significant improvement in OS was observed in the group with lymph node clearance with 2-years OS of 79% *vs* 71% in those who did not have it. Pts with pCR showed a non-significant higher median OS in comparison with no pCR (63 *vs* 46 months). Lymph node and pleural recurrences occurred in 19% pts and metastasis in 43% (bone, brain, adrenal gland, contralateral lung).

Conclusions: Our data showed that concurrent neoadjuvant radiochemotherapy followed by surgery is an effective approach in stage III NSCLC with excellent long - term OS and PFS as well as low treatment-related toxicity profile.

CO47

IMPACT OF ONCOLOGIC MULTIDISCIPLINARY TEAM MEETINGS LUNG (GOM LUNG A. O. PAPARDO) ON MANAGMENT AND OUTCOMES IN LOCALLY ADVANCED STAGE III LUNG CANCER PATIENTS

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Aims: This study aims to evaluate retrospectively Locally Advanced NSCLC patients treated in our Center relatively to the GOM Lung's (Radiation Oncologist, Medical Oncologist, Thoracic Surgeon, Radiologist, Pathologist) work and to the implementation of the intensity-modulated radiation therapy (IMRT) technique in our Center, since 2016 year. Primary end-point was Overall survival (OS), Secondary end-points were Progression-free Survival (PFS) and Radiation-induced lung injury (RILI).

Methods: Patients with Locally Advanced NSCLC between January 2012 and August 2019 were retrospectively reviewed. All patients underwent a pre-treatment imaging with FDG-PET/CT. The Radiation treatment planning provides: three-dimensional conformal radiation therapy (3D-CRT), intensity-modulated radiation therapy (IMRT) and, in some cases, Boost with Fractionated Stereotactic Radiotherapy (Boost-FSRT). The patients were treated according to three schemes: Exclusive Radiotherapy (eRT), Concurrent Chemo-Radiotherapy (cCRT: Paclitaxel 175 mg/mq g1+ Carboplatino AUC 5 g2 q21) and Sequential Chemo-Radiotherapy (sCRT: Gemcitabina 1250 mg/mq g1,8 + Carboplatino AUC 5 g2, q21, 3-5 cycles). Contrast enhanced CT on skull, thorax and abdomen was performed to all patients 2 months after the end of radiation treatment and, subsequently, every 3 months; FDG-PET/CT was performed every 6 months. RECIST criteria were assessed to evaluate the response to treatment and RTOG/EORTC scoring criteria were used to evaluate the radiation toxicities. Univariate and multivariate survival analysis were performed using Kaplan-Meier methods and Cox regression.

Results: A total of 110 patients were eligible for this analysis, 31 female (28.2%) and 79 male (71.8%) with a median age of 73 years (range 41-89 years) and a median follow-up of 16.3 months. The radiation treatments utilized were: 3D-CRT in 44, 3D-CRT+Boost FSRT in 6, IMRT in 56 e IMRT+Boost FSRT in 4. eRT was employed in 39 patients (35.5%), cCRT in 47 (42.7%) and sCRT in 24 (21.8%). The median OS was 42 months

(range 23.9-60.2) and the median PFS was 18.1 months (range 0.5 – 91.6 months). The incidence rates of RILI were 0.06% (7/110 patients). One patient died under treatment after rupture of major vessels. The multivariate analysis shows that since 2016 in patients treated in our Centre for locally advanced NSCLC was improved the OS response rates. The same data is found in patients with age ≥ 75 years.

Conclusions: The results of our study confirm the important role of GOM Lung's to define the Multidisciplinary approach of Stage III of Lung cancer to improve patients selection, access times to the cure allowing a better response rates to combine treatment. The use of the IMRT technique since 2016 compared to 3D-CRT, in elderly patients (≥ 75 years), has improved the survival and toxicity rates.

CO48

RE-DETERMINATION OF PD-L1 EXPRESSION AFTER CHEMO-RADIATION IN LOCALLY ADVANCED PD-L1 NEGATIVE NSCLC PATIENTS ("RECAL TRIAL"): RETROSPECTIVE MULTICENTRIC ANALYSIS

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Aims: The main purpose of this multicenter retrospective study is to evaluate the variation in PD-L1 expression before and after chemo-radiation treatment (CRT) in patients with unresecable stage III NSCLC. Secondary objective are: Impact of the re-determination of PD-L1 expression on the therapeutic process approach (possibility of administering maintenance Durvalumab), acute complications of the rebiopsy and the inter-observer variability in PD-L1 assessment at both diagnosis and post-therapy re-evaluation.

Methods: Twenty patients with unresecable stage III NSCLC, PDL1 negative at onset, who underwent CRT and subsequently re-biopsied to re-determinate PDL1 status were enrolled by 20 Italian center. Pre- and post CRT histological samples were centralized in a single laboratory for the review of PD-L1 expression. The percentage of patients undergoing Durvalumab after CRT, the percentage of non-diagnostic procedures, the acute complications of re-biopsy and the concordance between local test results and centrally reviewed tests were analyzed.

Results: The results of this study are still preliminary. Of all the patients analyzed, 2 currently showed a PDL1 expression switch with weak positivization and this gave the opportunity to start Durvalumab maintenance treatment, while in the other cases the negative result was confirmed at the re-biopsy. The re-biopsy procedure was well tolerated, however two patients experienced severe hypoxia requiring hospitalization, with recovery after two weeks.

Conclusions: Although the data analysis is still ongoing, the present study is the first work in the literature evaluating the re-determination of PDL1 after CRT. The positivization of PDL1 after CRT is not a frequent event and could be burdened with severe side effects, however it guarantees an important therapeutic chance that can influence the overall survival of these patients.

CO49

NATIONAL REGISTRY FOR THE FOLLOW-UP OF BREAST CANCER PATIENTS TREATED WITH RADIOTHERAPY: AIRO-LILT COLLABORATIVE PROJECT

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Aims: Radiation therapy in breast cancer has changed in the last two decades; in fact the improvement of the clinical indications and the availability of more effective systemic therapies allowed the adoption of personalized treatments. In daily practice many questions on the best therapeutic choices for many patients remain. For this reason a national radiotherapy follow-up program and data collection can help in guaranteeing the best treatment standards and the transferability of know-how, with a potential positive impact on the National Health System.

Methods: A collaborative project between LILT (Italian League Cancer Fight) and AIRO (Italian Association of Radiotherapy and Clinical Oncology) Breast Study Group is presented, with the aim of organizing a register for the radiotherapy follow-up in patients with breast cancer, in terms of efficacy and side effects. Breast IRRadiATA is a large dataset in a web based-application, consisting of 29 elements in 6 folders providing a drop-down list, with the possibility to select the appropriate answer about: Personal data, Surgery, Systemic therapy, Radiotherapy, Acute and late side effects. Username and password are requested for the access to all author-

ized users, to guarantee security and reliability of the register. The LILT operators of four Italian seats check the adequacy and correctness of data collection.

Results: The first purpose of the register is to create a database in breast cancer for epidemiological studies and to spread real life information about the benefits and risks of radiation treatment for breast cancer. The second purpose is the knowledge of the treatments in breast elderly patients (over 65) and their side effects in high hypo-fractionation regimens. The third aim is the assessment of the adherence of current clinical practice in Italian radiotherapy centres to the best standards of breast radiotherapy. A preliminary feasibility study is carried out in 16 Italian centres that asked to participate in the registry, to validate the simplicity and applicability of the software.

Conclusions: This project represents the implementation of a national radiotherapy follow-up registry and can help in the identification of critical issues in the radiation treatment of patients with breast cancer. The outcomes in terms of efficacy and side effects will be used to standardize treatments according to high quality level and to ensure the best care for breast cancer.

CO50

BREAST RE-IRRADIATION AFTER SECOND CONSERVATIVE SURGERY FOR IPSILATERAL BREAST CANCER RECURRENCE. SINGLE-INSTITUTION EXPERIENCE

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Aims: Standard therapy for patients with ipsilateral breast cancer recurrence (IBTR) after breast conserving treatment (BCT) is salvage mastectomy. However, there is a growing interest in second conservative therapy as a viable alternative. We reported the experience conducted on behalf of the Breast Unit ASL LT.

Methods: From 2012 to 2020 we recorded a constant increase in the number of patients suffering from breast cancer who underwent conservative surgery and subsequent moderate hypofractionated postoperative radiotherapy treatment (1279 patients). The data of these patients are entered in the Breast Unit ASL LT register and are subjected to continuous monitoring and updating of the follow-up. The hypofractionated schedule used was 42.56 Gy/16 fractions. In most cases a sequential Boost of 10 Gy/4 fractions was performed on tumor bed marked by surgical clips; in the last 5 years it was carried out according to tumor and patient related factors associated with a higher risk of IBTR (invasive breast cancer, higher tumor grade, positive excision margins, younger patient age, triple negative or HER2 positive disease). 5 of 1279 patients who developed IBTR underwent a second conservative surgery followed by re-irradiation. The hypofractionation schedule of 42.56 Gy/16 fractions on the entire breast already previously irradiated was performed again.

Results: All patients completed hypofractionated postoperative radiation treatment (retreatment after second conservative surgery) without interruption. After a minimum follow-up of 7 months (range 7- 36 months), we reported mild-moderate acute toxicity (skin erythema). Mild local late toxicity (fibrosis, skin dyschromia) and a cosmetic result that the patients defined as acceptable were reported.

Conclusions: In patients undergoing conservative surgery followed by moderate hypofractionated postoperative radiotherapy, a second conservative surgery followed by re-irradiation of the entire breast is a feasible alternative to mastectomy in selected cases of ipsilateral local recurrence diagnosis. More data and longer follow-up are needed.

CO51

SAFETY OF CONCURRENT ADJUVANT TRASTUZUMAB EMTANSINE (TDM-1) AND RADIATION THERAPY FOR RESIDUAL HER2-POSITIVE BREAST CANCER AFTER PRIMARY SYSTEMIC THERAPY

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Aims: Residual invasive disease after primary systemic therapy (PST) in patients with HER2-positive early breast cancer involves a higher risk of death and recurrence compared with patients with pathologic complete response (pCR). In the phase III KATHERINE trial, the use of adjuvant Trastuzumab Emtansine (T-DM1) reduced the risk of recurrence or death by 50% in this population compared to trastuzumab prosecution. A

recently presented subgroup analysis by Loibl et al showed an increase in grade ≥3 adverse events in the TDM-1 arm in patients treated with adjuvant radiotherapy as compared to patients not receiving radiotherapy (27.4% *vs.* 16.4%) or patients treated with trastuzumab with or without radiotherapy (15.6% *vs.* 14.6%). Our aim was to evaluate the acute side effects of TDM-1 administered concurrently with adjuvant radiotherapy in a real life multicentric register.

Methods: We retrospectively evaluated data of patients treated between January 2019 and December 2020 with concurrent TDM-1 and radiotherapy in an adjuvant setting. Left ventricular ejection fraction (LVEF) was assessed at baseline, before and after radiotherapy. All toxicities were evaluated and scored using Common Terminology Criteria of Adverse Events (CTCAE) version 5.0.

Results: A total of 25 women treated in 7 Italian institutions were included in the analysis. In the acute setting, G1-2 dermatitis was recorded in 20 patients (80%), with no G3 events described. Breast pain was reported in 3 cases (12%). Blood tests showed 3 cases of G1 leucopenia (12%) and 1 case of G1 anemia (4%); 6 patients had thrombocytopenia (24%), with 3 cases (12%) of ≥G2 toxicity. Nine cases (36%) of elevation of liver transaminases were reported, with 1 G2 (4%) and 1 G3 (4%) toxicities. Treatment with TDM-1 was interrupted in 4 patients (16%) due to the onset of thrombocytopenia or elevation of liver transaminases. Left ventricular ejection fraction (LVEF) remains stable between TDM-1 start and the end of RT with an average reduction of 0.79 point% (SD + 3.9), only 1 patient registered an asymptomatic LVEF reduction >10%.

Conclusions: The acute toxicity rate, especially focusing on skin and cardiac adverse events, were assumed acceptable in our cohort. To safely administer this concomitant treatment. Further evidence coming from larger series and prospective experiences are needed.

CO52

STEREOTACTIC RADIATION AND DUAL HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2 BLOCKADE WITH TRASTUZUMAB AND PERTUZUMAB IN THE TREATMENT OF BREAST CANCER BRAIN METASTASES

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Aims: Brain metastases (BM) are observed in 30% to 55% of metastatic HER2+ breast cancer (BC) patients. Dual HER2 blockade with trastuzumab and pertuzumab (TP) plus chemotherapy represents the first line therapy of metastatic HER2+ BC. TP showed to prolong BM free survival, however there is a lack of data on the association of TP with BM stereotactic radiotherapy (SRT). This study aims to assess the safety and efficacy of fractionated SRT (FSRT) and PT in patients with BCBM.

Methods: Patients with HER2+ BCBM who received FSRT from December 2015 to December 2019 were identified. Patients were included if they were treated with FSRT within 21 days of receiving PT. Planned total dose was 27 Gy prescribed to the 80% isodose line and delivered in three fractions. Prescription dose was reduced for lesions close to critical brain structures. Patients were evaluated 4–6 weeks after SRS and subsequently every 2–3 months with MRI re-imaging.

Results: Overall 49 patients with HER2+ BM were identified. Of these patients 9 were treated with concurrent PT to 31 HER2+ BCBM lesions. Most patients were HR+/HER2+ (6/9; 66.6%). The median dose of FSRT was 27 Gy (12–27 Gy) with a median dose per fraction of 9 Gy (4-9 Gy). The median PTV of lesions was 2.26 cm3 (0.8-54.4). With a median follow-up of 18.3 months (1.5-39.8 months) no local progression was observed. Overall response rate (complete + partial responses) was 77.5%. Only one patient developed radionecrosis to one cerebellar lesion. Median time to BM occurrence from the beginning of PT was 15.6 (1-40.5 months). Distant intracranial failure after FSRT occurred in 4/9 patients (44.4%). In 2 patients multiple lesions were observed at first follow-up MRI and after 8 months and systemic treatment was changed; in 1 patient two new lesions were observed 2 months after FSRT leading to new courses of FSRT; in another patient 3 new lesions appeared at first follow-up MRI and were treated with a subsequent course of FSRT; afterwards new other lesions were observed at follow-up MRI and the patient changed systemic therapy. Overall brain metastases median survival was 33.9 months (95%CI 24.1-43.6). Mean duration of PT treatment in these patients was 27.9 months (10.1-53.7 months).

Conclusions: In our single institution experience fSRT and TP showed to be a safe treatment for patients with BCBM with an adequate overall response rate. Thanks to fSRT duration of PT in these patients is similar to patients without BM.

CO53

GAMMA-KNIFE RADIOSURGERY OF BRAIN METASTASIS FROM BREAST CANCER

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Aims: Brain metastasis (BM) occur in about 10-16% of patients affected of advanced breast cancer (BC). In recent year overall prognosis of metastatic BC patients has improved with the introduction of new target therapies and the use of local ablative therapy in oligometastatic patients could offer an efficacy, non-invasive approach to control cranial metastasis. This report analyzes clinical outcome of BM from BC treated with GammaKnife Radiosurgery (GKRS).

Methods: Data of 58 consecutive BC patients and 149 metastases treated with GKRS for BM from November 2012 to August 2020 were retrospectively examined. We exploratory examined the relationships between clinicopathological factors and clinical outcome. Overall survival (OS), local control (LC) and distant brain control (DBC) were calculated from the date of GKRS using the Kaplan-Meier method.

Results: The median age at BMBC was 56,2 years (range: 31-80). RPA class was 1 in about half of patients (28 out of 57). Forty-two percent of patients had an estrogen receptor-positive BC, 44% were HER2 positive and 16% were Triple negative. In nineteen (34%) patients the brain was the only metastatic site. At the time of GKRS all patients had controlled extracranial disease. Mean number of brain metastasis treated with GKRS was 2.4 (range: 1-11). Mean prescription dose was 21 (15-24), 9 patients underwent a second radiosurgery course. Ten cases (17%) had a history of craniotomy and five (9%) cases had a prior WBRT. At the time of BM diagnosis 41 (72%) patients received GKRS and no change of chemotherapy schedule. Fifteen radiological radionecrosis were registered, however, three patients had symptomatic radionecrosis, two treated with steroids and one with surgery. Local control was 95%, 92% and 86% at 6, 12 and 24 months, respectively. Prior steroids therapy was related to poorer LC. Median distant brain control after GKRS was 47 months (95%CI:20-60 months), DBC was 85%, 72% and 63% at 6, 12 and 24 months, respectively. Median overall survival was 24 months (95% CI:15-45 months), overall survival was 85% at 6 months, 68% and 48% at 1 and 2 years. Patients with RPA class I had improved survival (median 45 versus 18 months, p=0.036, HR 2 C95% 1.1-3.9).

Conclusions: Our study showed that patients with no symptoms and at BM diagnosis demonstrated an improved prognosis after GK.

CO54

SHOULD NON-LUMINAL SUBTYPE BE CONSIDERED AS RISK FACTOR IN SELECTION PATIENTS FOR "ONCE-DAILY" PARTIAL BREAST IRRADIATION (OD-PBI)? OUR 10 YEARS EXPERIENCE

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Aims: The purpose of this study was to report clinical outcomes in patients treated with "once-daily" partial breast irradiation (OD-PBI), stratified as per molecular subtype and American Society for Therapeutic Radiology Oncology (ASTRO) patient selection criteria in order to determine whether molecular subtype should be recommended as one of the selection criteria for OD-PBI.

Methods: From December 2010 to November 2020, we treated 416 women with OD-PBI Tomotherapy: 38.5 Gy in 10 once-daily fractions. 397 pts had luminal subtype (A-B and B like), 19 pts (4,6%) had non-luminal subtype. Among these 13 pts (68%) had triple negative breast cancer (TNBC) and 6 pts (32%) were Her2+. Rates of ipsilateral breast tumor recurrence (IBTR), axillary failure (AF), distant metastases (DM), disease-free survival (DFS), cause-specific survival (CSS), and overall survival (OS) were analyzed for each molecular subtype and for the pooled cohorts. Clinical, pathologic, and treatment-related variables were analyzed including age, tumor stage/size, histology, grade of differentiation and lymph node status to determine their association with molecular subtype. Tumor and treatment characteristics across the subgroups were compared using the Pearson $\chi 2$ test or Fisher's exact test when sample sizes were small.

Results: With a median follow-up of 63.5 months, the rates of IBRT and AF in luminal cohort were 0.5% and 0,2%, respectively. The rates of IBRT and AF in non-luminal cohort was 0% and 10,5% respectively. Univariate analysis found that negative estrogen receptor status was the only factor significantly associated with AF (p=0.032; <.05). Non-luminal subtypes were related to treatment with adjuvant chemotherapy (p=0,002; <.05), while a trend was seen for stage (T1c-T2) (p=0.07; >.05). Between two cohort of patients no significant difference was found in terms of IBRT (0.5% *vs* 0%; p>.05), DFS (98.8% *vs* 84.6%; p>.05), DM (100% *vs* 84.6%; p>.05), CSS (100% *vs* 84.6%; p>,05) and OS (98.4% *vs* 84.6%; p>.05).

Conclusions: Excellent 5-year outcomes were seen after OD-PBI in all 416 patients. No significant differences in factors associated with IBRT were noted between cohorts. However, estrogen receptor negativity was related to adjuvant chemotherapy and was the only factor associated with AF, while a trend for stage (T1c-T2) was noted. Non-luminal subtype, as a predictive risk factor of nodal recurrence, could be considered an unsuitable criteria for OD-PBI.

CO55

HYPOFRACTIONATED RADIOTHERAPY IN 10 FRACTIONS IN NODE POSITIVE BREAST CANCER: 3 YEAR-FOLLOW UP TOXICITY OF A PHASE II STUDY

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AIMS Post-operative loco-regional (LR) hypofractionated radiotherapy (Hypo-RT) is an attractive approach in locally advanced breast cancer (LABC). The aim of this study is to report the preliminary results of the adverse effects of a 10 fractions hypofractionated schedule in patients (pts) with resected LABC. METHODS This is a single arm phase II study assessing toxicity in pts treated with 34 Gy/10 fxs/2 wks to the whole breast/chest wall and to the draining lymph nodes; an optional single fraction 8 Gy boost was administered with electrons to the tumor bed in patients who had undergone conservative surgery. Both acute (CTCAE v4.0) and late (LENT/SOMA) toxicity were collected. All pts except those who underwent mastectomy without reconstruction or with temporary expander were also asked to rate their cosmetic outcome according to the Harvard scale. Toxicity was assessed weekly during RT and then at each follow-up examination (1, 3, 6 months and then yearly). *Results:* From February 2015 to March 2019, 59 women (median age 60 years; range 31-84) with stage II to IIIA breast cancer were enrolled; 83% underwent conservative surgery, 17% mastectomy. All pts underwent axillary dissection. One patient withdrew consent to protocol follow-up. Of the 58 evaluable pts, 56 underwent neo-adjuvant (41%) or adjuvant (59%) chemotherapy. Trastuzumab was administered concomitant with RT in all HER2 positive pts (25%). RT was delivered with conformal 3D-CRT (32.8%) and then with optimized IMRT (67.2%) technique in order to improve dose distribution. A deep inspiration breath hold (DIBH) technique was used in compliant left-sided LABC pts (48.4%). All pts completed treatment as planned. At a median follow up of 42.3 months (IQR 31.4-57.2 mths), no locoregional failures were observed. Acute toxicity was as follows: grade 0, 30 pts (51.7%); grade 1, 25 pts (43.1%); grade 2, 3 pts (5.2%); no grade 2+ toxicity was recorded. Regarding late toxicity, 3 events were reported: fibrosis (1 pt, 1.7%), teleangectasia (1 pts, 1.7%), lymphedema (1 pt, 1.7%). One patient (1.7%) experienced grade 3 breast retraction. No other grade 2+ events were reported. Of eligible patients (N=51) patient-reported cosmetic outcome was excellent, good, fair and poor in 59%, 23.5%, 11.7% and 5.8% respectively. CONCLUSIONS These preliminary data support the feasibility and tolerability of our 10-fractions hypofractionated schedule after surgery for LABC.

CO56

MACHINE LEARNING-BASED MODELS FOR PREDICTING LOCOREGIONAL RELAPSE IN PT1-2 PN0-1 BREAST CANCER PATIENTS TREATED WITH MASTECTOMY

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Aims: While post-mastectomy radiotherapy (PMRT) is a mainstay for the treatment of locally-advanced breast cancer patients, indications for early-stages (namely, pT1-2 pN0-1) are less defined, and a cleared understanding of predictive factors of locoregional relapse is needed to better inform clinical indications. This study explores the potentials of machine learning (ML)-based algorithms in this clinical setting.

Methods: A total of 2632 patients, treated at the European Institute of Oncology IRCCS, between 1998 and 2006, who underwent mastectomy without subsequent radiotherapy was considered for the analysis. Three ML- and statistics-based regression models were trained to predict the locoregional recurrence and the hazard ratio associated to all the variables. For ML models a permutation method was used to estimate the importance of the clinical features on the outcome. The concordance index (c-index) was used to compare the performances.

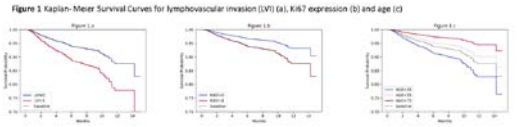

Figure 1.

Results: A total of 1823 patients was considered eligible for the analysis. Overall, Cox's proportional hazard model resulted comparable (c-index of 0.682) with the Random Survival Forest (RSF, c-index of 0.661) and the Survival Support Vector Machine (SSVM, c-index of 0.672). At statistical analysis, the most predictive features were the presence of lympho-vascular invasion (+90%), Ki67 expression (+86%) and advancing age (-3%) which reduces the overall risk of LRR. In the case of the RSF the variables that weight the most on the accuracy of the model were the lympho-vascular invasion (+0.020), the molecular subtype (+0.025) and Ki67 expression (+0.019); whilst for the SSVM were the lympho-vascular invasion (+0.020), the pT (+0.025) and Ki67 expression.

Conclusions: Even if ML algorithms do not allow to achieve quantitative estimation of the weight of patient- and

disease- related characteristics on the risk of locoregional relapse, the prediction accuracy is comparable in terms of c-index values between Cox's analysis and ML algorithms. Overall, Cox analysis only permits to quantify the risk, and to provide clearer and more interpretable indications on the need of performing post-mastectomy radiotherapy. In perspective, external validation would be beneficial in to confirm our results.

CO57

RE-IRRADIATION OF LOCALLY RECURRENT RECTAL CANCER: A NATIONAL SURVEY BY THE AIRO GASTROINTESTINAL STUDY GROUP

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Aims: In locally recurrent (LR) rectal cancer, achieving a radical resection (R0) is the most important prognostic factor for OS. Re-irradiation (re-RT) may increase the rate of R0 resection, however guidelines regarding prescribed dose, delivery techniques and dose constraints for re-RT in rectal cancer recurrence are lacking. The Italian Association of Radiation and clinical Oncology study group for gastrointestinal malignancies (AIRO-GI) proposed a national survey to investigate the current clinical practice in this setting of patients.

Methods: In February 2021 the survey was designed and approved between members of the AIRO-GI. In March 2021, the survey was administered to all members of GI group.

Results: The questionnaire consisted of 40 questions investigating center characteristics, clinical indications, dose and treatment techniques of re-RT in LR rectal cancer. Thirty-seven questionnaires were completed and returned. A multidisciplinary team and an expert radiation oncology dedicated to lower GI pathologies with at least 10 years of experience were present in the majority of responding centers (> 80%). The stage of LR rectal cancer was defined considering site of recurrence and pelvic organs infiltration in 80-90% of cases. In patients with resectable LR rectal cancer, neoadjuvant treatment, including re-RT, was an option in 40% of the responding centers reaching 60% in unresectable cases. For conventional fractionated radiotherapy (RT), the dose of 30-40 Gy (1.8-2 Gy/die) was preferred by 65% while dose up to 30-35 Gy in 5 fractions was chosen in 60% of centers for hypofractionated RT. High quality RT treatments (IMRT/SBRT) and daily IGRT protocols were employed in 94% of centers. Best timing to evaluate response to treatment was 7-8 weeks in 59%. Assuming a/b=5 Gy, the EqD2 of re-RT was 38-40Gy for 80% of responding centers while a total EqD2(a/b=5 Gy) considering re-RT and previously treatment was 90-100 Gy in 46%. Concomitant chemotherapy with capecitabine was prescribed by 50% of centers.

Conclusions: Our survey showed a high quality of treatment and management of LR rectal cancer. Multidisciplinary discussion is considered mandatory as well as daily IGRT protocols and IMRT technique. Substantial variability emerged in terms of dose and fractionation. Use of stereotactic treatment for re-RT is increasing, prospective trials are needed to better elucidate dose and fractionation, together with toxicity profile and oncological outcomes.

CO58

OUTCOME ANALYSIS OF DIFFERENT THERAPEUTIC OPTIONS IN LOCALLY ADVANCED PANCREATIC CANCER: A PREDICTIVE MODEL FROM A MULTICENTER STUDY (PAULA-1)

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Aims: Different treatment options are suggested by international guidelines in locally advanced pancreatic cancer (LAPC): definitive chemotherapy (CHT), chemoradiation (CRT), and stereotactic body radiotherapy (SBRT). The purpose of this analysis was to retrospectively compare these therapies in terms of: overall survival (OS), local control (LC), and distant metastasis free-survival (DMFS). Moreover, we developed a predictive model of LC in LAPC.

Methods: LAPC patients from a multicentric retrospective database (PAULA-1) were included. Survival curves were calculated with the Kaplan-Meier method and compared with the log-rank test. Multivariable analysis (Cox's proportional hazard model) was used to identify predictors of LC, OS, and DMFS. The LC predictive model was developed based on random forest machine learning method.

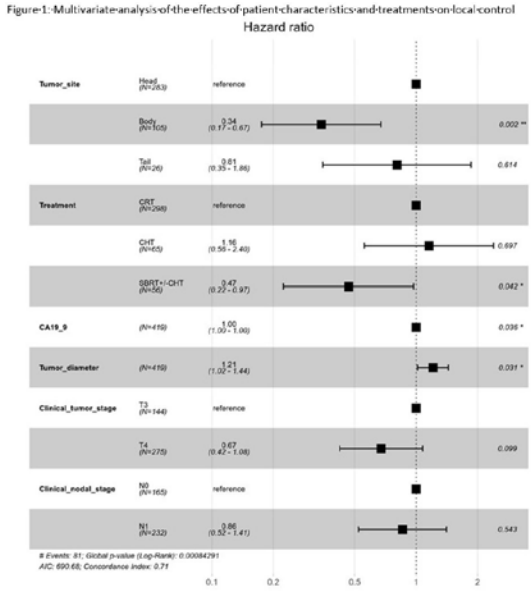

Figure 1.

Results: Median follow-up was 16.6 months (range: 3.0-92.0). Of 419 patients included, 298 (71.1%) were treated with CRT, 65 (15.5%) with CHT, and 56 (13.4%) with SBRT. At univariate and multivariable analysis, tumor of the pancreatic body (p=0.002) and SBRT (0.042) were both significantly correlated with improved LC (Figure 1). At univariate and multivariable analysis, both pancreatic tail as tumor site (p=0.043) and ECOG 2 status (p=0.009) were significantly correlated with improved and worse OS, respectively. At multivariable analysis, increased CA19-9 negatively impacted on OS, LC, and DMFS. Finally, the LC predictive model reached an AUC of 68% (CI 58.7%-77.4%).

Conclusions: Results after SBRT are similar to the ones after CHT and CRT in terms of OS and DMFS. An improved LC was recorded after SBRT. Furthermore, we proposed a predictive model for LC potentially useful for treatment personalization. Randomized trials are needed to confirm the role of SBRT and to evaluate if the improved LC can translate in better quality of life.

CO59

PROSPECTIVE PHASE II STUDY ON VOLUME DE-ESCALATION IN NEOADJUVANT CHEMORADIOTHERAPY OF RECTAL CANCER: DOSIMETRIC ANALYSIS AND CLINICAL IMPLICATIONS

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Aims: In the current study we analysed the dosimetric data on patients enrolled in a prospective phase II study on volume de-escalation in neoadjuvant chemoradiotherapy (CRT) of locally advanced rectal cancer (LARC) compared to an historical matched-control patient group.

Methods: Fifty-two patients with LARC (T2 low-lying/T3, N0-N1) were enrolled. Reduced treatment volumes, due to the exclusion of elective nodal irradiation, were delineated. The CTV included the primary tumor and mesorectum with vascular supply containing the perirectal and presacral nodes. The PTV was defined by the CTV with a margin of 1 cm in all directions. Radiation therapy was delivered with a total dose of 50.4 (28fx/1.8Gy). The control group (51 patients) received standard treatment. In both, concomitant fluoropyrimidine-based chemotherapy was associated. We analysed dose parameters of the main organs at risk (OARs) for the two groups (reduced *vs* standard volumes): small bowel (V5, V10, V15, V20, V30, V45), bladder (Dmax, V5, V10, V15, V20, V35, V50) and femoral heads (V52). Treatment interruptions (≥ 5 days) due to adverse events were the primary clinical endpoint of this analysis. The dosimetric variables were compared using the independent sample t-test. A 2-sided p value of 0.05 was consid-

ered significant.

Results: The mean volume of de-escalated PTV was 495.5cc±169.8cc (range, 231.0cc– 920.3cc) compared with standard PTV (mean 1055.37cc±204.44cc; range, 620.6cc – 1696.9cc). The V5, V10, V15, V20, V30, V45 of small bowel were significantly lower in the reduced volumes group (mean 170.9cc, 131.8cc, 54.1cc, 35.2cc, 25.5cc, 13.4cc respectively), in comparison with the standard group (mean 531.3cc, 429.4cc, 302.0cc, 231.8cc, 139.3cc, 60.2cc respectively; p<0.001). The Dmax, V5, V10, V15, V20, V35, V50 of the bladder were also significantly lower in the experimental group (mean 65.7Gy, 94.1%, 90.4%, 65.3%, 13.1%, 2.5% respectively) than in the control group (mean 55.9Gy, 100.6%, 99.2%, 94.1%, 56.7%, 6.6% respectively; p<0.033). Moreover, the left and right femoral heads V52Gy was lower in the first group (p=0.042). Treatment interruptions due to gastrointestinal toxicity in the two groups was 11.5% *vs* 41.1%, respectively (p=0.001).

Conclusions: This is the first study to show significant dose reduction for OARs given by the reduction of target volume in LARC, while improving clinical outcomes as shown in the final report of the study protocol. This is probably related to the biological effect associated with the low number of interruption days.

CO60

PROGNOSTIC FACTOR IN ANAL CANCER PATIENTS TREATED WITH CONCURRENT CHEMO-RADIATION

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Aims: Inflammatory profile has been widely evaluated in many solid tumors. Recently the Systemic Immune-inflammation Index (SII) has been used as a prognostic index in some solid malignant tumors. The baseline hemoglobin (Hb) level has been identified as a prognostic indicator of poor response to radio-chemotherapy treatment in patients with anal squamous cell carcinoma (SCC). A recent study developed a simple scoring system based on the previously mentioned laboratory indexes of inflammation (HEI index). Here we evaluate the HEI index in our patients.

Methods and Materials: Clinical records from patients with SCC of the anus treated with curative intent between January 2007 to January 2021 were retrospectively analyzed. We investigated the correlation between baseline clinical and laboratory variables and PFS and OS using Kaplan–Meier survival curves, and a p-value < 0.05 was considered statistically significant. NLR was defined as the neutrophil / lymphocyte ratio, the PLR as the platelet / lymphocyte ratio, the SII as platelets x neutrophils / lymphocytes. NLR and PLR were dichotomized based on the results of Receiver Operating Characteristic (ROC) curves. Previously identified cut-offs were used for SII, hemoglobin and eosinophils. HEI Index was calculated with a score=1 for each variable: Hb≤12 g/dL, SII≥560 and eosinophil count ≥100/μL, based on full blood exams before CHT-RT. According to HEI index, patients were stratified in low-risk (from 0 to 1 negative prognostic factors) and high-risk (from 2 to 3 negative prognostic factors).

Results: 38 patients were identified (Table 1). Univariate analysis showed an association between PFS and baseline hemoglobin levels ≥12 g/dL (p=0.0184) as well as with PLR <250 (p=0.05), while OS was statistically correlated with NLR <4 (p=0.0037). Univariate analysis showed a correlation between PFS and OS with HEI INDEX 0-1 (low risk, p=0.0090 and p=0.03 respectively). Multivariate analysis confirmed the association between HEI Index with OS (RR: 78, 95% CI: 1.5-3812, p=0.028) as well as with PFS (RR : 19.9, 95% CI: 1.24-320.4, p=0.034).

Conclusions: Our findings suggest that elevated pretreatment NLR and PLR are potentially associated with poor survival outcome in patients with anal cancer who undergo to definitive chemoradiation. Moreover, our results support the possible prognostic role of HEI INDEX with PFS and OS.

Table 1. Patients characteristic.

Characteristic	Value (%)
Gender	
Male	9 (24%)
Female	29 (76%)
Age (mean)	59 yrs
ECOG Performance Status	
0	24 (63%)
1	14 (37%)
2	0
HIV infection	
Yes	3 (8%)
No	35 (92%)
Smoking	
Yes	14 (37%)
No	24 (63%)
Clinical stage	
I	2 (5%)
IIa	5 (13%)
IIb	7 (18%)
IIIa	8 (21%)
IIIb	12 (32%)
IIIc	4 (11%)
IV	0
Chemiotherapy	
MMC/5-FU	14 (37%)
CDDP/5-FU	20 (52%)
5-FU alone	4 (11%)
Radiotherapy	
3D	21 (55%)
IMRT	17 (45%)

CO61

A PREDICTIVE MODEL OF 2 YEARS DISEASE FREE SURVIVAL DURING MR GUIDED RADIOTHERAPY NEOADJUVANT CHEMORADIOTHERAPY IN LOCALLY ADVANCED RECTAL CANCER PATIENTS

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Aims: Distant metastasis is the main cause of treatment failure in locally advanced rectal cancer (LARC) patients (pts), despite the recent improvement in the treatment strategies. This study aims to evaluate the "delta radiomics" approach in pts undergoing neoadjuvant chemoradiotherapy (nCRT) treated with magnetic resonance-guided radiotherapy (MRgRT), developing a logistic regression model able to predict 2-years disease-free-survival (2yDFS).

Table 1 and Figure 1.

	Number of Patients (%)
Median Age (range)	62 (40-87)
Sex	
• Male	31 (68.9%)
• Female	14 (31.1%)
cT	
• 2	5 (11.1%)
• 3	27 (60%)
• 4	13 (28.9%)
cN	
• 0	11 (24.4%)
• +	34 (75.6%)
Median Radiotherapy Dose [Gy] (range)	55 (50-59.4)
Median interval between end of nCRT and surgery [weeks] (range)	14.4 (5.9-22.6)
Surgical procedure	
• APR	2 (4.4%)
• AR	32 (71.2%)
• TEM/EL	2 (4.4%)
• No surgery	9 (20%)
ypT	
• 0	7 (19.4%)
• 1	1 (2.8%)
• 2	10 (27.8%)
• 3	18 (50%)
ypN	
• 0	27 (75%)
• +	9 (25%)
pCR/cCR	
• Yes	13 (28.9%)
• No	32 (71.1%)
Adjuvant CT type	
• Yes With Oxa	16 (35.6%)
• Yes Without Oxa	2 (4.4%)
• No	27 (60%)
2yDFS	
• Yes	38 (84.4%)
• No	7 (15.6%)

CT: chemotherapy; pCR: pathological complete response; cCR: clinical complete response; AR: anterior resection; APR: abdominal-perineal resection; TEM: transanal endoscopic microsurgery; EL: Local excision; 2yDFS: 2 years disease free survival

Table 1. Patient characteristics

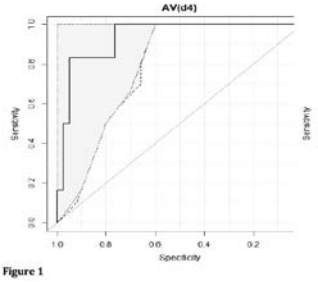

Figure 1

Methods: The pts enrolled come from two institutions: an Italian center and an American center (US). Italian patients underwent MRgRT with a simultaneous integrated boost (SIB) technique in 25 fractions with a boost of 55Gy on Gross Tumor Volume (GTV) plus the corresponding mesorectum. US pts delivered a sequential treatment reaching 50.4 Gy in 28 fractions to GTV and corresponding mesorectum. Concomitant chemotherapy with capecitabine/5-fluorouracil or an intensification schedule with oxaliplatin was prescribed, in relation to clinical stage and high risk factors. For each pt, a total of 6 T2*/T1 MR images were considered for the analysis at simulation and at 5, 10, 15, 20 and 25 fractions. A total of 90 radiomic features (RF) were extracted from each MRI considering the GTV as region of interest. The variations of RF during treatment were quantified calculating the delta RF, which were the ratio between the values calculated at different dose levels and the one extracted at simulation. The Wilcoxon–Mann–Whitney test was performed to identify the ability of each feature in predicting 2yDFS at the univariate analysis. A logistic regression model considering three delta RF was finally calculated, evaluating its performance in terms of ROC curve.

Results: Data regarding 45 LARC pts were collected and reported in Table 1. Pathological complete response was reached in 13 cases (28.9%), whereas 6 pts (13.3%) developed metastases. At the univariate analysis, a total of 76 RF resulted to be significant in identifying 2yDFS. The most significant RF was the variation in terms of area/surface ratio between fraction 20 and simulation, which showed an AUC of 0.93 (Figure 1).

Conclusions: The results of this study supports a promising role of delta radiomics analysis on low-field MR images in predicting 2yDFS for LARC pts. Further analyses including larger cohort of pts and an external validation are needed to confirm these preliminary results.

CO62

DOSE-PAINTING STEREOTACTIC BODY RADIATION THERAPY ON TUMOR-VESSEL AND DUODENAL INTERFACES FOR UNRESECTABLE PANCREATIC CANCER: A DOSIMETRIC ANALYSIS

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Aims: Stereotactic body radiation therapy (SBRT) is an important treatment option for pancreatic cancer (PC). This study was conducted to analyse the results of a dose-painting SBRT approach with higher biologically effective doses on tumor-vessel interface (TVI) to increase surgical resectability and reduced doses on simultaneous integrated protection (SIP) to protect duodenum for unresectable PC.

Methods: Frameless set-up was used for CT simulation. Gross Tumor Volume (GTV) was contoured by a dynamic co-registration of CT simulation with diagnostic

CT scan. Integrate GTV was delineated including tumor-vessel interface (iGTV= GTV+TVI). A Planning target volume (PTV) was obtained adding 5mm to Internal Target Volume (ITV), generated by 4DCBCT (Symmetry™). Within the PTV, two volumes were delineated: a PTV-SIP, inside which the prescription dose was reduced according to duodenum dose constraints, defined as the intersection between the PTV and the Planning Organ at Risk (PRV) for the duodenum (duodenum + 3 mm), and a PTV boost generated to administer higher doses to cover the tumor-vessel interface inside the GTV. A differential dose distribution by a Simultaneous Integrated Boost (SIB) technique was planned.

Results: Three pilot cases have been analyzed. Dose constraint for duodenum was set as maximum dose (0.5cc) <33Gy (5 fractions). Dose prescription on all cases was 35Gy (5 consecutive daily fraction, 60 Gy BED10), with minimal dose to PTVs of 25Gy, and 40Gy on PTV boost (72Gy BED10). Case1: PTV volume =52cc, PTVSIP volume =12cc, PTV boost volume =8cc. Case2: PTV volume =126cc, PTVSIP volume =15cc, PTV boost volume =57cc. Case3: PTV volume =107cc, PTVSIP volume =10cc, PTV volume boost=44cc. In the three cases, the mean dose on PTV were 35.5, 36,7 37.1 Gy, the mean dose on PTVSIP were 32, 31, 33 Gy, the mean dose on PTVs boost were 40, 41, 39 Gy and the maximum dose on PTVs boost were 41.7, 42.3, 41 Gy, respectively. Volumes and dose distribution of case 1 is showed in Figure 1.

Conclusions: Our preliminary results showed that SIB/ SIP approach in pancreatic SBRT is feasible and may prevent damage to duodenum giving a safe administration of ablative doses to the tumor. This dose-painting could facilitate the conversion to negative margin resection and to enhance local tumor control and survival, increasing the therapeutic window of clinical benefit. A prospective clinical study is currently ongoing to confirm the efficacy on outcomes.

Figure 1. PTV delineation (**a**) and dose distribution (**b**) of SBRT dose-painting approach with Simultaneous Integrated Boost (SIB) and Simultaneous Integrated Protection (SIP) for PC. PTV (red) = GTV (yellow) + tumor-vessel interface (TVI). PTV SIP (light blu) = overlap area between the PTV and PRV duodenum (white).

Figure 1.

CO63

STEREOTACTIC BODY RADIATION THERAPY (SBRT) IN PATIENTS WITH HEPATOCELLULAR CARCINOMA (HCC): A MONOCENTRIC EXPERIENCE

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Aims: In hepatocellular carcinoma (HCC), Stereotactic Body Radiotherapy (SBRT) commonly reserved for patients with unresectable disease, or in cases of lesions located near large vessels, just below the diaphragm, or larger than 4 cm, where other local treatment such as thermal ablation cannot be used. However, it is not included in major international guidelines as an initial treatment for HCC at any stage, mainly due to the absence of prospective randomized studies. The aim of this study was to analyze the results of a large monocentric group of HCC patients treated with SBRT, assessing the impact of this approach on the clinical outcome.

Characteristic	n	%
Number of patients	133	
Male	56	42
Female	77	58
Median age (range)	76 years (21-90)	
Child-Pugh class		
A	90	68
B	43	32
BCLC stage		
A	61	46
B	64	48
C	8	6
Hepatitis etiology		
Viral	83	62
Alcoholic	32	24
No hepatitis	18	14
Number of lesions	245	
1	61	46
2	40	30
3	24	18
4	8	6
Previous systemic treatment		
Yes	21	16
No	112	84
Previous local treatments		
Yes	93	70
No	40	30
Lesion diameter (mm)	36, median (17-99, range)	

Tabella 1. Patient's and disease's characteristics.

Methods: All HCC patients treated with SBRT

between 2010 to 2020 at our Institution were retrospectively assessed. Patients with up to 4 liver lesions, any maximum diameter and no extrahepatic metastases were included in our analysis. The gross tumour volume (GTV) coincided with the clinical target volume (CTV). The internal target volume (ITV) was generated by the CTV considering all the different respiratory phases to CT-scans. The Planning target volume (PTV) consisted of ITV plus an isotropic margin of 5 mm. Patients were treated with a dose of 30-75 Gy in 3-10 fractions using the technique of modulated arc volumetric therapy in its RapidArc form and flattening filter-free beams. Local control (LC) and overall survival (OS) were calculated.

Results: Overall, 133 patients for a total of 245 lesions were included. The details are described in Table 1. At a median follow-up of 19 months (range 3–100), 56 patients were alive 42.1%). One- and 2-years rates of LC were 87.9% (95% CI 81.1–92.4) and 79.5% (95% CI 69.0–86.8). In terms of OS, the 1- and 2-years rates were 78.6% (95% CI 69.8–97.6) and 48% (95% CI 37.2–58). In multivariate analysis, previous liver surgery (HR 0.74, 95% CI 0.27-0.85; p 0.012) HBV-related infection (HR 1.61, 95% CI 2.19-11.46; p 0.0001) and radiological response after SBRT (HR 0.29, 95% CI 1.13-1.57; p 0.0006) were significantly correlated with prolonged OS. No association was found between LC and patients/disease characteristics in Cox proportional-hazard regression analysis. Globally, SBRT was well tolerated with no grade 4 or 5 toxicity.

Conclusions: Our analysis confirms the efficacy of SBRT in the treatment of HCC patients with an acceptable toxicity profile.

CO64

HYPOFRACTIONATED RADIOTHERAPY AFTER INDUCTION CHEMOTHERAPY FOR ADVANCED PANCREATIC CANCER

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Aims: To assess feasibility, toxicity and outcome of hypofractionated radiotherapy (RT) concomitant to capecitabine (cape) after induction chemotherapy (iCT) for advanced pancreatic cancer (APC) in stage III or IV.

Methods: Patients (pts) with APC without distant progression after iCT were considered. RT consisted of 44.25 Gy in 15 frs to the tumor and involved lymph-nodes adding margins of 1-1-1.5 cm from GTV and was delivered concomitant to cape; 59 pts received a SIB of 48-58 Gy to a sub-volume infiltrating regional vessels (within a Phase I study) or to PET+ residual. Second and third line CT was allowed in case of progression after RTCT. All pts were evaluated for acute and late toxicity. Overall survival (OS), progression free survival (PFS), distant PFS (DPFS) and local PFS (LPFS) were assessed from the start of iCT only in pts with stage III. The predictive value of selected parameters was tested by univariate/multivariate Cox analyses: gender, age, iCT, number (n°) of CT cycles (≥ or < median n°), target volume, GICA value pre-RT (≥ or < median value).

Results: From 11/2004 to 06/2019, 244 APC, 206 stage III, 38 stage IV, were treated; median follow-up was 17.9 months (m). ICT consisted of GMC alone: 36 pts, combination CT with at least 2 drugs: 208 pts; median n° of cycles was 6. Three pts did not complete RTCT (1 early progression, 2 toxicity); median duration of RTCT was 20 days. Acute GI toxicity. G≥2: 52/244 pts (21.3%), G3: 8 pts (3.3%). Late toxicity. G ≥2: 20 pts (8.2%), G ≥3: 15 pts (6.1%). G ≥2 and G ≥3 late toxicity occurred in 11 (18.6%) and 9 (5.7%) out of 59 pts treated with SIB, respectively, significantly higher ($p<0.01$) compared to values in pts without SIB (9 and 6/185, 4.8% and 3.2% respectively). Median OS, PFS, DPFS and LPFS, assessed in stage III, were 26, 11.9, 12.8 and 15.1 m, respectively. At univariate analysis, gender, and GICA value pre-RT were the only predictive variables for OS. GICA pre-RT was confirmed at multivariate analysis: median OS was 20 and 29.3 m in pts with GICA pre-RT higher or lower to the median value (91), respectively ($p=0.05$). Gender ($p=0.03$) and GICA pre-RT ($p=0.04$) were also the only predictive variables for DPFS. None of all variables were associated to LPFS.

Conclusions: Hypofrationated RT after iCT is feasible with acceptable acute and late toxicity rate. A dose > 44.25 Gy is significantly more toxic even when delivered on small sub-volumes. Outcome of present study compares favourably with results obtained with standard fractionation.

CO65

ROLE OF RADIOTHERAPY AND HEI INDEX IN MCRPC PATIENTS

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Aims: The aims of the study are to evaluate how the addition of radiotherapy could extend the efficacy of Androgen Receptor-Targeted Agents (ARTA) in oligo-progressive metastatic Castration Resistant Prostate Cancer (mCRPC) patients and to study the Hemo-Eosinophils Inflammation (HEI) Index as a prognostic factor.

Methods: mCRPC patients have been treated with ARTA: Enzalutamide (ENZA) or Abiraterone Acetate plus Prednisone (AAP). No patients received docetaxel before ARTA while everyone maintained LHRH-analogue during

castration resistant phase. Patients with PSA progression during ARTA have been evaluated by 18F-Choline PET-TC and it was added ablative radiotherapy (SBRT) to the site of progression. Progression Free Survival 1 (PFS1) was calculated from the start of ARTA up to its end or the start of aRT; PFS2 from irradiation for oligoprogressive disease up to change or definitive end of systemic treatment. HEI Index was calculated with a score=1 for each variable: Hb < 12 g/dL, SII > 560 and eosinophil count ≥100/μL, based on full blood exams before ARTA. According to HEI index, patients were stratified in low-risk (from 0 to 1 negative prognostic factors) and high-risk (from 2 to 3 negative prognostic factors).

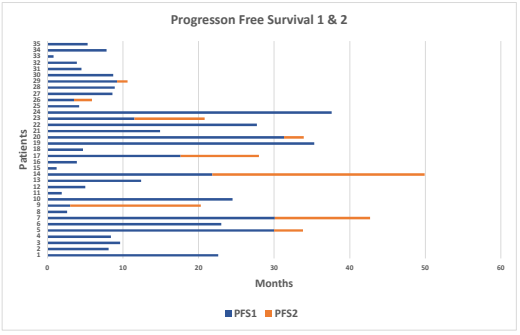

Figure 1. PFS1 and PFS2 for each patient.

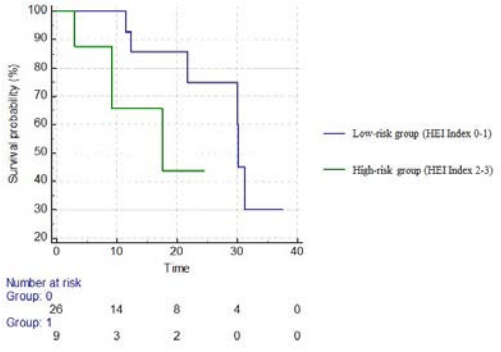

Figure 2. PFS1 in HEI Index high-risk group and low-risk group.

Results: From August 2016 to April 2021, 35 mCRPC patients (median age of 79 years) were treated with ARTA (20 APP, 15 ENZA) and 9 of them (6 AAP, 3 ENZA) received additional SBRT (4 bones, 4 lymph nodes, 1 local recurrence). A patient treated with SBRT recorded a Grade 1 urinary toxicity (CTCAE v.5). According to ISUP 2016 Classification, 3/35 patients were Grade 1, 4/35 Grade 2, 10/35 Grade 3, 11/35 Grade 4 and 7/35 Grade 5. Median PFS1 was 9,6 months; while PFS2 was 3.8 months (pt 5), 12,6 months (pt 7), 17,3 months (pt 9), 28,1 months (pt 14),10.4 months (pt 17), 2.6 months (pt 20), 9,3 months (pt 23), 2,4 months (pt 26) and 1,4 months (pt 29) (Figure 1). Based on HEI Index, the low-risk group consists of 26 patients (16 AAP, 10 ENZA), while the high-risk group of 9 patients (5 ENZA, 4 AAP). According to HEI index, median PFS1 was 30,1 months in low risk and 17,6 months in high risk (HR 0,18, 95% CI:0,026-1,30; p=0,09) (Figure 2) .

Conclusions: The results confirm how combination of ARTA and SBRT can delay other systemic therapy in oligoprogressive mCRPC patients. The HEI Index potentially correlates with PFS1 even with imprecise results, and it could be explored as a predictive factor in mCRPC patients.

CO66

PATTERN OF RECURRENCE AFTER SBRT IN PROSTATE CANCER PATIENTS WITH NODAL PELVIC RELAPSE

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Aims: Salvage radiotherapy is the main treatment option for biochemical relapse (BCR) after radical prostatectomy (RP). Novel imaging, such as Choline and PSMA PET, improved staging sensibility in BCR. However, no standard management is recommended for isolated pelvic nodal relapse, and comparative data between different strategies are lacking. One option is nodal stereotactic body radiotherapy (SBRT). We retrospectively analysed recurrence patterns after nodal SBRT in patients (PT) affected by pelvic oligometastatic relapse after RP.

Materials and Methods: Data about 93 PT consecutively treated in 5 different institutions. Inclusion criteria were BCR after RP with < 3 metachronous lymphoadenopathies under aortic bifurcation. PT underwent SBRT on all sites of disease. Concomitant ADT was allowed. PT treated on prostate bed +/- pelvic nodal volumes were excluded from the analysis.

Results: After a median follow-up of 20 months, 57 PT had post-SBRT radiological evidence of relapse, for a median disease-free survival (DFS) of 15 months (95% CI 9-24). Concomitant ADT was administered in 20 (21.5%) PT. Considering only PT in whom concomitant

ADT was not administered, median ADT-free survival was not reached. Overall, 8 (8.6%), 21 (22.6%) and 28 (30.1%) PT had prostate bed only, pelvic nodal or distant relapse, respectively. Concomitant ADT, ISUP pattern at diagnosis < or > 3, time to relapse < or > 12 months, PSA at recurrence < or > 1.10 ng/m and PSMA staging were not significantly associated with DFS. After relapse, 42 PT (45.2%) received a second SBRT course.

Conclusion: Nodal SBRT yielded encouraging DFS and ADT-free survival in this population. Despite the high rate of recurrences, only a minority of PT developed prostate bed recurrence, suggesting that local treatment may be safely avoided. Considering that the majority of PT developed distant metastases and were managed with a second SBRT course, upfront pelvic prophylactic treatment could be considered unnecessary in this population. In order to maximize the benefit of this approach in pelvic nodal relapse setting, reliable selection criteria are needed. Interestingly, early detection of nodal relapse with PSMA staging did not seem to influence the outcome in this setting.

CO67

TEN-YEAR RESULTS OF PELVIC IRRADIATION AND HIGH-DOSE MODERATELY HYPOFRACTIONATED SIMULTANEOUS BOOST ON PROSTATE IN UNFAVORABLE INTERMEDIATE, HIGH AND VERY HIGH-RISK PROSTATE CANCER

N.G. Di Muzio[1,2], C.L. Deantoni[1], C. Brombin[2,3], C. Fiorino[2,4], C. Cozzarini[1], F. Zerbetto[1], P. Mangili[4], R. Tummineri[1], I. Dell'Oca[1], S. Broggi[4], M. Pasetti[1], A. Chiara[1], P.M.V. Rancoita[2,3], L. Perna[4], A. Del Vecchio[4], M.S. Di Serio[2,3], A. Fodor[1]

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Aims: To report 10-year outcomes of pelvic lymph-nodal prophylactic irradiation (WPRT) and high-dose (HD) moderately hypofractionated simultaneous integrated boost (SIB) on prostate and seminal vesicles in unfavorable intermediate- (UIR), high- (HR) and very high-risk (VHR) prostate cancer (PCa).

Methods: From 06/2004-12/2015, 224 UIR, HR and VHR PCa pts were treated with Tomotherapy® (Accuray, Sunnyvale, CA) with WPRT to 51.8 Gy/28 fractions and SIB to 74.2 Gy (EQD2 88 Gy) to prostate and lower third of seminal vesicles. Neoadjuvant androgen deprivation therapy (ADT) was prescribed in 83% of pts for a median of 3.55 months (IQR: 2.45-5.3), adjuvant ADT in 80.8% of pts for a median of 22.71 months (IQR:13.69-31.70) and in 77.7% of pts both.

Results: Median follow-up was 96.3 months (IQR:71.0-124.6). Median age at diagnosis 74.9 years (IQR:71.3-78.1). Late gastro-intestinal (GI) toxicity was: 8% G2 and 8.5% G3. At the last follow up 3.1% of pts presented G3 GI toxicity. Late genito-urinary (GU) toxicity was 15.6% G2 and 12.5% G3-G4. At the last follow-up 8% of pts presented≥G3 GU toxicity. 10-year biochemical relapse-free survival (bRFS) was 79.1%(95%CI:71.5-87.5), clinical relapse-free survival (CRFS) was 87%(95%CI:80.8-93.6%), while overall survival from diagnosis was 65.7%(95%CI:58.2-74.1). Cause specific survival at 10 years from diagnosis was 94.9% (95% CI: 91% -99%). Only 2 pts presented local relapse. Very high-risk group *vs* unfavorable intermediate risk group resulted to be a significant risk factor for biochemical relapse (HR:2.8,95%CI:1.17-6.68,p=0.021). In the final selected multivariate model, only Gleason score 4/5 emerged as significant risk factor for biochemical relapse (HR=2.1,95%CI:1.05-4.37,p=0.036) (see Figure 1), while previous TURP (HR=3.5,95%CI:1.61-7.54,p=0.001) and acute toxicity ≥ G2 (HR=3.1,95%CI= 1.45-6.52,p=0.004) emerged as significant risk factor for GU toxicity≥G3. Hypertension was found to be a significant risk factor for developing GI toxicity≥G3 (HR=3.52,95%CI:1.025-12.09,p=0.046), while ADT played a protective role (HR=0.25,95%CI: 0.10-0.64, p=0.004)

Conclusions: WPRT, with HD moderately hypofractionated SIB to prostate and seminal vesicles, and ADT determines in PCa patients good bRFS and CRFS, with acceptable toxicity. Previous TURP and acute toxicity≥G2 predicted GU toxicity≥G3, while hypertension predicted GI toxicity≥G3. ADT was a protective factor for GI toxicity. Only GS score was determinant for bRFS and CRFS.

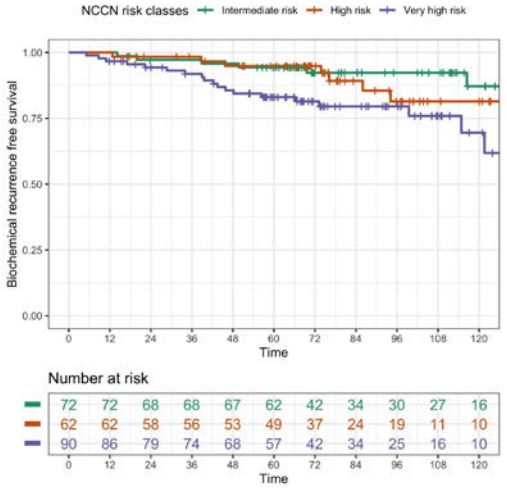

Figure 1.

CO68

STEREOTACTIC RADIOTHERAPY IN RECURRENT PROSTATE CANCER AFTER POSTOPERATIVE OR DEFINITIVE IRRADIATION

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Aims: Treatment options for local relapse in prostate cancer after postoperative or definitive radiotherapy (RT) include reirradiation, through external beam RT or brachytherapy. In our department we conducted a retrospective analysis reporting clinical outcomes of a cohort of patients treated with stereotactic reirradiation (reSBRT) through Cyberknife® robotic system. Here we present the updated results after a median follow up of 4 years.

Methods: We retrospectively reviewed data of 50 consecutively patients treated from June 2012 to February 2016 at our institution. All patients have been treated with external beam postoperative or definitive RT, had a biochemical relapse defined by European Urology Association criteria and had intraprostatic lesion or prostate bed macroscopic recurrence detected by 18F-choline PET/CT and MRI. Patients with metastatic or regional nodal disease were excluded. All patients underwent reSBRT with CyberKnife® robotic system (Accuray Inc, Sunnyvale, CA, USA). A total dose of 30 Gy in five fractions was prescribed to the 80% isodose line to cover 95% of the PTV. PSA was assessed at 2, 6 and every 3 months after the end of RT. Toxicity was assessed by the Common Terminology Criteria for Adverse Events toxicity scale v.4.03.

Results: After a median follow up of 48.2 months (6.4-86.3), 25 patients (50%) experienced biochemical relapse, with 13 patients (26%) developing metastatic disease and one cancer related death. Median biochemical relapse-free survival (BRFS) was 43 months (28-49); median metastasis free survival (MFS) was not reached. At univariate analysis Gleason score (GS)>8 and concomitant androgen deprivation therapy (ADT) were significantly related to worst median BRFS (46 *vs* 28 months, p=0.04 and 46 *vs* 19 months, p=0.02) and concomitant ADT was significantly related to worst MFS (not reached *vs* 32 months, p=0.002). At multivariate analysis both GS>8 and ongoing ADT showed to be independent predictors of BRFS (HR 2.42, 95%CI 1.09-5.41, p=0.02 and HR 2.83, 95%CI 1.17-6.8, p=0.02, respectively); only ongoing ADT was confirmed as an independent predictor of MFS (HR 4.75, 95%CI 1.52-14.8, p=0.007). Late grade 1-2 rectal and bladder toxicity occurred in three (6%) and 13 (26%) patients, respectively. One patient experienced both grade 3 acute and late bladder toxicity.

Conclusions: We confirmed our data about the safety and effectiveness of reSBRT. Careful patient selection is needed to maximize the benefit of this approach.

CO69

ADJUVANT VERSUS SALVAGE RADIOTHERAPY IN PATIENTS WITH PROSTATE CANCER: RESULTS OF A MONOCENTRIC EXPERIENCE.

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Aims: A much debated aspect over the years in prostate cancer therapy concerns timing of Radiotherapy after radical prostatectomy. Recently, Radicals-RT trial showed comparable results between men who underwent adjuvant RT soon after surgery and those who received rescue RT only at the time of disease recurrence. Purpose of our study is to verify the thesis supported by Radicals trial in order to understand if the radiotherapy approach can be avoided in subjects with PSA almost zeroed after surgery and proposed only at the time of a possible recovery of the disease.

Methods: We retrospectively evaluated 249 patients with prostate cancer who underwent prostatectomy alone or prostatectomy and lymphadenectomy treated with pre-RT (Adjuvant *vs* salvage) between January 2011 and December 2019; among these we have identified three subgroups, 40 pt with pre-RT PSA >0.5ng/ml, 209 with PSA < or =0.5ng/ml. Within the group with pre-RT PSA < or = 0.5ng/ml there were 165 patients with pre-RT PSA < or = 0.2ng/ml. 158 subjects were treated with adjuvant RT and 91 with rescue RT. All patients were stratified by Type of RT (adjuvant *vs* rescue), Gleason score, age, type of surgery, risk class, PSA at diagnosis, number of lymph nodes removed and margin status. Median follow-up was 112 months

Results: We did a multivariate analysis of Progression Free Survival factors risk by step-wise method finding: in the group of all 249 patients for those with adjuvant RT group HR 95% CI 3,195 *vs* rescue RT HR 95% CI 1,534-6,655 with p= 0,002. In the group of PSA < or = 0.5ng/ml for those with adjuvant RT group HR 95% CI 3,763 *vs* rescue RT HR 95% CI 1,509-9,380 with p=0,004. In the last group of PSA < or = 0.2ng/ml a significant confidence interval was not reached (p=0.35).

Conclusions: From our study it can be asserted that adjuvant radiotherapy has superior results in biochemical

disease control compared to salvage RT in patients who have a PSA prior to RT greater than 0.5. This advantage, on the other hand, is reduced by showing a p-value of 0.004 *vs* 0.002 in patients with pre-RT PSA <0.5 and substantially comparable results in patients with pre-RT PSA <0.2 (p-value 0.35).

CO70

PREDICTION OF URINARY TOXICITY AFTER PROSTATE CANCER RADIOTHERAPY: LONG TERM EVALUATION

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Aims: To assess factors affecting the incidence of (patient-reported) urinary toxicity (tox) at 5 years after radical radiotherapy (RT) for prostate cancer in a large group of patients (pts) enrolled in a prospective, multicentric trial

Methods: Pts were treated at different prescribed doses with conventional (74-80Gy @1.8-2Gy/fr) or moderately hypo-fractionated RT (65-75.2Gy @ 2.2-2.7Gy/fr) in 5fractions/week. All doses were corrected to 2Gy/fr, using the linear-quadratic model by applying α/β derived from maximum likelihood estimate (MLE). Bladder dose-volume histogram were reduced to equivalent uniform dose (EUD), with volume parameter n derived from MLE. Tox was evaluated every 6 months till 60 months. 4 endpoints were considered: (a) urinary incontinence as evaluated through the International Consultation on Incontinence Modular Questionnaire short form (ICIQ) and defined as the occurrence of an ICIQ value>5 (as calculated in the first 2 questions: frequency of urinary incontinence & amount of leakage) at least once between 6 and 60 months. Pts with baseline ICIQ>0 in the first 2 questions were excluded from the analysis. (b) urinary obstructive symptoms as evaluated with the International Prostate Symptom Score (IPSS) questionnaire and defined as the occurrence of an increase of IPSS of at least 10 points with respect to baseline at least once between 6 and 60 months. (c) grade 2+ haematuria as scored by the clinician. (d) obstruction requiring intervention. (e) a comprehensive moderate/severe toxicity defined as at least one among a/b/c/d. Logistic was used to determine association between urinary tox probability and the best dosimetric descriptor (determined MLE) and clinical risk factors. Internal validation was performed by bootstrapping. Nomograms were derived from logistic

Results: 312 pts were available. Rate for incontinence was 14%, 16.5% for obstructive symptoms, 3% haematuria, 2% obstruction and 26.6% for any moderate/severe tox. With the only exception of haematuria, for all the other tox endpoints MLE pointed toward the 2Gy-equivalent prescribed dose, with alpha/beta=1.5Gy, indicating a high sensitivity of urinary tox to fractionation and a possible relevant role of the urethra for these endpoints. Odds Ratios (OR) were 1.06, 1.09, and 1.06 for 1Gy increase for incontinence, obstructive symptoms and any tox, respectively. For haematuria the dose to 2cc of bladder (α/β=5Gy) was selected by MLE (OR=1.23).

Conclusions: A low α/β (1.5 Gy) for late urinary toxicity resulted in higher likelihoods, consistently with a high sensitivity of late urinary tox to fractionation. This points out that hypofractionation should to be coupled to optimization in the bladder-PTV overlap/urethra in order to reduce the risk of late urinary tox, especially for patients having other risk factors

CO71

CONCOMITANT NIVOLUMAB AND RT IN METASTATIC KIDNEY CANCER. BENEFIT OF ABLATIVE *vs* PALLIATIVE APPROACH

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Aims: Immune checkpoint inhibition (ICI) with Nivolumab is one of the cornerstones in metastatic renal cell carcinoma (RCC) both in I and in II-line settings. Despite the pre-clinical evidence of biological rationale for the additive effect of SBRT and ICI, its clinical evidence is still lacking, especially after NIVES trial failure in meeting its primary endpoint. To explore the benefit of SBRT compared to palliative only RT with ICI, we present a multicentric series of metastatic RCC patients treated with concomitant RT and Nivolumab.

Methods: Forty patients who underwent RT on overall 52 metastatic lesions within 4 months either before or after Nivolumab start were retrospectively analysed. RT was defined ablative if >5 Gy/fraction were administered. Patients treated with Nivolumab in I or II-line settings were included. Primary endpoints were OS (time between Nivolumab start and death from any cause) and PFS (time

between Nivolumab start and end).

Results: After a median follow-up of 11 months (IQR 4.7-17.6), 16 patients died; median PFS and OS were 6 (95% CI 5-10) and 24 months (95% CI 13-24), respectively [Figure 1]. Local progression occurred in 14 treated lesions, 5 and 9 in the ablative and palliative RT group, respectively. Distant progression was reported after treatment of 39 lesions, 19 and 20 in the ablative and palliative RT group, respectively. At univariate analysis, median PFS was significantly associated with the absence of metastasis at diagnosis (9 *vs* 4 months, p=0.005) and to ablative RT intent (20 *vs* 5 months, p<0.0001). Median OS was improved in patients without evidence of metastatic disease at diagnosis (not reached *vs* 11 months, p=0.02) and in those treated with concomitant ablative RT (not reached *vs* 11 months, p=0.001). At multivariate analysis, the only independent prognostic factor significantly associated with PFS and OS was RT ablative intent (HR 3.51, 95% CI 1.6-7.5, p=0.0012 and HR 2.8, 95% CI 0.99-8.07, p=0.05, respectively). 14 patients reported adverse events grade >2 (7 endocrinological, 2 cutaneous, 1 pneumological, 3 hepatic, 2 pancreatic).

Conclusions: Ablative if compared to palliative-only RT had a significant impact on PFS and OS in patients treated with concomitant Nivolumab treatment. Combination toxicity was mild, manageable and mainly related to Nivolumab. These results prompt further prospective evaluation of this combination strategy.

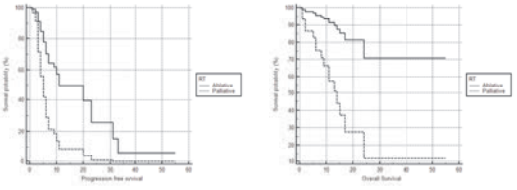

Figure 1. Cox proportional hazard model for Progression Free and Overall survival.

CO72

PROGNOSTIC FACTORS AND EFFICACY OF INVOLVED NODES STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR THE TREATMENT OF 117 LYMPH-NODE OLIGO-RECURRENCE PROSTATE CANCER

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Aims: The aim of the present study is to evaluate the efficacy of involved-nodes stereotactic body radiotherapy (SBRT) for oligo-rPC and to identify the prognostic factors that determine the outcome in this patient setting.

Methods: Patients with pelvic nodal oligo-rPC following primary surgery, radical radiotherapy or salvage radiotherapy who underwent involved nodes SBRT with biological effective dose (BED) > 120 Gy, with or without concurrent Androgen Deprivation Therapy (ADT), were retrospectively evaluated. Biochemical progression free survival (bPFS), distant progression free survival (DPFS), Overall survival (OS), related prognostic factors and toxicity outcomes were investigated.

Results: From November 2012 to December 2019, 74 patients for a total of 117 lesions met the inclusion criteria. Median follow up was 31 months (range 6-89 m). Concurrent ADT was administered in 58.1% of patients. 1y -2y and 3y DPFS ere 77%, 37%, 19% respectively; 1y -2y and 3y –OS were 98%, 98%, 95% respectively. The presence of a single target lesion showed a statistically significant influence on OS (p=0.021). Patients who reached early nadir (< 3months after SBRT) had a lower 3y survival (p=0.004). Value of PSA nadir after SBRT and the time between primary treatment and SBRT had an impact on biochemical Progression free survival. Concomitant ADT was correlated with improved DPFS in patients with more than 2 lymph-node involved. No acute or late adverse effect of any grade were reported.

Conclusions: SBRT is a safe and effective treatment for oligo-rPC, with a local control of 100%. It is not possible to clearly determine the need to postpone ADT in patients with 2 or more node metastases. Number of metastases, time-to-nadir (TTN), PSA nadir value and the time between first treatment and SBRT were identified as prognostic factors. Future prospective studies are expected to answer the questions that are still open.

CO73

A RADIOMIC MODEL TO PREDICT TWO YEARS OVERALL SURVIVAL IN LOCALLY ADVANCED CERVICAL CANCER PATIENTS TREATED WITH NEOADJUVANT CHEMORADIOTHERAPY

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Aims: The aim of this study is to determine if

radiomics features from T2-weighted 1.5 T magnetic resonance (MR) images could predict 2 years overall survival (2yOS), in patients with Locally Advanced Cervical Cancer (LACC) after neoadjuvant chemo-radiotherapy (NACRT).

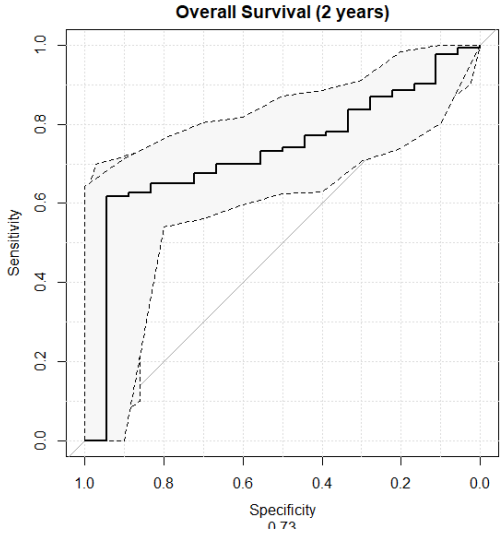

Figure 1.

Methods: We retrospectively enrolled 175 patients from two institutions (142 for the training cohort and 33 for the validation one) with LACC diagnosis (stage from IB2 to IIIC at International Federation of Gynecology and Obstetrics), that underwent NACRT followed by radical surgery from 2005 to 2018. A total of 1557 radiomics features belonging to four families (statistical, textural, morphological and fractal features) were extracted from pre-treatment MR images. The ability of each feature in predicting 2yOS was quantified in terms of Wilcoxon Mann Whitney test. Among the significant features, Pearson Correlation Coefficient (PCC) was calculated to quantify the correlation among the different predictors. A logistic regression model was calculated considering the two most significant features at the univariate analysis showing the lowest PCC value. The predictive performance of the model created was quantified out using the area under the receiver operating characteristic curve (AUC) as target metric.

Results: Based on this method, 46 different variables showed significance ($p<0.05$) at the univariate analysis. The radiomic model showing the highest predictive value combined the features calculated starting from the grey level co-occurrence based features, after the application of the Laplacian of Gaussian filter at two different kernel size (0.7 and 1). Such model exhibited an AUC of 0.73 (95% Confidence interval of 0.61-0.84) in the training set and 0.91 (0.72-1) in the validation set (Figure 1), suggesting its potential clinical use.

Conclusions: The proposed radiomic model has the ability to predict 2yOS in LACC patients before undergoing NACRT. To confirm the reliability of such results and translate the use of such model in clinical practice, larger studies with a consistent external validation are mandatory.

CO74

WHICH IS THE BEST TIME TO ASSESS COMPLETE RESPONSE AFTER CHEMORADIATION IN LOCALLY ADVANCED CERVICAL CANCER?

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Introduction/Background: The assessment of clinical response after exclusive chemoradiation in locally advanced cervical cancer (LACC) is recommended 3-6 months following completion of treatment, as per international guidelines. Aim of the present study was to investigate the best timepoint for assessing the clinical complete response in our series of LACC patients.

Methodology: Patients with histologically proven squamous cell cervical cancer or adenocarcinoma, stage IB2-IVA FIGO 2018 were retrospectively analyzed. All patients received intravenous cisplatin (40 mg/m²/weekly), external beam radiotherapy (45 Gy in 25 daily fractions±simultaneous lymph-nodes boost) and interventional radiotherapy (IRT, 28 Gy/twice/weekly). The primary endpoint was complete response evaluation, that we analysed at three timepoints with magnetic resonance imaging: 1) Assessment 1: At the end of external beam radiotherapy, before IRT (5-6 weeks from the start of treatment); 2) Assessment 2: 3 months after the end of IRT (18-20 weeks from the start of treatment); 3) Assessment 3: 6 months after the end of IRT (30-32 weeks from the start of treatment)

Results: 63 patients (median age: 55 years; 2018 FIGO stage IA: 1, IIA: 3, IIB: 15; IIIA: 1; IIIC1: 29; IIIC2: 10; IVA: 3; IVB:1) were analyzed. 57 patients had a squamous cell carcinoma, 6 adenocarcinoma. The treatment was well tolerated with a satisfactory compliance.

Complete clinical response was achieved in 16 patients at assessment 1, 40 of patients at assessment 2, and 45 of patients at assessment 3. Seven Patients (53%) with a partial response at assessment 2 had a complete response at 6 months from the end of the treatment. Nine patients were missing at the third assessment. Six months after treatment 80% of clinical complete response was registered (Figure 1).

Conclusions: Our data suggests that the optimal timepoint for assessment of complete clinical response after chemoradiation for LACC patients could be 6 months after exclusive treatment completion. This longer timeline could include patients not yet responders after 3 months, avoiding too early rescue therapies. Further and larger studies are needed to confirm this finding.

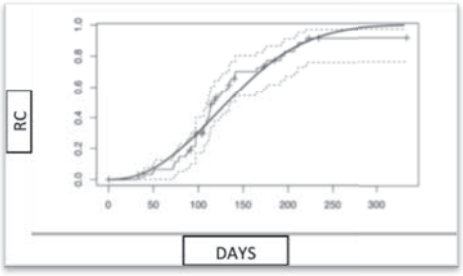

Figure 1.

CO75

RELIABILITY OF ALGEBRAIC SUM TO EVALUATE PELVIC RADIOTHERAPY AND BRACHYTHERAPY CUMULATIVE DOSES

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Aims: To study reliability of algebraic sum in evaluation of cumulative adjuvant external beam (APR) and brachytherapy (BRT) doses with respect to rigid plan fusion in gynecologic cancer patients (pts).

Methods: Between 2019 and 2020, we treated 50 gynecologic cancer pts with APR and endocavitary high-dose-rate BRT at 2 radiotherapy oncology centres. Of this group, 20 pts treated in supine position were retrospectively reviewed to compare algebraic sum to a rigid fusion of APR and BRT plans. A rigid box assessment on pelvis with MIM-Maestro software v 6.7.7. was adopted. On fused computed tomography (CT) rectum and bladder volumes and doses of the two separate CT plans were transferred. Organ at risk (OAR) cumulative dose volume histograms (DVH) were calculated, with respect to OAR volumes of APR and BRT. To limit OAR volume variability, the mean cumulative doses of each OAR was analysed. Following dosimetric parameters were examined: Dmax (0.5cc), D20% and D50% for rectum, Dmax (0.5cc) and D50% for bladder, for each parameter differences between the two methods adopted were reported as delta (D) values.

Results: Median age was 60 years (range,44-84) and median KPS 100% (range, 90-100%). 3 pts had squamous cell cervical cancer, 1 squamous cell vaginal cancer, and 11 endometrioid cancer (6 adenocarcinomas and 5 clear cell or mixed histology endometrial cancer). Pts have been submitted to surgery and subsequent APR with volumetric modulated arc therapy (V-MAT) at the dose of 25x2 Gy. A boost with endocavitary BRT at the dose of 2x5 Gy was performed in all pts. Differences between mean cumulative doses and algebraic sum of doses were calculated. For rectum, there were no significant differences: DDmax (0.5cc), -0,8%+/-8%; DD20%, -0.5% +/-2.5% (Figure 1); DD50%, 7% +/-19%. For bladder, DD50%, resulted similar, 0.5% +/-11%, whereas DDmax (0.5cc), was quite different ,31% +/-17%. For rectum and bladder D50%, BRT contribute resulted minimal. Bladder Dmax (0.5cc) was not reliable for the difference of bladder position during APR and BRT due to the bladder displacement caused by BRT applicator. All pts completed treatment without significant acute or late toxicities.

Conclusions: In gynecologic cancer pts submitted to APR and BRT, algebraic sum and rigid plan fusion of doses assure similar results in evaluating cumulative OAR doses. On the basis of our preliminary results, algebraic sum seems to be a reliable method to estimate cumulative doses. Moreover, algebraic sum of doses is easier to do, more accurate in calculating bladder Dmax (0.5cc), and remains the only available tool when APR and BRT are performed in different centres and DICOM files are not obtainable.

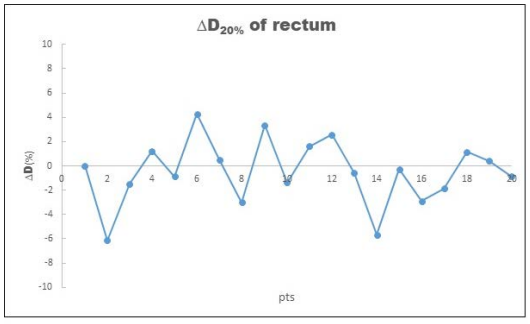

Figure 1.

CO76

PROGNOSTIC ROLE OF EARLY FDG-PET/CT IN LOCALLY ADVANCED CERVICAL CARCINOMA PATIENTS (LACC)

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Aims: To evaluate in patients with LACC the prognostic impact of FDG-PET/CT (early-PET) after exclusive chemoradiotherapy (CRT) and before intra-uterine brachytherapy

Methods: We included 23 pts with LACC (range 30-75 years) that referred to our institution between 2013 and 2019. Pts were treated with concomitant CRT and subsequent brachytherapy. FIGO STAGE: 1/23 were IIA, 12/23 IIB, 4/23 IIIB, 4/23 IIIC and 2/23 IVA. 9/23 pts had regional lymph node involvement and 2 pts had also positive lombo-aortic lymph nodes. Twenty/23 pts underwent radiotherapy and concomitant weekly chemotherapy with Cisplatin (40 mg/mq^2), 4 pts received neoadjuvant chemotherapy and 1 patient only radiotherapy. Nineteen/23 pts were treated with IMRT tecnique and 17 of them received IMRT-SIB (2.2 Gy x 28 fractions on GTV-cervix and GTV-LNs PET-positive, 1.8 Gy x 28 fraction on pelvis±LN lombo-aortics). The total brachytherapy dose was 21 or 28 Gy in 3-4 fractions, 7 Gy per fraction, with the aim to obtain a total dose (EBRT plus BT) in the range of 85-90 Gy (6 pts 28 Gy, 17 pts 21 Gy). All pts performed FDG-PET/CT after CRT and before brachytherapy (early-PET). PET images were rated as positive when there was focal uptake with a SUV max >3.

Results: At the end of CRT and before brachytherapy all pts performed early-PET: Thirteen/23 were negative and 10/23 positive. One/13 (7.7%) pts with negative early-PET showed a progressive/relapse disease: 1 systemic (lung-bones) progressive disease after 82 months from the end of brachytherapy. Six/10 pts (60%) with positive early PET-TC had progressive/relapse disease: 4 pts showed systemic (lung-bones) progressive disease and 2 pts showed nodal, cervical and bone relapse after a median time of 5 months from the end of brachytherapy. Median early-PET SUV max among these 6 patients was 5.8. Patients with early-PET- had statistically better 2-year OS and MFS compared to patients early-PET+, 100 *vs* 45% (CI 95%: 0.010-0.39; p 0.03) and 100 *vs* 60% (CI 95%: 0.010-0.56; p 0.01) respectively.

Conclusions: Our results showed that pts with positive early-PET before brachytherapy had statistically worst survival outcomes due to metastatic progression/local relapse. This setting of pts may benefit from adjuvant systemic treatment.

CO77

EVALUATION OF STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN THE MANAGEMENT IN EARLY-STAGE DISEASE ENDOMETRIAL CANCER

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Aims: Postoperative adjuvant radiotherapy (RT) in the management of early stage endometrial cancer (EC) is still controversial. We evaluate the feasibility of stereotactic body radiotherapy (SBRT) using the VMAT technique as a postoperative treatment on the vaginal cuff in stage I endometrial cancer.

Methods: Nine patients (pts) with stage I endometrial cancer were considered eligible for adjuvant vaginal brachytherapy (BV) but all pts, for medical or other reasons, were not candidates for BV and were therefore treated with VMAT-SBRT. During treatment simulation, all pts were positioned in supine position with arms on the chest. A soft radiopaque trans-vaginal probe was used to visualize the Clinical Target Volume (CTV) as the upper two thirds of the vagina. The Planning Target Volume (PTV) was created by isotropically expanding the CTV of 3mm. Bladder wall, rectum and femoral heads were contoured as Organs at risks (OARs). A prescribed dose of 30 Gy (6 Gy/fractions on alternate days) to the PTV was planned. The biological equivalent dose delivered was 40Gy (α/β=10) to the target and 54Gy (α/β=3) to the OARs. 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. Treatment was delivered with an Elekta Versa HD. For each patient, daily CBCT was performed before each treatment fraction to correct for translations and rotations of patient positioning. Acute Toxicity was scored according to the common Terminology Criteria for Adverse Events version 3.0 (CTCAE).

Results: With respect to CTV, mean D95% was 99%, while mean V95% was 99.9% (D2%>105% and D98%>97%). With respect to the PTV, mean D95% was 97%, while mean V95% was 96.7% (D2%>103% and D98%>95%). Mean D15cc, D1cc and maximum dose to the bladder wall were 14.7, 29.1 and 30.3 Gy respectively. Mean D20cc, D1cc and maximum dose to the rectum were 15.1, 28.4 and 29.3 Gy, respectively. Mean D10cc to the femoral heads was 9.9 Gy. Acute GI and GU toxicities were registered as follows: G0-G1 in 6 patients, G3 in 3 patients. No toxicity grade >G3 was observed.

Conclusions: SBRT using a VMAT technique is an effective and safe modality for the treatment of low risk early stage endometrial cancer as an alternative to BV. Longer follow-up is needed to obtain data on chronic toxicity and local disease control.

CO78

PATTERN OF FAILURE IN PATIENTS WITH CERVICAL CANCER TREATED WITH CHEMORADIOTHERAPY

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Aims: To describe pattern of failure of patients (pts) with locally advanced cervical cancer treated with radiotherapy (RT) +/- chemotherapy (CT) followed by brachytherapy (HDR).

Table 1.

Characteristic	No.
Age(y), median (range)	60 (31-89)
Histology	
Squamous	75 (91,5%)
Adenocarcinoma	6 (7.3%)
Undifferentiated	1 (1,2%)
Grade	
1	2 (2,4%)
2	16 (19,5%)
3	19 (23,2%)
Unknown	45 (54,9%)
FIGO	
I	3 (3,7%)
IIA	6 (7,3%)
IIB	63 (76,8%)
IIIA	2 (2,4%)
IIIB	4 (4,9%)
IVA	4 (4,9%)
IVB	0 (%)
Pelvic lymph node	
Positive	38 (46,3%)
Negative	44 (53,7%)
Para-aortic lymph node	
Positive	6 (7,3%)
Negative	76 (92,7%)
Chemotherapy	
Platinum based	39 (47,6%)
platinum + taxane based	9 (11%)
Unknown	24 (29,3%)
None	10 (12,2%)
Concomitant CT + RT	71 (86,6%)
EBRT Dose-fractionation schedules	
45 Gy in 25 fx	67 (81,7%)
50,4 Gy in 28 fx	14 (17,1%)
Other (44 Gy in 20 fx)	1 (1,2%)
Parametrial SIB	67(81,7%)
53,75 in 25 fx	11 (13,4%)
57,5 Gy in 25 fx	40 (48,8%)
58,8 Gy in 28 fx	3 (3,7%)
Pelvic Nodal SIB	
57,5 Gy in 25 fx	32 (39%)
Para-aortic lymph Nodal SIB	
58,8 Gy in 28 fx	4 (4,9%)
HDR-BT	
28 Gy in 4 fx	67 (81,7%)
30 Gy in 5 fx	10 (12,2%)

Methods: We retrospectively analyzed patients treated at our Institute from 2010 and 2019. All patients were staged with pelvic MRI, chest abdomen CT scan and 18-fluorodeoxyglucose (FDG) PET. External beam radiotherapy was delivered by 3D-CRT, VMAT/IMRT technique. Different dose-fractionation schedules were prescribed according to clinical stage for EBRT. Brachytherapy dose prescription was 28 Gy in 4 fx or 30 Gy in 5 fx. Primary endpoint was locoregional recurrence rate. Secondary endpoints were acute and late toxicity.

Results: Data of 82 patients were retrospectively recorded. Patient's characteristics were described in table 1. Median OTT from the beginning of EBRT to the end of HDR-BT was 56 days (range: 41 to 71 days). Median follow up was 51 months (range: 4-98 months). 11 of 82 (13,4%) patients were lost at follow up. 18 of remaining 71 (25,4%) patients presented a clinical relapse detected by imaging (CT, MRI, PET): 2 patients on primary tumor (respectively at 3 and 6 months from the end of radiation treatment); 5 patients on local lymph nodes (at 2, 3, 8, 9, 12 months from the end of radiation treatment), 14 patients on distant lymph nodes or visceral (at 2, 3, 3, 3, 4, 5, 6, 7, 8, 15, 18, 28, 31, 36 months). At last follow up 58 of 82 (70,7%) patients were alive and 24 patients deceased (29,3%). 12 of 24 (50%) patients deceased had a clinical relapse on primary tumor, local or distant lymph nodes or visceral. In 46 of 58 (79,3%) patients alive at last follow up there was no evidence of disease; in 8 of 58 (13,8%) progressive disease is detected; 4 (6,9%) patients alive were lost at follow up so clinical status was unknown. We estimated 5-year locoregional control (LRC) and 5-year metastasis free survival (MFS) using the Kaplan-Meier method. 5-year LRC was 88,7% and 5-year MFS was 73,2%.

Conclusions: Overall oncologic results are good. These data from our Institute experience show that standard treatment of locally advanced cervical cancer (external beam irradiation +/- chemotherapy followed by brachytherapy) is usually well tolerated.

CO79

HYPOFRACTIONATED RADIOTHERAPY AND CONCURRENT CHEMOTHERAPY IN CERVICAL CANCER EXCLUSIVE TREATMENT WITH OR WITHOUT BRACHYTHERAPY: A PRELIMINAR EXPERIENCE

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Aims: To evaluate feasibility and tolerability of hypofractionated external beam radiation therapy (EBRT) schedule with concurrent chemotherapy (weekly cisplatin 40 mg/m^2) in high volume and node positive cervical cancer (CC).

Methods: From March 2018 to July 2020, 15 consecutive patients, median age 59 (47-80) with locally advanced (IIB-IVa) high volume CC received exclusive chemoradiation. Hypofractionated EBRT was delivered using VMAT and a simoultaneous integrated boost. EBRT schedule was 66.08 Gy to primary, 59.92 Gy to positive nodes, 54.4 Gy to negative pelvic nodes and 50.4 Gy to lomboaortic nodes, when required, in 28 daily fractions. Pelvic RM was performed during the last week of EBRT to evaluate tumor response. Four patients received image guided brachytherapy boost (BRTb) (14 Gy in 2 weekly fractions), in 3 patients BRTb was technically not feasible, 2 patients were unfit to continue treatment, in 4 elderly patients BRTb was not planned. In 2 non responders patients, systemic therapy followed chemoradiation. Cone beam CT was acquired daily. Acute and late toxicity were registered using RTOG scales.

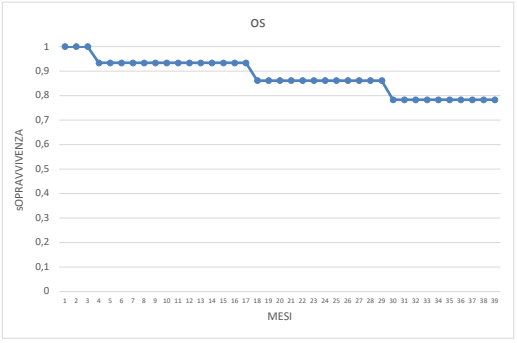

Figure 1. Overall Survival

Results: Median follow-up is 18.7 months (0.33-38). The oldest patient of the series (80 years) died early for a cardiovascular event. Other 3 patients died after 17, 45 and 50 months respectively. Eleven patients are alive, 10 without evident disease and one is lost at follow-up. Overall survival is shown in Figure 1. Acute genitourinary (GU) and gastroenteric (GI) toxicity was ≤ G2 and all patients completed treatment in 8 weeks. Late GU toxicity ≥ G3 was reported in patients who received BRT boost (in 2 patients G3 and in 1 patient G4, requiring temporary colostomy). No patients presented > G2 late GI toxicity.

Conclusions: At state of art, brachytherapy is mandatory within cervical cancer radiation strategies. A dose escalation with EBRT could provide to a tumor downsizing useful when only endocavitary without combined interstitial brachytherapy is available but insufficient to cover high volume residual primary. Unfortunately, in our series, hypofractionated EBRT plus BRT it's more toxic than standard treatment. Moreover, in elderly patients or in patients with technical impossibility to receive BRT, external dose escalation could represent an alternative and this schedule seems to be useful in local control. More trials including higher number of patients is necessary to define the real role of hypofractionation in cervical cancer.

CO80

A PROSPECTIVE TRIAL: DOSIMETRIC IMPACT OF RECTAL ENEMAS AND BLADDER FILLING ON HIGH-DOSE-RATE INTRACAVITARY CERVICAL CANCER BRACHYTHERAPY

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Purpose: To evaluate the effects of rectal-enemas and bladder-filling on dose constrains during radical High-Dose-Rate (HDR) intracavitary-cervical-Brachytherapy (BT).

Table 1.

Table 1: Rectal and Bladder volume and dose *

Factors	NO ENEMA 1 BRT fraction	ENEMA 2 BRT fraction	p-value**
Mean rectal volume (cc)	43,84±17	38,21± 13.16	0, 0052
Min **(cc)**	21 cc	16	
Max **(cc)**	88 cc	70	
Mean bladder volume (cc)	130±27.45	129±26.19	0,4443
Min **(cc)**	82	76	
Max **(cc)**	200	205	
Mean RECTUMD0.1cc (Gy)	7,4±0.94	6,74±0.81	0,0004
Mean RECTUM D2cc (Gy)	5,37±0.51	4,97±0.51	0,0003
Mean Bladder D0,1cc (Gy)	7,1±0.50	6,9±0.66	0,0951
Mean Bladder D2cc (Gy)	5,7±0.27	5,6±0.41	0,05262

*Data are expressed as mean ± SD
**Wilcoxon paired test was applied to assess significance : p < 0.05

Material and Methods: Between 2016 to 2020, 37 patients (pts) with cervical cancer (stage IIB-IIIA-IIIB-IVA) treated with external beam radiotherapy and concurrent chemotherapy followed by 3 fraction (fx.) CT-based HDR-BT were included in a prospective trial. Patients were instructed to try to evacuate before coming to the hospital for HDR-BT and the first brachytherapy fx. was considered the basal status. Patients were instructed to self-administer two rectal cleansing enemas before the second-Third fx. Dose-Volume-Histogram(DVH) values were generated for the rectum and bladder e correlated with their volume variation. Rectal volume differences at the first and second BT-fx were computed and compared, and their corresponding DVH-parameters (D0.1cc,D2cc) were assessed; the same evaluation was performed evaluating the maximum bladder volume in cc and the dose at 2 cc and 0.1 cc. All patients underwent pelvic CT scans at every BT fx., with 3-mm thick slices, in the supine posi-

tion with a Foley bladder catheter that instilled 60 mL of saline solution. The HDR-BT was performed using a Fletcher-style applicator. The total standard prescribed dose was 21 Gy in 3 fx.

Results: Significant differences in rectal volume and DVH parameters were observed between no enema and enema fractions ($p<0.05$) (Table 1). No differences were observed in bladder volume and dose at 2cc and 0.1cc ($p< 0.05$) (Table 1).

Conclusions: Our rectal cleansing protocol results in an improvement in dosimetric terms. A rectal volume without enema corresponds to an increase in the dose to the rectum. A standard bladder filling of 60cc through catheterization allows us to obtain constant bladder volumes respecting DVH-doses. Prospective studies are needed to investigate whether these data are linked to differences in rectal toxicity.

CO81

PLAQUE BRACHYTHERAPY FOR THE TREATMENT OF UVEAL MELANOMA: OUR STRATEGIES AND RESULTS

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Aims: The objective of this study was to assess the results of the treatment of uveal melanoma, with brachytherapy (BT), using ruthenium-106 (106Ru) and iodine-125 (125I) plaques, in terms of local control, enucleation free survival and patients survival.

Material and Methods: Medical records of 147 patients (median age 71 years; range 31-88 years) treated with ruthenium and iodine plaques BT for uveal melanoma (UM) between 2010 and 2020, were retrospectively reviewed. UM was diagnosed with A-scan and B-scan standardized echography, optical coherence tomography, fluorescein angiography, indocyanine green–angiography and/or magnetic resonance. The tumor was located in choroid (83%), iris (11%) and ciliary body (6%). The largest basal diameter ranged from 4 mm to 18 mm (median, 10.25 mm), tumor height ranged from 1.8 mm to 11.2 mm (median, 3.25 mm). American Joint Committee on cancer (AJCC) I-II (<6 mm in height) stage were treated with 106Ru plaque with a prescription dose of 110Gy to the tumor apex, as well as AJCC II-III (> 6mm in height) stage were treated with 125I plaque with a prescription dose of 85Gy to the tumor apex.

Results: The ophthalmic evaluation at three months after BT showed a complete response [CR] in all the patients. Median follow-up was 70.7 months (range 12-120 months). We reported a total of 9 (6.1%) local recurrences and 11 (7.5%) metastatic diseases. The most frequent Common Terminology Criteria for Adverse Events (CTCAE v 5.0) grade 1-2 late adverse event was ischemic retinopathy (30.0%), followed by exudative detachment (21.0%). Five (3.4%) patients, who were treated with 125I plaque underwent enucleation: two (1.3%) for local recurrence and three (2.0%) for comorbidities (neo-vascular glaucoma symptoms). Only 9 patients (6.1%) died of disease; other 5 patients (3.4%) of age and/or comorbidities. The 5-year actuarial local control (LC), disease-free survival (DFS), overall survival (OS) and enucleation free survival (EFS) rates were 95%, 92%, 97%, and 97%, respectively.

Conclusions: Plaque BT offers an effective and safe approach for selected cases of uveal melanoma, due to the reported satisfactory results in terms of local control, eye conservation and survival.

CO82

TOTAL BODY IRRADIATION (TBI) IN HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT). RETROSPECTIVE SURVIVAL ANALYSIS IN 16 YEARS MEDIAN FOLLOW-UP. FOCUS ON TECHNIQUE

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Aims: Total Body Irradiation represents one important component of pre-hematopoietic stem cell transplant in patients(pts) with Acute Lymphoblastic Leukemia(ALL), Myeloblastic Leukemia and others hematological diseases. We retrospectively investigated overall survival(OS) in pts undergoing TBI in our Center and evaluated different techniques used.

Methods: Since 1994 to 2020, 276 TBI treatments were performed in our Center in pts aged 16-66years (median age 37y,SD13). Median weight was 68kg, range 40-112,SD14. Median height was 170cm, range 140-198,SD9.7. 110pts were affected by ALL, 105pts by Acute or Chronic Myeloblastic Leukemia. The others were affected by refractory Non-Hodgkin Lymphoma(26) and Myelodysplastic Syndromes(35). The hematological indications for HSCT have not changed over time, as well as chemo-conditioning regimes. Only 13pts were transplanted twice, after a previous ineffective transplant without TBI. “Human Leukocyte Antigens(HLA) identic sibling” donor was possible in112pts, “HLAmatched unrelated” donor in116pts, “HLAmismatched unrelated” in28, cord blood in13 and “HLAaploidentical” in7. 187HSCT were conditioned by myeloablative regimes (TBI prescribed dose=12Gy). 89HSCT by nonmyeloablative regimes (<12Gy). Since1994 to2015 the standard

procedure for TBI was in a sitting position with lung lead attenuators and antero-posterior irradiation (1994to2000 using Cobalt gamma rays, 2000to2015 6MeV Xrays). Since2016 to2020 the set-up was modified in a more comfortable supine position with solid water compensators and lateral-lateral irradiation 6MeV Xrays. A previsional plan was calculated with TPS on TCimages. In vivo dosimetry was maintained. Survivals have been evaluated by KaplanMeyer method and the inference by LogRank test.

Results: Median follow-up was 16ys. Mean accrual was 10.2pts/y. 2ys-OS was 54.5%, 4ys 48.6%, 10ys 44%, 20ys 37%, 26ys 36%[1]. Younger age (<50y) seems to predict better survival p=0.0005[2]. No significant difference in OS was found between two regimes (ablative *vs* no) p=0.07[3], type of donor(except cord blood and HLAaploidentical)[4], techniques p=0.46[5].

Conclusions: Long follow-up confirms that the OS reaches a plateau after 2ys. A statistical significance has been found according to age. It's seems that there is a trend between conditioning regimes but this is due to the selection of pts, that depends on age. Survival is not affected by the type of donor; neither by the irradiation technique, although a longer follow-up is recommended to confirm the last result.

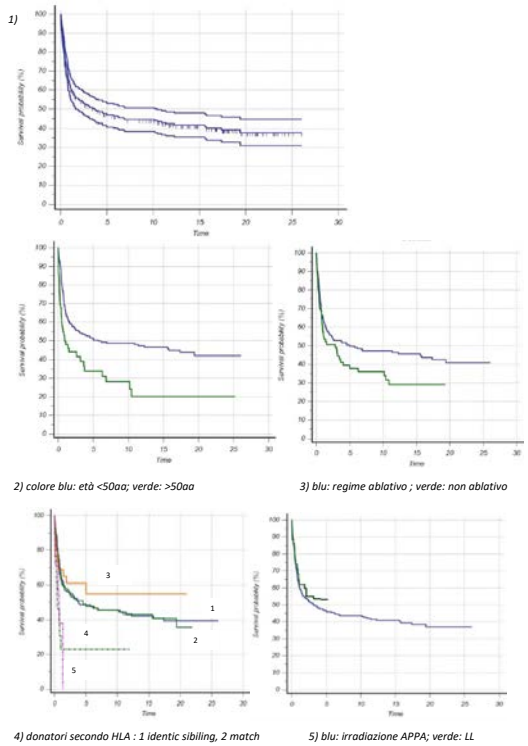

Figure 1.

CO83

PRELIMINARY RESULTS OF PARTICLE BEAMS RADIOTHERAPY FOR MALIGNANT PERIPHERAL NERVE SHEATH TUMORS

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Aims: To investigate outcome and toxicity of patients (pts) affected by malignant peripheral nerve sheath tumors (MPNST) treated with high-dose protontherapy (PT) and carbon ion radiotherapy (CIRT).

Materials and Methods: We retrospectively analyzed the outcome of 23 patients with MPNST treated between July 2013 and December 2020. Twenty one pts (91.3%) were treated with post-operative RT. Residual disease was macroscopic in 12 pts (52%), 9 pts (40.9%) were treated for local recurrence after surgery. Two unresectable pts underwent definitive radiotherapy after biopsy. The most frequent tumor site was brachial plexus. Twenty one pts were irradiated with CIRT to a median total dose of 63.9 Gy(RBE) (range, 54-76.8), 2 pts underwent PT to a median total dose of 64 Gy(RBE) (range, 60-68). Primary endpoints were overall survival (OS), local control (LC) and progression-free survival (PFS), calculated with Kaplan Meyer method. Secondary endpoint was toxicity, assessed according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

Results: Median follow-up was 23 months (range, 2 – 80). Three patients were lost to follow-up after median time of 28 moths (range, 16-41). Twelve local progressions (52%) were observed with a median time to local recurrence of 14 months (range, 1 – 66 months). Two distant metastases (8.7%) were recorded. OS at 2 and 3 years was 70% and 49%, respectively. LC at 2 and 3 years was 52% and 37%, respectively. PFS at 2 and 3 years was 52% and 37%, respectively. Acute toxicities of grade 2 (erythema and paresthesia) and grade 3 (erythema) in 5 patients were observed. Severe late radiation related toxicity of grade 3 (peripheral motor neuropathy and brachial plexopathy) was recorded in 2 patients.

Conclusions: High dose CIRT and PT show favorable results with acceptable toxicities in patients with gross residual and local recurrence after surgery, or unresectable malignant peripheral nerve sheath tumors. Patients accrual by multidisciplinary approach is still ongoing to confirm these findings and investigate on this challenging disease.

CO84

TOTAL BODY IRRADIATION (TBI) WITH VOLUMETRIC MODULATED ARC THERAPY (VMAT): A FIRST CLINICAL EXPERIENCE

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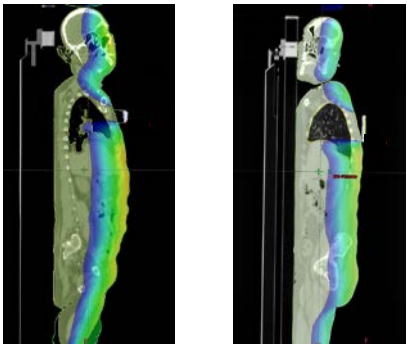
Aims: TBI is an important part of the conditioning regimen for patients (pts) with acute myeloid leukemia (AML) or acute lymphoid leukemia (ALL) undergoing hematopoietic stem cell transplantation (HCT). The most utilized method of delivering TBI is with the pts standing or lying down at a wide source-to-skin distance, with poor pts compliance and depending on the dimensions of the bunker. Our aim is to describe the implementation of VMAT for the treatment of such pts.

Figure 1 and Table 1.

Fig. 1 Treatment plan supine and prone



Tab.1 Planned Dose (PD) and Measured dose (MD) in the prescription point (ombelicus) and OARs: lung right (LR) and lung left (LF).

Patients	PD prescription point (ombelicus) cGy	MD prescription point (ombelicus) cGy	PD LR cGy	MD LR cGy	PD LF cGy	MD LF cGy
1	1211.5	1175	848.8	880	884.8	865
2	1200.6	1211	840.4	846	865.7	820
3	1203.1	1201	842.2	871	840.3	845

Notes: in vivo dosimetry is not required for patients (2) treated at TBI low doses; a patient candidate for TBI high dose was planned, but the start of treatment was postponed due to disease recurrence during induction CT

Methods: from January 2021 to May 2021 6 pts were treated: 5 male and 1 female (median age: 53 years, range 37-69), affected by ALL (3 pts), AML (2 pts) and one with CMML. All pts were relapsed and 4 of them had previously been subjected to HCT. 4 pts were treated with TBI high dose (200 cGy BID for 3 fr.) and 2 to with TBI low dose (2-4 Gy in one fr.). For each patient two computed tomography (CT) image sets were performed, with a slice thickness of 4 mm. The target volume for is whole body, including the skin. Pts who were treated with TBI high dose, the following were contoured: heart, lung right and left, diaphragm right and left, hilum lung right and left. The contouring of such structures is necessary for the definition of lung shielding lead blocks. The TBI treatment plans were generated using the RapidArc™ software, provided within the Eclipse™ treatment planning system. The radiation therapy was performed with a dedicated bed and the addition of a spoiler in such a way that - with the alignment of the beam- SSD remains approx. 2 meters .

Results: In our cases the lungs were the only OAR (mean lung dose accepted between 8-10 Gy). The arc beam is modulated in order to create a homogeneous profile in the prescription point (ombelicus), which is usually defined at the hemi-thickness of the pt (Figure 1). During the first session, in vivo dosimetry is performed with Mosfets applied at predetermined points along the body and the correct position of lung shielding lead blocks checked through RX image. The planned dose was in line with the measured dose via Mosfets (Tab.1). All pts well tolerated RT. No acute toxicity related to RT treatment was found.

Conclusions: The RT with VMAT technique can be considered as a treatment option for the pts that need TBI in the conditioning regimen before the HCT with good compliance of the pts , without the limitations related to the bunker and provides an homogeneously, reproducible and reliable irradiation of the patient.

CO85

ROMIDEPSIN (FK228) FAILS IN COUNTERACTING THE TRANSFORMED PHENOTYPE OF RHABDOMYOSARCOMA CELLS BUT EFFICIENTLY RADIOSENSITIZES, *IN VITRO* AND *IN VIVO*, THE ALVEOLAR PHENOTYPE SUBTYPE

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Aims: Herein we describe the in vitro and in vivo activity of FK228 (Romidepsin), an inhibitor of class I HDACs, in counteracting and radiosensitizing embryonal (ERMS, fusion-negative) and alveolar (ARMS, fusion-positive) rhabdomyosarcoma (RMS).

Methods: RH30 (ARMS, fusion-positive) and RD (ERMS, fusion-negative) cell lines and human multipotent mesenchymal stromal cells (HMSC) were used. Flow cytometry analysis, RT-qPCR, western blotting and enzymatic assays were performed. Irradiation was delivered by using an x-6 MV photon linear accelerator. FK228 (1.2 mg/kg) *in vivo* activity, combined or not with radiation therapy (2 Gy), was assessed in murine xenografts.

Results: Compared to HMSC, RMS expressed low levels of class I HDACs. *In vitro*, FK228, as single

agents, reversibly downregulated class I HDACs expression and activity and induced oxidative stress, DNA damage and a concomitant growth arrest associated with PARP-1-mediated transient non-apoptotic cell death. Surviving cells upregulated the expression of cyclin A, B, D1, p27, Myc and activated PI3K/Akt/mTOR and MAPK signaling, known to be differently involved in cancer chemoresistance. Interestingly, while no radiosensitizing effects were detected, in vitro or in vivo, on RD cells, FK228 markedly radiosensitized RH30 cells by impairing antioxidant and DSBs repair pathways *in vitro*. Further, FK228 when combined with RT *in vivo* significantly reduced tumor mass in mouse RH30 xenografts.

Conclusions: FK228 did not show antitumor activity as a single agent whilst its combination with RT resulted in radiosensitization of fusion-positive RMS cells, thus representing a possible strategy for the treatment of the most aggressive RMS subtype.

CO86

PRIMARY ORBITAL LYMPHOMA: A REPORT OF A SINGLE INSTITUTION EXPERIENCE

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Aims: Orbital non-Hodgkin's Lymphomas are rare tumors that represent the second type of primary eye cancer in the adult. 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 clinical features, toxicity and prognosis in patients with orbital non-Hodgkin lymphoma treated with RT.

Methods: In the period from 2002 to 2020 73 patients with orbital non-Hodgkin Lymphoma were treated at our institute. This patient's cohort was retrospectively assessed. Diagnosis was confirmed by surgical biopsy using incision, excision or orbitotomy. The median radiation dose was 36 Gy (20-36 Gy), most commonly given as fractions of 1.5-2 Gy.

Results: Follow up data were available for 71 patients. The median age was 64 years, and 44% of patients (n=31) were male. In 31 cases (43.7%) there was involvement of the right orbit, in 37 cases left orbit (52.1%) and in 3 cases synchronous bilateral eye involvement (4.2%). The most common histology was marginal B-cell lymphoma (n=48, 68%). Patients presented with typical symptoms like periorbital swelling. At a median follow-up of 38 months (1-226), 64 patients were alive (OS 90%), with 10 patients relapsed (1 locally, 1 in controlateral eye, and 8 distant, PFS 86%). 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 toxicty was reported in 14.1% of cases. Cataracts were detected in 6 patients (8.5%), hyperaemia in 1 (1.4%), dry eye managed with application of artificial tears in 2 (2.8%), maculopathy in 1 (1.4%).

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, the toxicity profile was tolerable.

CO87

THE 0,7,21 HYPOFRACTIONATEDRADIOTHERAPIC REGIMEN IN THE MELANOMA METASTASIS TREATMENT: OUR EXPERIENCE

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Aims: To evaluate Response Rate (RR), Progression Free Survival (PFS) and Overall Survival (OS) in melanoma metastatic patients treated with 0-7-21 hypofractionatedradiotherapic regimen.

Methods: Of the 50 patients treated from January 2013 to March 2020 in our center with melanoma metastasis, we enrolledin our study 10 patients.

Results: The median age was 77 years (range 55-86 years). Sites of treatment were: lymph nodes in 5 patients, bone in one and skin in 4 patients. The delivered dose was 24 Gy in 3 fractions, at the time 0-7-21, 8 Gy for fraction.In only one patient was observed the BRAF V600K mutation. All patients have been treated with immunotherapy:three with Pembrolizumab, four with Nivolumab, one with Pembrolizumab and Ipilimumab, one with Ipilimumab and Nivolumab, and one with Vemurafenib, Pembrolizumab, Ipilimumab, and Dabrafenib combined with Trametinib.We observed a RR of 100% with a median PFS of 12,5 months (range 4-13 months),no local progression was observed. The median OSwas 100% and 78% at 6 and 12 months, respectively.

Conclusions: The 0-7-21 regimen allowed to obtain good responses in the treatment of melanoma metastases. Important results have been seen on long-term local control. Our experience encourages the use of this fractionation in the palliative treatment of melanoma metastasis.

CO88

ADJUVANT RADIOTHERAPY IN PLEOMORPHIC LEIOMYOSARCOMA OF THE SPERMATIC CORD: EFFICACY AND TOLERANCE

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Aims: To assess efficacy and tolerance of adjuvant radiation treatment in patient affected by recurrent pleomorphic leiomyosarcoma of the spermatic cord with positive margins at last surgery. This tumor is a rare disease. The mainstay of treatment is radical surgery with wide excision margins and adjuvant therapies have been suggested in selected patients, but there are no clear guidelines due to few data in literature.

Methods: We report the case of a 68 years old man, affected by pleomorphic leiomyosarcoma of the right spermatic cord who had many local relapses, between 2016 and 2020. All relapses were treated with surgery and also adjuvant chemotherapy. In March 2020 he underwent last surgery that removed inguinal bulky lesion and showed positive margins. Therefore, we decided to deliver adjuvant radiotherapy. The clinical target volume (CTV) was tumor bed and right inguinal nodes. The Planning target volume (PTV) was defined with an anisotropic margin of 7 mm around the CTV. A total dose of 54 Gy in 27 fractions was prescribed to PTV and the technique used was VMAT with daily-CBCT (cone beam-CT). Organ at risk were rectum, bladder, femoral heads, large bowel and penile bulb. The patient was seen twice a week during treatment and for follow-up visits four weeks after completion of treatment, than three months' interval with pelvic MRI and/or PET/TC with FDG. Acute and long-term toxicities were verified according to CTCAE v4.0 staging system.

Results: The patient showed no toxicity in the first part of treatment, but experienced G2 skin toxicity (dermatitis) towards the end of the treatment, without treatment interruptions. First follow-up at four weeks from the end of treatment showed complete resolution of acute skin toxicity with topic therapy. With a follow-up of 12 months we reported no toxicities and no clinical or radiological evidence of disease.

Conclusions: In patients affected by pleomorphic leiomyosarcoma of the spermatic cord with a high risk of local recurrence, adjuvant radiotherapy should be considered. This is a safe and well tolerated treatment especially with modern techniques. However, we need a long-term follow-up to assess its efficacy on local control, in order to verify therapeutic success.

CO89

RISK-GROUP CLASSIFICATION BY RECURSIVE PARTITIONING ANALYSIS FOR PATIENTS AFFECTED BY OLIGOMETASTATIC KIDNEY CANCER TREATED WITH STEREOTACTIC ABLATIVE RADIOTHERAPY

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Aims: Incidence of renal cell carcinoma (RCC) is increasing worldwide and almost half of the patients will develop metastases during diseases' course, with poor survival. The role of radiotherapy in the management of RCC is now emerging thanks to the introduction of Stereotactic ablative radiotherapy (SABR). Aims of this retrospective analysis were to evaluate survival of patients treated with SABR for cranial and extracranial oligometastases and to stratify them into prognostic risk classes.

Methods: End points of our study were overall survival (OS), progression-free survival (PFS), local control (LC) and out-field progression-free survival (OPFS). The binary classification tree approach with recursive partitioning analysis (RPA) was applied to stratify patients into risk groups based on OS.

Results: From 2008 to 2021, 129 patients received SABR on 242 oligometastases from kidney cancer. Median age was 65.0 years (29.8 – 88.4) and the majority of patients was male (136, 82.93%). Brain was the most common site of treated metastases (84, 34.71%), followed by lung (62, 25.62%), and lymph node (44, 18.18%). Median SBRT dose was 36 Gy (16 – 75) delivered in 1 to 10 fractions. Median biological effective dose (BED10) was 81.6 Gy (28.8 – 262.5). Median follow-up was 19.4 months (3–234.9). The 3-year OS rate was 55.1% (95%CI 44.6–64.4) and, at multivariable analysis, increasing age (HR 1.03, 95%CI 1.00-1.04; p=0.014) and brain disease (HR 4.46, 95%CI 2.16–9.22; p=0.000) were significantly associated with lower survival. The 2-year PFS rate was 28.8% (95%CI 21.2–36.8) and brain disease (HR 2.34, 95%CI 1.55 – 3.53; p=0.000) and number of treated lesions (HR 1.33, 95%CI 1.07 – 1.64; p=0.008) were significantly associated with worse PFS. The 2-years LC rate was 95.2% (95%CI 90.7–97.6), and median OPFS was 11 months with 2-yr rate of 33.4% (95%CI 25.0–42.0). RPA identified 4 prognostic OS classes: Class 1 (age≤65, body metastases) with 3-years OS of 82.6% (95%CI 65.3–91.8); Class 2 (age>65, body metastases, no bone disease) with 2 years OS of 67.9% (95%CI 45.5–82.6); Class 3 (age>65, body metastases, bone disease) with rate of 37.5% (95%CI 5.5–71.6), and Class 4 (brain disease) with 9.7% (95%CI 1.8–25.7).

Conclusions: SABR for oligometastatic kidney can-

cer appears to be effective, both for cranial and extracranial lesions. Selection of patients need to be investigated in prospective trials to clarify the role of combined treatment in unfavorable risk classes.

CO90

A LARGE, MULTICENTER, RETROSPECTIVE STUDY ON EFFICACY AND SAFETY OF STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN OLIGOMETASTATIC CERVICAL CANCER (MITO-RT2/RAD STUDY): A COLLABORATION OF MITO, AIRO GYN, AND MANGO GROUPS

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Aims: Data supporting stereotactic body radiotherapy (SBRT) for oligometastatic gynecological cancer patients are increasing, but stereotactic treatments have not yet been fully explored. The aim of this retrospective, multicenter study (MITO RT-02) was to define efficacy and safety of SBRT in a very large, real life dataset of metastatic/persistent/recurrent cervical cancer (MPR-CC) patients.

Methods: Clinical and SBRT parameters have been collected in order to fulfill primary endpoints, i.e. the rate of complete response (CR) to SBRT, and the 24-month actuarial local control (LC) rate on "per lesion" basis. The secondary end-points were acute and late toxicities. Objective response rate (ORR) included CR and partial response (PR). Clinical benefit (CB) included ORR and stable disease (SD). Toxicity was evaluated by RTOG/EORTC and CTC-AE scales, according to center policy.

Table 1. Patients and treatments characteristics.

	N. (%)
Patients	84
Lesions	126
Age, yrs	
Median (range)	58 (30-92)
ECOG Performance Status	
0-1	79 (94.1)
2-3	5 (5.9)
Histotype	
Squamous	77 (61.1)
Adenocarcinoma	36 (28.6)
Adenosquamous	5 (4.0)
Clear cell	3 (2.4)
Other	5 (4.0)
N. lesions per patients	
1	61 (72.6)
2	13 (15.4)
≥3	10 (12.0)
Type of lesion (%)	
Lymph node	70 (55.5)
Parenchyma	46 (36.5)
Bone	10 (8.0)
Anatomic Site	
Neck	7 (5.5)
Thorax	34 (27.0)
Abdomen	32 (25.4)
Pelvis	46 (36.6)
Bone	7 (5.5)
Metachronous lesions	
No	99 (78.6)
Yes	27 (21.4)
N. patients undergoing previous radiotherapy in site	
No	53 (63.1)
Yes	31 (36.9)
Equipments	
LINAC	108 (85.7)
Cyberknife	10 (7.9)
Tomotherapy	1 (0.8)
MRI LINAC	7 (5.6)
Type of treatment	
SRS, stereotactic radiosurgery (single fraction)	26 (20.6)
SBRT, stereotactic radiotherapy (more fractions)	100 (79.4)
PTV	
Median, range (cc)	16.8 (1.8-223.3)
Total dose, Gy	
Median (range)	35 (5-60)
Dose/fraction, Gy	
Median (range)	7 (2.5-26)
Dose prescription	
Specific isodose	48 (38.1)
Isocenter	32 (25.4)
Target mean	46 (36.5)

Results: Fifteen centers participated to the study; after evaluation of inclusion/exclusion criteria, 84 CC patients, carrying a total of 126 lesions treated by SBRT between March 2006 and February 2021, were selected for the analysis. Patient characteristics and treatment data are summarized in Table 1. Complete and partial response, as well as stable disease were observed in 73 (57.9%), 30 (23.8%), and 16 (12.7%) lesions, respectively, reaching

about 94% CB rate. With a median follow-up of 14 months (range: 3-130), the 24-month actuarial LC, DFS and OS rate were 61.8%, 22.3%, 52.9%, respectively. Mild acute toxicity was experienced in 14 (16.6%) patients; late toxicity was documented in 4 patients (4.7%).

Conclusions: This study confirms the efficacy and safety of SBRT in MPR-CC patients. The low toxicity profile suggests a wider use of this treatment in this setting, however combinations with new drugs are needed to improve outcomes.

CO91

STEREOTACTIC BODY RADIOTHERAPY FOR LUNG OLIGOMETASTASES: A RETROSPECTIVE MONO-INSTITUTIONAL ANALYSIS OF PREDICTIVE FACTORS FOR CLINICAL OUTCOMES

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Purpose: In this study, we report the retrospective data of a cohort of patients who received stereotactic body radiotherapy for pulmonary oligometastases and we assess the clinical factors potentially affecting the clinical outcomes.

Methods: The present series reports the outcomes of a cohort of 71 patients with pulmonary oligometastases. All patients were treated with SBRT performed with image-guided volumetric modulated arc therapy (VMAT-IGRT), up to 5 secondary lesions. Local control (LC), distant-progression free survival (DPFS) and overall survival (OS) were assessed using Kaplan-Meier method. Univariate and multivariate analyses were performed to assess any potential predictive factor for survival outcomes. A $p<0.05$ was assumed as statistically significant. All statistical analyses were carried out using Graphpad Prism v9.0.2 (Graphpad, San Diego, CA, USA).

Results: A total of 98 lesions in 71 patients were treated from February 2014 to August 2020: 57 lesions were oligorecurrent, 25 were oligoprogressive, 16 were oligopersistent. The most frequent histology subtypes were: colo-rectal in 37.7%, lung cancer (both small and non-small cell lung cancer) in 44.8%, head and neck cancer in 8.1%, other in 9.4%. Median patients' age was 71 (range, 32-93 years). Concurrent systemic therapy was administered in 32.3%. SBRT was performed after a median disease free-interval of 26 months (range, 2-226) delivering a median total dose of 60 Gy (range, 55-70 Gy) in 3-10 fractions for a median BED10=105 Gy (range, 96-180 Gy). Median PTV volume was 10.3 cc (range, 0.3-70.3 cc). Median follow-up was 29.5 months (range, 6-81); acute and late toxicity was negligible with no G>2 adverse event. Our LC rates at 2 and 4-years were 92.4% and 89.8%. DPFS rates at 2- and 4- years were 45.3% and 27.2%. The most frequent site of relapse was lung in 27 cases (38%). A second SBRT course was proposed in 21 cases (29.5%) who developed a further oligoprogression, resulting in median time to second progression of 9 months (range, 2-44) for a 2-year PFS2 rate of 42.4%. At univariate analysis, patients who developed a sequential oligometastasis reported better OS rates (p=0.002). This was also confirmed at multivariate analysis, where also distant progression was associated with worse OS (p=0.022). Interestingly, higher local control rates were associated with better PFS (p=0.04). The 2- and 4- OS rates were 61% and 39.7%

Conclusions: SBRT is feasible for pulmonary oligometastasis with favorable local control and minimal toxicity. At multivariate analysis, patients who develop a further oligometastatic progression maintain a survival advantage compared to polymetastatic dissemination. Also, local control was found to be significantly related to improved PFS rates.

CO92

LUNG OLIGOMETASTASES TREATED BY STEREOTACTIC BODY RADIATION THERAPY: A RETROSPECTIVE SINGLE CENTER ANALYSIS.

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Aims: The lung is one of the most common metastatic sites of malignant tumors. Following the encouraging results reported in curative setting for early stage primary NSCLC, the interest in using stereotactic body radiotherapy (SBRT) as a local treatment modality for patients with lung oligometastases is increasing. In this scenario we investigated the efficacy and safety of SBRT for lung oligometastases in terms of local control (LC), progression-free survival (PFS), overall survival (OS) and toxicities.

Methods: This study retrospectively enrolled a total of 90 patients (143 lesions) treated in our department from January 2017 to June 2020. Lung oligometastases status was defined as the presence of up to 5 metastatic lesions in the lung and with both the primary tumor and any extra-thoracic metastases being controlled. OS was defined as the time between the end of SBRT and death, PFS as the time between SBRT and desease progression. All parameters were estimated using the Kaplan-Meier method. The patient group consisted of 59 men (65.5%) and 31 women (34.5%), with a median age of 70 years (range, 45–93 years). Median tumor volume was 8.745 cm^3 (range, 0.65–143.7 cm^3). The median prescription dose was 45 Gy (range, 20-60 Gy) in 1-5 fractions.

Results: All patients completed the treatment as

planned, and the median follow-up time was 18 months (range, 3-46 months). The median PFS time for all patients was 12.5 months. The 1-, 2- and 3- years actuarial progression free survival (PFS) rate following SBRT were 54, 33 and 18.7% respectively. The median OS for the entire group was 22 months, with an actuarial 1-, 2- and 3- year OS of 78.8%, 56.2% and 48% respectively. Among the 143 lesions in the whole group, 5 (5.55%) lesions had local recurrence (LR). The acute toxicity rate was 13.3%. No patient developed acute grade 3 or 4 toxicity.

Conclusions: SBRT is feasible for lung oligometastases with favorable local control and minimal toxicity. SBRT could also allow to delay the administration of systemic treatments in different settings of lung oligometastases.

CO93

SINGLE *vs* MULTIFRACTION RADIOSURGERY IN BRAIN METASTASES: A MONOISTITUTIONAL EXPERIENCE

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Aims: Stereotactic radiosurgery (SRS) has revolutionized the initial management of patients with brain metastases. The most common late-delayed radiation effect of SRS is the development of brain radionecrosis (RN), which is often associated with the presence of different degrees of neurologic deficits. MF-SRS (2-5 fractions) has been used as an alternative to SF-SRS, with the aim to reduce the incidence of late radiation induced toxicity while maintaining high local control (LC) rates.

Methods: In this mono-institutional analysis, 90 consecutive patients with one or two brain metastases treated with SF or MF-SRS, were included. Endpoints of the analysis were acute toxicity, LC, progression-free survival (PFS), overall survival (OS) and RN in SF and MF-SRS.

Results: 90 patients were eligible and treated with SRS from June 2017 to June 2020 and retrospectively analysed. Metastases were treated with Linac based radiotherapy, using VMAT tecnique. A total of 98 lesions were treated: 82 patients had single metastasis, while 8 patients had two metastases. Median follow up was 20 months (range 8-36 months). Patients were divided into two groups. Group A (35 patients) received a single fraction with a dose ranged from 21 Gy to 24 Gy; Group B (55 patients) received 3 fractions with a dose ranged from 24 Gy to 27 Gy. Size limits were metastases <2cm in longest diameter, largest tumor <4 ml in volume. 6 patients (7%) experienced toxicity grade 1 on the RTOG scale; 2 patients (2%) experienced toxicity grade 2. Every patient undergoing to perfusion and spectroscopic MRI before SRS and then every 3 months. At first follow up (3 months) 70% of patients had CR and 30% had SD, no PD.

The 1-year local control rates were 80% in the SF-SRS group and 92.7% in the MF-SRS group. The 1-year PFS cumulative rate was 85.7%, 83.3% in the group A and 87% in the group B. The 1-year OS cumulative rate was 54.4%, while 51.4% in the group A and 56.4% in the group B. 7 patients (20%) undergoing SF-SRS and 5 (9%) subjected to MF-SRS experienced brain RN; the 1-year incidence rate of RB was 16.6% and 6.4%, respectively.

Conclusions: MF-SRS at a dose of 27 Gy or 24 Gy in 3 daily fractions seems to be an effective and safety treatment modality for brain metastases, associated with better local control and a reduced risk of radiation-induced RN as compared with SF-SRS at dose ranged from 21 Gy to 24 Gy.

CO94

LYMPH-NODAL SBRT VERSUS EXTENDED SALVAGE NODAL RADIOTHERAPY IN OLIGOMETASTATIC GYNECOLOGIC TUMORS, COMPARISON OF TWO DIFFERENT TECHNIQUES

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Aims: To compare outcomes and toxicity of salvage extended nodal radiotherapy (ENRT) versus Stereotactic body radiotherapy (SBRT) on lymph nodal (LN) relapse in oligometastatic gynecological cancer patients (pts).

Methods: From 03/2007 to 05/2021, 53 gynecological cancer patients with LN relapse after previous radical therapies were treated with fluoro-deoxy-glucose positron emission tomography/computed tomography (PET/CT) guided-salvage RT in our Institution: 28 with ENRT+SiB on positive PET/TC LN (group 1) and 25 with SBRT (group 2) on positive PET/TC LN. Primary histology was: ovarian in 20pts, endometrial in 18pts, cervix in 11pts and others in 3pts, almost equally distributed in the two groups. In group 1 two target were defined: the first one included the lymph-nodal chain of interest (pelvic, para-aortic or mediastinal) as clinical target volume (CTV1), adding a 7mm isometric margin to obtain the planning target volume (PTV1). The PTV2 was obtained adding a 5mm isometric margin to GTV-PET. In group 2 the PTV was obtained adding 3 mm isometric margin to GTV-PET. The prescription dose was 50.4Gy/28 fractions (fr) to PTV1 and median dose of 61.01 (50.4-65.5)Gy to PTV2 in group 1, while in group

2 the median dose to PTV was 36 (30-45)Gy in 3-5 fr (6-12Gy/fr). The treatment was delivered with TomoTherapy® or RapidArc® (Varian Medical Systems, Palo Alto, CA) in group 1 and CyberKnife®(Accuray, Sunnyvale, CA) in group 2.

Results: Median follow-up was 32.2 (3.4 – 142.4) and 13.92 (2.08-39.11) months for group 1 and 2, respectively. Acute toxicity were almost negligible in SBRT and mild, in the ENRT group, (see table 1). Local relapse was registered in 4/28 pts and 2/25 pts in group 1 and 2, respectively, while systemic progression in 50% of pts in both group (53% *vs* 48%). Kaplan Meier estimates of 12 months OS were 88% *vs* 93% (p=0,21), while 12-months DFS was 54 *vs* 58% (p=0,99).

Conclusions: In oligometastatic pts lymph-node PET-guided radiotherapy is feasible ensuring good (88.7%) local control. Even considering the limitation due to the difference between the median follow-up, of the two groups, the results seem similar in terms of DFS and OS. ENRT+ SIB toxicity was acceptable but SBRT toxicity was lower. Longer follow-up is necessary to confirm these results.

Table 1.

Table 1 Acute Toxicity ERNT vs SBRT groups.

	Gastro-Enteric	Rectal	Genito-Urinary	Genital	Hematological	Other
Grade	ENRT+SIB (total patients: 28)					
G0	13 (46%)	28 (100%)	25 (89.3%)	25 (89.3%)	22 (78.6%)	26 (92.9%)
G1	10 (35.7%)	0 (0%)	3 (10.7%)	2 (7.1%)	2 (7.1%)	2 (7.1%)
G2	5 (17.9%)	0 (0%)	0 (0%)	0 (0%)	1 (3.6%)	0 (0%)
G3	0 (0%)	0 (0%)	0 (0%)	1 (3.6%)	3 (10.7%)	0 (0%)
	SBRT (total patients: 25)					
G0	20 (80%)	25 (100%)	25 (100%)	25 (100%)	25 (100%)	24 (96%)
G1	4 (16%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
G2	1 (4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
G3	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)

CO95

REIRRADIATION FOR LOCALLY RECURRENT HEAD AND NECK CANCER WITH STEREOTACTIC RADIOTHERAPY USING CYBERKNIFE®

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Aims: Pts with recurrent squamous cell carcinoma of the head and neck (rHNC) have a poor prognosis and reirradiation is a valid option and a potentially curative treatment. SBRT has emerged as a viable treatment modality for pts with rHNC because offers comparable disease outcomes with shorter treatment time and decreased toxicity. Some studies suggested higher rates of CBOS after SBRT. We aimed to evaluate safety and efficacy of SBRT re-irradiation using Cyber-Knife® system (CK) in rHNC. *Methods:* We retrospectively reviewed 29 pts with rNHC reirradiated with CK-SBRT between March 2013 and August 2020. Overall survival (OS) was calculated from date of the end prior-RT (OS-1), and from the date of CK re-RT (OS-2) to last follow-up/death; progression-free survival (PFS) was calculated from date of CK re-RT until documented tumor progression/death. D0,1cc, D1cc, D2cc, Dmean and Dmax to carotid artery during re-RT were recorded.

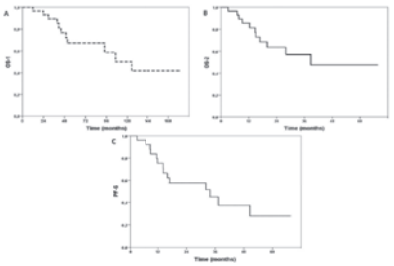

Fig1: 'A' Overall Survival-1 (OS-1) from the end of RT to last follow-up median time 125 months (77-172); 'B' Overall Survival-2 (OS-2) from the end of re-RT to last follow-up median 38 months (n.e.); "C" Progression-free Survival (PF-S) from the end of re-RT to PD (progression disease) median 34 months (4.7-63).

Figure 1.

Results: 20 (69%) were treated with SBRT at first recurrence: 18 pts had in-field recurrence and 2 pts out-field recurrence; 9 pts (31%) were treated after second relapse (7 in-field and 2 out-field recurrence) from primary treatment. No pts received concurrent chemotherapy during re-irradiation. The median re-RT total dose was 25 Gy (range, 20-37.5 Gy) with median of 5 fractions (range, 5 - 15). 6 pts were treated daily and 23 every other day. Median OS1 was 125 months (range, 77-172 months), median OS2 was 38 months (n.e.); median PFS was 34 months (range, 4.7-63 months), Figure 1. Univariate analysis showed that time from the first RT course to first recurrence (>18 months) was a favorable predictive factor for OS1. Instead, GTV and PTV volumes (<16 cc) were favorable predictive factors for OS1, OS2 and PFS. Multivariate analysis revelated that GTV volume (≧16cc) was a statistically significant predictor for OS1 and OS2 and PTV volume (≧16cc) was statistically significant for OS2. Median cumulative BED3Gy was 161.2 Gy (range, 85.6-230.6 Gy) for the left carotid arteries and 151.2 Gy (range, 30.9-227.2 Gy) for the right carotid arteries. No carotid blowout syndrome was reported in our study cohort.

Conclusions: SBRT using CK in patients with rHNC is a safe and feasible treatment option with clear potential for prolonged disease control. Furthermore, CK thanks to its high accuracy, can allows to reduce the risk of CBOS

while maintaining radiobiological parameters described in the literature.

CO96

MAGNETIC RESONANCE GUIDED STEROTACTIC BODY RADIATION THERAPY (MRGSBRT) FOR METASTATIC PATIENTS: A SINGLE CENTER EXPERIENCE

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Aims: SBRT is an increasingly used technique for the treatment of metastases in both poly- and oligo- metastatic patients. The new available hybrid linear accelerators with MR (MR-Linac) combine the best soft tissue contrast resolution offered by magnetic resonance (MR) imaging with cutting-edge online gating methods and the possibility of online treatment plan optimization (online adaptive radiotherapy).

Magnetic resonance-guided stereotactic radiation therapy (MRgSBRT) takes full advantage of the opportunities offered by hybrid technology to perform dose escalation protocols while respecting dose constraints to surrounding organs at risk (OARs). The aim of this retrospective, mono-institutional study was to define the feasibility and clinical benefit of MRgSBRT in a case series of metastatic patients.

Methods: Clinical and dosimetric data from metastatic patients treated with MRgSBRT were consecutively collected. The primary objectives were to define the 12-months local control (LC), progression free survival (PFS) and overall survival (OS) rate. The objective response rate (ORR) included complete response (CR) and partial response (PR). Clinical benefit (CB) was defined as the achievement of ORR and stable disease (SD). Acute and late toxicities were assessed according to the CTCAE version 4.0 scale.

Results: From February 2017 to April 2020, 75 consecutive metastatic patients, accounting for a total of 119 lesions in 109 treatment sessions, were treated by MRgSBRT. Patients and treatment characteristics are summarized in Table 1. Complete and partial response, as well as SD were observed in 6 (5%), 12 (10.1%), and 40 (33.6%) lesions, respectively, reaching a 48.7% CB rate with a 15.1% of ORR. With a median follow-up of 12 months (range: 1-45 months), the 12-month actuarial LC, PFS, and OS rate were 55.1%, 52.6%, 98.6%, respectively. Mild acute toxicity was experienced in 14 (15.3%) patients; no acute toxicity was reported. Late toxicity was observed in 12 patients (10,9%) (pulmonary fibrosis G1).

Conclusions: This study confirms the feasibility of MRgSBRT with a satisfying CB. Treatment was well tolerated reporting low toxicity levels.

Table 1. Patients and treatments characteristics.

	N. (%)
Patients	75 (100)
Lesions	119 (100)
Age, yrs	
Median (range)	69 (34-87)
ECOG Performance Status	
0-1	72 (96)
2	3 (4)
Primary tumor	
Non-small cell lung cancer	9 (7.6)
Pancreas	18 (15)
Melanoma	17 (14.3)
Colorectal cancer	51 (42.9)
Breast	4 (3.4)
Gynecological malignancies	7 (5.9)
Other	13 (10.9)
N. lesions per treatment	
≤5	62 (52,1)
>5	57 (47,9)
Anatomic Site	
Adrenal	7 (5.9)
liver	68 (57.1)
pancreatic	3 (2.5)
lung	41 (34.5)
Metachronous lesions	
No	13 (11)
Yes	26 (21.8)
Yes (>12 months)	80 (67.2)
PTV	

Discussed Poster

DP01

PRELIMINARY REPORT OF TOXICITY AND QUALITY OF LIFE OF THE FIRST 100 PATIENTS TREATED WITH 1.5T MR-GUIDED STEREOTACTIC BODY RADIOTHERAPY FOR PROSTATE CANCER

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Purpose: In the present series we report preliminary acute and late toxicity of the first 100 patients who received 1.5T MR-guided daily-adaptive stereotactic body radiotherapy for prostate cancer.

Methods: We report the outcomes of the first 100 patients treated from October 2019 to December 2020. All the patients were enrolled in a prospective study (MR Linac n°XXXX). Before the treatment, the insertion of the rectal spacer was proposed as optional and applied in 37 patients. Hormone therapy was prescribed according to international guidelines in 32 patients. Toxicity was prospectively collected and assessed using Common Terminology Criteria for Adverse Events (CTCAE v5.0). Quality of life was assessed using IPSS, ICIQ-SF, IIEF-5, EORTC QLQ-C30, QLQ-PR25 and EPIC-26 questionnaires.

Results: A total of 100 patients were treated: 34 were low risk, 29 were favorable intermediate-risk, 31 were unfavorable intermediate-risk, 2 high risk, 4 were low-volume M1 patients. The median age was 71 years (range, 52-84 years), median IPSS was 3 (range, 0-7); SBRT was delivered using 1.5T MR-guided daily adaptive radiotherapy in 5 sessions for a median total dose of 35 Gy (35-36.25 Gy) on consecutive (n=75) or alternate days (n=25). The adapt-to-shape workflow was mainly adopted (480/500 sessions). The median treatment time was 40 minutes (range, 33-83 minutes). The median PTV volume was 105.8 cc (range, 13.98-196.4cc). Acute toxicity rates were as follows: 5 acute G2 genitourinary tract pain events, and two cases of urethral stenosis requiring catheterization fully resolved within the first follow-up. For gastrointestinal toxicity, only 4 cases of G2 events (rectal tenesmus or proctitis) were observed. All the G≥2 events occurred after an average time of 30 days from the end of RT. With a median follow-up of 6 months (range, 2-15 months), for late events, we have recorded 3 late G2 GU events (urinary tract pain) and only one G2 GI proctitis. All patients are alive and in disease control except for one M1-low volume patient who developed distant progression two months after RT. Preliminary QoL assessment revealed a transient decline in fatigue, fully recovered after first follow-up.

Conclusions: Our preliminary report on the first 100 patients of patients who received 1.5T MR-guided daily-adaptive SBRT for prostate cancer reports excellent results in terms of acute toxicity, and minimal impact on QoL. More mature data are warranted.

DP02

IMPACT OF HYDROGEL PERI-RECTAL SPACER INSERTION ON SEMINAL VESICLES INTRA-FRACTION MOTION DURING 1.5 T-MRI-GUIDED ADAPTIVE STEREOTACTIC BODY RADIOTHERAPY FOR LOCALIZED PROSTATE CANCER

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Objectives: MR-guided daily-adaptive radiotherapy is improving the accuracy in the planning and delivery phases of the treatment. Rectal hydrogel-spacer may help in mitigating organ motion, but few data are currently available.

Methods: We aimed to assess any potential impact of the device on seminal vesicles motion by measuring translational and rotational shifts between the pre- and post-treatment MRI scans of a total of 50 fractions in the first 10 patients who underwent MR-guided prostate SBRT (35 Gy/5fx). Of them, 5 patients received the hydrogel-spacer. The comparative analysis was performed using the Mann-Whitney U-Test

Results: Median rotational shifts were: in antero-posterior 0° (range, 0.097°/0.112°; SD=0.05°) *vs* 0° (-0.162/0.04°; SD=0.07°) in the no-spacer subgroup (p=0.36); lateral shifts were 0° (-0.1°/0.54°; SD=0.28°) *vs* -0.85° in the no-spacer cohort (-1.56°/0.124°; SD=0.054°; p=0.22). Cranio-caudal shifts were 0° (-0.121°/0.029°; SD=0.06°) in the spacer-cohort *vs* 0° (-0.066°/0.087°; SD=0.69°; p=0.53). (Table 1 – Figure 1) Median translational shifts were: in antero-posterior 0.9 mm (-0.014 mm/0.031 mm; SD=0.036 mm) in the spacer-group *vs* 0.030 mm (-0.14 mm/0.03 mm; SD=0.032 mm; p=0.8); latero-lateral shifts were -0.042 mm (-0.047 mm/0.07 mm; SD=0.054 mm), *vs* -0.023 mm (-0.027 mm/-0.01 mm; SD=0.023 mm) in the no-spacer group (p=0.94). In cranio-caudal, statistically significant shifts were reported: 0.082 mm (0.06 mm/0.15 mm; SD=0.04 mm) *vs* 0.06 mm (-0.06/0.08 mm; SD=0.09 mm) in the no-spacer cohort (p=0.031) (Table 1 – Figure 2).

Conclusions: A favorable impact of the hydrogel-spacer on seminal vesicles motion was observed only in cranio-caudal translational shifts. Further studies are required to fully investigate the potential contribution of this device on vesicles motion.

Table 1. Rotational and translational shifts with and without spacer.

	Spacer			No Spacer			p-value
	Median	SD	Range	Median	SD	Range	
Rotational shifts (degrees)							
AP	0	0.05	0.097/0.112	0	0.07	-0.162/0.04	0.36
LL	0	0.28	-0.1/0.54	-0.85	0.054	-1.56/0.124	0.22
CC	0	0.06	-0.121/0.029	0	0.69	-0.066/0.087	0.53
Translational shifts (mm)							
AP	0.009	0.036	-0.014/0.031	0.030	0.032	-0.14/0.03	0.8
LL	-0.042	0.054	-0.047/0.07	-0.023	0.023	-0.027/-0.01	0.94
CC	0.082	0.04	0.06/0.15	0.060	0.09	-0.06/0.08	**0.031**

AP=antero-posterior; CC=cranio-caudal; LL=latero-lateral; SD=standard deviation

Figure 1. Rotational Shifts.

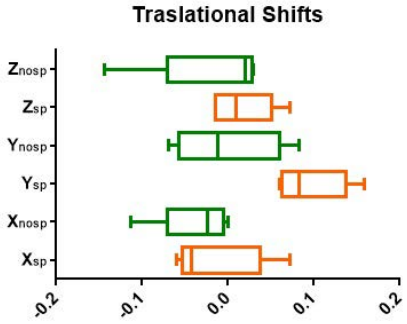

Figure 2. Traslational Shifts.

DP03

THE IMPLEMENTATION OF KNOWLEDGE BASED PLANNING FOR VOLUMETRIC ARC THERAPY IN LEFT SIDE BREAST CANCER

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Aim: Knowledge-based planning (KBP) is a promising technique that can improve plan quality and efficiency. The purpose of this study was to evaluate plan quality with the implementation of KBP in volumetric modulated

arc therapy (VMAT) plans for left-sided breast cancer patients.

Methods: The model libraries were populated with 70 expert clinical plans from treated patients who previously received left-sided breast-conserving surgery and VMAT with simultaneously integrated boost with or without Deep Inspiration Breath Hold technique. The libraries were created on the Varian RapidPlan™. Subsequently, twenty left side breast treatment VMAT plans were generated manually (MP) and with KBP. Total dose was 48 Gy on tumor bed, and 40.5 Gy for left breast in 15 fractions. The plan qualities were compared between MP and KBP plans, in terms of dose coverage and dose to organ at risks (OAR: lung right, lung left, heart, esophagus, spinal cord).

Results: All plans were capable of achieving the prescription requirement (V95% more than 95%). There were almost no statistically significant differences in terms of the planning target volume coverage and dose conformality without differences in terms of doses OARs, between MP and KBP. KBP could save time in generating VMAT plans compared to MP (roundly 60-90 minutes *vs* 30 minutes).

Conclusions: As shown by other analysis, it is feasible to generate acceptable VMAT plans after implementing KBP for left-sided breast cancer, if the model library is populated by expert clinical plans. However, KBP could faster generate comparable MPs for left side breast cancer.

DP04

ASSESSMENT OF REAL-TIME INTRAFRACTION ORGAN MOTION DURING VIRTUAL BRACHYTHERAPY WITH PROSTATE SBRT

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Aims: Extreme hypofractionation requires tight CTV to PTV margins, high dose gradients, and strict adherence to planning criteria in terms of patient positioning and organ motion mitigation. An electromagnetic (EM) transmitter-based tracking device for Virtual Brachytherapy (VB), meant as dose escalated prostate prostate SBRT, was implemented. The aim of this study was to evaluate the intra-fraction organ motion in this setting.

Methods: Thirteen patients with prostate cancer underwent VB in 4 or 5 fractions (BED1.5= 279 Gy and 253 Gy, respectively), using Volumetric Modulated Arc Therapy (VMAT) techniques with flattening filter free (FFF) beams on Linac platform. The EM tracking device consisted in an integrated Foley catheter with a transmitter in a dedicated lumen. Signals sent by the transmitter were detected by antennas in a specific receiver placed on the Linac couch. The system was calibrated to the treatment room isocenter and allowed treatment localization in addition to motion tracking. Starting from the daily CBCT and during the delivery, the organ motion was tracked and VB was interrupted when a 2-mm threshold was trespassed and mandated a new CBCT, unless the offset was transient. Real-time assessment of the duration and magnitude of prostate displacement along the three directional axes was recorded for each fraction.

Table 1. RF transmitter shifts by direction during each phase of patient set-up and treatment delivery.

Total treatment	LAT (mm)		LNG (mm)		VRT (mm)	
Pt	mean	SD	mean	SD	mean	SD
1	0.03	0.30	-0.46	0.93	-0.85	0.73
2	-0.27	0.41	-0.48	0.96	-0.60	1.00
3	0.21	0.28	-0.34	0.49	-0.51	0.59
4	-0.65	0.76	-0.29	0.92	-1.03	1.02
5	-0.45	0.79	0.22	0.69	0.03	0.84
6	-0.30	0.23	0.61	0.52	-0.12	0.26
7	-0.36	0.65	0.12	0.38	-0.37	0.76
8	-0.15	0.45	0.01	0.71	1.06	1.90
9	0.05	0.21	0.04	0.44	0.00	0.67
10	-0.50	0.91	0.04	0.58	-0.07	0.53
11	-0.34	0.37	-0.50	0.71	-0.94	1.11
12	0.04	0.40	0.49	1.96	-0.13	0.60
13	0.33	0.25	0.61	0.78	0.16	0.62
average	**-0.18**		**0.01**		**-0.26**	

Results: Total treatment time lasted on average 10.2 minutes [range 5.5-22.7], 6.7 minutes [range 2.7-17.8] for setup and 3.5 minutes [range 2.5-7.3] for beam delivery. In 45% of the monitored fractions, a new CBCT was mandated. The CBCT was repeated during the initial setup phase in 15 out of 56 fractions, while the beam delivery was interrupted in 10. The transmitter shifts along x, y, and z axes for every treated patient during each phase of setup and beam delivery are reported in table 1. The mean value of the target average deviation was -0.18 mm, -0.01 mm, and -0.26 mm in vertical, lateral, and longitudinal direction, respectively. The prostate was found within 1 mm from its initial position in 83% of the treatment time, between 1 and 2 mm in 13.0%, and exceeds 2 mm only in 4%.

Conclusions: Our findings show that EM tracking is a reliable technique for real-time non-ionizing prostate monitoring during VB, allowing to keep the average target motion within 2 mm. Using FFF VMAT beams shortened the treatment time and significantly contributed to reduce the intra-fractional motion.

DP05

DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING AND HADRONTHERAPY: WHICH ROLE FOR LOCALLY RECURRENT RECTAL CANCERS?

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Aims: Functional Magnetic Resonance Imaging (MRI), such as Diffusion-Weighted Imaging (DWI), has been investigated for tumor characterization and assessment of oncologic treatment response. This retrospective study aims to evaluate the association between pre-treatment DW-MRI and radiological response in patients (pts) with unresectable locally recurrent rectal cancer (LRRC) treated with Carbon Ion Radiotherapy (CIRT).

Methods: Clinical and radiological data of 17 consecutive pts (age range, 34-78 years, M:F=16:1) treated with CIRT as re-irradiation for LRRC (11 pre-sacral, 5 perineal and 1 pre-coccygeal), between 2014 and 2019, were retrospectively collected. Manual contouring of each lesion on pre-treatment DWI acquired with b=1000 smm^{-2} (b1000) and respective Apparent Diffusion Coefficient (ADC) maps were performed with ITK SNAP. ADC and b1000 lesion histogram distributions were described by the following continuous variables (DWI features): median, inter-quartile (iqr), skewness and kurtosis. Pts were stratified as 1-year-responder (R) and 1-year-non-responder (NR) based on their radiological findings at 12 months according to morphological criteria. Non-paired Mann-Whitney U test (α=0.05) was performed to test statistically significant differences of any DWI feature among R and NR patient groups. Such predictive relevant DWI features were fed to K-means clustering algorithm to evaluate its capability in stratifying LRRC patients before CIRT.

Results: Enrolled pts were stratified as follows: 6 NR and 11 R. Volume dimensions for NR and R were respectively 67883,52±121208,29 mm^3 and 16341,56±40686,20 mm^3 (median±iqr). b1000 values for NR and R were respectively 62,5±23,9 and 34±13, while ADC values were respectively 942,5±339 um^2/s and 963±277 um^2/s (median±iqr). All b1000 features showed statistically significant differences between NR and R groups, while only ADC kurtosis showed statistically significant differences. The most relevant features were b1000 median and iqr ($p<0.01$), thus they were fed to K-means clustering. Pts were accordingly stratified into two clusters with an accuracy score of 0,88.

Conclusions: DW-MRI showed promising results in predicting CIRT outcome in LRRC pts. Particularly, b1000 features, especially median and iqr, showed remarkable potentiality of being a biomarker of CIRT response, while poor results were exploited from ADC features. Further investigations should be carried out on a larger cohort of LRRC pts to confirm these data.

DP06

RADIATION THERAPY AND CARDIOVASCULAR IMPLANTED ELECTRONIC DEVICES: A SINGLE CENTER TEN YEARS EXPERIENCE

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Aims: Cardiovascular Implanted Electronic Devices (CIED) are becoming more frequently implanted in oncologic patients (pts). Arrhytmologist and Radiation Oncologist need to cooperate for the management of these pts. *In vitro* and *in vivo* studies demonstrated several malfunctions of CIED following direct exposure to high-energy photons beam. During the treatment planning process CIEDs must be considered as Organ at Risk with specific constraint. In 2018 AIRO and AIAC proposed guidelines for CIED management during radiotherapic care path. Based on CIED dependency, dose at CIED, treatment site and photon beam energy, pts are classified in 3 risk groups (low, moderate and high).

Methods: Since 2010, every pt with CIED was evaluated by a dedicated Arrhytmologist before Radiation Therapy. During the treatment session every pt was followed by ECG/pulse-oximeter + audio-visual monitoring and magnet positioning. After the daily session, every pt was revaluated by the same Arrhytmologist. The contouring of CIED and Lead was integrated into RT plan in order to avoid Maximum Dose > 2 Gy apart from some specific situation. Photon beam energy was 6 MeV for all treatments.

Results: Between 2010 and 2020, 119 CIED pts were treated in our Radiation Department. We report the data related to 75 pts (63.0%), where the CIED was included in the CT-Scan and identified as OAR. 60 pts (80%) had thorax radiotherapy, while for 15 pts (20%) RT was extra thoracic. Twenty-three (30%) pts were at high risk. Median Dmax and Maximum Doses delivered to CIED and Lead were 1.23 Gy- 20.0 Gy and 17.23 Gy- 64.16 Gy

respectively. 45 CIEDs (60%) received <2 Gy, 26 CIEDs (34.7%) a Dmax between 2 and 10 Gy, and 4 CIED (5.3%) received a Dmax> 10 Gy. 34 Leads (45.3%) received > 10 Gy. During CIED interrogations, no hardware failure was detected, neither in CIED, nor in Lead.

Conclusions: In our experience, CIED pts can undergo safely to radiation treatment. Even for high-risk pts, especially where Dmax at CIED was > 2 Gy no CIEDs failures were observed. To the best of our knowledge, this study is the first that included CIED and Lead as distinct OAR, in order to evaluate their dose distribution. Even if Dmax of Lead was high, the effect was not clinically significant.

DP07

NIVOLUMAB IN ADVANCED HEAD AND NECK SQUAMOUS CELL CARCINOMA OLDER PATIENTS COHORT: SAFETY, EFFICACY DATA AND PREDICTIVE VALUE OF GERIATRIC ASSESSMENT

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Aims: The purpose of this retrospective study was to evaluate efficacy and tolerability of Nivolumab in elderly and frail patients affected by locally advanced or recurrent/metastatic head and neck squamous cell carcinoma (HNSCC).

Methods: We retrospectively collected data from HNSCC patients treated at our institution with Nivolumab monotherapy. Overall Survival (OS) and Progression Free Survival (PFS) were determined as outcome measures. Immune-related adverse events (irAEs) were scored according to Common Terminology Criteria for Adverse Events scale version 4.03. Geriatric-8 score (G8) and Age-adjusted Charleson Comorbidity Index (ACCI) were retrospectively extrapolated from medical records. Student's t test and Mann Whitney U test were used to compare continuous variables, while the Chi square test or Fisher's exact test were used to compare categorical variables in differently frail subgroups.

Results: 23 elderly HNSCC patients aged over 70 years and treated with Nivolumab from April 2018 to May 2021 were included in our analysis. Median Age at baseline was 77,9 years (range 70-88). Four patients had ECOG PS 0 at diagnosis, while thirteen patients had PS 1 and six patients had PS 2. All patients had G8 score lower or equal to 14, while ACCI was 4 for one patient, 5 for three patients, 6 for two patients and 7 or higher for seventeen patients. Primitive tumor location was oropharynx (26,1%), hypopharynx (4,3%), larynx (8,7%), oral cavity (47,9%) and paranasal sinuses (13%). At data cutoff, 10th of May 2021, mOS was 7 months (range 0-27) and mPFS was 5,5 months (range 0-27). Mean number of Nivolumab cycles received was 11, with 43,5% of patients receiving more than 13 cycles. irAEs of any grade were observed in 56,5% of patients, most common being grade 1 cutaneous rash and hypothyroidism (21,8% each) and there was only one irAE of grade 3, being cutaneous rash. Only 1 patient discontinued treatment due to remittent G3 cutaneous rash. Statistical tests conducted did not show significant differences between patients with PS 0-1 *vs* PS 2 or ACCI <7 *vs* ≥ 7 in duration of treatment, outcome or incidence of irAEs.

Conclusion: Nivolumab in our elderly HNSCC patients demonstrated good efficacy and safety profile regardless of PS or selected frailty scores, suggesting that they may not be as realiable in predicting prognosis and tolerability in this setting of patients. Further data is needed to confirm our findings.

DP08

STEREOTACTIC RADIOTHERAPY BOOST IN LOCALLY ADVANCED CERVICAL CARCINOMA PATIENTS (STARBACS): A PHASE II, SINGLE-ARM, MONOCENTRIC STUDY

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Aims: To evaluate feasibility, toxicities and clinical outcomes (LC, PFS e OS) in locally advanced cervical cancer patients treated with platinum-based chemotherapy concomitant to radiotherapy followed by SBRT consolidation boost.

Methods/design: The STARBACS study was designed as a phase II, single-arm, monocentric study. Inclusion criteria comprehend histologic diagnosis of cervical cancer; clinical and radiological diagnosis of locally advanced (M0) disease; subscribed quality of life questionary (QoL- SF36) at the enrolment. The radiological evaluation provided inferior abdomen-pelvis Magnetic Resonance Imaging and 18F-FDG-PET. Patients will be assigned to platinum-based chemotherapy (40 mg/m^2) plus radiotherapy to a total dose on clinical target volume (CTV) of 46Gy. An SBRT-boost (12-21Gy) on gross tumour volume (GTV) will be delivered after loco-regional restaging with contrast-enhanced MRI. An isotropic margin of 2mm (PTV1-2) both on CTV and GTV will be applied. For contouring, delineation will be matched simulation-TC 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) will be used. The primary endpoint is toxicity evaluation according to Common

Terminology Criteria for Adverse Events (CTCAE v4). Grade 1 and 2 of the scale will be considered as ordinary adverse events, Grade ≥ 3 toxicities will be defined as severe adverse events. Local control (LC) is defined as the time from the SBRT-boost to loco-regional progression, defined as measurable tumour lesion increase of more than 25% compared to initial diameters according to the Response Evaluation Criteria in Solid Tumours (RECIST) response criteria; PFS was considered as the time from concurrent radio-chemotherapy to locoregional or distant failure. OS was calculated from the diagnosis to the date of death or last registered follow-up. The patients will be submitted to clinical re-evaluation at a pre-established three months interval and radiological evaluation at six months according to the international guideline.

Expected Results The STARBACS study will provide on feasibility and clinical efficacy of SBRT-Boost in LACC compared to brachytherapy.

DP09

VMAT STEREOTACTIC RADIOTHERAPY FOR BRAIN METASTASES SURGICAL CAVITIES: HYPERARC AND RAPIDARC DOSIMETRIC COMPARISON

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Aims: HyperArc (HA) is a non-coplanar volumetric modulated arc therapy (VMAT) treatment approach with single isocenter for intracranial stereotactic radiotherapy. HA provide the advantage of delivering high dose to target volume while minimizing dose to normal tissue for single or multiple targets compared to the conventional VMAT technique. Stereotactic radiotherapy for brain metastases resection cavities represents a challenge because of large volume and irregular shape with related high toxicity. HA plans were calculated for 10 consecutive patients who received hypofractionated stereotactic radiotherapy on resection cavity with VMAT Varian RapidArc (RA).

Methods: HA plans were generated with 6MV FFF for a TrueBeam LINAC equipped with 2.5 mm central leaves. RA plans previously delivered on a TRILOGY LINAC equipped with 5 mm leaves MLC with 6MV. All plans were calculated with Acuros XB algorithm on Eclipse TPS. Homogeneity index (HI), RTOG and Paddick conformity index (CI), gradient index (GI) and V2Gy-25Gy for normal brain tissue were compared as indicator of PTV coverage and brain tissue spare. Monitor units (MU) per fraction were evaluated as an indicator of irradiation efficiency. Dose was prescribed to the minimum of the target (100% of the prescription dose to 100% of PTV) for both HA and RA plans. For HA plans Dmax was limited to 130% of the prescription dose. Total dose was 27-35 Gy in 3-5 fractions. Mean PTV was 31.37 cc (range 7.20-81.31).

Results: HA and RA provided comparable RTOG CI (mean±SD 1.14±0.03 vs.1.16 ±0.04, p=0.28) and Paddick CI (0.88±0.02 *vs* 0.87±0.30, p=0.29). HI (1.22±0.06 *vs* 1.15±0.05, p<0.01) and GI (2.31±0.22 *vs* 2.59±0.34, p<0.01) values were more favorable for HA than RA. V2Gy of normal brain tissue values were similar for HA and RA plans (539.8±249.4 *vs* 568.1±257.9 cc, p=0.11). Low-to-moderate dose spreads (V4Gy-V18Gy) were significantly reduced (p<0.01) in the HA plans over that of RA. Mean V18Gy was 24.6±14.2 cc *vs* 26.4±17.5 cc (p<0.01) and V25Gy was 11.7±7.9 cc *vs* 11.8±8.7 cc (p=0.35) for HA and RA respectively. Mean MU per fraction were 2910±1129 *vs* 3740±1061 for HA and RA plans respectively.

Conclusions: HA plans provide steeper dose fall-off and comparable conformity with respect to the delivered RA plans. HA plans reduce MU delivering by one third resulting in more efficient irradiation technique.

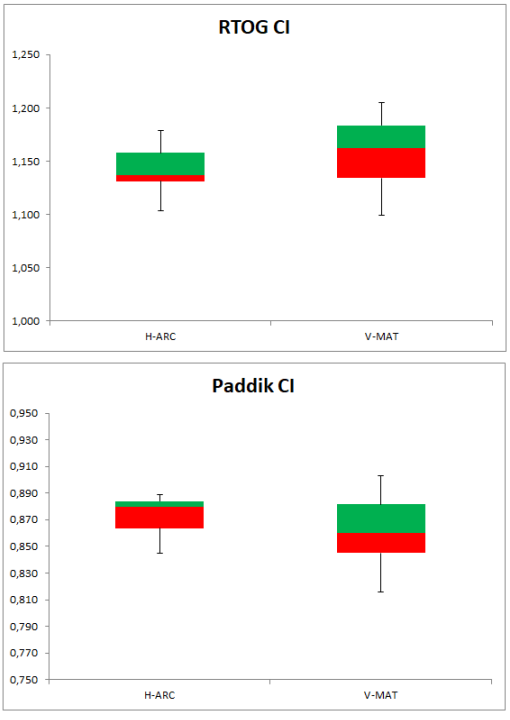

Figure 1.

DP10

LONG-SURVIVING GLIOBLASTOMA PATIENTS TREATED WITH POSTOPERATIVE RADIO-CHEMOTHERAPY: A RETROSPECTIVE ANALYSIS

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Aims: Glioblastoma (GBM) is a highly aggressive tumour with a median Overall Survival (OS) of 12-15 months and a Relapse Free Survival (RFS) of 7-10 months after surgery. The long-term survivors (LTS), defined as patients (pts) alive two years after diagnosis, are only 9-13%. Five- and 10-year survival is less than 5% and 1%, respectively. We retrospectively evaluated the characteristics of LTS treated with adjuvant radiochemotherapy.

Methods: We analysed patient characteristic of 32 LTS (18 males and 14 females). We also correlated OS and RFS with their characteristics and with the received treatment. Therefore, we examined pts with OS >5 and >10 years.

Results: Median age was 57 years (range 18-71) and median Karnofky performance status (KPS) was 90% (range 70-100%). MGMT methylation was known in only 5 cases (methylated in one) and IDH mutation (wild type) only in 2 cases. Tumour site was frontal lobe in 12 cases and temporal lobe in 17. After surgery (radical resection except one), all pts received adjuvant radiotherapy (60 Gy in 30 fractions); 30 of them were treated with concomitant TMZ and 29 with adjuvant TMZ for a median of 20 cycles (range 2-120). Of the 29 pts, only 4 pts received adjuvant TMZ for 6 cycles or less, 16 pts were treated with 7-24 cycles (median 12) and 12 pts were treated with >24 cycles (median 54, range 26-120). No toxicity was observed in pts treated with adjuvant chemotherapy. Sixteen pts (50%) received induction chemotherapy for 1 cycle due to waiting list problems and three of them had G4 hematologic toxicity. Local relapse was observed in 17/29 cases after a median of 22 months (range 9-58). After relapse, 4 pts were treated with surgery plus chemotherapy, 4 with chemotherapy alone, 1 with radiotherapy alone and 8 with best supportive care. Eight pts (28%) are alive with complete remission after a median of 76 months (range 34-151), 21 pts (72%) died with a median of 31 months (range 24-86). There was a statistically significant difference between OS and RFS in pts receiving more or less 24 cycle of adjuvant TMZ (OS: 59 *vs* 29 months and RFS: 47 *vs* 19.5 months, p>0.001). OS was >5 years for ten (31%) pts and >10 years for 4 of them (the so-called extreme survivors). OS at 2-, 5- and 10-years was 17%, 5% and 2%, respectively.

Conclusion: Our analysis confirmed previously published data, showing a better prognosis with younger age, good performance status and radical surgery. With the limitations of the small number of patients, our study showed an improved OS and RFS for pts treated with >24 cycles of adjuvant TMZ.

DP11

RE-IRRADIATION OF RECURRENT MEDULLOBLASTOMA IN ADULTS PATIENTS: A SINGLE INSTITUTION EXPERIENCE

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Aims: To evaluate safety and efficacy of re-irradiation (re-RT) with 3D-conformal radiation therapy (3D-CRT) and radiosurgery (RS) with both single and multisession approaches, in terms of toxicity and survival for recurrent medulloblastoma (RMB).

Methods: Study population consisted of adult patients diagnosed with RMB and treated with either RS or 3D-CRT at our Institute. Clinical, dosimetric and radiological data were retrospectively collected and analyzed.

Results: Twenty-two patients treated from October 2002 to May 2020 were enrolled. Median age at first diagnosis was 32 (range 4- 56). All patients were already treated with upfront surgery followed by craniospinal irradiation plus boost to the posterior fossa and 17/22 (77%) patients received adjuvant chemotherapy, mainly platinum-based. At relapse, 20/22 (91%) patients underwent RS and 2/22 (9%) 3D-CRT; 4/22 (18%) received both. 11/22 (50%) patients received 2 or more courses of re-irradiation. Median age at first recurrence was 38 (range 19-60) and median interval from primary irradiation to first re-RT was 36 months (range 4-438 months). For single and multi- session RS median prescribed total dose was 18 Gy (range 9-20 Gy) and 21 Gy (range 10-25 Gy/2-5 fractions), respectively. For 3D-CRT median total dose was 25 Gy (range 20-30.6 Gy/5-17 fractions). At a median follow up of 19 months (range 1-104 months), treatment response was evaluable in 18/22 (82%) patients. Local control was achieved in 7/18 (39%). Acute toxicity occurred in 4/22 (18%). Main symptoms were fatigue (3/22, 14%), nausea (2/22, 9%), local pain (2/22, 9%) and lower limb paraesthesia (2/22, 9%). We also registered a single case of paraplegia and lower limb anesthesia. The MRI imaging showed spinal cord compression at D11 due to perilesional oedema. The patient was treated medically with high dose steroids with optimal clinical response. No late post-irradiation side effects were recorded. As of April 2021, 3/22 patients (14%) were alive. Global median overall survival was 79 months (range 26-440 months). For patients treated with

2 or more courses of re-RT median overall survival was 73 months (range 27–154 months).

Conclusions: To date the treatment of RMB, especially in adults, is still not standardized due to lack of clear guidelines and a limited number of literature studies. Re-RT can be considerate a safe and well-tolerated approach. However, doses, fractionation and techniques are still under debate.

DP12

CARBON ION RADIATION THERAPY FOR LOCALLY ADVANCED HEAD AND NECK MUCOSAL MELANOMA: CLINICAL EXPERIENCE IN 40 CONSECUTIVE PATIENTS

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Aims: To retrospectively analyze toxicity (tox) and outcome of patients (pts) with locally advanced head and neck mucosal melanoma (LAHNMM) treated with carbon ion radiotherapy (CIRT) at our institution.

Methods: LAHNMM pts who received curative CIRT from June 2013 to June 2020 were included in this analysis. Tox was scored using CTCAE v.5.0 criteria. After CIRT, MRI was performed every 3 months (mo.) in the first 2 years, then every 6 mo. until the 5th year, then once a year. Pts were restaged with total body CT or 18F-FDG PET once a year or according to Medical Oncologist's indications. Local control (LC), overall survival (OS) and progression free survival (PFS) were calculated with Kaplan-Meier Method.

Results: Overall, 40 pts were included for analysis. Median age was 70 years (range 39-87). Tumor (T) site was nasal cavity/paranasal sinuses/other in 77.5%/12.5%/10%, T status was naïve/recurrent in 77,5%/22,5% of pts. T stage was T3/T4 in 17(42,5%)/23(57,5%) pts. Mutational status was unknown in 12(30%), wild type in 23(57,5%), NRAS/BRAF/c-KIT-mutated in 3(7,5%)/1(2,5%)/1(2,5%) pts. 28 (70%) pts were treated after surgery, 10 (25%) with exclusive CIRT, 2 (5%) pts received systemic therapy before and after CIRT (chemotherapy in one case, immunotherapy in the other). For operated pts, surgery was endoscopic/open/combined in 22(78,6%)/3 (10,7%)/3(10,7%) cases, with R0/R1/R2 margins in 2(7%)/19(68%)/7(25%) pts. Mean GTV volume, outlined in R2 postoperative and definitive cases, was 137 cc (range 5-276 cc). CIRT total dose was 65.6 Gy(RBE) and 68.8 Gy(RBE) in 22(55%) and 18(45%) pts, respectively (16 fractions, 4 fractions/week). 18 pts (44%) received immunotherapy after CIRT. Median follow-up (FU) time was 18 mo (range 5-81 mo). Acute tox at the end of CIRT was G1-G2 in 95% and G3 in 5% of pts, with no tox >G2 at 3 mo. follow-up. Late tox was G0 in 10% and G1-G2 in 81% of pts; 2 pts (5%) had G3 events (unilateral hearing impairement in one case and unilateral visual impairement), 1 pt had a G4 unilateral visual loss (expected tox). At last FU, LC was maintained in 33 pts (84,6%). 2 year- LC, PFS and OS were 84.5%, 33% and 59%, respectively.

Conclusions: CIRT in LAHNMM pts is promising in terms of LC and safety. Impact of mutational status and immunotherapy are still under investigation. Prospective trials and further multidisciplinary efforts are required to improve pts' prognosis and survival.

DP13

ARTIFICIAL INTELLIGENCE FOR REAL TIME TUMOR TRACKING IN THORACIC RADIOSURGERY WITH RADIXACT SYSTEM

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Aims: Herein we report preliminary results of a pilot study of single fraction SABR in elderly and multiple lung oligometastatic patients. This study investigates the feasibility and the compliance to lung radiosurgery.

Materials: Lung tumor tracking allows to reduce the healthy tissue irradiation and is theoretically faster than the gating technique. Single fraction SABR in lung nodules is established as an appropriate treatment in oligometastatic patients. However, the risk of target missing in single fraction is higher than in fractionated SABR. Recently and only present in few centers worldwide, Accuray Int, developed a free breathing real time tumor tracking based on artificial intelligence for helical IMRT delivery (Synchrony on Radixact system). 28 Gy single fraction SABR was planned in 6 patients in both peripheric and central lesions. In room time, nodule volumes, local response, real time tracking verification have been assessed for all the patients involved.

Results: Mean patients age was 79 years old (75-84) and 4 ones were men and the remaining 2 were women; in all cases their PS was 0. All patients had oligometastatic disease: primary melanoma (2), primary NSCLC (2) and CRC (1). Concurrent immunotherapy (respectively Pembrolizumab, Nivolumab and Ipilimumab) was delivered in 3 patients. Lesions were both central (3/6) that peripheral (3/6). Mean GTV volume was 8,50 cc (from

1,9 cc up to 18,2 cc), minimum diameter of lesions was 129 mm to 312 mm. Median beam on time was 17,6 min (910 sec – 1255 sec). The analysis of the cumulative vector of nodules movement, measured a median excursion of 7 mm with a median respiratory cycle time of 4 seconds. No lesions progressed, due to the short follow up, the shrinkage timevolume plot is currently under evaluation. Median follow-up was 2 months, during which we observed no clinical acute toxicity, only one patient showed a radiological pattern of diffuse consolidation.

Conclusions: The preliminary results of our pilot study, showed that lung SABR executed throughout Synchrony on Radixact system is a high compliance treatment in elderly oligometastatic patients. This advanced technique needs a high expertise of all the personnel but is very promising in specific cohort of patients.

DP14

PROSPECTIVE TRIAL OF STEREOTACTIC ABLATIVE RADIOTHERAPY TO PRIMARY LOCALLY ADVANCED TUMOR IN OLIGO-METASTATIC NON-SMALL CELL LUNG CANCER PATIENTS: GOOD NEWS FOR A NEW STANDARD OF CARE!

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Aims: Stereotactic Ablative Radiotherapy (SABR) has shown high rates of local control and prolonged survival in early-stage non-small cell lung cancer (NSCLC), though its role in oligometastatic disease is undefined. This study aimed to evaluate SABR as a local consolidative therapy in oligometastatic (oligoM) NSCLC patients.

Methods: In this prospective trial, we sought to evaluate SABR to primary locally advanced (LA) tumor and metastatic sites in oligoM NSCLC patients. Fit patients received initial systemic therapy according to international guidelines. Patients without progression after front-line therapy (chemotherapy, immunotherapy and targeted therapy) were evaluated by an 18F-FDG-PET/CT to receive consolidative SABR to the primary and all metastatic sites (≤ five lesions).

Results: Between May 2018 and February 2021, 17 oligoM NSCLC were included. Median age was 71 years (range, 38-85), 14 (82%) were male and 10 (59%) had adenocarcinoma histology. The main site of metastasis was bone, adrenal gland and brain in 7 (41%), 4 (23%) and 3 (18%) patients, respectively. 15 (88%) patients received systemic front-line therapy: chemotherapy in 8 (47%), immunotherapy in 4 (23%) and a tyrosine kinase inhibitor in 2 (12%). The median administered dose to primary LA tumor was 45 Gy (range,35-50) in 5 fractions. Median follow-up achieved 16 months (range, 6-37). 3 (18%) and 7 (41%) patients developed local relapse and distant metastasis after a median time of 14 months (range,9-15) and 4 months (range,3-6), respectively. No adverse events of ≥G3 was recorded. At las follow-up 16 (94%) patients are alive, only 5 (33%) discontinued first front-line therapy and started second-line therapy.

Conclusions: The use of SABR on primary LA tumor in oligoM NSCLC patients was well tolerated and showed favorable clinical outcomes regarding second line therapy-free survival and overall survival. Also considering the results of other prospective trials, consolidative SABR to primary LA tumor should be included as standard of care in oligoM NSCLC patients.

DP15

STEREOTACTIC ABLATIVE RADIOTHERAPY AFTER NEOADJUVANT CHEMOTHERAPY IN LOCALLY-ADVANCED NON-SMALL-CELL LUNG CANCER ELDERLY PATIENTS UNFIT TO CONCURRENT CHEMO-RADIOTHERAPY: FEW FRACTIONS FOR A GREAT OUTCOME!

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Purpose: Although the standard of care in LA-NSCLC is concurrent chemo-radiotherapy (ChT-RT), there is a lack of prospective trials regarding the best treatment in elderly patients. We enrolled in a phase II trial unresectable locally advanced non-small cell lung cancer (LA-NSCLC) elderly patients unfit to concurrent ChT-RT, to assess effectiveness and safety of stereotactic ablative radiotherapy (SABR) after neoadjuvant chemotherapy (ChT).

Methods and materials: The cutoff of age ≥70 years was chosen as a commonly used definition of elderly in LA-NSCLC patients. All patients were unfit for concurrent chemo-radiotherapy (ChT-RT). The tumor volume included primary tumor (T) and CT-PET positive node/s (N). A simultaneous integrated boost (SIB) was optimized to differentiate the dose for primary tumor (T) and lymph-node/s (N).

Results: 27 LA-NSCLC elderly patients unfit for concurrent ChT-RT were recruited. Median age was 73 years (range,70-85) and 21 (78%) were male. Histology was squamous cell carcinoma (SCC) and adenocarcinoma (ADK) and in 17 (63%) and 10 (37%), respectively. The stage was IIB, IIIA, IIIB and oligometastatic IV in 2 (7%), 9 (33%), 10 (37%) and 6 (22%) pts, respectively. All patients had "ultra-central" located tumor with PTV overlapping the major airways. In 14 (52%) cases T and N were separately treated using SIB technique to administer a higher dose to T. Median prescribed dose was 40 Gy (range, 35-50) and 40 Gy (35-45) in 5 fractions to T and N, respectively. During a median follow-up of 19

months (range, 4-45), 7 (26%) and 11 (41%) patients had experienced local recurrence (LR) and nodal regional recurrence at a median time of 9 (range, 4-24) and 9 months (range, 4-28), respectively. 11 (41%) patients developed distant metastases after a median time of 9 months (range, 3-27). At last follow-up, 21 (78%) patients were alive, 10 (48%) without radiological evidence of disease. Treatment compliance was 100% and no patients developed ≥ G3 acute and late toxicities.

Conclusions: In our phase II prospective trial, SABR after neoadjuvant ChT in LA-NSCLC elderly patients was safe and effectiveness. The treatment compliance was excellent and no patients experienced ≥G3 toxicity. Few fractions of SABR could represent an attractive option to obtain a "great" outcome in LA-NSCLC elderly patients unfit for concurrent ChT-RT.

DP16

A SURVEY AIMED TO TEST PATIENTS NEEDS FOR THE DEVELOPMENT OF A MOBILE APPLICATION FOR PATIENTS UNDERGOING BREAST RADIOTHERAPY (RADIOSA PROJECT)

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Aims: Breast cancer requires integrated multimodal treatments, including surgery, chemotherapy, and radiation therapy. Monitoring of symptoms during treatment can help to identify those patients who needs medical interventions. Use of mobile Apps in the radiotherapy-oncology field gives the possibility of daily monitoring and supportive care for patients undergoing breast radiotherapy. A few mobile Apps are specific to breast cancer and to best of our knowledge no App is specific for patients treated with radiotherapy. The aim of this survey is to test the acceptability and satisfaction related to the development of a dedicated mobile application (RADIOSA project: Mobile Application on Breast Radiotherapy) among breast cancer patients undergoing radiotherapy.

Methods: Qualitative questionnaires were administered from May 17, 2021 to June 4, 2021 on a sample of female patients undergoing breast adjuvant radiotherapy treatment to understand which aspects could be most useful for them to be included in the new mobile App.

Results: 30 patients completed the questionnaires (median age 62 years; range 41-88 years). All patients (100%) welcomed the proposal for dedicated mobile App. Of these, 90% of patients preferred the possibility of requesting an emergency visit, to view tutorials on the management of local side effects such as skin toxicity, to perform physiotherapy exercises to facilitate correct positioning of the arm during radiotherapy. 87% of patients were in favor of FAQ area and the possibility of breast massage tutorials, while 80% of patients appreciated the option of following a calendar with planning of all radiotherapy sessions. Instead, 67% of patients showed no interest in receiving notifications regarding the timing of cream application, while 57% patients showed little interest in viewing tutorials on how to hold their breath for those radiotherapy sessions involving the technique of voluntary inspiration (however among these patients, only 14% of patients was receiving breast hold radiotherapy). Finally, only 7% patients provided their suggestion in the free section of survey, asking to insert a dedicated section for psychological support.

Conclusions: "RADIOSA" project was welcomed by all patients. After this preliminary phase, we have decided to add a section for the request of psychological support in the mobile App. We are now proceeding to develop the application with the goal of creating the simplest and most intuitive interface as possible.

DP17

FRACTIONATED SRT ASSOCIATED TO SYSTEMIC THERAPY IN PATIENTS WITH BREAST CANCER BONE METASTASES: FEASIBILITY AND EFFICACY

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Aims: This study aims to assess the safety and efficacy of fractionated SRT (FSRT) associated to systemic therapy in patients with breast cancer bone metastases.

Materials and Methods: Patients with breast cancer bone metastases who were treated with FSRT within 21 days of receiving systemic therapy were identified. All lesions were treated with LINAC-based FSRT. Treatment was delivered using IMRT or VMAT in supine position using vacuum-locked or other customized devices. All patients received systemic therapy in relation to molecular pattern. Local control was evaluated at least after two months after treatment completion by means of radiological exams, while pain responses assessed at the end of treatment and every three months thereafter. Acute toxicity were reported and graded as per standardized Common Toxicity Criteria for Adverse Events 4.0 criteria.

*Results:*From January 2019 to March 2021,a total of 40 patients with breast cancer bone metastases were identified. The median age of patients at the time of RT was 54 years. All patients were treated with higher doses of radiotherapy delivered in three fractions according to the lesion's site (Total dose 18 Gy, 21Gy or 27Gy). The most common treated site was axial skeleton (83%). 18 patients for a total of 29 lesions, were treated with FSRT and concurrent systemic therapy. Administrated sistemic therapy was as follow: 10 patients (55.6%) received

CDK4/6 inhibitors (12 radiotherapy courses), 6 patients (33.3%) trastuzumab (12 radiotherapy courses), 2 patients (11,1%) Eribulin. The most common collateral effect observed was neutropenia, in particular in association with CDK4/6 inhibitors. All patients completed treatment without interruptions. During the follow-up the most used diagnostic exam was the PET/CT. With a median follow-up of 7 months (range: 1-24 months), we recorded: patients treated in association with CDK4/6 inhibitors had 2 complete response (CR), 4 partial response (PR), 5 stable disease (SD), 1 progression disease (PD); patients treated with trastuzumab 3 CR, 3 PR, 4 SD, 2 PD; all patients treated with Eribulin had SD. 13 treatments determined a pain relief, of which eight a complete pain response. Nobody developed pathologic fractures.

Conclusions: Highly hypofractionated radiation therapy is a feasible and tolerable treatment for bone metastases. Longer follow-up will be needed to accurately determine response and late effects.

DP18

EVALUATION OF RADIOMICS AS PREDICTIVE AND PROGNOSTIC FACTOR IN PATIENTS WITH BREAST CANCER UNDERGOING NEOADJUVANT CHEMOTHERAPY FOLLOWED BY SURGERY±RADIOTHERAPY

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Aims: Over years, neoadjuvant chemotherapy (NAC) has been increasingly used in breast cancer initially to reduce the tumor load in patients scheduled for mastectomy, and at present time to achieve pathological Complete Response (pCR). Recent advances in radiomics have provided insights in personalized medicine related to tumor detection, sub-type classification, and assessment of treatment response. Among other strategies to predict response to NAC, radiomics features extracted from pre-treatment contrast-enhanced Magnetic Resonance Imaging (CE-MRI) have shown promising results. The aim of this study is to predict pCR of NAC in patients affected by breast cancer using radiomics features calculated from pre-treatment CE-MR images.

Methods: This retrospective observational study 39 patients with histologically confirmed breast cancer treated between July 2014 and July 2020. All patients underwent NAC, MRI evaluation before and after NAC, clinical examination, standard imaging (breast ultrasound and mammography). 28 patients (72%) responded to NAC while 11 patients (28%) did not.

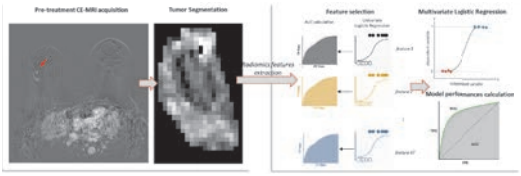

Figure 1. Analysis pipeline: 47 radiomics features were extracted from segmented CE_MR images acquired before NAC. Univariate logistic regression analyses were performed to select a subgroup of these features in terms of their ability capability of classifying patients between responders and non-responders to therapy [criterium AUC>0.65]. Multivariate logistic regression was then run by using this sub-set of radiomics features.

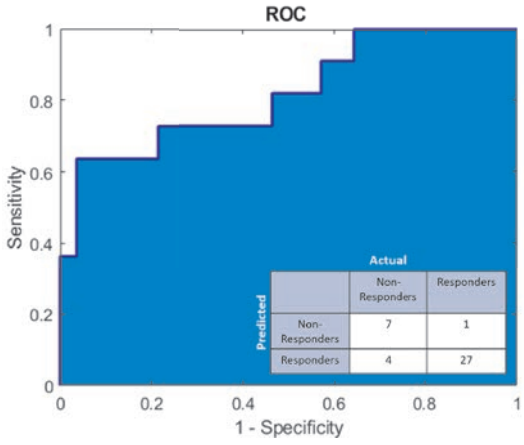

Figure 2. ROC curve and confusion matrix associated with the multivariate classification model.

Figure 1 shows an overview of the analysis pipeline. After manual contouring and masking of tumor tissue on pre-NAC CE-MR images, 47 quantitative features were computed using 'Radiomics', an open-source MATLAB© toolbox. Subsequently, univariate logistic regression models (dependent variable: pathological response) were fitter for each feature. 10 features which yielded an area under the Receiver Operating Characteristic (ROC) curve (AUC) > 0.65 and were fed to a multivariate logistic regression classifier which was trained to discriminate responders *vs* non-responders at pathological specimen. Model were evaluated in terms of AUC, sensitivity and specificity.

Results: Figure 2 shows the ROC (AUC=0.818) which characterizes the multivariate classifier along with the corresponding confusion metrics. The model correctly classified 27 responders (out of 31) and 7 non-responders (out of 8), corresponding to a specificity of 0.871 and a sensitivity of 0.875.

Conclusions: This retrospective observational study demonstrates the usefulness of radiomics features in the prediction of patients' response to NAC. Indeed, by using

only radiomics features calculated from CE-MR images acquired before therapy inception, we were able to discriminate responders from non-responders with high specificity and sensitivity (both larger than 0.87). This may open novel avenues for better treatment selection as well as patient stratification for future clinical trials.

DP19

PHASE II STUDY OF INDUCTION FOLFIRINOX FOLLOWED BY RADIOCHEMOTHERAPY IN BORDERLINE RESECTABLE OR UNRESECTABLE LOCALLY ADVANCED PANCREATIC CANCER: RESULTS OF THE PLANNED INTERIM ANALYSIS

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Aims: The aim of this study was to evaluate the safety and efficacy of induction treatments in patients with borderline resectable or unresectable locally advanced pancreatic cancer and the efficacy of pre-operatory staging with PET-CT and laparoscopy in addition to CT scan.

Methods: From 2015 to 2020 we evaluated 42 patients with borderline resectable or unresectable pancreatic cancer. A pre-treatment staging was performed with CT scan, 18FDG PET-CT scan and laparoscopy. Patients with metastatic disease were excluded. Suitable patients received induction treatments with FOLFIRINOX, after 4 cycles patients were restaged with CT scan and 18-FDG PET-CT. Patients without evidence of metastatic disease started radiochemotherapy with weekly gemcitabine. After radiochemotherapy, before surgery evaluation, patients performed CT scan and 18-FDG PET-CT scan.

Results: Fifteen patients (39.5%) were excluded from the protocol because of the evidence of metastatic disease, and thus a total of twenty-three patients were consequently enrolled. Four patients (1.5%) had a progression of disease after induction chemotherapy. Median follow-up 12.6 months. Nineteen patients (50%) completed radiochemotherapy. Six patients (15.8%) had a progression of disease after radiochemotherapy. Four patients are currently treating. Eleven patients underwent surgical radical resection (28.9%). The Median OS and the Median PFS in patients who have completed radiochemotherapy were 15.7 months and 13 months respectively. One-year OS, 1-year PFS, 1-year LPFS and 1-year MPFS were 87.1%, 58.6%, 89.2% and 60% respectively. Patients who underwent resection had a significant longer median OS compared with non resected patients (17 months *vs* 13.2 months, $p<0.05$). The median PFS for resected patients was 14.5 months compared with 8.1 months for non resected patients ($p=0.007$). For the entire cohort of patients the treatment was well tolerated. Only nine patients (23.7%) had haematological grade 3-4 toxicities.

Conclusions: Altough the follow-up time is limited, these preliminary data of the protocol treatment show promising results for patients with borderline resectable and unresectable pancreatic cancer. The best results were observed in patients who were resectable after the end of study protocol. The enrollment is actually ongoing. Continued optimization in multimodality therapy and an accurate patient selection are crucial for the appropriate treatment of patients.

DP20

PREDICTIVE VALUE OF NEUTROPHIL–LYMPHOCYTE RATIO ON PATHOLOGICAL RESPONSE AFTER NEOADJUVANT CHEMORADIATION FOR LOCALLY ADVANCED RECTAL CANCER

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Aims: Neoadjuvant chemoradiotherapy (NCRT) followed by total mesorectal excision is a standard of care in locally advanced rectal cancer (LARC) patients. However, patients show a wide variation in responses and oncological outcomes and currently, it remains difficult to predict treatment outcomes. The identification of reliable biomarkers for the oncologic outcomes could be relevant to guide in risk-adapted treatment strategies. The aim of this study was to investigate the role of haemoglobin and systematic inflammation evaluated by neutrophil–lymphocyte ratio (NLR) and platelet–lymphocyte ratio (PLR) as effective markers to predict tumor response and prognosis of LARC patients after NCRT.

Methods: Seventy LARC patients, treated with long-course NCRT and radical surgery, were retrospectively analysed. Pathological tumor response was evaluated according to Mandard tumor regression grade (TRG). Venous blood samples were obtained within one week before NCRT and during the last week of treatment. To explore the prognostic impact of haemoglobin, NLR and PLR on TRG and outcomes, as local control, disease-free survival and overall survival, a t-test analysis between independent groups was performed. Post-NCRT values have been also evaluated.

Results: TRG 1-2 was obtained in 44 patients (62.9%). The median values of pre-NCRT haemoglobin, NLR, and PLR were 13.10g/dL, 2.10, and 124.19, respectively. The median values of post-NCRT haemoglobin, NLR, and PLR were 12.75g/dL, 6.09, and 296.69, respectively. A statistically significant correlation between pre-treatment median value of NLR and TRG rates (p=0.011) was showed: 1.9 (range: 1.5-2.7) in TRG 1-2 *vs* 2.5 (range: 2.0-3.3) in TRG 3-4 (Figure 1). No statistically significant correlations were found for pre-NCRT haemoglobin value and PLR with TRG1-2 versus TRG3-4 (p= 0.930 and p=0.710, respectively). No significant correlation was reported with clinical outcomes. Post-NCRT blood values did not result in significant correlation with TRG neither outcomes.

Conclusions: The prognostic significance of NLR has been explored in several cancers. In our study a higher (2.0 - 3.3) pre-NCRT NLR resulted predictive of poor pathological tumor response. The study is still ongoing in order to be validated in a larger number of patients and to investigate further variables helpful to define predictive models for personalize treatments with a possible intensified therapy in poor-responders' patients.

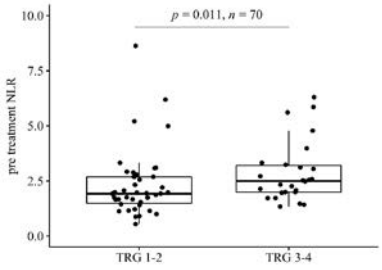

Figure 1. Box plot for pre-treatment NLR measured in 70 subjects divided according to their TRG. The median is 1.9 [1.5 - 2.7] in TRG 1-2 and 2.5 [2.0 - 3.3] in TRG 3-4. For all subjects involved the median is 2.1 [1.7 - 2.9].

Figure 1.

DP21

REIRRADIATION OF PROSTATE CANCER WITH STEREOTACTIC VOLUMETRIC MODULATED ARC IMAGE-GUIDED RADIATION THERAPHY (VMAT-IGRT): INTERIM ANALYSIS OF A MONOISTITUTIONAL PROSPECTIVE TRIAL

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Aims: The management of the locally recurrent prostate cancer patients (pts) continues to be debated. The aim of this phase II study is to explore the efficacy and safety of prostate re-irradiation with stereotactic volumetric modulate arc image-guided 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 February 2021 17 pts were re-irradiated to the prostate with stereotactic VMAT-IGRT, the total dose was 30Gy in 5 daily fractions. Pts were followed by clinical examination and PSA value 1 month after treatment and every 3 months thereafter. The primary outcome is to estimate the efficacy of the salvage stereotactic VMAT-IGRT in terms of biochemical relapse-free survival (bRFS,), local control (Lc), and androgen deprivation therapy free interval (ADTFI). Secondary outcomes are acute and late genitourinary and gastrointestinal toxicities evaluated according to Common Terminology Criteria for Adverse Events version 4.03.

Results: After a median follow-up of 9,5 months (range 1-33), 14 of 17 pts accrued were evaluable. No G3 acute urinary toxicity was registered, whereas gastrointestinal acute toxicity was not observed. In the first six months all but one pts had a decrease in serum level PSA, three pts had a progressive increase in serum PSA at the ninth, twelfth and fifteenth months, respectively. The four pts with biochemical failure showed a metastatic 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 acute toxicity profile. We reserve further evaluations regarding late toxicity and analysis of other outcomes.

DP22

SIMULTANENEOUS INTEGRATED EXTERNAL BEAM BOOST AFTER DEFINITIVE RADIOCHEMOTHERAPY IN LOCALLY-ADVANCED CERVICAL CANCER

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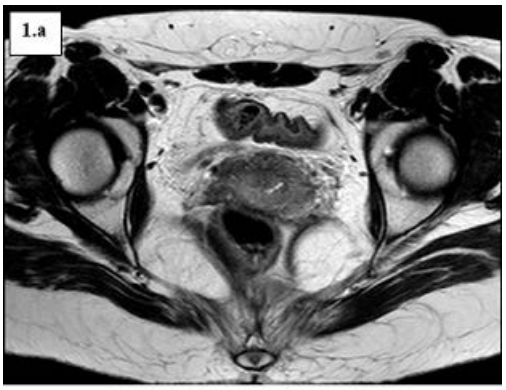
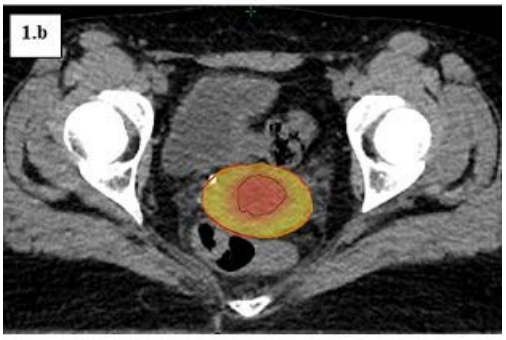
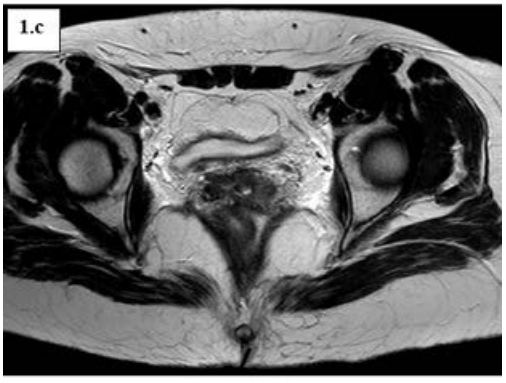
Aims: The standard treatment in locally-advanced cervical cancer (LACC) is external beam radiotherapy (EBRT) with concomitant chemotherapy (CH) and interventional radiotherapy/brachytherapy (IRT). In this study we analyzed the potential utility of external beam boost in patients (pts) unfit for IRT.







1.a MRI before RT boost. **1.b** Boost RT planning.
1.c MRI after RT boost.

Figure 1.

Methods: 15 pts with median age of 51 years (range 32-83), affected by LACC, were treated between July 2017 and July 2020. The stage at diagnosis, according to FIGO 2018 classification, ranged between IB3 and IIIC2. 10/15 pts (66%) were affected by squamous cell carcinoma, 4 pts (27%) by adenocarcinoma and 1 patient (7%) had neuroendocrine carcinoma. All pts underwent pelvic EBRT with Volumetric Modulated Arc Therapy (VMAT) and concomitant weekly platinum-based CH. To evaluate the residual tumor, an MRI was performed at the fourth week of EBRT (Figure 1a). IRT was unfeasible due to undetectable cervical canal: consequently, a sequential VMAT boost to residual primary tumor was delivered. We identified two different Clinical Target Volumes (CTV): the whole cervix (CTV1) and MRI residual tumor (CTV2) (Figure 1b). During treatment a daily CBCT was performed. A routine follow-up was planned with MRI every three months (Figure 1c), periodic CT and PET-CT scans.

Results: The median total dose to the pelvis was 45 Gy/1.8 Gy/fraction (range 45–50.4 Gy). A median 54 Gy (range 50-56.25 Gy) simultaneous integrated boost was administered to positive PET-CT lymph nodes in 7/15 pts. Concerning the cervical boost, the median prescribed dose to the CTV1 was 19.8 Gy (range 17-27.5 Gy), while a median total dose of 30 Gy (range 20-33 Gy) was delivered to CTV2, in 10-11 total fractions. The EQD_2 total dose to CTV2 ranged between 76.8 and 82.1 Gy (α/β 10). After a median follow-up of 12 months (range 6-29), 7 pts had local complete response; a partial response was observed in 6 pts: 1 patient had hepatic progression while a second one pelvic lymph node progression. Additionally, 1 patient with partial local response underwent surgical hysterectomy with complete residual tumor excision. Local and systemic progression occurred in 2 pts. No gastrointestinal and genitourinary acute or late toxicity > G2 was detected, according to Common Terminology Criteria for Adverse Events v.4 scoring criteria.

Conclusions: Standard treatment in LACC is chemoradiation followed by IRT, but, in our experience, a dual level dose EBRT boost with VMAT technique is a feasible and safe option when IRT can not be performed.

DP23

STEREOTACTIC BODY RADIATION THERAPY (SBRT) BOOST IN PATIENTS WITH CERVICAL CANCER INELEGIBLE FOR INTERVENTIONAL RADIOTHERAPY/BRACHYTHERAPY BOOST: AN UPDATE OF OUR INSTITUTIONAL EXPERIENCE RESULTS:

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Aims: Standard treatment in cervical cancer is external beam radiotherapy (EBRT) concomitant with platinum-based chemotherapy, followed by Interventional Radiotherapy/Brachytherapy boost (BT). Stereotactic body radiation therapy (SBRT) could be used to treat the final boost volume in cervix patients who are ineligible for BT.

Methods: Since October 2012 to July 2020, 9 consecutive women with cervical cancer were treated with

SBRT as a final boost to the high-risk volumes. Eight patients with cervical cancer were treated with chemotherapy during conventionally fractionated EBRT: cisplatin weekly 40 mg/m^2 for 5–6 cycles. The patients were treated with a stereotactic boost with a total dose of 12-25 Gy in 2-5 fractions (5-7 Gy for fraction). SBRT was delivered by volumetric-modulated arc therapy (V-MAT). All patients underwent image-guided radiotherapy (IGRT) using cone-beam computed tomography (CBCT) system as daily pre-treatment imaging.

Results: The median age was 52 years (range 38–79). The majority of patients (88%) had squamous cell carcinoma. The most frequent reason for forgoing BT was the cervix canal and/or vaginal stenosis (5 patients), refused treatment (2 patients) and hematological disease (2 patients). Median boost dose for patients completing the treatment was 15 Gy (range: 12–25 Gy); the median dose per fraction was 5 Gy (range: 5–7Gy). The median follow-up in months was 27 (range 12-58 months). After SBRT boost only one local recurrence was observed at 8 months in a patient with FIGO stage IVA. The systemic progression of metastatic disease was seen in four patients. The median survival was 36 months (range 22–65 months) and the actuarial 2-year OS and DFS was 87% and 66.6% respectively. Acute bladder toxicity G1 was reported in 2 of 9 (22%) patients, vaginal toxicity G1-G2 is not reported and there was 1 case (11%) of G1 gastrointestinal toxicity observed. Late vaginal G1 toxicities were reported in 2 of 9 (22%). Late vaginal toxicity G2 was recorded 1 of 9 (11%) patients and G3 was reported in 1 of 9 patients (11%). Late urinary and gastrointestinal G2 toxicities were reported in 2 of 9 patients (22%).

Conclusions: Despite the limited number of patients investigated in our study, external beam boost using SBRT technique in cervical cancer patients ineligible for BT showed acceptable survival outcomes and particularly a safe toxicity profile.

DP24

PROGNOSTIC VALUE OF HPV STATUS IN A COHORT OF PATIENTS AFFECTED BY ADENOCARCINOMA OF THE UTERINE CERVIX

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Aims: The aim of this study is to evaluate the impact of human papilloma virus (HPV) status in the clinical outcome of patients affected by adenocarcinoma of the uterine cervix treated with surgery followed by concurrent chemo-radiotherapy (CCRT) +/- brachyteraphy (BT).

Methods: We retrospectively evaluated 39 patients (median age 52 years, range 33-75 years) with FIGO (IB2-III) stage cervical adenocarcinoma, who were treated in our Institution, from January 2012 to December 2020; 29 patients (74%) were HPV (mostly HPV 16 or HPV 18) associated adenocarcinoma subtype (HPVA) and 10 patients (26%) were HPV not associated (NHPVA). Twenty-one patients (54%) received combined neoadjuvant chemotherapy of taxane and platinum, with or without anthracycline. All the women underwent surgery (type II-III radical hysterectomy with bilateral pelvic lymphadenectomy) followed by adjuvant pelvic RT (45-50.4Gy in 25-28 daily fractions) and 23 women (59%) received concomitant chemotherapy (weekly cisplatinum 40 mg/m^2). Sequential vaginal high-dose rate (HDR)-BT boost, up to a dose of 10Gy in 2 fractions of 5Gy, was delivered in 20 patients (51%). Pelvic RT was performed with a 6-15 MV beam using four-field conformal technique or Volumetric Modulated Arc Therapy (VMAT). Vaginal HDR-BT was delivered using a 192Ir source, HDR afterloader, with a vaginal applicator set.

Results: Two-years and five years overall survival (OS) were 92% and 73%, and two-years and five years progression free survival (PFS) were 72% and 59%. At log rank test analysis, HPVA patients had a significant lower risk of death (p=0.004), as well as in the same cohort there was a trend for a lower risk of progression (p=0.098).

Conclusion: Adenocarcinomas of the uterine cervix consist of a large heterogenous group of tumours, with about 35% correlated to HPV infection. The prognosis of these malignancies is worse than for other histologies. As shown in other organs, in our study HPV status significantly affects prognosis. So HPV status in cervical cancer may be a useful prognostic biomarker before treatment.

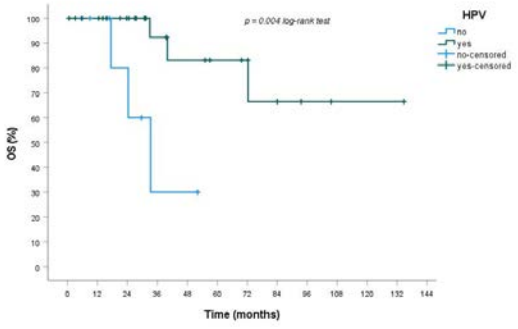

Figure 1.

DP25

STEREOTACTIC RADIOSURGERY, A REALLY PROMISE IN THE MANAGEMENT OF SELECTED UVEAL MELANOMA

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Aims: Uveal melanoma (UM) is the most common primary intraocular malignant tumor. This malignancy is frequently treated using brachytherapy, stereotactic radiotherapy or proton therapy. The objective of this study was to assess the role of stereotactic radiosurgery (SRS) in the treatment of large and/or juxtapapillary UM.

Methods: From January 2014 to December 2020 we treated 56 patients (median age 71 years; range 31-89 years) affected by UM, diagnosed with A-scan and B-scan standardized echography, optical coherence tomography, fluorescein angiography, indocyanine green–angiography and/or magnetic resonance. Inclusion criteria were Eastern Cooperative Oncology Group [ECOG] performance status [PS] ≤ 2; life expectancy > 6 months, thickness >10 mm and\or diameter >16 mm or juxtapapillary UM. The treatment was delivered with a TrueBeam™ LINAC and RapidArc® technique, using 6 MV FFF beams. All the lesions were treated with one single fraction of 27Gy [Biological Effective Doses (BED) ≈ 100Gy, assuming an α/β of 10].

Results: The ophthalmic evaluation at three months after SRS showed a complete response [CR] in all the patients. We reported poor acute toxicities, whereas overall late toxicity occurred in 35 (62.5%) patients. The most common Common Terminology Criteria for Adverse Events (CTCAE v 5.0) grade 1-2 late adverse event was neo-vascular glaucoma (21.4%), followed by ischemic retinopathy (14.3%). Sixteen patients (28.5%) underwent enucleation: 8 (14.3%) for local progression and 8 (14.3%) for grade 3-4 treatment comorbidities. The 5-year disease-free survival (DFS), overall survival (OS) and enucleation free survival (EFS) rates were 41%, 60% and 65%, respectively. In univariate and multivariate analysis, only American Joint Committee on cancer (AJCC) stage significantly influenced progression disease (p=0.001 and 0.032; respectively) and death (p=0.001 and 0.008; respectively). The Bruch's membrane rupture had a significantly high risk of death in univariate and multivariate analysis, (p=0.046 and 0.049, respectively). In univariate and multivariate analysis, the patients who achieved local control (LC) had a lower risk of enucleation, (p<0.001 and 0.013, respectively).

Conclusions: SRS offers an effective and safe approach for selected cases of uveal melanoma, due to the reported satisfactory results in terms of local control, eye conservation and survival.

DP26

BRACHITHERAPY OF NON-MELANOMA SKIN CANCERS IN AGED PATIENTS

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Aims: Non-melanoma skin cancers (NMSCs) are the most common malignancy worldwide, of which 99% are basal cell carcinomas (BCCs) and squamous cell carcinomas (SCCs) of skin. Mainstays of treatment remain surgery and radiotherapy, particularly in older patients (≥70 years old).. High-dose-rate interventional radiotherapy (HDR-IRT) seems to be an excellent option for NMSC.

Methods: Between November 2011 and May 2021, we treated 15 patients for a total of forty lesions in aged patients with NMSC with HDR-IRT. Patients underwent brachytherapy treatment for a total dose ranging from 30 to 40 Gy (10 Gy per fraction). Toxicities were recorded using the Common Terminology Criteria for Adverse Events scale (CTCAE) v. 4.03.

Results: Median age was 82 years. Acute toxicity was recorded in all patients. Grade 1 erythema appeared in 11 cases (27.5%) and it was self-resolved with the application of eudermic cream in 10 days; Grade 2 erythema appeared in all 27 cases(67,5%). Towards the end of each treatment schedule, epidermolysis developed which was resolved within 3 weeks; Grade 3 skin toxicity apperars in 2 cases (5%) and was managed with dressings and close outpatient follow-up until complete resolution in 5 weeks. Late toxicity: Grade 1 skin atrophy and pigmentation changes in field were observed in all patients. At last follow-up, all patients were disease free.

Conclusions: Personalized HDR-IRT appears to be safe for older patients and management of skin toxicity is manageable. Furthermore, the treatment of the lesions avoids the complications associated with the progression of the disease.

DP27

RADIOTHERAPY PRACTICE FOR NON-MELANOMA SKIN CANCER AMONG CENTERS OF AIRO EMILIA ROMAGNA AND MARCHE WORKING GROUP

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G. Aluisio[13], G. Capezzali[2], M. Benedetti[12], F. Bunkheila[2], N. D'Abbiero[5], G. Frezza[4], C. Iotti[11], F. Lohr[14], G. Mantello[3], F. Mauro[10], A.G. Morganti[1], M. Giannini[8], D. Piva[7], A. Romeo[6,9], A. Stefanelli[13], E. D'Angelo[14]. On the behalf of the Italian Association on Oncological Radiotherapy (AIRO) Emilia Romagna and Marche Working Group.

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Aims: Basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (cSCC) are the two most common subtypes of non-melanoma skin cancer. The aim of this multicenter, retrospective analysis is to describe the role of RT in the management of patients (pts) affected by BCC and cSCC.

Methods: AIRO Emilia Romagna and Marche Working Group collected and analysed data of pts affected by BCC and cSCC undergone radiotherapy (RT) between January 2016 and December 2019.

Results: We retrospectively analyzed 464 pts treated in 11 Centers in Emilia Romagna and Marche. All but 28 pts had histological confirmation before undergone RT: 277 (59.7%) cSCC and 160 (34.3%) BCC. Median age at diagnosis was 83 years (range 32-112). Definitive and postoperative RT (PORT) has been delivered in 44.1% and 37.7% of pts, respectively, while palliative RT has been used in 18% of cases. In the definitive RT subgroup, 68 (33.8%) pts and 78 (38.8%), and recurrent 21 (10.5%) and 17 (8.5%), were treated for cSCC and BCC respectively. In the PORT setting, 141 (81.9%) pts received RT after resection of the primary tumor and 31 (18%) after surgery of the recurrence. Palliative RT was performed in 65 pts and 8 pts, for cSCC and BCC respectively. Different RT techniques and many treatment schedules have been used (Figure1). Median RT dose was 45 Gy (range: 24-80), 50.4 Gy (range: 24-66), and 25 Gy (range: 6-66) in definitive, PORT, and palliative treatments, respectively. With the objective to compare different schedules biological equivalent dose (BED) was calculated assuming α/β=10 for tumoral tissue (Table 1).

Conclusions: Radiotherapy plays an important role in the management of non-melanoma skin cancer pts. The heterogeneity of techniques and RT schedules observed, suggest the importance to include these pts in prospective trials for a better evaluation of outcomes.

Table 1.

RT INTENT	Number of pts	BED_{10} (range)	BED_{10} (average)	BED_{10} (median)
CURATIVE	201	28,8-120	69,93	67,1
PORT	172	28,8 – 81,3	65,69	67,2
PALLIATIVE	82	9,6-81,3	37,66	66,3

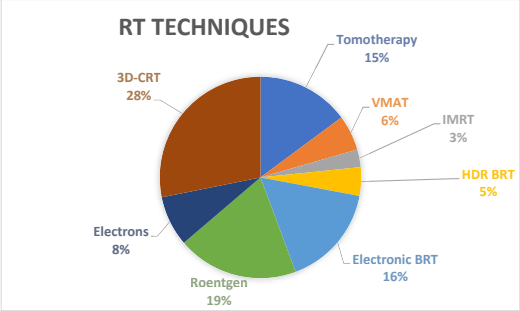

Figure 1.

DP28

LATE CARDIAC COMPLICATIONS HODGKIN AND NON-HODGKIN LYMPHOMA PATIENTS UNDERGOING CHEMOTHERAPY AND RADIOTHERAPY

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Aims: The primary endpoint of this multicenter prospective observational study was to evaluate the prevalence of late (five years from the end of therapy) cardiovascular toxicity in patients with Hodgkin (HD) and non-Hodgkin lymphoma (LNH) treated with antracycline-based chemotherapy (CHT) and 3D conformal radiation (3D-CRT) on the mediastinum. Secondarily, we cor-

relate clinical and/or subclinical cardiac damage with cardiac substructures RT dosimetric data.

Materials and Methods: Patients underwent cardiovascular screening based on cardiological examination, complete blood chemistry tests, blood thyroid function, blood troponin and NT proBNP o BNP, electrocardiogram, echocardiogram, cardio-pulmonary exercise test and supraortic trunk echocolor-doppler. Specifically, the following parameters are retrospectively evaluated: total dose, dose by fraction and technique used for cardiac, pulmonary and thyroid. The assessment of toxicity is obtained through the contouring of the heart chambers and cardiac structures, lungs, thyroid and carotids and the dose volume histogram (DVH) evaluation. Based on the expected prevalence of the primary endpoint of 16%, after 5 years, a sample of 207 patients was estimated assuming a margin of error of 5% and a confidence interval of 95% (CI 95%). For time to event endpoints the survival curve will be estimated using the Kaplan Meier method and the comparisons will be based on the log-rank test.

Results: Since November 2019 to date we enrolled 10 patients affected by mediastinal HD and LNH, respectively one and nine. Patient ages ranged from 31 to 73 years (median 42 years). All patients were treated since July 2006 to April 2016 with CHT and 30 Gy/15 fractions 3D-CRT on the mediastinum. Median FUP was 89 months (range 50-1470 months). Mean dose (Gy) for heart, heart V25 (%), pericardium, left atrium V25 (%), left ventricle V10 (%), right ventricle V20 (%), left main coronary artery V20 (%) was 11.4, 12.7,6.25, 14.8, 18.5, 11.6, 74.5 respectively. Only one patient showed grade I left ventricular dysfunction and high BNP serum level (108.5 pg/ml). The expected duration of the study is 24 months so the study itself and its results are still ongoing.

Conclusions: The results of this study could have an impact on daily clinical practice, proposing a specific cardiological screening program reserved for selected category of patients considered at risk of developing late cardiotoxicity.

DP29

COMBINATION OF RADIOTHERAPY AND CAR-T CELL THERAPY IN REFRACTORY NON-HODGKIN B LYMPHOMA: SINGLE-CENTER EXPERIENCE

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Aims: Anti-CD19 chimeric antigen receptor (CAR) T-cell therapy (tp) is an effective option for the treatment of relapsed/refractory diffuse large B-cell lymphoma. In order to control lymphoma progression during the manufacturing period, a bridge tp regimen is required for most patients (pts). Radiotherapy (RT) may be used for pts with localized chemorefractory disease as a bridge tp, or as salvage treatment for pts with localized residual/relapsed disease after infusion.

Methods: Here we report a case series of 8 pts treated in our CAR-T Unit with RT in the peri-infusional setting: 1 primary mediastinal, PMBCL, and 7 diffuse large B-cell lymphoma, DLBCL. Figure 1 summarizes the treatment history. All pts received tisagenlecleucel (tisa-cel), except one who received axicabtagene-ciloleucel (axi-cel). We used RT as bridging regimen for 6 pts. The dose of RT was 30 Gy in 15 fractions (fr). The site was mediastinum for pt 001, abdominal adenopathy for pt 002, 003 and 005, inguinal adenopathy for pt 004, laterocervical adenopathy for pt 007. Median volume of irradiation was 270 ml (min 79,6 ml, max 635 ml). We also used RT as salvage tp for localized disease relapse 3 months after infusion in 2 cases. The dose of RT was 30 Gy in 15 fr in pt 006 and 30Gy in 10fr in pt 008. The site was inguinal adenopathy for pt 006 (volume of irradiation 129.5ml), and mediastinal adenopathy for pt 008 (volume of RT 29.1ml).

Results: Response to bridging RT was achieved in 3/6 pts (2 partial response, 1 complete response), one pt had stable disease, and one pt had disease progression at the time of CAR-T infusion. One pt died for severe Covid19 pneumonia before receiving the planned CART infusion. The outcome is favorable at the time of writing for all infused pt except one, who died for progression 3 months after infusion (the one with progressive disease at the time of infusion). Response to salvage RT was a complete remission in both 2pts, and one of them underwent consolidation with allogeneic stem cell transplantation. Toxicity was manageable both in bridging and salvage RT, with no grade 3-4 CRS; maximum CRS grade was 2 in 3 cases. Only one pt receiving axi-cel needed admission at ICU for grade 4 ICANS, with complete resolution after treatment with high dose steroids.

Conclusions: We showed that RT is feasible and well tolerated as bridging or salvage tp, and an effective treatment option for localized residual disease in the peri-infusional setting for CAR-T pt.

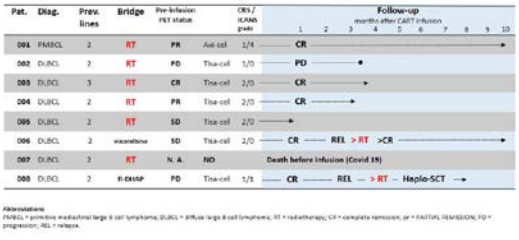

Figure 1.

DP30

L'ENTINOSTAT RADIOSENSIBILIZZA LE CELLULE DI RABDOMIOSARCOMA

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Aims: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma of childhood. Radiotherapy (RT) plays a crucial role on local control but it is often unable to achieve overall survival improvement due to the emergence of radio-resistant cell populations. HDACs are deregulated in tumors and Class I HDAC inhibitors (HDACi) demonstrated preclinical anti-cancer effects in several tumors among which RMS.

Methods: As HDACi are able to radio-sensitize different types of cancer cells partly by blocking DNA repair, we evaluated here the activity of MS-275 (Entinostat), a Class I and IV HDACi, as single agent or in combination with RT on radio-sensitive parental and radio-resistant RMS cells in vitro and in vivo.

Results: MS-275 hampered cell survival in vitro in a reversible manner in FN-RMS RD (RASmut) and irreversibly in FP-RMS RH30 cell lines by inducing cell accumulation in the G1 Phase of the cell cycle, down-regulating the expression of cyclin A, B, and D1 and up-regulating that of p21 and p27 in both cell lines as well as reducing the activity of ERKs and expression of c-MYC in RD and those of PI3K/Akt/mTOR and MYCN in RH30 cells. HDACi treatment resulted in non-apoptotic cell death associated to BCL2 and BCL-xL protein levels increase in surviving cells. Further, MS-275 impaired the ability of RH30 cells to form colonies in vitro and enhanced their response to RT promoting radio-sensitivity while RD cells were unhindered. However, DNA damage repair inhibition was induced by MS-275 and RT as single treatments and markedly increased by combined treatment in both cell lines. Reactive Oxygen species formation was also stimulated by MS-275 compared to RT alone and paralleled by down-regulation of anti-oxydant genes such as NRF2, SOD, CAT and GPx4. These effects were strengthened combining MS-275 and RT and associated to improved ability of RT to induce growth arrest in G2, the most radio-sensitive phase of the cell cycle. In vivo RT treatment partially affected tumor growth of RD while had no effects on RH30 xenografts. MS-275 significantly inhibited tumor growth in RH30 cells while its effects on RD cells were modest. Finally, MS-275 + RT combined treatment had a partial inhibitory effect on the growth of xenografted RD cells while strongly prevented that of RH30 xenografts.

Conclusions: Altogether, these findings suggest that MS-275 could be considered as a radio-sensitizing agent for the treatment of intrinsically radio-resistant PAX3-FOXO1 RMS.

DP31

STEREOTACTIC BODY RADIOTHERAPY IN PATIENTS AFFECTED BY OLIGOMETASTATIC SOFT-TISSUE SARCOMA: A NEW THERAPEUTIC OPTION

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Aims: Stereotactic body radiotherapy (SBRT) is emerging as a valid alternative to metastasectomy in patient with advanced soft-tissue sarcoma, who are unfit or refuse surgery. The aim of our study was to evaluate the efficacy of SBRT on disease control and survival in oligometastatic (≤ 5 lesions) STS.

Methods: From December 2012 to March 2021, 83 consecutive patients, corresponding to 126 lesions, were treated at our institution with SBRT. Every patient was judged unsuitable for surgery by Multidisciplinar Tumor Board. Local control (LC), progression free survival (PFS) and overall survival (OS) from SBRT were assessed. Acute and late toxicities were evaluated.

Results: Median follow-up time was 41 months (1-125 months). Median age at SBRT was 60 years (20 - 88) and the majority of patients were female (54, 65%). The most common primary site was trunk (37, 44.6%), followed by pelvis/uterus (22, 26.5%) and limbs (21, 25.3%). The most frequent histological subtypes were leiomiosarcoma, liposarcoma and undifferentiated pleomorphic sarcoma (68, 81.9%). Lung (78, 61.9%) and liver (17, 13.4%) were the most common site of metastases. Median SBRT dose was 48 Gy (18 - 67.5 Gy) delivered in 1 - 8 fractions, while median biologically equivalent dose (BED_{10}) was 106 Gy (40 - 220 Gy). Local control at 2 years was 96.39% (median not reached). The 1-year and 2-years PFS rates were 35.6%±5.5 and 16.3%±4.4, respectively; at multivariate analysis, the ECOG performance status (PS) was correlated with poorer PFS (HR 1.69, 95%CI 1.11- 2.57; p=0.0138). The 1-year, 2- and 3-years OS-from-SBRT rates were 88.8%±3.7, 74.9%±5.3 and 62.3%±6.2, respectively. At multivariate analysis, ECOG-PS (HR 2.05 95%CI 1.22 – 3.42; p= 0.006), nuclear grading (HR 1.93 95%CI 1.06 – 3.50; p=0.0292) and BED_{10} (HR 0.67 95%CI 0.46 – 0.99; p=0.0452) were associated with lower OS from SBRT. Only one patient suffered from acute G2 toxicity; no G3 or more, acute and late, toxicities have been registered.

Conclusions: In patients affected by oligometastatic STS, SBRT appears to yield an excellent local control with minimum toxicity. Optimal dose/fractionation regimen has still to be found, considering the lack of literature in this field. Future prospective trials are needed to estabilish the role of SBRT in this setting.

DP32

KI-67 CAN PREDICT RADIOSENSIBILITY IN NET TUMORS? RETROSPECTIVE ANALYSIS OF A MULTIDISCIPLINARY CENTRE

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Aims: Predictive biological markers of radio-sensitivity in NETs are not yet known and the true impact of radiotherapy in NETs is still unknown. This is a retrospective analysis of the correlation between Ki-67 expression and radiotherapy (RT) response in our series of consecutive patients.

Material and Methods: Data on patients with NETs underwent radiotherapy between 2015 and 2020 at the Radiotherapy Department of the European Institute of Oncology in Milan were retrospectively collected. Cox proportional hazard regression models was applied. Informed consent to scientific research and the study was required. The study was notified to our Ethical Committee.

Results: Among 43 patients, there were 36% GEP-NENs, 36% pulmonary NENs, and 29% were NENs from other sites. The Ki-67 was < 3% in 9/45 patients, 3-20% in 9/45 and >20% in 14/33 patients. Almost all patients were metastatic at the time of radiotherapy. The purpose of the radiotherapy was symptoms control (43%) or cytoreductive (44%), in association or not with analogs therapy (48%) or with other systemic therapy (41%). The RT technique were: 3DC (24%), IMRT (19%) and SRT (52%). The most frequent sites were the bone level (44% between spines and other bones) and extra-regional lymphnodes (24%). At a median time of 3 months follow up (FU) there was local complete response in 9 patients (14%), a local partial response in 17 (27%), stable disease in 23 (37%) and local progression disease in 14 treatments (22%). At 1.9 years median FU, the were not statistically significant differences in terms of overall survival based on grading based on Ki-67 (p=0.770). Moreover, in a Cox proportional hazard regression models with Ki-67 in continuous, +10% increase shows an HR (95% CI): 1.14 (0.82-1.59), p=0.44. There was not statistically significant correlation between the objective response rate (ORR) and Ki-67 in an unadjusted model considering all the lines of the therapies. There was not correlation also in an adjusted model taking into account the systemic therapies and schedules and in an adjusted model with Ki-67 in continuous, +10% shows an ORR: 1.17 (p=0.19)

Conclusions: This retrospective study does not seem to suggest a possible correlation between Ki67 and the response to RT at the first interim analysis even using a categorical or continuous scale. However, considering the bias in selecting population, further studies are needed in a more homogeneous population to explore this purpose.

DP33

POSTOPERATIVE MANAGEMENT OF KELOIDS WITH HIGH-DOSE-RATE BRACHYTHERAPY

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Aim: The effectiveness of postoperative interventional radiotherapy (POIRT) in preventing keloid recurrences after surgical excision has already been confirmed. We report our updated monocentric experience on the adjuvant high-dose-rate (HDR) interstitial brachytherapy.

Methods: We retrospectively analysed the medical records of 133 consecutive patients (104 female; 29 male) with 164 keloid. Patients receiving complete surgical excision and HDR-POIRT treatment from October 2004 to February 2021. Median age at the time of treatment was 43 years (range 31-51). The lesions were localized at the breast (32%), the sternal area (13%), the abdomen (12%), the ear lobe (16%), the arm (6%), the neck (6%),the chest wall (excluding breast and sternal area) (5%) and other regions (9%). During the surgical procedure, at the end of the scar excision, the dedicated plastic tube for brachytherapy was inserted as deep as possible through the centre of the wound. Surgical wound was considered as the target volume, and the irradiation usually started within 4-6 hours after surgery. The scheduled dose was 12 Gy in 4 fractions, two fraction per day with at least 6 hours in-between. Recurrence was defined as the presence of a new keloid in a previously treated site (both along the scar or only at its extremity).

Results: 32 patients were lost at follow-up, therefore

the data of 101 patients and 126 keloids are presented. No complication, such as bleeding or scar infections, occurred during treatment or after catheter removal; the most frequent early toxicity was erythema (14%), but most of the patients had no toxicity (84%). Over a median follow-up time of 35 months (range, 10 - 83), 43 treated keloids (26%) relapsed; the median time of relapse was 8 months (range, 5 – 17). 7 patients receive a re-treatment (surgery and brachytherapy) after the relapse of the keloid lesion.

Conclusions: Brachytherapy for keloids adjuvant treatment after surgical excision is an effective and safe treatment. Use of relatively low brachytherapy dose may partially explain the relapse rate observed in our series. Further prospective investigation with different treatment schedules will be planned in order to establish the optimal dose that should be employed in the postoperative treatment of this benign condition.

DP34

FEASIBILITY OF INTRAOPERATIVE REAL-TIME MPTRUS GUIDED BIOLOGICAL HDR INTERVENTIONAL RADIOTHERAPY PLANNING IN LOCALIZED PROSTATE CANCER: EARLY MONO-INSTITUTIONAL EXPERIENCE

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Aims: To report the feasibility and early results of a mono-institutional series of intraoperative real-time multiparametric transrectal ultrasound (mpTRUS) guided biological dose planning in organ confined intermediate to high-risk prostate cancer patients treated by high-dose-rate interventional radiotherapy (HDR-IRT) with or without supplementary external beam radiotherapy.

Materials and Methods: Twenty-one patients were treated for a total of twenty-seven HDR-IRT fractions delivered between 2014 and 2021. All patients had a histologically proven organ confining prostate cancer. Fifteen patients received 15 Gy fraction to the dominant intraprostatic lesion (DIL) followed by a conventionally fractionated complementary external beam radiotherapy (46 Gy); in six HDR-IRT monotherapy patients two weekly fractions of 13.5 Gy were delivered. The Clinical Target Volume (CTV) for Dref was identified by cognitive matching of multiparametric MRI, PET-Choline (when available) and intraoperative mpTRUS imaging (grayscale + color Doppler). The Planning Target Volume for Dref included CTV+ 3mm margin. DVH parameters, organ at risks doses and toxicity results were recorded.

Results: The median follow-up was 41 months, the mean age was 68 years, and the mean initial prostate-specific antigen (PSA) was 11.2 ng/mL. Mean prostate volume was 32.3 cc. We treated T2 in 20%, T3a in 47.5% and T3b in 32.5% whereas N stage was N0 in 95% and N1 in 5%, respectively. ADT was administered in 18/21 patients according to the following internal protocol: No ADT in case of favorable intermediate risk, 6 months in unfavorable intermediate risk and 2 years after clinical complete response in high risk. LHRH analogues were used unless the patient refused (antiandrogen was given in those cases). Median PSA nadir was 0.01 ng/mL with a median time to PSA nadir of 22 months. Organs at risk parameters specifically for urethra (u) and for rectum (r) were as follows: uD0.1: 12.9 Gy and rD2: 8.2 Gy, respectively. We observed exclusively G1 and G2 urinary toxicity in 8/21 and 2/21 patients, respectively. No rectal toxicity was recorded. Intraoperative mpTRUS procedure prolonged the HDR-IRT application time with only 5-8 minutes per fraction.

Conclusions: Intraoperative real-time mpTRUS guided biological dose planning HDR-IRT in intermediate to high-risk prostate cancer with or without supplementary external beam radiotherapy is feasible and resulted in a low toxicity profile and in an effective PSA response.

DP35

OLIGO-AIRO: A NATIONAL SURVEY ON THE ROLE OF RADIATION ONCOLOGIST IN THE MANAGEMENT OF OLIGO-METASTATIC PATIENTS

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Aim: To explore the role of Italian Radiation Oncologists in the management of oligometastatic patients

Material and Methods: The questionnaire was sent via e-mail on May 2020 to all the AIRO members. Topics included personal working and educational information, criteria for the definition of the oligometastatic disease, responders' clinical attitude to the treatment of the oligometastatic disease in different clinical scenario, combination of SBRT with other treatment modalities. For each question, the agreement was considered reached when more than 80% responders chose the same response.

Results: 105 AIRO members answered the questionnaire. The median number of oligometastatic lesions per patient treated in each Center was 2 for 55% of the responders, 3 metastases in 22% of the cases, >3 lesions in 12%, and 1 in 11%. When choosing a treatment option for fit patients with a single oligometastatic focus, 52% of the responders agreed in proposing only SBRT, the combination of SBRT and systemic therapy was the second option (30%), and 18% of the responders considered exclusive surgery. Interestingly, no responders considered systemic therapy alone as a viable treatment option. On the contrary, in the case of unfit patients with a single oligometastatic lesion, the consensus has shifted in favor of the SBRT alone (89%), while the combination of SBRT and systemic therapy was 9%, and surgery alone 2%. In the case of patients with >1 oligometastatic lesion, the responders did not reach a consensus about the treatment strategy to propose: 42% chose the combination of SBRT and a new systemic treatment line, 39% opted to continue the same systemic treatment line and to add SBRT, 17% proposed SBRT alone, and 2% a new systemic treatment line. In the oligoprogressive setting, 41% of the responders opted to continue the current systemic treatment and to add SBRT, 38% chose a systemic treatment switch plus SBRT, 1% a new systemic treatment line, and no responders opted for surgery. In the case of oligoresidual disease, 70% of the responders was in favor of adding SBRT and continuing the current systemic treatment, 18% opted for a systemic treatment switch plus SBRT, 12% chose SBRT and the interruption of the systemic treatment.

Conclusion: The present survey represents a picture of Italian Scientific Radiation Oncology Community in 2020 regarding oligometastatic disease.

DP36

CLINICAL OUTCOMES OF STEREOTACTIC ABLATIVE RADIOTERAPY IN OLIGOMETASTATIC GYNECOLOGICAL CANCERS

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Aims: Patients (pts) with oligometastatic disease may benefit from treatment of all metastatic sites with stereotactic body radiation therapy (SBRT). In this retrospective study we analyzed the efficacy and safety of SBRT for oligometastatic gynecological cancers in terms of local control (LC) and toxicity.

Methods: From 4/2009 to 2/2021, 82 lesions in 45 pts were treated with SBRT. Five lesions of 4 pts were treated with helical Image Guided-Intensity Modulated Radiotherapy (IG-IMRT) to a median dose of 54 (35-63) Gy in 6 (5-10) median fractions prescribed to 95% of the Planning Target Volume (PTV). Seventy-seven lesions of 41 pts were treated with robotic SBRT to a median dose of 40 (18-60) Gy in a median of 5 (1-8) fractions, prescribed to a median isodose of 80% (68-84%). Nine PTVs (10.8%) were in the same field of previous adjuvant or salvage radiotherapy performed with IG-IMRT with a median dose of 50.4Gy. Primary histology was: ovarian in 33.3%, endometrial in 42%, cervical in 17.8% and other (fallopian tubes, vulva and vagina) in 6.7% of pts, respectively. Target locations were 53.7% lymph nodes, 33% lung, 6% bone, 6% central nervous system and 1.2% liver. Gross tumor volume was defined by the fusion of CT, PET/CT and/or MRI images. Toxicity was assessed using CTCAE version 4.03 criteria.

Results: Median follow-up was 15.1 months (0.69–75.4). Eleven pts (24%) presented grade (G) 1-2 acute toxicity. No grade ≥3 acute toxicity was observed. Two pts presented late toxicity: one had G2 rib pain persistent 28 months after the end of the treatment, and the other, irradiated on D12, a spine fracture 12 months later, with G3 bilateral leg pain and motor deficit, and underwent surgical decompression. After treatment 75.6% of targets had a complete response, 13.4% a partial response and 11% progression disease. Systemic progression occurred in 66.7% of pts. Disease Free Survival (DFS) was 5.6 months (0.56-67.2). Overall survival (OS) at 6 and 12 months was 77.8% and 55.5%, respectively. Twelve-months local control was 86% (Figure 1).

Conclusions: SBRT is an effective local treatment, with acceptable toxicity in pts with oligometastatic gynecological disease. Distant progression remains the primary site of failure in these pts, and this confirm the need

for further research of effective salvage systemic therapy.

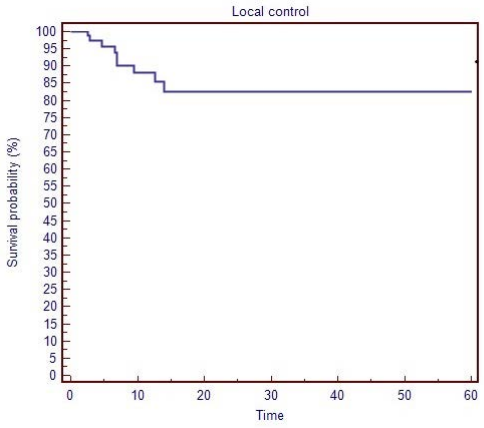

Figure 1.

DP37

OLIGOMETASTATIC PATIENTS WITH SPINAL METASTASES TREATED WITH A VMAT RADIOTHERAPY BOOST: A DOSE ESCALATION STUDY

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Purpose. To report the final results of a dose escalation study of volumetric intensity modulated arc radiosurgery (VMAT-SRS) boost after 3D-conformal radiotherapy (3D-CRT) in patients with isolated spinal metastases (iSM).

Material/Methods. Patients with iSM and less than 5 visceral metastases were included in this study. 25 Gy 3D-CRT radiotherapy was delivered in 10 daily fractions (2 weeks) to metastatic lesion, affected vertebrae and adjacent ones (one cranial and one caudal vertebrae). Sequentially, the dose to spinal metastasis (plus a personalized margin) was progressively increased (8 Gy, 10 Gy, 12 Gy) in the patient cohorts. Dose-limiting toxicities (DLTs) were defined as any treatment-related non-hematological acute adverse effects rated as G ≥ 3 or any acute hematological toxicity rated as ≥ 4 by RTOG scale.

Results. Fifty two lesions accounting for 40 consecutive patients (M/F: 30/11; median age: 69 years; range 38-85) were treated from November 2010 to June 2020. Most patients had a primary prostate (65.0%) or breast cancer (22.5%); in particular 14 patients could be classified as oligo-recurrent and 26 patients as oligo-progressive. Thirty two lesions received 8 Gy VMAT-SRS boost (total BED10: 45.7 Gy), 14 patients received 10 Gy (total BED10: 51.3 Gy), and 6 patients received 12 Gy (total BED10: 57.6 Gy). With a median follow-up of 15.2 months (range 1-91), no acute toxicities > grade 2 (Table 1) and no late toxicities > grade 1 were recorded. Overall response rate based on CT/PET-CT/MR was 78.8% with a complete response rate of 55.7%. Two year-actuarial local control (defined as irradiated site progression-free) was 88.4%, while the 2 year-actuarial overall survival was 90.5% .

Conclusion. A VMAT-SRS boost on iSM delivered after a 25 Gy 3D-CRT to adjacent vertebrae resulted to be feasible with encouraging tumor response, local control rate and toxicity profile.

Table 1. Acute toxicity (RTOG scale).

Toxicity	Grade	Dose Levels* I: 33Gy	II: 35Gy	III: 37Gy
Skin	1	5	1	0
	2	0	0	0
	3-4	0	0	0
Superior GI Tract	1	2	2	0
	2	1	0	0
	3-4	0	0	0
Larynx	1	0	0	1
	2	0	0	0
	3-4	0	0	0

*Total dose accounting for 25Gy 3D-CRT+ boost dose escalation (8 Gy, 10 Gy, 12 Gy)

DP38

STEREOTACTIC ABLATIVE RADIOTHERAPY IN COMBINATION WITH ANDROGEN RECEPTOR-TARGETED THERAPY FOR OLIGOPROGRESSIVE CASTRATION-RESISTANT PROSTATE CANCER PATIENTS

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Aims: To evaluate stereotactic body radiotherapy (SBRT) efficacy as a metastasis-directed therapy in patients with oligoprogressive (≤ 5 metastases) metastatic castration-resistant prostate cancer (mCRPC) during first-line treatment with androgen receptor-targeted therapy (ARTT).

Methods: A retrospective multi-institutional analysis was conducted in mCRPC patients treated with SBRT to oligoprogressive lesions during ARTT. SBRT was delivered to a median total dose of 30 Gy in 3 to 5 fractions with a Biological Effective Dose (BED) > 100 Gy in all cases, using an α/β ratio of 3. Clinical outcomes were time to next-line systemic treatment (NEST), radiological progression-free survival (r-PFS) and overall survival (OS). Toxicity was evaluated according to Common Terminology Criteria for Adverse Events (CTCAE) v4.0. The Kaplan-Meier method and the Cox proportional hazards model were used for univariate and multivariate analysis (MVA), respectively.

Results: Data from 34 patients treated from May 2015 to March 2020 were analyzed. Median NEST-free survival, r-PFS and OS were 16.97, 13.47 and 38.3 months, respectively. At MVA, worse NEST-free survival and r-PFS resulted significantly affected by > 3 metastases at diagnosis of metastatic hormone sensitive disease (mHSPC) (Hazard Ratio [HR] 3.66, p=0.009; HR 3.03, p=0.034), PSA ≤ 7 ng/ml at mCRPC diagnosis (HR 0.23, p=0.017; HR 0.19, p=0.006) and PSADT ≤ 3 months at mCRPC diagnosis (HR 3.39, p=0.026; HR 2.79, p=0.037). The high metastatic burden at mHSPC diagnosis was related to a decreased OS (HR 4.68, p=0.029). No acute or late grade ≥ 2 toxicity was reported.

Conclusions: In our series, SBRT to all oligoprogressive lesions in mCPRC patients led to a sustained period of disease control, resulting safe and effective, positively affecting the disease course.

DP39

PALLIATIVE SHORT-COURSE RADIOTHERAPY IN PATIENTS WITH RECTAL CANCER.

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Aims: Palliative radiation therapy (RT) is used to treat symptomatic rectal cancer although clinical benefits and toxicities are poorly documented. There is no consensus about the optimal RT regimen and clinical practice undergoes significant changes. Our aim was to evaluate the efficacy and toxicity of short-course (SC) RT in this setting of patients.

Methods: Charts from patients with locally advanced disease not candidates for standard treatment or with symptomatic metastatic rectal cancer treated with SCRT (25 Gy/5 fractions in 5 consecutive days) were retrospectively reviewed. Clinical outcome measures were symptomatic response rate and toxicity.

Results: From January 2007 to December 2017, 59 patients received SCRT; 53 were evaluable. Median age was 80 years (range 49-93 years) and median KPS 70% (range 50-100%). Forty-one (77%) patients had lower rectal cancer, 9 (17%) had local relapse and 26 (49%) metastatic disease. Thirty-one (58%) patients had not received previous oncologic treatment and forty-six (87%) had disabling comorbidities such as cardiovascular and bronchopulmonary diseases, diabetes, stroke. Seventeen (77%) out of twenty-two patients receiving previous treatments (surgery and/or chemotherapy) were referred to the radiation oncologist for a locally progressive disease. The median follow-up was 8 months (range, 1-70). Clinical response to RT for bleeding, pain and tenesmus was 100%, 95% and 89%, respectively. The compliance to the treatment was 100% and no patient experienced acute severe (≥ grade 3) toxicities. Median time to symptoms recurrence was 11 months (range 3-69). Fifteen (28%) patients had the symptom resumed, while 38 (72%) did not have symptom's recurrence until the death or the last clinical update. Globally, the median overall survival was 12 months.

Conclusions: SCRT is a safe and effective regimen in symptomatic rectal cancer and may be considered the regimen of choice for standard treatment in unfit patients.

DP40

RADIATION THERAPY FOR TREATMENT OF SIALORRHEA IN AMYOTROPHIC LATERAL SCLEROSIS: A CASE REPORT

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Aim: To consider palliative radiotherapy efficacy in order to reduce sialorreha in Amyotrophic lateral sclerosis (ALS), a progressive, paralyzing condition that affects primarily lower motor neurons.Methods :the patient was a 32-year-old man with history of ALS diagnosed 8 years before RT treatment. At the time of treatment he presented locked-in-syndrome with quadriplegia and loss of motor function to the lower half of his face,PEG-tube placement, and tracheostomy with ventilator use.He also developed sialorrhea. He underwent medical therapy , but when symptoms recurred, on March 2020, the patient was referred to radiation oncology for palliative RT, because of sialorrhea symptoms continuing to be annoying and requiring costant aspiration, also during night sleep.The recommendation was for radiotherapy to the bilateral parotid (or two-thirds of the bilateral parotid glands) and submandibular glands with 20 Gy in 4 fractions or 12 Gy in 2 fractions, delivered twice weekly. To restrict access to the hospital during SARS COV2 pandemic period, we decided to prescribe the dose of 12 Gy in 2 fractions delivered twice weekly. Computed tomography simulation was performed in the supine position with arms at sides and a 3-point Aquaplast mask was utilized for motion management, opened for eyes in order to communicate with the patient through the movement of the eyelids.The two-thirds of the bilateral parotid glands and submandibular glands were contoured bilaterally, and treatment was planned using 3DCRT technique with 6 MV photon beams prescribed to a calculation point at the 95% isodose line. On October 2020, after 6 months, sialorrhea symptoms reappearance requiring frequent suctioning,also during night sleep so he received one more fraction of 6 Gy.

Results: Time to symptomatic improvement was less than 1 month after treatment.He tolerated treatment well, with a subjective decrease in the amount of secretions and increased thickness of saliva by the final fraction requiring less suctioning during the day, and no aspiration during night sleep.The only acute adverse effects noted were temporary beard hair loss, low edema, erythema of the bilateral skin neck after the final fraction.*Conclusions:* EBRT is an effective and well-tolerated treatment option for Sialorrhea in ALS and for these reason it could be considered as a first alternative option.Dose fractionation schemes ,most frequently reccomended ,are 12 Gy in 2 fractions or 20 Gy in 4 fractions.

Poster

P0001

WHOLE BRAIN RADIOTHERAPY FOR METASTASES FROM DIFFERENT PRIMARIES: ESTIMATION OF SURVIVAL IN A MONOINSTITUTIONAL EXPERIENCE

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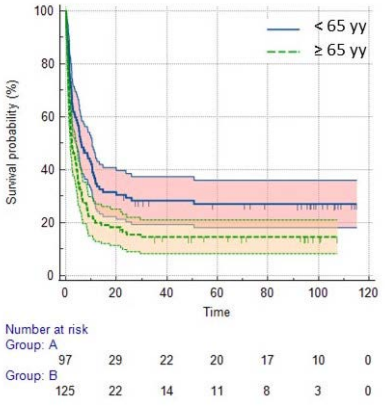
Aims: To analyze the effect of whole brain radiotherapy (WBRT) on overall survival (OS) in patients with brain metastases.

Methods: A database of 222 patients undergoing WBRT for multiple brain metastases from 2010 to 2020 was retrospectively analyzed at the Department of Radiotherapy, San Martino Hospital, Genoa. Medical records and clinical variables were extracted from a pool of originally 234 patients. A 3DCRT technique was used in all patients. Primary endpoint was OS stratified according to number of lesions, age, primary tumour and symptoms at diagnosis.

Results: 117 females and 105 males were included in this analysis, median age was 66 years (range: 25-92). 163 (73.5%) patients, 30 (13.5%), 18 (8.1%) and 11 (4.9%) presented multiple, single, two and 3 lesions, respectively. Patients with single or two lesions received WBRT and not SBRT due to primary histology (SCLC), site and size of lesions or previous radiosurgery treatment. The most common WBRT fractionation regimen were 30 Gy in 10fx in 132 (59.5%) pts and 20Gy in 5fx in 80 (36%) pts. The imaging for initial diagnosis and evaluation consisted in CT-scan in 178 (80.2%) pts and MRI in 44 (19.8%) pts. Brain metastases were most frequently associated with lung cancer in 114 (51.3%) patients (55 ADK, 26 NSCLC; 21 SCLC); breast cancer in 43 (19.4%) patients with the IDC being the most frequent histological variant in 84% of patients and other histologies as melanoma or renal carcinoma in the remaining 65 (29.3%) pts.



Figuure 1.

At the time of WBRT 158 (71.2%) pts were symptomatic, the most common symptoms were gait and limb ataxia in 45 cases, nausea and vomit in 24 patients, neu-

rocognitive alteration in 17 patients, speech difficulty in 9 patients and focal weakness reported in 9 patients. 64 (28.8%) patients were reported as asymptomatic. Median OS from the end of radiotherapy was 3.9 months (95% CI: 2,433 to 5,200), the median OS from the diagnosis of brain metastases was 5.9 months (range: 0.8-120). 2 yy OS was 21.7%. 2 yy OS was 29.5% and 33.2% (p=0.0025) for pts <65 yy and over 65yy (Figure 1). No significance difference in OS according to symptomatic *vs* asymptomatic patients (p=0.8168), number of lesions (≤3 *vs* >3, p=0.1552), primary tumour (breast *vs* lung *vs* others, p=0.5301) and fractionation (30Gy/10fx *vs* 20Gy/5fx) was detected.

Conclusions: According to our analysis WBRT was related to a significant difference in OS in younger patients (< 65 years) compared to elderly patients.

PO002

ARTIFICIAL INTELLIGENCE IN BREAST CANCER CONTOURING (WHOLE BREAST, REGIONAL LYMPH NODES AND ORGANS AT RISK): A PILOT STUDY

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Aims: Modern software based on artificial intelligence (AI) may represent a relevant contribution in radiotherapy contouring and treatment planning. Aim of this study is to present a single institution experience based on a new software for AI contouring of breast cancer target volumes and Organs at Risk (OaRs) on computer tomography (CT) images.

Methods: We tested a new cloud-based software (MVision AI, MVision AI Oy, Helsinki, Finland) for automatic OAR contouring of CT-images according to the ESTRO and RTOG guidelines. Three Radiation Oncologists (ROs) experienced in breast cancers performed the process of relevant OaRs contouring on 10 patients previously treated in our department. Moreover, they recorded the time needed to complete the task. Then, the same CT scans were automatically contoured by MVision and the time needed to complete the process was registered. Finally, the automatic contouring was checked and corrected by the same ROs, always measuring the time of the process. The quality of automatic contouring was scored by the ROs using a five-point Likert scale, with grades ranging from 1 (very bad) to 5 (very good). The contouring times were compared using the T-test.

Results: Seventeen CT (10 patients) were contoured by three experienced ROs, in 64.9 +/- 16.1 minutes (mean +/- SD) for each contouring, by delineating the whole breast, regional lymph nodes (CTVn_L1, CTVn_L2, CTVln_L3, CTVn_L4, CTVn_IMN, CTVn_ITP) and seven OaRs (Body, Heart, Left and Right Lung, Spinal Cord, Trachea, and contralateral breast). The MVision software contoured a median of 29 structures in 3.8 +/- 0.4 (mean +/-SD) minutes. The subsequent corrections of MVision contours by ROs were performed in 19.6 +/- 6.9 minutes (mean +/- SD). A statistically significant difference was found between contouring time spent by ROs and AI contouring plus ROs correction time (p<0.001). The ROs scored the automatic contouring quality as grade 4 (good), and grade 5 (very good) in 58.8% and 41.2% of cases, respectively.

Conclusions: AI-based contouring resulted a useful tool to reduce working time, with theoretically improved homogeneity of the contouring process. The quality of AI-based delineation was considered more than satisfactory by experienced ROs.

PO003

OPTIMIZATION OF CTV AND REDUCTION OF INTRA- AND INTER-OBSERVER VARIABILITY IN PROSTATE CANCER DELINEATION WITH A STANDARDIZATION TOOL

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Aims: Delineation of treatment volumes is a fundamental issue in Radiotherapy and Artificial Intelligence (AI) tools can favor the contouring procedures, integrated with the clinical knowledge of the physician. We investigated the role of the new software Anatom-e 3 on the cloud (Anatom-e Information Sytems Ltd., Houston, Texas, 2021) to improve the contouring quality for prostate cancer, according to reference Guidelines, in a multicentric setting.

Methods: A multicentric contouring protocol was implemented within the Radiotherapy Network of Lazio Abruzzo and Molise (AIRO-LAM). Two clinical cases of not operated prostate cancer were enrolled for contouring, with two complete CT series: the first one was a cT2c N0 M0, Gleason 7 (3+4), scheduled for radiation, only prostate and seminal vesicles; the second one was an high-risk cT3b N1 M0, Gleason 8 (4+4), scheduled for extended radiotherapy on prostate and pelvic nodes. For each center a Radiation Oncologist (RO) with high expertise, another with low expertise and a senior Resident were selected to identify volumes. Participants were asked to manually segment clinical target volumes (CTVs), in the first phase (4 weeks long) according to 2018 ESTRO ACROP consensus guideline and 2009 Radiation Therapy Oncology Group atlas and afterwards (next 4 weeks) with the aim of the software. All the contours were sent to a single RT structures storage.

Results: A preliminary "Consensus Meeting" with contouring laboratory was organized before the start of the study, to agree on the whole contouring workflow. All the centers were provided with the same CT series, and target volumes and organs at risk were imported in the TPS used in each center. After a specific training with remote sessions and instructions, participants were asked to manually, semiautomatically, automatically or AI based contouring, to segment clinical target volumes (CTVs), for both patients. Intraobserver (Intra-OV) and interobserver (Inter-OV) variability were evaluated with the *DICE* similarity coefficient and reported in the results.

Conclusions: In the era of AI this trial has been performed to assess the role of Anatom-e 3 software in the contouring workflow, to mitigate uncertainties and discrepancies provided by independently done contouring, autocontouring and AI deep learning-based algorithms. For our trial, we choose the newest consensus guidelines available, which offer improved patient care with the cost of slight increase in complexity.

PO004

IMPLEMENTATION OF AUTO-CONTOURING ON MR IMAGES FOR HEAD AND NECK CANCER

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Aims: The use of MRI-only radiotherapy is growing due to the better soft-tissue visualization on MR images and the possibility to acquire functional information. Unlike CT, MRI signals do not depend on electron densities (ED), required by the Treatment Planning System (TPS) to calculate the dose distribution. Therefore, it is necessary to convert MRI data to ED maps to allow the dose calculation in the TPS, obtaining synthetic-CT (sCT). The sCT are achieved by assigning bulk-density to the contoured Organ at Risk (OARs) and also to air and bone regions. This work aims to evaluate the use of ADMIRE® software (research version 3.18, Elekta AB) for the multi-atlas-based segmentation of head and neck (H&N) structures on MRI to optimize and to automatize the process.

Methods: Images of 11 cases were acquired using a T1 Dixon-Vibe sequence of H&N volume on a 1.5T Aera scanner (Siemens Healthcare). The MRI sequences were acquired in the same setup of CT simulation, including a thermoplastic mask fixed on a flat table. A flexible 16-channels body receiver-coil was placed over the head, neck and shoulder region, in addition to a spine coil under the patient. A radiation oncologist (RO) contoured 26 structures (OARs, bone and air) on each MRI dataset with the support of a neuroradiologist. To evaluate the geometric accuracy of 3 auto-segmentation methods implemented on ADMIRE® (STAPLE, Patch Fusion (PF) and Random Forest (RF), a leave-one-out cross-validation approach was used. We used three auto-segmentation methods for each patient dataset, using only the other ten as MR-based atlases.

Results: The contours, automatically and manually generated, were compared using the Dice Similarity Coefficient (DSC). The OARs manually segmented by the radiation oncologist served as the gold standard. For STAPLE, PF and RF, respectively, mean DSC ($\pm 1\sigma$) was as follows: 0.95±0.04, 0.97±0.03 and 0.98±0.01 for external body; 0.80±0.05, 0.67±0.03 and 0.85±0.05 for bones; 0.83±0.07, 0.84±0.06 and 0.86±0.04 for air; and

0.77±0.06, 0.80±0.05 and 0.83±0.05 for the parotids. The RF method showed overall better results, but also some difficulties in dealing with small structures such as lens, cochlea and optical nerves.

Conclusions: The ADMIRE® software was found to be adequate for auto-contouring H&N structures on MRI using an Atlas-Based Autosegmentation approach. It can serve as a useful tool to reduce physicians' workload, improve image workflow and implement the use of MRI-only radiotherapy.

PO005

ARTIFICIAL INTELLIGENCE IN THE CONTOURING OF UPPER ABDOMEN ORGANS AT RISK: A PILOT STUDY

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Aim: Modern software based on artificial intelligence (AI) may represent a relevant contribution in radiotherapy contouring and treatment planning. Aim of this study is to present a single institution experience based on a new software for AI-based contouring of Organs at Risk (OaRs) on computer tomography (CT) images.

Method: We have recently tested the new cloud-based software MVision AI Oy (Helsinki, Finland) for automatic OAR segmentation of CT-images contouring according to the ESTRO and RTOG guidelines. Two Radiation Oncologists (ROs) experienced in upper gastrointestinal cancers performed the process of relevant OaRs contouring on 11 patients previously treated in our department. Moreover, they recorded the time needed to complete the task. The same CT scans were then automatically contoured by M-Vision and the time needed to complete the process was registered. Finally, the automatic contouring was checked and corrected by the same ROs, always measuring the time of the process. The quality of automatic contouring was scored by the ROs using a five point Likert scale, with grades ranging from 1 (very bad) to 5 (very good). The contouring times were compared using the T-test.

Results: Fifteen CT (11 patients) were contoured by two experienced RO in 26.26 +/- 9.60 minutes (mean +/- SD) for each contouring and by delineating six OaRs (Liver, Stomach, Spinal Cord, Body, Left and Right Kidney). The M-Vision software automatically contoured a median of 12 OaRs (range:12-13) in 2.56 +/- 1.72 minutes (mean +/- SD). The subsequent corrections of M-vision contours by ROs was performed in 7.00 +/- 7.05 minutes (mean +/- SD). The total time, considering automatic contouring and ROs corrections, was 9.56 +/- 7,12 minutes (mean +/- SD). The difference among the contouring time spent by ROs, and automatic contouring plus corrections was statistically significant (p=0.0004). The ROs scored the automatic contouring quality as grade 3 (sufficient), grade 4 (good), and grade 5 (very good) in 6.7%, 60.0%, and 33.3% of cases, respectively.

Conclusion: AI-based contouring resulted an useful tool to reduce working time, with theoretically improved homogeneity of the contouring process. The quality of AI-based delineation was considered more than satisfactory by experienced ROs.

PO006

SETUP DISCREPANCY BETWEEN CONE-BEAM COMPUTED TOMOGRAPHY AND EXACTRAC X-RAY SYSTEM FOR PROSTATE IMAGE-GUIDED RADIOTHERAPY

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Aims: Intensity-modulated radiotherapy (IMRT) has become a mainstay for the treatment of prostate cancer because IMRT techniques allow for dose escalation while minimizing toxicity to surrounding organs. With recently innovations more accurate image-guided systems using direct visualization of the prostate have been developed. The aim of this study was to evaluate the setup discrepancy measured with two image-guided radiotherapy (IGRT) techniques, ExacTrac X-Ray 6 degree-of-freedom (6D) and kilo-voltage cone-beam computed tomography (CBCT). The first device employs an X-Ray imaging system that verifies the target position using bone anatomy. CBCT imaging allows positioning verification using not only bone anatomy but also soft tissues.

Methods: Setup data were collected on a Novalis-TrueBeam STx treatment unit for 57 patients with prostate cancer. Prescription doses ranged from 67.5 to 80 Gy in 25 to 40 fractions. All patients were initially positioned at the isocenter, setup corrections were determined using registrations of ExacTrac X-Ray images with the corresponding digitally reconstructed radiographs using the ExacTrac 6D fusion software. After correction through the 6D robotic couch, the residual setup errors were determined by means of registrations of CBCT images with the planning CT using online 3D fusion software, and for each session, displacements were evaluated to compare the setup differences between ExacTrac system and CBCT.

Results: A modest difference in residual setup errors was found between CBCT and ExacTrac X-Ray system. The average residual error differences were 1.11±1.01 mm, 1.10±0.97 mm and 1.07±1.39 mm in the lateral, lon-

gitudinal and vertical directions, respectively. The root-mean-square (RMS) of the differences were less than 1.66 mm for translations and 0.9 degrees for rotations.

Conclusions: We found a good agreement in the setup accuracy between ExacTrac X-Ray system and CBCT. Both IGRT systems achieved reasonably low residual errors after initial correction, but ExacTrac offers additional benefits such as the capability to quantify all rotational errors, fastest automated positioning in 6D and smaller doses; on the other hand, CBCT, sometimes seems preferable to ExacTrac for the capability to appreciate soft tissues. Further clinical investigations are needed to determine whether ExacTrac X-Ray system is a good alternative or a complement to CBCT for prostate cancer patients.

PO007

ARTIFICIAL INTELLIGENCE IN THE CONTOURING OF FEMALE PELVIC VOLUMES OF INTEREST: A PILOT STUDY

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Aim: Modern software based on artificial intelligence (AI) may represent a relevant contribution in radiotherapy contouring and treatment planning. Aim of this study is to present a single institution experience based on a new software for AI-based contouring of Volumes of Interest (VoIs) on computer tomography (CT) images in female patients with pelvic tumors.

Methods: We tested the new cloud-based software MVision AI (MVision AI Oy, Helsinki, Finland) for automatic segmentation of VoIs on CT-images according to international guidelines. Three Radiation Oncologists (ROs; two inexperienced and one experienced in gynecological cancers) performed the process of relevant VoIs contouring on ten patients previously treated in our department. Moreover, they recorded the time taken to complete the task. Then, the same CT scans were automatically contoured by MVision and the time taken to complete the process was registered. Finally, the automatic contouring was checked and corrected by the same ROs, always measuring the time of the process. The quality of automatic contouring was scored by the ROs using a five-point Likert scale with grades ranging from very poor to very good. The contouring times were compared using the T-test.

Results: The contoured VoIs by ROs and MVision were nine: body, bladder, rectum, right and left femoral heads, bilateral kidneys, bowel bag, cord, and uterus/cervix. Three ROs manually contoured ten CT scans in 37.2±6.4 and 24.8±3.1 minutes (mean±SD), for the two inexperienced ROs and the expert one, respectively. The time required by MVision for this process was 4.9±3.3 minutes (mean±SD). Automatic contouring and ROs corrections' total time was 31.4±8.1 minutes for inexperienced ROs and 21.2±4.2 minutes (mean±SD) for the expert one. The difference between time spent by ROs and time required for automatic delineation plus manual correction was statistically significant for inexperienced ROs (p:0.004) but not for the expert one (p:0.09). The quality of automatic segmentation was scored as poor, sufficient, and good in 6%, 41%, and 53%, respectively.

Conclusions: AI-based contouring resulted an useful tool to reduce the working time for inexperienced ROs, with theoretically improved homogeneity of the contouring process. The quality of AI-based delineation was satisfactory in most cases.

PO008

ARTIFICIAL INTELLIGENCE IN THE CONTOURING OF MALE PELVIC ORGANS AT RISK: A PILOT STUDY

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Aim: New software based on artificial intelligence (AI) have been proposed for radiotherapy contouring, especially of Organs at Risk (OaRs). Here we report on a single center experience based on a new AI software used for automatic delineation of male pelvic OaRs.

Methods: MVision AI (MVision AI Oy, Helsinki, Finland), a cloud based software for automatic OaRs contouring of CT-images, was tested in this analysis. Twelve male patients previously treated in our institute for pelvic

malignancy were randomly selected. Two Radiation Oncologists (ROs), with over ten years of experience in the management of male pelvic neoplasms, delineated OaRs and registered the time to complete the process. The same CT scans were sent to MVision and the time taken for automatic contour was also recorded. Then, the ROs revised the AI-based contouring and recorded the duration of this process. Finally, the quality of MVision contouring was evaluated by ROs with a five point Likert scale ranging from 1 (very bad) to 5 (very good). The contouring times were compared using the T-test.

Results: Twelve CT-scans (corresponding to 12 patients) were contoured by two ROs and eight OaRs were identified (body, bowel bag, rectum, recto-sigmoid junction, bladder, penile bulb, left and right femoral head). Mean time for each CT-scan contouring was 24.2 (SD: 6.3) minutes. The MVision software contoured a median of 13 OaRs in 2.9 +/-1.4 (mean +/-SD) minutes. ROs corrections were performed in 9.2 +/- 4.5 (mean +/- SD). Times for automatic contouring and ROs correction were added together, resulting in 12.1 +/-5.2 (mean +/- SD) minutes. A statistically significant difference was found between contouring time spent by ROs and AI contouring plus ROs correction time ($p<0.001$). The quality of MVision contouring was evaluated by ROs as grade 4 (good) and 5 (very good) in 41.7% and 58.3% of cases, respectively.

Conclusions: AI software can be a useful support in the contouring process of male pelvic OaRs, significantly reducing the working time. Moreover, a reduced intra-observer variability is expected. Finally, the quality of AI-based contouring was judged as more than satisfactory by ROs.

PO009

ARTIFICIAL INTELLIGENCE IN CHEST ORGANS AT RISK CONTOURING: A PILOT STUDY

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Aim: Modern software based on artificial intelligence (AI) may represent a relevant contribution in radiotherapy contouring and treatment planning. Aim of this study is to present a single institution experience based on a new software for AI contouring of Organs at Risk (OaRs) on computer tomography (CT) images.

Method: We have recently tested a new cloud-based software MVision AI (MVision AI Oy, Helsinki, Finland) for automatic OAR contouring of CT-images according to ESTRO and RTOG guidelines. Two Radiation Oncologists (ROs) experienced in thoracic cancers performed the process of relevant OaRs contouring on 12 patients previously treated in our department. Moreover, they recorded the time needed to complete the task. Then, the same CT scans were automatically contoured by MVision and the time needed to complete the process was registered. Finally, the automatic contouring was checked and corrected by the same ROs, always measuring the time taken to complete the process. The quality of automatic contouring was scored by the ROs using a five point Likert scale with grades ranging from 1 to 5. The contouring times were compared using the T-test.

Results: Twenty-four CT (12 patients) were contoured by two experienced ROs in 13.7 +/- 1.8 minutes (mean +/- SD) for each contouring and by delineating seven OaRs (Body, Esophagus, Heart, Left and Right Lung, Spinal Cord, and Trachea). The MVision software automatically contoured a median of 12 OaRs (range: 12-13) in 2.2 minutes +/- 0.1 (mean +/- SD). The subsequent corrections of MVision contours by ROs was performed in 1.3 minutes +/- 1.0 (mean +/- SD). The total time, considering automatic contouring and ROs corrections, was 3.4 minutes +/- 1.0 (mean +/- SD). The difference among the contouring time spent by ROs and automatic contouring plus corrections was statistically significant ($p<0.0001$). The ROs scored the automatic contouring quality as grade 1-3 (very bad-sufficient), grade 4 (good), and grade 5 (very good) in 0%, 8%, and 92% of cases, respectively.

Conclusion: AI-based contouring resulted an useful tool to reduce working time, with theoretically improved homogeneity of the contouring process. The quality of AI-based delineation was considered good-very good by experienced ROs.

PO010

HEART AND LEFT ANTERIOR DESCENDING CORONARY ARTERY DOSE FOR THE TREATMENT OF LEFT-SIDED BREAST CANCER PATIENTS USING THE CATALYST™/SENTINEL™ SYSTEM FOR DEEP INSPIRATION BREATH-HOLD RADIOTHERAPY

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Aims: The deep inspiration breath-hold technique (DIBH) helps to prevent adverse cardiovascular effects in breast cancer patients treated with postoperative radiotherapy. The breath-hold can be achieved with different techniques: spirometric methods, voluntary BH or optical/thermal tracking of the chest wall. Aim of this study was to evaluate treatment of left-sided breast cancer patients with an optical tracking system in terms of dosimetric impact on heart and left anterior descending coronary artery (LAD).

Methods: During a period of 5 months (January 2021-May 2021) twenty-three patients with left breast cancer candidates to postoperative radiotherapy were enrolled in our study since they were able to respect the DIBH protocol. The respiratory gating systems were Sentinel and Catalyst HD; patients used a tablet for the visual feedback of the breathing position. CT scans were acquired in free-breathing positions (FB) and in DIBH and dual treatment plans were arranged for each patient. All treatment plans were calculated with the Raystation® 10A version treatment planning system and radiotherapy was administered using an Elekta Versa HD™ linear accelerator with a total dose of 42.56 Gy in 16 fractions to the whole breast. Dosimetric parameters: mean dose, V10 and V20 for the heart, mean and maximum doses for the LAD were extracted from the dose-volume histograms and compared using the Wilcoxon-test in both plans. Dosimetric parameters were expressed in terms of mean (± Standard Deviation). In this study, a $p<0.05$ was considered statistically significant.

Results: Mean heart dose was 182 (±42) cGy for FB while it was 110 (±20) cGy for DIBH with a reduction of the 39% ($p<0.001$). V10 for the heart was 3.06 (±0.2)% for FB while it was 0.7 (±0.3)% for DIBH with a reduction of the 77% ($p<0.001$). V20 for the heart was 1.5 (±0.4)% for FB while it was 0.35 (±0.16)% for DIBH with a reduction of the 76% ($p<0.001$). Mean LAD dose was 1043 (±166) cGy for FB while it was 365 (±110) cGy for DIBH with a reduction of the 65% ($p<0.001$). Maximum LAD dose was 3470 (±38) cGy for FB while it was 925 (±90) cGy for DIBH with a reduction of the 73% ($p<0.001$).

Conclusions: Our analysis confirmed previous published data reporting dose reduction to the heart and LAD with breath-hold technique. DIBH using the Catalyst™/Sentinel™ system is a valid approach for left-sided breast radiotherapy. This option is recommended to reduce late cardiac toxicity.

PO011

CLOSE TO PACEMAKER (PMK) AND OVER – STEREOTACTIC MAGNETIC RESONANCE (MR) - GUIDED ADAPTIVE RADIATION THERAPY (SMART) ON PARACARDIAC NODE IN PATIENT WITH PMK

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Pacemaker and cardiac devices represented a serious challenge for MR imaging and a main obstacle for nearby radiotherapy treatment (RT), especially for ablative doses. SBRT associated with new technologies could acquire new targets unthinkable before. In this case we report paracardiac SMART on patient with PMK device. Herein we present the case of a 65 years old man with severe obesity, BPCO and atrial fibrillation controlled by PMK implantation in 2019. His oncologic history starts in 1997 with first diagnosis of Schwannoma of left scapula. He runs a long history of several relapses: firstly local recurrences treated with local excisions and subsequently SBRT on lung metastasis, with complete clinical response. Last clinical disease presentation occurred in a paracardiac site, anterior to the left ventricle, very close to the PMK leads. After multidisciplinary briefing with cardiac electrophysiologist concerning of feasibility of this hard treatment, our medical physicists proceeded to planning SBRT treatment on cardiac metastasis with critical recommendation to lower doses as much as possible to the PMK leads. The prescribed total dose for this tough treatment of SMART was 45 Gy in 5 fractions on the core of the cardiac lesion (Prescribed dose at the 98% of target volume) Max dose reported to cardiac leads was 7.5 Gy, with minimum registered distance from the PTV was about 4 mm. The SBRT was delivered every other day, from 29 March to 08 April 2021; for each RT-day patient underwent pre- and post- treatment PMK calibration, in secure "MRI SCAN" mode. During RT, executed on MRIdian® Linac, we maintain continuous visual and verbal contact, monitoring heart rate using a pulse oximetry. No acute toxicity or PMK malfunction were detected during overall treatment time, whilst surprisingly, we observed a significant mass interfraction reduction, already comparing the first and last fraction. Waiting for first diagnostic follow-up, our case report suggests feasibility of mediastinal/thoracic SMART in patient with cardiac devices, even in proximity of OAR or electronic components. Highly selected cases, based on Multidisciplinary evaluation and treatment, could benefit of ablative stereotactic treatment with Online advanced MR-Guided RT (SmartVISION®). If in last years, especially in the era of oligometastatic chronic disease, SBRT acquired new therapeutic fields with new emerging boundaries, SMART can go beyond limits and borders unbelievable before.

PO012

DOSIMETRIC EVALUATION OF A CUSTOM-MADE SILICON BOLUS BASED ON A 3D-PRINTED MOLD OF PATIENT ANATOMY FOR THE TREATMENT OF A CUTANEOUS LYMPHOMA OF THE FACE

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Aims: To evaluate the treatment plans obtained with and without the use of a custom-made silicon bolus for a patient affected by a T-cell cutaneous lymphoma of the face.

Methods: A 23 years old patient with primary cutaneous Peripheral CD8+ T-cell Lymphoma was referred for radical radiotherapy. The disease diffusely involved the nasal vestibule with skin and cartilage erosion of the columella and of the lateral crus, the skin of the cheeks and the superior lip. In order to overcome the skin-sparing effect of megavoltage-photon beams, for a target with difficult anatomy and several skin-air interfaces, a planning CT of the head was acquired and a 5mm thick custom–made silicon bolus (Ecoflex® 00-10, with a 1.04 g/cc density) was realized from a 3D printed mold, encompassing the residual nasal vestibule and the skin of the cheeks. We then acquired a new CT scan with the silicon bolus in place and we optimized the treatments plans both on the CT with and without bolus for two different Treatment Planning Systems (TomoPlan and Monaco-VMAT using a 6MV photon beam from Synergy BM). To assess the PTV coverage at the skin surface we extracted from the PTV three contiguous slices, 1 mm thick, at increased depth from the skin: PTV1mm, PTV2mm and PTV3mm.

Results: The comparison of the two Tomotherapy plans showed an excellent PTV1mm coverage for the plan with bolus and a lower coverage without bolus (V90%, V95% and V98% of 98%, 96,1% and 93,1% with bolus and 91,1%, 38,2% and 6,3% without bolus respectively). The coverage of the PTV2mm and of the PTV3mm was slightly better with bolus but was satisfactory also without bolus (V98% of the PTV2mm at 93,1% *vs* 89,0% with and without respectively). The comparison of the two VMAT plans showed a good PTV1mm coverage for the plan with bolus with the same lower coverage without bolus (despite lower than with Tomotherapy, with V90%, V95% and V98% of 96,4%, 91% and 74% with bolus and 80,7%, 34,3% and 6,2% without bolus respectively). The coverage of PTV3mm was again better for the plan with bolus but satisfactory for both plans, while the PTV2mm coverage of the plan without bolus resulted inadequate (V95% and V98% of 95,7% and 90,6% with bolus but 83,4% and 58% without bolus respectively).

Conclusions: The use of CT-based custom-made silicon bolus can be useful to treat patients with tumors involving the skin in anatomical sites where electron beams are not an adequate choice, and this benefit was more pronounced in VMAT plans.

PO013

HEALTHCARE-WORKERS TRAINING FOR THE TREATMENT OF LEFT-SIDED BREAST CANCER PATIENTS USING THE CATALYST™/SENTINEL™ SYSTEM FOR DEEP INSPIRATION BREATH-HOLD RADIOTHERAPY

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Aims: The deep inspiration breath-hold technique (DIBH) helps to prevent adverse cardiovascular effects in left breast cancer patients treated with postoperative radiotherapy by reducing the dose to the heart and to the coronary artery. Aim of this study was to evaluate the training time of healthcare-workers in our experience of left-sided breast cancer patients' treatment with the optical tracking system Catalyst™/Sentinel™.

Methods: From January 2021 to May 2021, thirty-two patients with left breast cancer were candidates to postoperative radiotherapy with DIBH. Radiotherapy was administered with an Elekta Versa HD linear accelerator giving a total dose of 42.56 Gy in 16 fractions to the whole breast with or without an electron beams boost. The respiratory gating systems were Sentinel for simulation and Catalyst HD for treatment. Moreover, patients used a tablet for the visual feedback of the breathing position. CT scans were acquired in free-breathing positions and in DIBH. Dual treatment plans were arranged for each patient. Time of training for each fraction was calculated by registering the time when the patient entered the linear accelerator room and again when the patient left the room after the radiotherapy treatment.

Results: Twenty-three patients were eligible for our study. Nine of them were excluded from the analysis since they were not able to maintain the DIBH position during the pre-planning CT scan (7 patients) or they could no longer maintain the treatment position before the radiation therapy starting (2 patients). Five of them were >75 years old, four suffered of anxiety disorders. Mean time of radiotherapy treatment varied from 40 to 17 minutes for each patient due to the training of all the healthcare-

workers, particularly of radiographers. Mean delivery time for each patient treated with DIBH was 40 minutes (range 35-45 minutes) during the first week; 30 minutes (range: 28-32 minutes) during the second week; 20 minutes (range: 18-22 minutes) after two weeks and 17 minutes (range: 14-19 minutes) after one month.

Conclusions: DIBH using the Catalyst™/Sentinel™ system is a valid approach for left-sided breast radiotherapy with considerable sparing of organs at risk. Our experience showed a mean time of treatment of 17 minutes after only one month of training. Following initial healthcare-workers training, DIBH was reliable and time-efficient.

PO014

STEREOTACTIC RADIOTHERAPY IS SAFE AND EFFECTIVE IN OLIGOMETASTATIC CANCER: RESULTS OF DIFFERENT SCHEDULES OF A SINGLE CENTRE

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Purpose: The aim of our study was to evaluate the effectiveness, PFS, interval of free time systemic therapy and toxicity in oligometastatic cancer patients (pts) treated with SBRT using different schedules.

Materials and Methods: We retrospectively analysed 26 oligometastatic pts receiving SBRT. 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. PTV was obtained by GTV + margin of 3-5 mm. For a better GTV definition, if necessary, image-fusion software were used. The dose prescription was 24\27 Gy in 3 fractions (ff) or 30 Gy in 5 ff; for lung lesions 50 Gy in 5 ff given 2-3 times at week (alternate days). PTV isodose line of 80% in 30% pts and PTV dose coverage of 95/105% in 70% pts. The treatment was performed with Versa HD™ linear accelerator of Elekta company (Stockholm- Sweden) using a VMAT technique. OS, PFS and LC control were calculated using Kaplan- Meier curve and SPSS 22 version software.

Results: From January 2017 to March 2021, 26 pts underwent SBRT; 17 of them (65,3%) were male and 9 (34,7%) were female. The mean age was 69 years old (range 51 to 81). The treated lesions were lymph nodes 73,3%, lung 15,3%, brain lesion 3,8%, bone 3,8% and prostate 3,8%. Of them 25 (96,84%) had a CR or PR and only 1 had a non-response with SD (3,15%). The mean PTV of treated lesions was 17,78 cc (range 3,67 cc to 90,5 cc). After mean follow-up of 17 months (range: 3-47 mnths) 1 year and 3 year PFS was 62% and 54%, respectively. Overall, 7 pts (26,9%) received systemic treatment before and during treatment, in remaining 18 pts SBRT managed to delay systemic treatment by 15 months. During follow-up only 3 (11%) pts experienced local recurrence in the treated site with a LC of 89%. Overall, ten (38,4%) pts experienced systemic disease progression. Finally, pts with a PTV < 21 cc had statistically significant advantage in PFS compared to pts with PTV > 21 cc ($p<0.043$). We did not observe any other factor influencing PFS. The treatment was well tolerated without acute or late toxicity.

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 due to define the optimal dose for fraction, considering physics features, kind of lesions and site of treatment.

PO015

DOSIMETRIC COMPARISON OF 3DCRT, VMAT AND TOMOTHERAPY FOR SYNCHRONOUS BILATERAL BREAST CANCER RADIOTHERAPY AFTER MASTECTOMY AND DEFINITIVE PROSTHESES

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Aims: Aim of our analysis was to compare the dosimetric characteristics in terms of PTV coverage and organ-at-risk dose of 3DCRT, VMAT and helical tomotherapy (HT) for bilateral chest wall plus right supraclavicular irradiation for synchronous breast cancer treated with mastectomy and definitive prostheses.

Methods: A case of synchronous bilateral breast cancer treated with mastectomy and definitive prostheses was selected. PTVs were defined as follows: PTV-R for the right chest-wall, PTV-L for the left chest-wall and PTV-R-SCL for the right supraclavicular target. Radiotherapy was scheduled with a total dose of 50 Gy (2 Gy per fraction). All treatment plans were calculated with the Raystation® treatment planning system. 3DCRT plan was realized using tangential beams, HT plan was realized with helical arc, VMAT plan was realized with two 360° arcs. V98, V107, homogeneity index (HI) and conformity index (CI) were compared. The mean doses for lung, heart and left-anterior-descending coronary artery (LAD), maximum dose to LAD, percentage volume of ipsilateral lung receiving 5 Gy (V5), 20 Gy (V20) and that of heart receiving 5 Gy (V5), 20 Gy (V20) were extracted and compared using the Wilcoxon-Test.

Results: VMAT and HT plans showed similar PTVs coverage and similar HI (VMAT = 0.91 *vs* TOMO = 0.93) and CI (VMAT = 0.70 *vs* TOMO = 0.74). CI and HI for 3DCRT were 0.35 and 0.30 respectively with a statistically significative difference with those of VMAT and HT

($p<0.001$). For HT plan: V98 was 99.66% for PTV-R, 99.26% for PTV-L, 99.87% for PTV-R-SCL. For VMAT plan: V98 was 98.42% for PTV-R, 98.52% for PTV-L, 99.81% for PTV-R-SCL. For HT plan: V107 was 0% for PTV-R, 0.15% for PTV-L, 0% for PTV-R-SCL. For VMAT plan: V107 was 0.19% for PTV-R, 0.17% for PTV-L, 0% for PTV-R-SCL. Lung dose was lower with VMAT plan (mean left lung dose: 3DCRT = 10.22 Gy, VMAT = 7.42 Gy, TOMO = 8.25 Gy; mean right lung dose: 3DCRT = 10.10 Gy, VMAT = 9.52 Gy, TOMO = 9.75 Gy). VMAT plan also showed a lower mean heart dose and a lower heart V5 while HT plan showed lower dose to LAD (Mean LAD Dose: 3DCRT = 27.60 Gy, VMAT = 9.27 Gy, TOMO = 6.49 Gy). Patient was treated with VMAT technique with an Elekta Versa HD™ linear accelerator since delivery time was 3 minutes instead of 15 minutes calculated for HT plan.

Conclusions: In our case PTV coverage was similar with VMAT and HT techniques. The dose to OARs is significantly reduced with both these modalities. 3DCRT is not to be considered yet a valid technique for this kind of treatments that require more complex plans. VMAT seems to reduce the dose to the lung and the heart with shorter delivery time.

PO016

PHANTOM SIMULATION AND PROTOCOLS DEFINITION FOR DEEP INSPIRATION BREATH HOLD (DIBH), CT ACQUISITION AND RADIOTHERAPY TREATMENT

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Aims: Clinical practice shows that cardiac toxicity is multifactor, patient and therapy method dependent. Our aim is to implement a new customized phantom in order to investigate DIBH in breast cancer radiotherapy using a laser based surface scanning system technology. Phantom simulation and protocols for DIBH in CT and RT are explored to assure quality and safety in left breast cancer radiotherapy.

Methods: Catalyst™/Sentinel™ (C-RAD, Sweden), were used and an innovative customized phantom was implemented, based on CIRS Dynamic Thorax Phantom, mimicking human respiration. Phantom was obtained adapting a thermoplastic brain mask on a human body, and after the necessary cooling time, fixed on the surrogate plate of the CIRS Dynamic Thorax Phantom. Pipe line from CT acquisition to RT treatment was defined. All steps were assessed by measurements of chest positions.

Results: Phantom movements, Catalyst™ and Sentinel™ respiratory studies and TPS evaluation were consistent with a position error less than 0.3mm. CT acquisition and RT treatment were feasible. DIBH work flow was designed, adjusted and confirmed during phantom tests.

Conclusions: The customized phantom warranty position and movement assessment in DIBH CT and RT treatment. DIBH work flow was defined and consistent. Radiographer training was feasible by Dynamic Phantom warranting test and retest in the work flow procedures. Position errors were less than 0.3mm and respiration curve measured with Sentinel and Catalyst were consistent with the position assessed with TPS

PO017

A SOLUTION FOR INTEGRATION BETWEEN RADIATION ONCOLOGY INFORMATION SYSTEM (OIS) WITH HOSPITAL INFORMATION SYSTEM (HIS)

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Aims: To obtain a fully integration between Oncology Information Systems (OIS), MOSAIQ by Elekta, and Hospital information System (HIS), GPI with three goals: increase efficiency, increase quality and safety, streamline workflows and processes.

Methods: We have started with a MOSAIQ configuration to obtain the most efficient paperless model. Routinely, Radiation therapy equipe used different sections of Mosaiq software, to process and visualize the information stored as patient custom properties; to store the data real-time generated during the RT process for each patient.

Results: Patient's visit is booked through HIS and demographic information is sent to the OIS and is stored in the OIS archive. This first step reduces repeated entry data and the mistake probability.

Radiation oncologists verifies the captured billing info (in RT ambulatory, in CT-simulator, in planning, in treatments), then sends it electronically as a financial transaction message to the Hospital Billing System. This mechanism would reduce errors and every record which is captured for billing would have an automatic corresponding evidence for NHS. Patient planning should be done in HIS, with a different agenda based on the type of visit (first visit or follow up). These appointments are immediately sent to the OIS. Modification or deletion in HIS is reflected in OIS. Patient documents of the first visit, follow up, and final treatment summary are sent to HIS via the OIS treatment summary, in order to share the patient's RT treatment status.

Conclusions: The automatic information exchange between OIS and HIS, that we have created, allows to

solve the problem of the registration of the incoming patient, of the outgoing billing data and the radiation oncology schedules and documents. These integrations eliminate redundant workflows, unnecessary work and paper.

PO018

NEW STRATEGIES AND INNOVATIONS IN RADIOTHERAPY TO TREAT CHALLENGING POSTMASTECTOMY BREAST CANCER PATIENTS: A CASE REPORT

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Purpose: We report a challenging case of left post mastectomy radiation treatment patient affected by severe preexisting comorbidities treated in our radiotherapy Unit by all these cutting edge technologies.

Material/Methods: A 71-year-old woman underwent surgery for an invasive left breast cancer classified as pT2N1a. In the past she underwent a lobectomy and a mechanical valve positioning. Her ejection fraction was around 50-55%. At the Multidisciplinary Tumor Board chemo-/radiotherapy was excluded due to the comorbidities and exclusive hormonal therapy was prescribed. Due to the radiotherapic indication albeit the comorbidities, a feasibility dosimetric study by all cutting edge technologies available in our arsenal was proposed. Chest wall as well axillary and supraclavicular nodes were contoured according to RTOG guidelines. In order to reduce the organs at risk (OARs) dose, Active Breathing Coordinator (Elekta@) device to treat the patient by moderate deep inspiration breath hold (DIBH) technique was used. Four different plans were generated and compared: a hybrid approach combining 3D-conformal and IMRT (HMRT plans), a hybrid approach combining 3D-conformal and VMAT (HVMAT plans) technique, a fully manual VMAT plan and a fully automated VMAT plan (AP-VMAT).

Results: Chest-wall and nodal areas planning target volumes were 465.5 cc and 117.2 cc, respectively. Target coverage criteria followed ICRU83 recommendations. Due to the co-morbidities, stringent objectives were applied (Table 1). The AP-VMAT was the only technique able to decrease the mean dose to the heart to the required objective of 4 Gy. In addition, the NTCP estimates for lung pneumonitis was below 1% only for the AP-VMAT. The mean dose of the contralateral breast was similar between techniques. Moreover AP-VMAT reported a large reduction of heart and ipsilateral lung irradiation in all dose ranges, down to 5 Gy. Therefore, fulfilling at best the target coverage criteria and OARs dose constraints, the AP-VMAT plan was proposed. A total dose of 50 Gy to the PTVs in 25 fractions for both chest wall and lymph-nodal area were delivered without the appearance of severe acute toxicity. Six months later, no adverse events e.g. skin fibrosis, or heart failure, or disease recurrence have been reported.

Conclusion: This case highlights the importance of the multidisciplinary approach to complex cases and showed as new technologies or cutting-edge updates can potentially change the therapeutic approach.

Table 1.

			Plan			
Structure	Metric	Objective	HMRT	HVMAT	MP-VMAT	AP-VMAT
PTV CW	D95 (Gy)	≥ 47.5	47.5	48.5	49.5	49.5
	D98 (Gy)	≥ 45.0	45.8	47.5	48.1	47.8
	D2 (Gy)	≤ 53.5	54.8	53.7	53.3	52.4
	Dmean (cGy)	50.0	51.3	50.8	51.4	50.5
Homogenity	HI	minimize	18	12.4	10.4	9.2
PTV SCL	D95 (Gy)	≥ 47.5	47.8	47.5	49.5	49.6
	D98 (Gy)	≥ 45.0	46.5	46.2	48.5	49.0
	D2 (Gy)	≤ 53.5	53.3	52.8	53.3	52.9
	Dmean (cGy)	50	50.5	50.2	51.6	51.1
Homogenity	HI	minimize	13.6	13.2	9.6	7.8
Conformity	CN		0.57	0.64	0.68	0.76
Heart	Dmean (Gy)	< 4	5.9	6.1	6.2	4.0
	V5 (%)		15.1	18.3	34.8	14.1
	V10 (%)		10.5	14.7	15.5	6.9
	V20 (%)	≤ 10	7.4	11.8	9.2	3.6
	V30 (%)	≤5	6.1	9.2	4.5	2.2
	$NTCP_{per}$	minimize	0	0	0	0
	$NTCP_{lung}$	minimize	0	0	0	0
Left lung	Dmean (Gy)		16.3	16.2	14.4	12.5
	V5 (%)	< 50	54.5	55.2	87.1	55.4
	V10 (%)	< 35	42.1	44.1	44.2	36.1
	V20 (%)	< 20	31.2	35.2	24.4	21.3
	V30 (%)		26.1	28.8	16.2	15.5
	$NTCP_{pneu}$	minimize	5.1	4.8	2.6	0.8
Right lung	Dmean (Gy)		0.7	0.6	2.4	2.4
Contralateral breast	Dmean (Gy)	< 2	1.1	1.1	1.4	1.3

PO019

RT TREATMENT STRATEGY BASED ON 18F-FDG-TC/PET RADIOMIC ASSESSMENT IN PATIENTS WITH HEAD AND NECK CANCER

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Aims: The aim of this retrospective study is to attempt to tailor radiotherapy treatment for Head and Neck Squamous Cell Carcinoma on the basis of texture analysis of both morphological and functional imaging. In this study patients were stratified the in two groups: those with residual or recurrent lesion in head-neck district after treatment (NLC) and patients without lesion in the same district (LC). Their evaluations were based on the results of post-treatment multimodality imaging (18-FDG PET/CT).

Methods: The study cohort included 70 patients. A 18-FDG PET/CT exam was performed both for staging and for treatment planning. 3DSlicer [https://www.slicer.org/] was used to perform feature extraction from semi-automatically segmentation both of primary lesion (T) and of the active lymph node nearby. The segmentation was carried out first on PET and then propagated on CT images. Processing and statistical analysis of radiomic features were performed by RadAR, a new computational tool to perform comprehensive analysis of radiomic datasets (https://github.com/cgplab/ RadAR). All patients were treated with radiation conventional fractionation associated with chemotherapy. P16 immunohistochemical overexpression was recorded for each patient. A radiomic signature including a selection of relevant features, was developed for both imaging modalities.

Results: The radiomic analysis clearly highlights the different signals resulting from lesions and lymph node, as expected. Two different prognostic model on CT and PET images were developed. A selection of six and nine best features were results respectively on CT and PET model. Both models showed very high sensibility to detect a treatment response (AUC rages from 85% of CT model to 94% of PET one).

Conclusions: Radiomic prognostic model applied to pre-treatment ^{18}F-FDG PET/CT could allow to distinguish patients in LC and NLC groups. Based on model, for LC patients, even if developed toxicity during treatment, total higher dose had to be still achieved, when functional constraints allow it. Our study demonstrates that using texture analysis in addition to clinical variables may impact on treatment strategy.

PO020

MEDULLOBLASTOMA TUMORS: RADIOMIC AND DOSIOMIC PROFILING OF PAEDIATRIC PATIENTS TREATED WITH IMRT

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Aims: The aim is to investigate imaging-based biomarkers of clinical outcomes in paediatric patients affected by medulloblastoma.

Methods: A retrospective exploratory MR-based radiomics and dosiomic analysis based on machine-learning technologies and statistical analysis was performed. 50 paediatric medulloblastoma patients treated with surgery, chemotherapy and radiotherapy (RT) were selected. Tumor characteristics, dosimetric parameters, baseline and pre-RT and follow up MRI (T1w, T2w and FLAIR image sets) and CT were available for all patients. Images were extracted with PyRadiomics and analysed with two different programs, a homemade script and RadAR (Radiomics Analysis with R). To reduce the amount of variables involved, while maintaining 90% of the variability of the data, was used the Principal Component Analysis technique. Ten features were associated with radio-induced toxicity occurrence. Random Forest classifier was trained on different combinations of the available data. RadAR performs analysis of radiomic features, implementing multiple statistical methods. To compare multiple features together, scaling and normalization were applied. An unsupervised analysis based on hierarchical clustering was used together with the Fisher's exact test to estimate statistical significance.

Results: With a 5-fold cross validation scheme the machine learning performance was evaluated . For every iteration a different test set consisting of an equivalent number of patients with and without toxicity was used. Individual dose, T1w, T2w and FLAIR data were not predictive, leading to average accuracies of 0.44±0.21, 0.56±0.16, 0.59±0.16 and 0.41±0.07, respectively. While combining all multiparametric information a better prediction performance was obtained: 0.62±0.09. In Figure 1 is reported the correlation matrix used to evaluate the degree of redundancy of feature data in the dataset. The result of Fisher's test is displayed by Kaplan-Meier plot in Figure 2. All the features available were predictive with a specificity of 0.79 and sensitivity of 0.65.

Conclusion: Good results were obtained by applying

the Random Forest classifier and statistical analysis to the radiomic and dose characteristics of pediatric patients. This multimodal and multiparametric approach could lead to great benefits for precision medicine as radiomic biomarkers are non-invasive and can be applied to pre-existing imaging data.

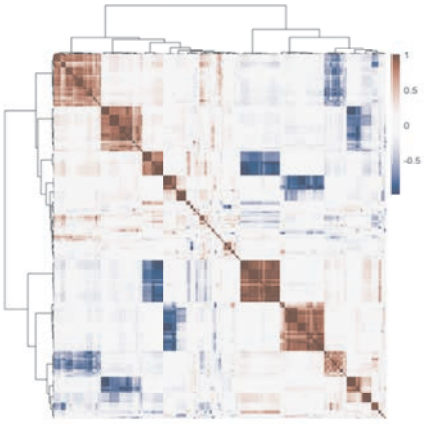

Fig. 1 Correltion matrix

Figure 1.

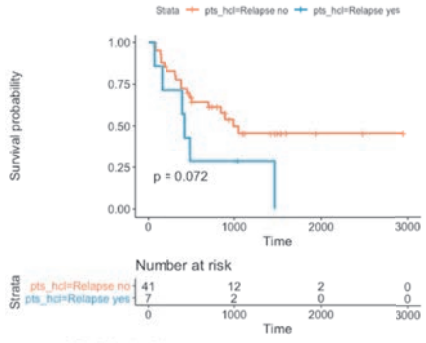

Fig 2. Kaplan-Meier plotof the result of the Fisher's test

Figure 1.

PO021

PRE-PROCESSING AND FEATURE/VOLUME CORRELATION FOR COMPUTED TOMOGRAPHY RADIOMICS IN NON-SMALL CELL LUNG CANCER: A STEP BACKWARDS TOWARDS METHODOLOGICAL IMPLEMENTATION

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Aims: Radiomics is increasingly used to implement clinically-based prognostic models for non-small cell lung cancer (NSLCL). However, no evidence supports the choice of specific imaging pre-processing methodologies. Admittedly, dedicated investigations could contribute to the refining of both reproducibility and performance of radiomic studies. As the volume of the primary tumor is a well-recognized prognosticator, our purpose is to assess how pre-processing may impact on the feature-volume dependency in computed tomography (CT) images of NSCLC patients treated with radiotherapy.

Methods: Images were retrieved from the publicly available repository NSCLC-Radiomics of The Cancer Imaging Archive (TCIA). Four hundred eighteen images were included in the analysis following manual inspection and editing of the segmentations; nodal disease- if any- was not included. Pyradiomics was used to extract 93 features; which were grouped as follows: first-order, shape-based (3D), shape-based (2D), gray level co-occurrence matrix (glcm), gray level run length matrix (glrlm), gray level size zone matrix (glszm), neighboring gray-tone difference matrix (ngtdm) and gray level dependence matrix (gldm). Twenty built-in pre-processing methods (filters) were applied, including wavelet and its possible permutations, Laplacian of gaussian and local binary pattern (lpb); each feature except those belonging to the shape category was computed once per filter, and on the original CT image. The Spearman correlation coefficient (ρ) was used; with thresholds of ≥0.7 and ≤0.5 defining strong and weak correlations, respectively.

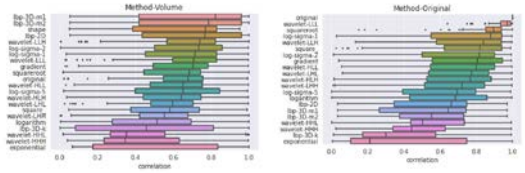

Figure 1.

Results: Overall, features of the glcm category were the least correlated with volume (ρ=0.5). The feature/volume correlation was found to be filter-dependent: the highest correlation was found when lpb-3D-m1 was applied (ρ=0.82), while the lowest correlations with volume were identified for the HHL and HHH-wavelet filters, and for the exponential method (ρ=0.35, 0.30 and 0.18, respectively). These results were confirmed when

features computed per each pre-processing modality were compared to the original image. An overview of the results is displayed in Figure 1.

Conclusions: Our data support the hypothesis that pre-processing does impact on features values; and provide a proof of concept that further standardization is warranted for radiomic studies. Further analyses will focus on how these findings impact on the performance of radiomic-based survival models.

PO022

SAMPLE PAIRING ("MIXUP") AS A DATA AUGMENTATION TECHNIQUE FOR DEEP MEDICAL IMAGE SEGMENTATION

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The problem of generalizability, or "overfitting," is a major impediment to deeplearning networks in all their forms. A key approach to improve the general-ization performance of deep image processing networks is through the extensiveuse of data augmentation techniques such as random flips, rotations, and de-formations. A data augmentation technique called mixup, which constructsvirtual training samples from convex combinations of inputs, was recently pro-posed for deep classification networks. The algorithm contributed to increasedperformance on the standard ImageNet-2012, CIFAR-10, CIFAR-100, Googlecommands, and UCI classification datasets, but has not yet been evaluated forimage segmentation tasks. In this paper, we evaluated the performance of themixup algorithm on a medical image prostate segmentation task with a standarddeep convolutional neural network. This was done on a set of 100 T2-weightedpelvis magnetic resonance image volumes from prostate cancer patients. Theperformance was quantified as the testing error (measured by the Dice similaritycoefficient and mean surface distance) from a reference segmentation made byan experienced radiologist. Our results suggest that mixup offers a statisticallysignificant boost in performance of up to 2% increased Dice and 22% decreasedsurface distance compared to non-mixup training.

PO023

EVALUATION OF FEATURES ROBUSTNESS IN RADIOMIC STUDIES: THE IMPORTANCE OF PARAMETERS HARMONIZATION WHEN USING MULTIPLE PLATFORMS

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Aims: Increasing efforts have been made to implement radiomics in the clinical practice. Features variability still represents one of the most critical pitfalls in the radiomic workflow, especially in magnetic resonance imaging (MRI). The aim of this study is to quantify the features robustness when using different radiomic packages and to provide harmonized parameters settings to allow for the greatest possible consistency among them.

Methods: Data from fluid-attenuated inversion recovery (FLAIR) MRI images of two patients diagnosed with glioblastoma who underwent surgery and chemoradiotherapy were included in the analysis. A subset of 20 radiomic features was selected according to the literature, and then extracted using Imaging Biomarker EXplorer (IBEX v1.0 beta) and PyRadiomics v3.0.1, with their default parameters settings. Harmonization methodology was derived from the study by Joseph James Foy (doi:10.6082/uchicago.2253). The harmonization effect was rated both intra-platforms and inter-platforms, through a Harmonization Necessity Factor (HNF) and PyRadiomics-Related Deviation (PyRD), respectively (Figure 1a). HNF values of 2 or higher were associated with high sensitivity to harmonization, while PyRD values ≤0.01 were associated with excellent agreement in feature values among platforms.

Fig. 1a

$$HNF = \frac{|FeatureValue\_Harmonized - FeatureValue\_Default|}{|FeatureValue\_Default|}$$

$$PyRD = \frac{|IBEXFeatureValue\_Harmonized - PyRadiomicsFeatureValue\_Harmonized|}{|PyRadiomicsFeatureValue\_Harmonized|}$$

Fig. 1b

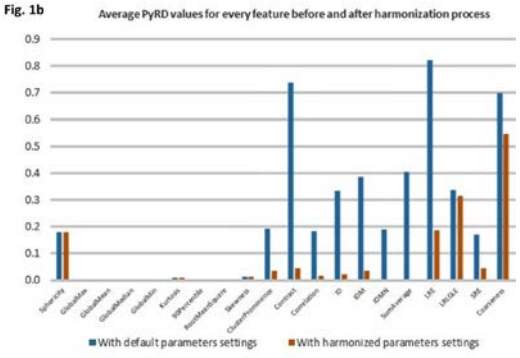

Figure 1.

Results: Harmonized parameters settings led to the greatest coherence, in terms of lowered PyRD values compared to default ones (Figure 1b). For each patient 16/20 features reflected excellent PyRD agreement in feature values among packages, with only *sphericity*, *Long Run Emphasis (LRE)*, *Long Run Low Gray Level Emphasis (LRLGLE)* and *coarseness* having a PyRD value in the order of magnitude of 0.1. Based on HNF

values, harmonization process had no effect on shape and first order features while *ClusterProminence* and *Contrast* showed to be the most sensitive, both in PyRadiomics and IBEX. Conversely, harmonization process had little impact on *Short Run Emphasis (SRE)*, *Inverse Difference Moment Normalized (IDMN)* and *Correlation*.

Conclusions: With default settings, most features showed significant differences in computed values between packages. First order features proved excellent agreement based on PyRD factor, while second-order features showed a relatively poor agreement between packages. Overall, harmonization allowed to achieve a higher degree of consistency. Our preliminary findings suggest that features harmonization could be beneficial in the radiomic workflow and foster results comparison across different centers towards clinical application.

PO024

TOXICITIES AND CLINICAL OUTCOMES IN LUNG TUMOURS TREATED WITH RADIOTHERAPY: THE PROGNOSTIC AND PREDICTIVE ROLE OF RADIOMICS AND "DOSIOMICS" FEATURES EXTRACTED BEFORE THERAPY, DAILY DURING IRRADIATION AND AT THE END OF TREATMENT

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Aims: To determine the potential prognostic and predictive role of radiomics features, including delta-radiomics and dosiomics, to create an analytical model predicting toxicities, and clinical outcomes, in patients treated with lung irradiation and submitted to daily onboard CBCT. Moreover, it will be possible to evaluate the correlation of objective treatment planning parameters (i.e. dose target planning delivered, alpha-beta ratio, BED, mean lung dose), associated to clinical/biochemical parameters as spirometry, DLCO, plasma TGF-β1, IL-8.

Patients and Methods: In a first phase will be retrospectively analyzed CT pretreatment, daily CT during therapy, and follow-up CT in a statistically predetermined patients' number. Using the commercial software MIM, serial 3-dimensional (3D) CT scans will be collected from one week before the start of treatment and daily thereafter. This procedure will be implemented according to the specific recommendation of the IBSI, to allow comparison between image data from different samples, or cohorts. Feature selection, useful for "radiomic" and "dosiomic" purposes, will be made using a learning algorithm (*i.e.* Pearson correlation coefficient). Subsequently, using software package which could be built on the MATLAB platform, machine learning algorithms will use the signature to construct predictive models by learning the decision boundaries of the underlying data distribution. DICOM files will be imported to MATLAB using the CERR. In the second phase, the model will be prospectively validated. Both phases (I-II) will be completed in three years.

Results: To demonstrate the potential prognostic and predictive role of radiomics features and the machine learning system as an analytic model of outcomes and toxicities in lung tumors patients. To evaluate if this innovative model can better predict OS, PFS, and toxicities.

PO025

DEVELOPMENT AND IMPLEMENTATION OF A CANCER REGISTRY FOR PATIENTS TREATED WITH HADRONTHERAPY: THE REGISTRY TRIAL (REGAL)

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Aims: Knowledge generation on treatment outcomes of cancer patients (pts) treated with hadrontherapy is essential. To do so we aim at constructing a pts registry to retrospectively and prospectively collect standardized real-world data on all cancer pts treated with hadrontherapy.

Methods: REGAL is an open-ended prospective and retrospective non-interventional and non-therapeutic multicohort study that includes routine clinical practice data derived from pts diagnostic tests and treatments. The retrospective enrollment takes into account all pts treated at our Institution from 2011 up today. This registry allows to analyze the disease course and treatment performed by collecting demographic, disease characteristics and delivered treatment; to register details about the radiotherapy treatment and biological parameters for developing predictive models (outcome and toxicity); to manage outcome data (in terms of overall survival, progression free-survival and local control); to define acute, intermediate and late toxicities; to collect Quality of Life questionnaires and PROMS. All information are managed according to pts' population and typical disease subsite. For this reason, 8 pre-specified sub studies have been created: Brain, skull base and spinal cord tumors; Ocular melanomas; Head and Neck tumors; Tumors of thorax and/or abdomen; Pelvic tumors; Sarcomas and tumors of limbs; Pediatric tumors; Mobile spine and sacral tumors. All pseudonymised pts' data obtained are recorded in an Electronic Data Capture system (RedCap platform). Standardized medical coding dictionaries will be used in the latest version available (Table 1).

Table 1. Standardized medical coding dictionaries.

ICD-10-CM	International Classification of Diseases, 10th Revision, Clinical Modification
ICD-O-3	International classification of diseases for oncology (ICD-O) – 3rd edition
MedRA	Medical Dictionary for Regulatory Activities
CTCAE	Common Terminology Criteria for Adverse Events – v. 5.0
ATC	Anatomical Therapeutic Chemical classification system

Results: A total number of 3400 pts have been treated at our Institution since 2011, divided into 1893 carbon ions and 1507 protons treatments (Figure 1). The collection and analysis are still ongoing.

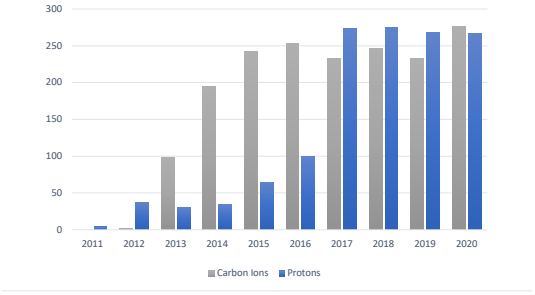

Figure 1. Particles treatments distribution through the years.

Conclusions: This registry will be used to generate clinical evidence and high-quality data of heavy ions particles therapy. By collecting data according to standardized dictionaries, REGAL will become a resource for the scientific community. Our registry is prepared for data sharing at the national and international cooperation to generate new evidence.

PO026

NEW OPPORTUNITIES FOR THE RADIATION ONCOLOGIST AND IMAGING SPECIALIST: THE PECULIAR FEATURES OF "BIOMEDICAL OMICS", A NEW MASTER'S DEGREE OF THE UNIVERSITY OF MILAN

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Aims: Omics disciplines have the potential to provide useful information about the cancer state and represent a powerful tool for the radiation oncologist to personalize treatments. One of the most representative examples is radiomics, which has emerged only recently, but already appears to be game changing in radiotherapy. A plethora of omics have arisen in recent years, and the newly inaugurated Master Program in Biomedical Omics (BO) of the University of Milan in Italy aims to address the unmet need of training novel specialists with a broad understanding of omics disciplines.

Methods: The course is structured over two years and admits students with a bachelor's degree in Biotechnology, Biology, Chemistry or Pharmaceutical Sciences. All teaching activities are fully held in English. The feedback of the students after the end of the first semester was collected through an online questionnaire encompassing questions about coordination among different courses, overall teaching effectiveness, interaction with lecturers and quality of the complementary didactic activity.

Results: Nine students enrolled in the first academic year and attended the courses of Radiomics, Genomics and Epigenomics, Proteomics and High-Throughput Screenings. The course of Radiomics was chaired by a Radiation Oncologist and a Radiologist, and showed the strongest multidisciplinary character, as clinicians, bioengineers, biotechnologists, physicists and PhD students with specific background on Radiomics for radiation oncology were involved in teaching activities. In general, faculty with different background were recruited according to the treated subject. Due to COVID-19 pandemic, laboratory activities were temporarily suspended while lectures, Journal Clubs and tests were mainly held online. The survey showed that coordination among the different courses and overall teaching effectiveness was positively evaluated. Students were satisfied with the interactions with lecturers as well as with the level of the proposed teaching modules. Webinars, seminars and classes overall met students' expectations.

Conclusions: At the end of the first semester, despite the difficulties brought by COVID-19 pandemic, the course overall met the expectations of students and realized a positive and effective didactic experience. In the next future, the novel professional figure of the omics specialist could be integrated in the already high multidisciplinary radiotherapy teams in Italy.

PO027

PREVALANCE OF PAIN IN RADIOTHERAPY DEPARTMENTS: RESULTS OF A MULTICENTER STUDY ON 2104 PATIENTS (ARISE)

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Aim: Pain is one of the most common symptom among cancer patients, occurring in 30-50% of patients undergoing active neoplastic therapy and in 75-90% of patients with advanced stage cancer. Furthermore, studies on pain assessment during radiotherapy are lacking. The aim of this multicenter observational prospective trial was to evaluate the prevalence of pain in radiotherapy departments using the Numeric Rating Score (NRS). Moreover, we analyzed the correlation of NRS with potentially predictive factors.

Methods: In this study we enrolled 2104 patients from 13 Italian radiotherapy departments. Radiotherapy aims, and patients and pain characteristics were recorded, using a collection form, during patients visits (in the course or at the end of treatment). Pain was classified as cancer pain, not-cancer-related pain, and mixed pain. The Pain Score was graded from 0 (no pain; NRS: 0) to 3 (severe pain; NRS: 7-10). The Analgesic Score was graded from 0 (no pain medication) to 3 (use of strong opioids). This study was approved by the Ethical Committee of the participating centers (ARISE-1 study).

Results: Of all enrolled patients, 67.0% complained of pain. For the purposes of this analysis we selected only patients with pain or under analgesic treatment (1409 patients). Among them, 47.3% complained of intermediate to severe pain. The results of the multivariable analysis are shown in Table 1. The parameters significantly correlated with higher mild-severe pain rates were: younger age (compared to older patients), worst (2-3) ECOG Performance Status (compared to ECOG=1), geographical location of the radiotherapy center (central-southern *vs* northern Italy), and opioids as analgesic drugs (compared to no pain medication).

Conclusions: The high prevalence of pain (particularly of intermediate-severe pain) among patients attending radiotherapy centers suggests inadequate attention to the treatment of this symptom during referral and therapy planning/delivery. Educational strategies are needed in radiotherapy departments to reduce this non-negligible percentage of patients with pain.

Table 1. Results of the multivariable analysis.

	OR (95% CI)	p-value
Age, years (analyzed as a continuous variable)	0.989 (0.980-0.998)	0.019*
ECOG-PS		
1	ref	
2	2.485 (1.816 - 3.400)	0.000*
3	2.400 (1.532 - 3.760)	0.000*
4	2.469 (0.796 - 7.652)	0.117
Geographical location of the radiotherapy center		
Nord of Italy	ref	
Center of Italy	1.646 (1.055 - 2.568)	0.028*
South of Italy	1.795 (1.307 - 2.465)	0.000*
Analgesic score		
No Therapy	ref	
No Opioids	2.015 (1.491 - 2.723)	0.000*
Opioids	7.734 (5.372 - 11.135)	0.000*

Legend: *: statistically significant; ECOG-PS: Eastern Cooperative Oncology Group Performance Status Scale; OR: odds ratio; 95% CI: 95% confidence interval.

PO028

MONOCENTRIC, RANDOMIZED CLINICAL TRIAL ABOUT THE EFFECT OF YOGA PRACTICE ON QOL, PHYSIOLOGICAL DISTRESS AND FATIGUE, ON PATIENTS AFFECTED BY BREAST CANCER UNDERGOING ADJUVANT RADIOTHERAPY

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Aim: Research on the effect of yoga in cancer patients has increased considerably over the past decade and a variety of yoga programs applied to cancer patients have reported improvements in stress and QOL.

Methods: Patients with stage 0 to III breast cancer were recruited before starting RT and were randomly assigned to yoga group (YG) two times a week for five weeks during RT or control group (CG). Self-report measures of QOL, fatigue and sleep quality, and blood samples were collected at day 1 of treatment, day 15 of treatment, end of treatment and 1, 3 and 6 months later. Cortisol blood level, IL6, IL10, IL1RA and TNFα were analized. Patients started XRT and yoga classes in October 2019. Due to COVID-19 pandemic and the DPCM of the 8th of March 2020 we closed the enroll-

ment at that time. We enrolled 24 patients, 12 YG and 12 CG, they all finished XRT the 6th of march 2020.

Results: There was no evidence of significant effects for PCS, MCS, BFI and PSQI. The analysis of cortisol revealed a significant interaction (p=0.04) between yoga practice and time on cortisol level. In particular YG has a lower cortisol level with respect to CG at the end of RT (p-adj =0.02) and cortisol levels were significantly lower at 15 days of RT and the last day of RT compared to 1-month follow up in YG. TNF-α was never expressed. There was no evidence of significant effects for IL-6 and IL-10. The analysis of IL-1Ra revealed a significant interaction effect (p=0.04). The effect of time on IL-1Ra level was significant in both YG and CG groups (p<0.001, p=0.008). In particular in YG group IL-1Ra was significantly lower at first day of RT, 15 days of RT, last day of RT and 1-month follow up with respect to 3-months follow up (p-adj<0.001, P-adj<0.001, P-adj<0.001, p=0.02), and at last day of RT with respect to 6-months follow up (p-adj=0.01). In CG group, instead, the values of IL-1Ra were significantly lower at the last day of RT, 1-month follow up and 3-months follow up compared to 6-months follow up (p-adj<0.001, p-adj<0.001, p=0.01).

Conclusions: This study shows that stress and inflammation levels are lower in YG than in CG and is also maintained over time. We should carry out a study with larger numbers of patients, possibly multicentric, which considers other inflammatory or pro-inflammatory factors in order to improve the compliance of patients undergoing adjuvant breast RT and reduce the costs of adjuvant pharmacological therapies that are often not successful.

PO029

RADIOTHERAPY FOR BREAST CANCER IN WOMEN WITH AUTOIMMUNE RHEUMATOLOGIC DISEASES: A MONOISTITUTIONAL EXPERIENCE

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Aims: Autoimmune rheumatologic diseases (ARDs) are chronic and heterogeneous disorders, described as an absolute or relative contraindication for radiotherapy (RT) due to increased RT-related toxicity. This study describes the management of breast cancer patients with ARDs who had the indication for adjuvant RT in our Center.

Methods: Patients affected by breast cancer and ARDs treated from January 2014 to January 2021 were retrospectively reviewed for treatment adherence and RT-related toxicity, according to CTCAE scoring scale.

Results: We considered 41 women with ARDs (mean age 59y). All the patients underwent multidisciplinary (dermatologic or rheumatologic) evaluation before RT. In 9 patients (21.9%) the severe active-phase disease or sequelae of chronic disease contraindicated the execution of RT. While 32 patients (75%) completed RT without breaks, 1 patient with Behçet Syndrome temporally suspended RT because of systemic exacerbation until resolution, following specialist suggestion. Thirteen women (31.7%) were in treatment with immune-system suppressant agents, interrupted during RT in all cases, except for steroids. Patients and treatment characteristics are shown in Table1. Hypofractionation was administered in 3 cases (7.3%), while 1 patient (2.4%) received 44,2 Gy (1,7 Gy/die) according to specialist opinion. Acute skin toxicity was recorded in 17 patients (41.5%) as grade 1, in 11 cases (26.8%) as grade 2. Late skin toxicity was: grade 1 (hyperpigmentation) in 4 cases (9.7%), grade 2 (telangiectasia) in 1 (2.4%). No G3-G4 toxicities were reported. Median follow-up was 29 months. After RT all the patients repeated specialist evaluation, and still now none of them presented disease exacerbation or needed further therapy for their autoimmune condition.

Conclusions: Literature experiences in irradiating patients with ARDs are in the form of exiguous retrospective studies and case reports, and we have no data to assess the best-tolerated dose and fractionation schedules in this subset. In our experience, a multidisciplinary evaluation allowed to exclude 9 patients at potential high-risk of adverse effects. On the contrary quiescent-phase ARDs seemed not to affect radiotherapy toxicity and all the reported adverse events were low grades. Considering the growing incidence of immune diseases and cancer, the interaction between RT and ARDs needs to be clearer.

Table 1.

Table 1: Patients, tumor and treatment characteristics			Treatment characteristics		N (%): 32
Patients characteristics		N (%): 41	RT sede	Whole breast	28 (87,50)
Autoimmune rheumatologic diseases (ARDs)	Behcet syndrome	1 (2,44)		Whole breast + IVC	3 (9,38)
	Dermatomyositis	1 (2,44)		Chest wall + IVC	1 (3,12)
	Fibromyalgia	7 (17,07)	RT total dose	≥ 5000	28 (87,50)
	Rheumatoid arthritis	16 (39,02)		4005-4256	3 (9,38)
	Sclerodermia	3 (7,32)		4420	1 (3,12)
	Sjogren syndrome	3 (7,32)	RT dose/ fraction	200	28 (87,50)
	Systemic lupus erythematosus	6 (14,63)		266-267	3 (9,38)
	Undifferentiated connective tissue disease	1 (2,44)		170	1 (3,12)
	Combined diseases	3 (7,32)	Boost	Yes	25 (78,12)
Tumor characteristics		N (%): 41		No	7 (21,88)
Side	Right breast	19 (46,35)	Ormone therapy	Yes	23 (71,87)
	Left breast	21 (51,22)		No	9 (28,13)
	Bilateral breasts	1 (2,43)	Chemotherapy	Neoadjuvant	7 (21,88)
Stage (pathological)	IA	30 (73,18)		Adjuvant	7 (21,88)
	IB	6 (14,64)		No	18 (56,24)
	IIA	3 (7,30)			
	IIB	2 (4,8828)			
Grade	G1	11 (26,83)			
	G2	26 (63,42)			
	G3	4 (9,75)			

PO030

TAPER: TRACK PALLIATIVE RADIOTHERAPY

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Aims: The primary objective is the global care of the symptomatic cancer patients. That being so, the collaboration between the Radiation Oncology Department and the Palliative Care Units of our Hospital was born. The intent was to promote multidisciplinary management also for this type of patients (pts). Encouraging an exchange between specialists is essential to obtain the best possible results for the patient and his family and to ensure the continuity of care between hospital and territory.

Methods: In November 2020, two paths were activated, both dedicated to advanced/metastatic patients. The first one is "The Multidisciplinary Radiotherapy Clinic - Palliative Care" (MRPC) a simultaneous care ambulatory dedicated to pain therapy. The second is "Fast-Track", which gives the possibility to treat patients with a reduced performance status, prioritarily (FLASH-RT). Both paths can be activated by the General Practitioner or by the reference specialist, by sending a dedicated email TAPER@aulss9.veneto.it. In 2020 to this setting of patients it was delivered FACIT-F, furthermore, we have collected these characteristics: gender, age, histology, site of the lesion, intensity of pain (valued with Numeric Rating Scale and pain score), type of pain, prescribed analgesic score, ECOG Performance Status (PS).

Results: One hundred patients with symptomatic metastatic cancer were admitted to our department between March 2020 and March 2021. We have analyzed the proposed questionnaires on the quality of life and the adequacy of pain therapy. Fifty patients are treated after the activation of the aforementioned pathways. A significant increase of compliance emerged with the introduction of MRPC and FLASH-RT. In all examined questionnaires, there was an increase of quality of life and a more rapid control of symptoms.

Conclusions: The improvement in oncological treatments has led to a progressive increase of the number of long-term survivors, it's more frequent to treat patients with RT in all stages of the disease. In an advanced/metastatic setting , it is very important to point our attention to quality of life to obtain the best compromise for a tailored treatment single.

PO031

PREVENTION OF RADIATION-INDUCED DERMATITIS DURING RADIOTHERAPY FOR BREAST CANCER: A PRELIMINARY EXPERIENCE USING A SILICONE-BASED TOPIC SUPPORTIVE THERAPY

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Aims: Radiation-induced dermatitis (RD) is the most common side effect related to radiotherapy for breast cancer, expericenced by approximately 95% of patients during and/or after treatment. Spectrum of RD includes different clinical features like pain and discomfort, erythema, itching, edema, desquamation, pygmentation, fibrosis, vascular injury and atrophy. It can have a negative impact on patients' quality of life and compliance, leading to possible reduction of doses, treatment discontinuance and increase of overall treatment time, with direct consequences on oncologic outcomes. Although basic recommendations for regular skin care can be suggested, at present there is still no consensus in the way of prevention and treatment of RD. In the present work we evaluated the role of a silicone gel-based topic agent used to prevent and to treat acute skin toxicity during adjuvant radiotherapy for breast cancer. To our knowledge, this is one of the few studies taking into account this kind of silicone gel-based supportive therapy.

Methods: We enrolled 15 female patients from March to April 2021, who received adjuvant radiotherapy for breast cancer. All treatments were 3D-CRT. In 14 cases (93.33%) patients were previously treated with conservative surgery, while in 1 case (6.67%) mastectomy was performed. 11 lesions (73.34%) were histologically classified as ductal carcinoma, 1 lesion (6.65%) as mucinous carcinoma, 1 lesion (6.65%) as squamous-like carcinoma and 2 lesions (13.36%) as ductal-in situ carcinoma. Median age was 59 years (range 36-78 years), and median breast size was 4 (range 2-8). According to VIII TNM classification, pathologic findings revealed 2 (13.34%) pTis, 11 (73.32%) pT1, 2 (13.34%) pT2. 5 patients (33.33%) received neoadjuvant chemotherapy with antracycline and taxane and 1 of them also received adjuvant chemotherapy with capecitabine. During the first physical examination, all patients got a waterproof, bacteriostatic, silicone gel-based wound dressing, to apply directly on mammary skin once a day for the whole treatment. Acute skin toxicity was assessed using RTOG criteria.

Results: Results are summarized in Table 1.

Conclusions: Despite the limited number of enrolled patients, according to literature, this kind of silicone gel-based wound dressing demonstrated its efficacy in preventing high grade skin toxicity during breast radiotherapy. Further studies are required to define and validate an unique approach to prevent and treat RD.

Table 1.

	50 Gy 25 fractions	45 Gy 20 fractions	40.05 Gy 15 fractions	Total
G0 toxicity	–	–	–	–
G1 toxicity	1	4	6	11
G2 toxicity	1	2	1	4
G3 toxicity	–	–	–	–
G4 toxicity	–	–	–	–
Total	2	6	7	15

PO032

SUPPORTIVE CARE IN THE TREATMENT OF PANCREATIC-BILIARY TUMORS. A CHALLENGING MANAGEMENT

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Aims: The therapy and management of patients with pancreatic and biliary tract cancers are real challenges for the Radioncologist. These tumors are often inoperable at the onset of the disease, quickly lead to pancreatic or hepatic insufficiency and radical radio-chemotherapy treatment is not always well tolerated by patients. It is important for the Radioncologist to be able to personally carry out supportive care for these patients.

Methods: In the last 3 years (2019-2021) we have treated 32 patients with pancreatic or biliary tract neoplasia in our center. The patients had a mean age of 63 years (range 50-77). There were 14 males, 18 females. All patients underwent radiotherapy with IMRT or 3DCRT technique with a dose of 50-55 Gy in daily fractions of 2-2.5 Gy. 25 patients underwent chemotherapy in our department with Gemcitabine-Oxaliplatin, Cisplatin-Gemcitabine, Fluorouracil-Oxaliplatin, Fluorouracil-Irinotecan-Oxaliplatin protocols. During therapy, many patients required blood draws and supportive care with rehydrating infusions, blood and platelet transfusions, albumin or immunoglobulin infusion, total parenteral nutrition, pain therapy. During hospitalization, stents or percutaneous drains were placed in patients with biliary tract or pancreatic duct stenosis.

Results: Due to the complexity and intensity of the integrated radio-chemotherapy treatment, 27 patients required supportive therapy. The toxicities found were nausea, vomiting, epigastric pain, severe thrombocytopenia, bleeding with anemia, jaundice, ascites, malnutrition with weight loss, dehydration. Toxicities were expertly managed and all patients completed integrated radio-chemotherapy treatment.

Conclusions: The data reported show that it is extremely important for the radio-oncologist to be able and to know how to manage the toxicities of the radio-chemotherapy treatment of pancreatic and biliary tract tumors. The supportive care allowed the continuation of the oncological treatments which, alternatively, would have been interrupted or permanently suspended. Completion of treatments results in a significant increase in overall survival and progression-free survival.

PO033

COMBINATORIAL EFFECT OF MAGNETIC FIELD AND RADIOTHERAPY IN PANCREATIC DUCTAL ADENOCARCINOMA ORGANOIDS: A PILOT STUDY

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Background: Pancreatic ductal adenocarcinoma (PDAC) is highly refractory to systemic treatment, including radiotherapy (RT) either as alone or in combination with chemotherapy. Magnetic resonance (MR)-guided RT is a novel treatment technique which conjugates the high MR imaging contrast resolution to the possibility of re-adapting treatment plan to daily anatomical variations. Magnetic field (MF) might exert a biological effect that could be exploited to enhance radiation effect. The aim of the present study was to lay the preclinical basis of the MF effect by exploring how it modifies the response to radiation in organoid cultures established from PDAC.

Material and Methods: The short-term effect of radiation, alone or in combination with 1.5T MF on UnityTM (Elekta Inc., Sweden), was evaluated in patient-derived organoids (PDOs). Cell viability, apoptotic cell death, and organoid size following exposure to the treatment were evaluated. Organoid cultures were treated with 6 Gy with or without 60 min MF exposure.

Results: We selected and tested four PDOs. While MF alone had minimal effect on viability of 3 out of the 4 PDOs tested, the combination of 6 Gy and MF further reduced cell viability in all cultures as compared to monotherapy with RT. We measured induction of apoptotic cell death following exposure to RT alone or in combination with MF by incubating organoid cultures with a fluorogenic substrate for the activated executioners Caspases 3 and 7. In keeping with ATP-based measures, combination of RT and MF significantly increased cell death of 59% and 33% compared to control while reducing organoids size in PDAC1- and PDAC2-PDO, respectively. No induction of apoptotic cell death could be observed in PDAC4 culture following treatment, yet organoids reduced in size. Overall, PDAC-PDOs dis-

played heterogeneous responses both to the radiation and to the MF, thus suggesting that not all patients are likely to respond to the treatment. Sensitivity could not be cross-referenced to peculiar morphological or genetic characteristics of the PDOs. PDAC4 showed the least sensitivity and, interestingly, it was derived from a patient who has been treated with adjuvant radiotherapy, but treatment was soon suspended as the patient rapidly progressed.

Conclusions: Long-time exposure to 1.5T MF can increase the therapeutic efficacy of radiation in PDAC organoids. This is the first evidence of a potential therapeutical combination of RT and MF.

PO034

IMMUNE CHECKPOINT INHIBITORS AND RADIOTHERAPY IN ADVANCED NON SMALL CELL LUNG CANCER: A META-ANALYSIS OF PUBLISHED STUDIES

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Aims: To assess the effects of Immune checkpoint inhibitors (ICIs) plus radiotherapy (RT) combination, in NSCLC patients, on the increase in overall survival (OS) and progression-free survival (PFS).

Methods: The MEDLINE and CANCERLIT (1970–2020) computerized bibliographic were searched, and the reference lists of included studies were supplemented with manually searches. Studies were included if they were comparative studies between combination ICIs-RT and ICIs or RT alone in advanced or metastatic NSCLC patients. Overall survival (OS) was analyzed according to the treatment strategy. Data on population, intervention, and outcomes were extracted, by two independent observers, from each study, in accordance with the intention-to-treat method, and combined using the DerSimonian method and Laird method.

Results: The six studies, that were included in the pooled analysis, included 8435 patients, in two studies ICIs and RT associations were compared to RT alone and in the remaining four studies to ICIs alone. ICIs-RT significantly increased the 1-year and 3-year OS RR by 0.75 (95% CI 0.64–0.88; p=0.0003) and 0.85 (95% CI 0.78–0.93; p=0.0006), respectively. Furthermore, there was a statistically significant benefit on 1- and 3-year PFS (RR 0.73 (95% CI, 0.61–0.87; p=0.0005) and RR 0.82 (95% CI 0.67–0.99; p=0.04), respectively).

Conclusions: ICIs and RT associations, in patients with advanced or metastatic NSCLC, increases 1- and 3-year OS and PFS compared to ICIs or RT alone.

PO035

PRELIMINARY RESULTS OF NEUTRALITY PROTOCOL (COHORT B, HISTORICAL ARM): EVALUATION OF "NEUTROPHILS-TO-LYMPHOCYTE RATIO" (NLR) IN PATIENTS AFFECTED BY LOCALLY ADVANCED INOPERABLE NON SMALL CELL LUNG CANCER (NSCLC) TREATED WITH RADIOCHEMOTERAPY

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Aims: To assess the role of Neutrophils-to-lymphocyte ratio (NLR) as a parameter of prognosis in patients with locally advanced stage III Non Small Cell Lung Cancer (NSLC) underwent chemotherapy (CHT). Primary endpoint is the evaluation of the relation between (NLR) and Local Relapse (LR), Progression Free Survival (PFS) and Overall Survival (OS). Secondary endpoints are the evaluation of the relation between systemic inflammation index (SII), LDH, PCR, VES and LR, PFS and OS.

Methods: The study population is divided into two cohorts: A (Durvalumab Arm) composed by patients who underwent a radical radio-chemotherapy (RT-CHT) treatment plus durvalumab; B (Historical Arm) composed by patients radically treated (RT-CHT) without immunotherapy. 85 patients were enrolled from 5 Italian centers. Median age of patients was 65 years (range 42-84); Performance status was 0 in 51 patients (60%) and 1 in 34 patients (40%). All patients were III stage: 37 (44%) IIIA, 39 (46%) IIIB, 9 (10%) IIIC; Histology was adenocarcinoma for 43 patients (51%), squamous cell carcinoma for 37 (44%) others for 5 patients (5%). PDL1 was (24%) in 20 patients, not evaluable for 65 patients (76%). 56 patients (66%) underwent concomitant RT-CHT, 29 (44%) sequential therapy. All patients underwent 3D Conformational Radiotherapy or Intensity Modulated Radiotherapy with a range dose 44-74 Gy and a mean dose of 61.6 Gy for concomitant and 61.1 Gy for sequential treatment.

Results: The median follow up was 21,8 months (range 4-110). Local relapses were 27; 36 patients had distant relapses. At 3 months after treatment 13 patients (15.3%) had stable disease (SD), 42 (49.4%) partial response (PR), 1 (1.2%) complete response, 1 (1.2%) pseudoprogression and 22 (25.8%) progression disease. At 12 months 18 (21.2%) SD, 3 (3.5%) PR, 1 (1.2%) CR, 12 (14.1%) PD. We reported toxicity during RT-CHT in 73 patients (85.8%), grade ≥ 3 in 29 patients (39.7%). LC resulted 83,6% at 1 year, 71,1% at 2 years, 57,3% at 3 years. PFS was 44,6% at 1 year, 30,1% at 2 years, 21,7%

at 3 years. OS was 71,6% at 1 year, 51,8% at 2 years, 34,4% at 3 years. The analysis showed a relation between NLR and stage disease, patients IIIC had higher NLR and worse OS and prognosis.

Conclusions: LC, PFS and OS of our preliminary analysis were in agreement with standard arm of Pacific and RTOG 0617 studies. The role of NLR as a prognosis parameter will be further evaluated in the framework of this study with longer follow up.

PO036

RADIATION THERAPY AS BRIDGING STRATEGY BEFORE INFUSION OF CAR T-CELLS IN NON-HODGKIN LYMPHOMA PATIENTS

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Aims: Chimeric antigen receptor (CAR) T-cells are autologous genetically engineered T cells recognizing tumor surface antigens. CAR-T cell targeting CD19 antigen has transformed salvage approach in relapsed/refractory B-cell lymphomas, achieving high response rates and durable remissions. However, several issues still need to be resolved to further optimize outcomes. One this challenges is to identify the optimal therapeutic regimen to maintain disease control prior to infusion of anti-CD19 CAR T-cells, during the 4 weeks period of product manufacturing (so called bridging therapy). In this context, radiation therapy (RT) may be a valuable bridging therapy to CAR T-cell therapy, offering tumor control and reduced toxicity, especially when disease burden is limited. Preliminary data from retrospective analysis showed early evidence that RT can be safe and effective as a bridging treatment. Therefore, RT may have complementary immunomodulatory activity with CAR-T cells. Here we describe a case series of our patients affected by high grade non Hodgkin Lymphoma, receiving radiation as a bridge therapy to anti-CD19 CAR T-cells.

Methods: Between August 2020 and March 2021, 5 patient (2 M, 3 F) received bridging radiation before anti-CD19 CAR T-cells. Median age was 44 years (34-53). Patient were affected by Diffuse Large B cell Lymphoma relapsed and/or refractory to chemotherapy and autologous stem cell transplantation, with a median of 5 lines of prior therapy (2-12). All patients received 2 to 2.5 Gy/fraction to a median dose of 32.4 Gy (20-42) with extended field RT surrounding disease involvement. One patient received concurrent chemotherapy. Median time from the end of RT to CAR-T cell infusion was 39 days (16-66).

Results: After the end of RT and before CAR-T cell infusion, 2/5 patient experienced haematological toxicities (1 grade III pancytopenia; 1 grade IV pancytopenia in the patient treated with concomitant chemotherapy), while 3/5 patients showed no significant toxicities. Disease assessment by PET-CT after RT in 4/5 patient, showed 3 complete remissions and 1 stable disease. At a median follow-up was 3.8 months (2–8) after CAR-T cell therapy, all patient are in complete remission.

Conclusions: RT can be considered as a safe and effective bridge approach to CAR-T cell therapy in patient affected by Diffuse Large B cell Lymphoma. Future investigation is warranted to optimize timing and dose of bridging radiation before CAR T therapy.

PO037

SAFETY AND EFFICACY OF CONCOMITANT CDK4/6 INHIBITORS AND RADIATION THERAPY IN HORMONAL RECEPTOR (HR)-POSITIVE HER2-NEGATIVE BREAST CANCER

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Aims: The association of cyclin-dependent kinase 4/6 inhibitors (CDK4/6i) with endocrine therapy (ET) is the current standard of care for I-II line treatment in metastatic hormone receptor (HR)-positive HER2-negative breast cancer patients. In this setting, radiation therapy (RT) with either palliative or ablative intent is often required. The aim of our study was to evaluate the safety and efficacy of concomitant CDK4/6i and RT in metastatic HR+/HER2- breast cancer patients compared to patients who did not receive RT.

Methods: We analysed data of 133 patients consecutively treated with CDK4/6i in two European institutions from September 2017 to February 2020. Both hematologic and non-hematologic acute toxicity have been evaluated and scored according to CTCAE v.5.0.

Results: We performed an analysis by simple cross-tables with chi-square test and logistic analysis to confirm emerged associations between outcomes and several parameters. Median age of patients was 59 years (range

37-86). At the time of metastatic disease diagnosis, 111 patients (83.5%) were postmenopausal. One-hundred twelve patients (84.2%) were treated with palbociclib, 19 with ribociclib, 2 with abemaciclib. Forty-six percent of patients received letrozole (I line) and 54% fulvestrant (II line). At a median follow up of 13.2 months, PFS rate was 53.4%. Fifty-nine patients received concomitant RT with palliative (79.7%) or ablative intent (20.3%) during CDK4/6i, while 74 patients did not. Bone was the most frequently treated RT site (81.4%), with 3-dimensional conformal radiation therapy (3D-CRT) as the most used technique (79.7%). RT was not significantly associated with ≥G2 (p=0.45) and any grade toxicity (p=0.69); there was no association with RT and CDK4/6i dose reductions (p=1.0) and discontinuations (p=0.07) [Table 1]. The use of CDK4/6i plus ET in first or second line did not show any impact on ≥G2 toxicity development (p=0.71). Postmenopausal status was the only factor associated with a significantly increased risk of ≥G2 toxicity (p=0.005). Among patients who received RT, no significant associations were found regarding RT intent, technique, and bone or visceral RT site [Table 2].

Conclusions: Our study showed that concomitant administration of RT with either palliative or ablative intent during CDK4/6i is safe and effective, without increased toxicity and significant impact on systemic treatment conduction. Further studies on larger series are needed to confirm these findings.

Tables 1 and 2.

RT administration (yes/no)	*p-values*
Any grade ≥2 toxicity	0.45
Any grade toxicity	0.69
CDK4/6i dose reductions	1.0
CDK4/6i discontinuation	0.066

Table 1. Association of RT administration with toxicity development and CDK4/6i dose reductions and discontinuation.

Parameter	*p-values*
Site of RT (bone vs visceral site)	
Any grade ≥2 toxicity	0.73
Any grade toxicity	1.0
CDK4/6i dose reductions	1.0
CDK4/6i discontinuation	-
RT technique (3D vs IMRT/CK)	
Any grade ≥2 toxicity	0.041
Any grade toxicity	1.0
CDK4/6i dose reductions	0.76
CDK4/6i discontinuation	-
Intent of RT (palliative vs radical)	
Any grade ≥2 toxicity	0.18
Any grade toxicity	1.0
CDK4/6i dose reductions	0.76
CDK4/6i discontinuation	-

Table 2. Association of RT site, intent and technique with toxicity development and CDK4/6i dose reductions and discontinuation.

PO038

APPLICATION OF THE TIME-SCHEDULE OF "RETE RADIOTERAPICA VENETA" IN THE REAL LIFE OF TWO RADIATION DEPARTMENTS

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Aims: Validate the congruence in terms of material and human resources of the staff of two different radiotherapy departments in Veneto, based on the schedule developed by "Rete Radioterapica Veneta"(RRV).

Methods: The RRV analysed in detail the radiotherapy workflow dividing it in various steps: first visit, Immobilization, Simulation, Imaging acquisition, Segmentation, Discussion and approval of treatment plans, IGRT, Treatment and control visit. Some activities were reimbursed by the health regional system and others were coded to obtain a bench marking possibility. For each of these, the RRV has associated an average time (minutes) spent by medical, technical and nursing staff. Our two radiation departments use MOSAIQ by Elekta as Oncology Information Systems (OIS) to manage the workflow automatically. That being so, it was simple to calculate numbers of registered activities. The amount of working hours per month for each professional figure was defined according to the employment contract, with exclusion of holidays, radiological risk and professional updating: 112/month hours for medical doctors and 116/month hours for technicians and nurses. The analysed period was the first three months of 2021.

Results: The two departments performed a total of 10953 and 16689 activities respectively, which involved the radiation oncologist for 5546 and 4843 activities, the radiation technicians for 5421 and 9461 activities and nurses for 1731 and 3354. We have generated the working hours for radiation oncologists, for radiation technicians and for radiation nurses. From these data derives a need respectively for the two departments: 10 and 13 radiation oncologists, 13 and 21 radiation technicians and 5 and 7 radiation nurses.

Conclusions: The data makes us think that the radiotherapy workflow is very complex and the new techniques (increasing the benefit for patients) are more time consuming than previous. A serious review of treatment staff is required.

PO039

RETROSPECTIVE EVALUATION OF THE "NEUTROPHIL-LYMPHOCYTE RATIO" (NLR) IN PATIENTS AFFECTED ADVANCED INOPERABLE STAGE III NON SMALL CELL LUNG CANCER (NSCLC) TREATED WITH DURVALUMAB INCLUDED IN THE ITALIAN EXPANDED ACCESS PROGRAM (EAP)

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Aims: The primary endpoint is to evaluate the association between Neutrophils-to-lymphocyte ratio (NLR) on blood count test and Local Relapse (LR), Progression Free Survival (PFS) and Overall Survival (OS) in inoperable locally advanced Non Small Cell Lung Cancer (NSCLC). The secondary objectives are to assess the association between systemic inflammation index (SII), LDH, CRP, ESR on blood count test and LR, PFS and OS.

Methods: Retrospective multicentric evaluation of the role of NLR, in patients with locally advanced NSCLC who underwent radical radio-chemotherapy in two cohorts of patients: cohort A (Durvalumab Arm) is composed by patients yet enrolled in the Durvalumab Italian Expanded Access Program for inoperable locally advanced NSCLC and cohort B (Historical Arm) is composed by patients who underwent a radical radio-chemotherapy treatment, without immunotherapy for locally advanced inoperable NSCLC. Exclusion criteria is life expectancy less than 6 months (GPA score <2).

Results: The two cohorts will be analyzed separately and compared, in order to explore both the prognostic and the predictive value of NLR for the different outcomes. Collected data refer to the blood count test, steroid therapy, immunomodulatory drugs and antibiotics during immunotherapy treatment, CT and will be recorded at several scheduled timepoints. Timepoints for cohort A are: Within 10 days from the beginning of immunotherapy, at 8-16-24-32-48-56 weeks from the beginning of immunotherapy (+/- 7 days), for cohort B are at the beginning and at the end of the chemo-radiation treatment. Patients will be followed up from the diagnosis of stage III unresectable, for 48 months after the end of the treatment, with a first evaluation after 24 months. This protocol expects the enrolment of approximately 220-300 patients: 150-200 patients will be enrolled in the cohort A, and 70-100 patients will be enrolled in the cohort B. The differences between the subgroups will be evaluated through the log-rank test. The multivariate analysis of the parameters will be performed with the Cox regression analysis. Survival data will be studied with Kaplan-Meier survival analysis.

Conclusions: The study hypothesis is that an increase of NLR, SII, LDH, CRP and ESR on blood count tests are associated with a poor prognosis even if will be further evaluated in the framework of this study.

PO040

CLINICAL STUDIES ON ULTRAFRACTIONATED CHEMORADIATION: A SYSTEMATIC REVIEW

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Aim: The efficacy of low-dose fractionated radiotherapy (LDFRT) and chemotherapy (CHT) combination has several preclinical but only few clinical evidence. Therefore, the aim of this review was to collect and analyze the clinical results of LDFRT plus concurrent CHT.

Methods: A systematic literature search was conducted on PubMed using the PRISMA methodology. Only studies based on the combination of LDFRT (< 1 Gy/fraction) and CHT were included. End-points of the analysis were tumor response, toxicity, and overall survival, with particular focus on any differences between LDFRT-CHT and CHT alone.

Results: Twelve studies (307 patients), on different clinical settings, fulfilled the selection criteria and were included in this review. Two studies were retrospective, one was a prospective pilot analysis, six were phase II trial, two were phase I study, and one was a phase I/II open label trial. No randomized controlled trials were found. Seven of eight studies comparing clinical response showed higher rates after LDFRT-CHT compared to CHT alone. Three out four studies comparing survival reported improved outcomes after combined modality treatment. Three studies compared toxicity among the two treatments and all of them reported similar adverse events rates (Table 1). In most cases toxicity was manageable with only three likely

treatment-unrelated fatal events (1%).

Conclusion: The role of LDFRT plus CHT is not supported by robust evidence. However, most comparisons showed improved outcomes without worse toxicity.

Table 1. Comparisons between low-dose fractionated radiotherapy plus chemotherapy and chemotherapy alone.

Study	Setting	Main findings
Arnold et al. 2004	Locally advanced SCCHN	LDFRT + CHT well tolerated with higher ORR (delivering less CHT cycles) compared to CHT alone. Toxicity profile similar to CHT alone.
Regine et al. 2007	Unresectable (5), M1 pancreatic (liver) (4), unresectable small bowel cancer (1)	ORR and survival rates higher than CHT alone.
Valentini et al. 2010	Relapsed or metastatic cancer of lung (12), H&N (7), breast (2), esophagus (1)	ORR higher than CHT alone in different settings.
Mantini et al. 2012	Advanced NSCLC	ORR and median OS higher than CHT alone. Toxicity profile similar to CHT alone.
Nardone et al. 2012	Breast cancer stage IIA/B-IIIA	Toxicity profile similar to CHT alone.
Nardone et al. 2014	Breast cancer stage IIA-IIIA	PMRR: 33.3%, similar to CHT alone.
Konski et al. 2014	Locally advanced or metastatic pancreatic cancer	Median OS in pancreatic cancer patients: 6 months with gemcitabine alone versus 9.1 months with LDFRT + CHT.
Balducci et al. 2014	Recurrent/ progressive GBM	Very low toxicity profile using LDFRT + CHT compared to the same group of patients treated with different approaches in GBM patients.
Beauchesne et al. 2015	Newly diagnosed inoperable GBM	Median OS of 16 months higher than OS rates reported in EORTC/NCIC trial (conventional RT + CHT versus conventional RT alone).
Das et al. 2015	Locally advanced SCC of the cervix (stage IIB–IIIB)	LDFRT + CHT followed by CHT + standard RT: ORR: 100% (CR: 40%; PR: 60%, based on MRI) and 3y-OS: 80%; CHT + standard RT alone (the latter treatment scheme done with higher number of CHT cycles): ORR: 70% and 3y-OS: 68%. Lower toxicity grade with LDFRT + CHT followed by CHT + standard RT compared to treatment scheme using CHT + standard RT alone (the latter done with higher number of CHT cycles).
Morganti et al. 2016	Metastatic colorectal cancer	2-y PFS: 63.9% and 31.2%, ORR: 83.3% and 33.3% in irradiated and not irradiated lesions, respectively (irradiation delivered with LDFRT).
Mattoli et al. 2017	NSCLC (stage IIIA-IIIB)	LDFRT + CHT: median OS higher than CHT alone.

Legend: CHT: chemotherapy; CR: complete response; GBM: glioblastoma multiforme; H&N: head and neck; LDFRT: low-dose fractionated radiotherapy; MRI: magnetic resonance imaging; NSCLC: non small cell lung cancer; ORR: overall response rate; OS: overall survival; PFS: progression free survival; PMRR: pathological major response rate; PR: partial response; RT: radiotherapy; SCCHN: squamous cell carcinoma of the head and neck.

PO041

ELECTROCHEMOTHERAPY AS A RADIOSENSITIZER IN PRECLINICAL AND CLINICAL SETTINGS: A SYSTEMATIC REVIEW

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Aims: Electrochemotherapy (ECT) is a local treatment combining electroporation (EP) and chemotherapeutic agents. ECT can overcome the chemo- or radioresistance acquired by tumor cells after multiple local and systemic treatments. Moreover, both ECT and irradiation (IR) could activate the immune system towards neoplastic cells. The aim of this review is to evaluate the potential role of EP and ECT as radiosensitizers.

Methods: In vitro and *in vivo* studies reporting on ECT or EP combined with IR were included in this systematic review. Studies not reporting tumor response or radiosensitivity parameters were excluded. The search was based on Medline, Scopus, and The Cochrane Library databases.

Results: The literature search, after removing of duplicates, led to the identification of 713 papers. Eleven studies (preclinical data in 10 studies and one clinical study) were included in the final analysis. Tumors were treated with EP alone and with ECT in two and nine studies, respectively. IR was delivered only with a single fraction in 10 studies, while hypofractionated treatment in one to five fractions was reported in one study. Despite the heterogeneity in reporting treatment response and the different subgroups analyzed in each study, ECT achieved improved tumor response when associated with IR compared to any single therapy or treatments combination. In fact, in vitro studies showed that EP significantly enhances the tumor control rates achieved with IR alone. Moreover, both higher IR total dose and dose per fraction improve the results of EP-IR combination. All preclinical and clinical in vivo studies showed a synergistic effect of ECT and IR as compared to single treatments and to other combinations of them, in terms of tumor growth delay and of IR dose required to achieve tumor control, regardless of tumor histology.

Conclusions: Based on this analysis, the combination of ECT and IR seems to improve local tumor control suggesting a radio-sensitizing effect of ECT. The mechanisms underlying this interaction and the possible role in the clinical setting deserve further studies.

PO042

TELEHEALTH DURING COVID-19: THE EXPERIENCE OF SCALIGERA RADIATION THERAPY DEPARTMENT

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Aims: To report our experience of the rapid incorpo-

ration of telehealth due to significant changes in care delivery related to the widespread coronavirus disease (Covid-19).

Methods: In march 2020 our department began to use telehealth for post treatment and follow up controls. Visits captured in the OIS Mosaiq from March to June 2020 were reviewed and categorized as in-person or telephonic visits.

Results: From march to June 2020, we observed a 35% decrease in captured visits as far as concern post treatment and follow up visits than in the same period of previous year (477 and 572 respectively). Globally, in person visits were 20% (95) and 80% (382) of appointments were performed by telephone. The patient's age and type of disease was associated with a major likelihood of telephone controls. New patients were continued to see in presence.

Discussion: Since the onset of the Covid-19 pandemic, we have been able to move to telehealth the majority of post-treatment and follow up visits. Telehealth was not used for new consults.

PO043

NON-INVASIVE ABLATION OF REFRACTORY VENTRICULAR TACHYCARDIA WITH STEREOTACTIC RADIOTHERAPY: A CASE REPORT

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Aims: Ventricular tachycardia (VT) caused by myocardial scarring is an important cause of mortality and morbidity. VT is routinely treated by antiarrhythmic drug therapy (AAD) and catheter ablation but both treatments have limited efficacy and potential adverse effects. Stereotactic radiotherapy emerged as a new tool in VT management.

Method: A 78-years old man, with previous anterior myocardial infarction in 1994, experienced a cardiac arrest caused by ventricular tachycardia. He underwent implantable cardioverter defibrillator implantation and, due to the presence of a thrombosis to the apex, an epicardial-only ablation was performed. After two months the patient suffered incessant VT recurrences despite treatment with amiodarone. Firm apical adherences did not allow to reach the isthmus in the second epicardial mapping. The patient referred to our department and we planned a stereotactic radioablation of the apical substrate. The patient received 25 Gy in a single fraction (PTV of 33.5 cc) delivered using a Linac dedicated for SBRT.

Results: After a follow up of 12 months, the patient did not experience any VT recurrence and no detectable adverse events related to SBRT occurred.

Conclusion: Cardiac SBRT is a promising and non-invasive option for the management of refractory VT. A longer follow-up on larger cohorts is warranted to evaluate the efficacy and safety of this technique

PO044

THE ROLE OF RADIOIMMUNOTHERAPY IN THE TREATMENT OF LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF THE SKIN: CASE REPORT OF THE RADIOTHERAPY DEPARTMENT PIACENZA HOSPITAL

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Purpose: Evaluation of the impact in terms of efficacy and toxicity of symptomatic radiotherapy treatment associated with sequential immunotherapy in locally advanced squamous cell carcinoma (LASCC) of the skin.

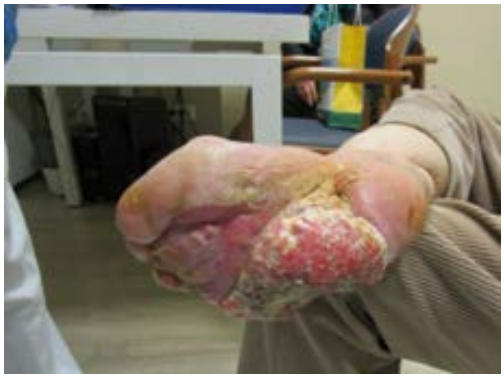

Figure 1. LASCC before the radiotherapy.

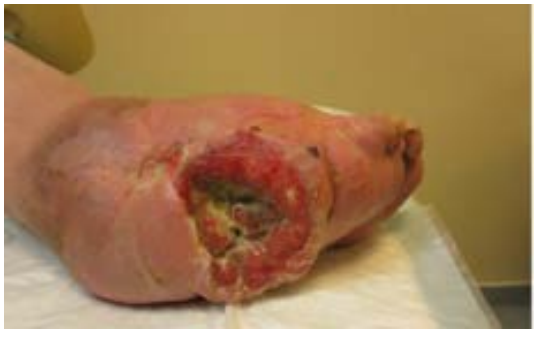

Figure 2. LASCC at the end of radiotherapy.

Method: In March 2021, an 85-year-old patient with LASCC of the right congenital clubfoot (ulcerated exophytic lesion of about 10 cm in diameter, Figure 1) underwent radiotherapy treatment by means of roengentherapy. The radiotherapy treatment was delivered through an anterior direct field with X-rays at low energies (180 Kv). The total dose was 45 Gy (3Gy/fr) in 15 fractions. After 15 days from the end of radiotherapy (Figure 2), the sequential immunotherapy treatment was started three times a week (cemiplimab - anti PD-1 monoclonal antibody).

Result: The radioimmunotherapy combination allowed to obtain a clear reduction in size of the treated lesion and a significant improvement in the symptoms reported by the patient (bleeding, edema, local pain).

Conclusions: Two months after the end of the radiotherapy treatment (Figure 3), our experience showed the integrated radioimmunotherapy treatment in the patient with LASCC of the skin was effective and with a low toxicity profile.

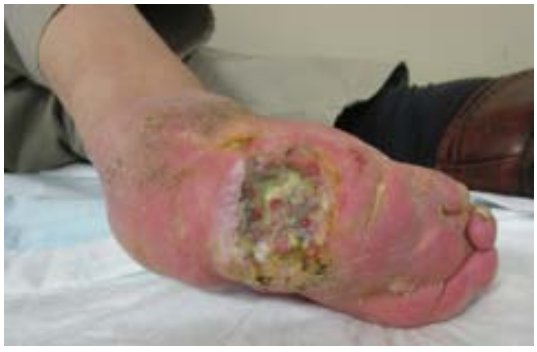

Figure 3. LASCC after the third cycle of sequential immunotherapy (two months after radiotherapy).

PO045

STEREOTACTIC RE-IRRADIATION OF RELAPSED BRAIN METASTASES IN PATIENT WITH NSCLC EGFRM

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Aim: Brain metastases (BM) are common in patients with non-small cell lung cancer (NSCLC). In the past, patients with multiple brain metastases were treated with whole-brain radiation therapy (WBRT). In recent years, the role of fractional stereotaxic radiotherapy (FSRT) has gained greater importance in the treatment of BM, especially in patients who can use target and immune therapy. In this report, we describe the case of re-irradiation of brain metastases with FSRT.

Method: We report the case of a female 66-year-old patient with stage IV NSCLC epidermal growth factor receptor (EGFR) mutated with multiple secondary lesions in the brain and bone. In March 2016, she started taking Afatinib and performed palliative radiotherapy on the pelvic bone. In December 2017 she underwent GammaKnife on 11 brain metastasis (22 Gy). Since October 2018, she has developed a slowly progressing disease with millimeter-sized lesions on the brain. It was decided not to submit the patient to WBRT and to change the cancer therapy to Osimertinib. In April 2020, MRI showed disease progression of 2 lesions (6 and 5mm). The patient underwent FSRT with HyperArc (24 Gy @ 8). In September 2020, MRI showed a complete response of the 2 lesions but the appearance of 7 new lesions (4 ÷ 6 mm) and the progression of a lesion treated with GammaKnife (7 mm). In November 2020 we repeated the FSRT with HyperArc on 8 lesions (27 Gy @ 9 on 7 new lesions and 24 Gy @ 8 on re-irradiated lesion). The HyperArc solution allows the simultaneous treatment of multiple brain lesions even at different doses. The dose and treatment delivery optimization algorithm allow for a sharp drop in dose distribution at low doses. The developed treatment plan was added to the previous treatment plans to check the trend of dose distribution.

Result: The patient never reported neurological symptoms during FSRT. The last MRI performed on May 12, 2021, shows the complete response of 2 lesions and good response of the remaining 6. Another 4 new metastases ranging in size from 2.5-3.5 mm appeared. The patient will perform a new MRI in July to check the progress of the lesions and decide on a possible other treatment.

Conclusion: This case demonstrates the efficacy and safety of FSRT with Hyper Arc in the treatment of multiple brain injuries and also their eventual re-irradiation. Furthermore, the FSRT proved to be more effective and less neuro-degenerative than the WBRT, allowing the maintenance of the patient's quality of life.

PO046

ABSCOPAL EFFECT AFTER STEREOTACTIC RADIOTHERAPY DURING IMMUNOTHERAPY IN OLIGOPROGRESSION PATIENTS AFFECTED BY RENAL CANCER

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Aims: To synergise innate and adaptive immunity against cancer cells, as well as to bypass immune tolerance and exhaustion, with the aim of facilitating tumour

regression using radiotherapy and immunotherapy in oligoprogression.

Methods: Between November 2020 and March 2021, we identified 2 metastasis each to promote immune stimulation with radiotherapy. Patients were treated with anti programmed cell death-1(PD-1), which were continued during radiotherapy.

Results: The first patient presented to CT multiple renal metastases, underwent stereotactic radiotherapy (5 Gy in a single fraction) on the largest lesion, being monorene patient for nephrectomy for renal carcinoma. A partial response was observed at the revaluation CT on all locations of metastases, even non irradiated. The second patient showed new PET/FDG hyper-fixation s at the lymph node and renal level for which he underwent stereotactic treatment (24 Gy in 3 fractions) at the level of the lymph node at the level of D10 with reduction of PET hyper-fixation of revaluation, also on the primitive. Low-dose radiation appears to provide beneficial responses in secondary tumors and may yield durable systemic responses to immunotherapy according with preclinical studies.

Conclusions: We supposed that radiotherapy, and anti-PD1, could act as immune-primers for abscopal effect modifying the immune tumor microenvironment. This cases supports the immune hypothesis for the abscopal effect, and illustrates the potential of combining radiotherapy and immunotherapy in the treatment of renal cancer. We also considered that low doses could be sufficient to induce abscopal effect.

PO047

HEEL SPUR AND RADIOTHERAPY: CASE REPORT AND SYSTEMATIC LITERATURE REVIEW

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Aims: Heel Spur (HS) is a chronic inflammatory condition causing pain and other typical symptoms. Therapeutic recommendations include the use of several drug or orthotic/physical therapies, performed alone or in combination. Surgery is usually reserved for refractory conditions. Radiotherapy has been showed to assure good clinical outcomes in this clinical setting. A systematic review was performed in order to describe feasibility and effectiveness of RT in the treatment of heel spur, evaluating its role in alleviating pain and consequently ensuring a better quality of life.

Methods: A systematic database search was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The systematic review included studies describing HS treatment and providing complete information about radiation treatments.

Results: A total of 15 articles ranging from 1996 to 2020 were reviewed. Studies characteristics analysis resulted in 7 prospective randomized studies and 8 studies retrospective experiences.

Conclusions: RT treatment of painful HS appears to be safe and effective, with high response rates even at low doses and with an overall favorable toxicity profile. Predictive parameters and modern tailored treatment should be investigated with further studies.

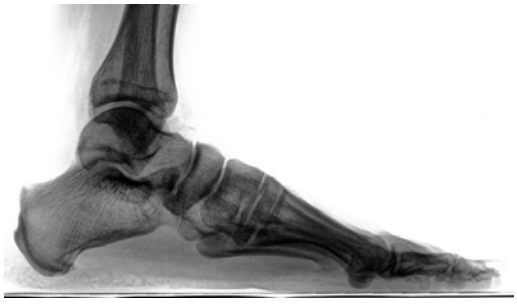

Figure 1.

PO048

THE ADDITION OF SILIBININ TO THE STANDARD TREATMENT IN GLIOBLASTOMA

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Aim: Glioblastoma (GBM) is the most common primary malignant brain tumor in adults. At diagnosis, the standard of care is represented by maximal safe surgery and adjuvant chemoradiation therapy. However, GBM is associated with high mortality and the median overall survival is inferior to 24 months, with a progression free survival (PFS) at 6 months around 48-59%. Silibinin, a natural polyphenolic flavonoid (with antioxidant and hepatoprotective effect) has been shown to inhibit in vitro cell growth in several cancer models, including malignant gliomas (by inhibition of STAT 3, keyprotein in cell proliferation mechanism). Based on this background, we hypothesized that silibinin would improve the efficacy of standard treatment in GBM.

Methods: Between April 2020-April 2021, we proposed treatment with silibinin to all patients with newly diagnosed GBM. The current standard of care involves maximal safe surgical resection followed by conventional

radiotherapy (cRT) (60Gy/30fractions) or hypofractionated radiotherapy (hRT) (40Gy/15fractions) with concurrent temozolomide (TMZ) followed by adjuvant TMZ. Silibinin in the form of 650 mg capsules (Sillbrain) was administrated at the following dosage: two capsules a day for the first two weeks of radiotherapy, then one a day continuously. Clinical, histological and molecular data were recorded for all patients. Standard follow-up was performed, included clinical examination, blood tests and brain MRI with contrast every 3 months, up to progression of disease. Any toxicity was recorded according to the CTCAE v4.0 classification. Second-line treatment was eventually chosen case by case.

Results: Overall, 10 patients (4 female and 6 male) accepted to integrate silibinin in their cancer treatment, concomitantly with RT and during follow up. The median age was 52 years (range 37-67) and median ECOG was 2 (range 1-3). All patients have histological diagnosis of GBM IDH1 wild-type and 3 cases showed MGMT methylation. Total resection was performed in 5 patients while subtotal resection in 5 cases. 6 patients underwent to cRT+TMZ and 4 to hRT+TMZ. Adjuvant TMZ was administrated in all cases. At median follow-up time of 12 months (range 8-24), all patients are alive; the median PFS was 9.8 months and 1-year PFS was 38%. Any acute or late toxicity of grade ≥ 2 were reported.

Conclusions: The addition of silibinin to the standard treatment is well tolerated by patients and it might be helpful to improve therapeutic results for GBM.

PO049

SINGLE- AND MULTI-FRACTION POST-OPERATIVE RADIOSURGERY FOR BRAIN METASTASES: CLINICAL AND DOSIMETRIC EVALUATION

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Aims: To explore the rate of local control and the risk of brain radiation necrosis in both single fraction (SF) and multi fraction (MF) approaches in the setting of post-operative radiosurgery (SRS) for brain metastases.

Methods: We retrospectively analyzed clinical, dosimetric and radiological data of 52 patients who underwent post-operative SRS for brain metastases from April 2011 to May 2020 at our Institution. Survival and local control were correlated to both clinical and dosimetric data.

Results: Median age at SRS time was 55 (range 26-79). 20/52 patients had NSCLC histology, 15/52 breast histology, 4/52 melanoma, 3/52 had colon carcinoma, 10/52 had other histologies. 22/52 patients received SF-SRS (range 14-20 Gy/1 fraction); 30/52 patients received MF-SRS (range 21-24 Gy/3 fractions). Patients with prior whole brain radiation therapy (WBRT) were excluded. After a median radiologic follow up of 30 months, 9/22 patients (40%) and 3/30 patients (10%) experienced recurrence disease in the SF-SRS and in the MF-SRS group, respectively. 6/12 recurrences underwent salvage surgery, and the other half salvage radiotherapy (SRS or WBRT). The SF-SRS and MF-SRS 1-year cumulative local control rates were 40% and 56%, respectively. Three patients (13%) in the SF-SRS group and only 1 (3%) in the MF-SRS group experienced brain radiation necrosis. These 3 cases of radiation necrosis in the SF-SRS group, had a V12Gy (brain volume receiving 12 Gy) value > 5 ml, but 2/3 of these occurred after cavity re-irradiation. The only case of brain radiation necrosis in the MF-SRS group had V20Gy > 20 ml. No other toxicities > G2 were reported. As of May 2021, 25/52 patients (48%) were alive. 15/27 of them died because of brain progression disease (PD), 9/27 because of extra-cranial PD, 1 for both brain and extra-cranial PD, 2/27 patients as a consequence of other causes. Median OS at last follow-up was 44.5 months (95% CI 22.2-77.2). 12- and 24-month median OS was 84.6%(95% CI 71.5%-92.0%) and 63.5%(95% CI 48.3%-75.3%), respectively. Lesion volume and histology did not affect OS nor local control. Stable extracranial disease was significantly correlated with better OS (77% versus 17%).

Conclusions: Our analysis shows that both MF-SRS and SF-SRS approaches provide good local control without relevant toxicities for post-operative brain metastases treatment. MF-SRS setting seems to be associated with a lower risk of brain radiation necrosis.

PO050

IMAGE-GUIDED VOLUMETRIC MODULATED ARC THERAPY (IG-VMAT) WITH HIPPOCAMPAL SPARING AND SIMULTANEOUS INTEGRATED BOOST FOR THE TREATMENT OF 1-3 BRAIN METASTASES

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Aim: The present study was aimed to report the local control and toxicity of a simultaneous integrated boost with whole brain radiotherapy for palliative treatment of Oligometastatic (<5 total metastases) and/or oligoprogressive (<5 progressive metastases in the context of otherwise stable metastatic disease)patients with < 3 brain

metastases (BM).

Methods: Fifteen patients with 1 to 3 BMs were retrospectively studied between November, 2018 and February, 2021. Ten patients (66,6%) had 1-2 BMs. Otherwise, 3 BMs were seen in 5 patients (33,4%). GTV (Gross tumor volume) contouring was based on the fusion imaging of MRI-CT, WBRT was prescribed in 30 Gy/10 fractions with a simultaneous integrated boost to the BMs of 45 Gy/10 fractions. All plans were optimized for dose coverage of the whole brain and lesions using Image-Guided Volumetric Modulated Arc Therapy (IG-VMAT). Contoured organs at risk (OARs) included brainstem, chiasm, optical nerves, eyes, lens and hippocampus. The Italian version of the Mini-Mental State Examination (MMSE), and the Rey- Auditory Verbal Learning Test (RAVLT) was used to assess the hippocampal-dependent episodic memory 3 months after treatment.

Results: The 1-year local control rates were 73% at the lesion level. Four patients showed a brain progressive disease which was out of boost field in 2 patients. The 6-month and 1-year OS were 93% and 80% respectively. Four patients (26,7%) reported minor (grade 1-2) neurologic findings consisting of headache and nausea. No patient was hospitalized due to radiation treatment. No patient developed radionecrosis and late toxicity during follow-up. Patients had no significant declines in Mini-Mental State Examination (MMSE), and the Rey-Auditory Verbal Learning Test (RAVLT) pre- and post-treatment.

Conclusions: WBRT with SIB to gross lesions using VMAT planning appears to be safe and effective in the treatment of brain metastases without significant cognitive decline. This treatment strategy should be considered in oligoprogressive patients not amenable for radiosurgery.

PO051

INTENSITY MODULATED RADIATION THERAPY WITH SIMULTANEOUS INTEGRATED BOOST TO SPARING BRAIN STRUCTURES IN PEDIATRIC INTRACRANIAL GERMINOMA

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Aims: Intracranial germinoma (IG) is a rare tumor of childhood with highly sensitive to radiotherapy (RT) and chemotherapy (CH). Survival rate is as high as 94% five years after RT alone resulting in the onset of potential late side effects related to the treatment. Intensity modulated radiation therapy (IMRT) to the whole ventricles (WV) with sequential boost (SB) to the tumor bed (TB) is considered a well-established treatment for localized IG. IMRT-WVI with simultaneous integrated boost (IMRT-SIB) to TB could achieve more conformal dose distribution to spare organ at risk (OAR). In this study we performed a dosimetry comparison between IMRT-WVI with sequential boost and IMRT-WVI with SIB to TB.

Materials and Methods: We treated a 15-year-old patient affected by non-metastatic ponto-mesencephalic multifocal germinoma enrolled in the SIOP CNS GCT II protocol. Patient received two cycles of CarboP-E with partial response at MRI brain post-CH, followed by 24Gy IMRT-WV in 15 fractions (fr) and 16Gy sequential boost to TB in 10fr. Pre and post CH contrast T1 e T2 MRI was anatomically registered to the CT planning to facilitate volume definition. Planning target volumes (PTV) 24Gy (PTV low) and 16Gy (PTV high) were generated according to SIOP RT guidelines. The following OAR were contoured: normal brain, brainstem, cerebellum, optic chiasm, pituitary gland, right and left cochlea-hippocampus-temporal lobe-lens-optic globe-optic nerve. IMRT plan was generated using 7 co-planar beams (0°-52°-104°-156°-256°-308°).

Results: We retrospectively analyzed the plan scheduling IMRT-WVI with SIB to TB. Biological equivalent dose was calculated to deliver 25,16 Gy in 1.5fr to the WV and 34,34 Gy in 2.0fr to the TB (17 total fr). IMRT-SIB plan was generated using 9 co-planar beams (0°-40°-80°-120°-160°-200°-240°-280°-320°). Both techniques achieved excellent target coverage (V95% >95); V100% was superior for IMRT-SIB (PTV low V100%: 90,75% SIB *vs* 20% SB); PTV high-V100%: 58% SIB *vs* 41% SB). Most of the OAR granted an advantage in terms of sparing with the IMRT-SIB (especially right and left cochlea, hippocampus, lens, and temporal lobes). Comparison dose for all OAR and dose distributions are reported in figure.

Conclusions: IMRT-WVI with SIB to TB is dosimetrically promising compared to IMRT-WVI with sequential boost in the treatment of localized IG to sparing OAR. It could be translated in fewer late side effects in this group of pediatric patients

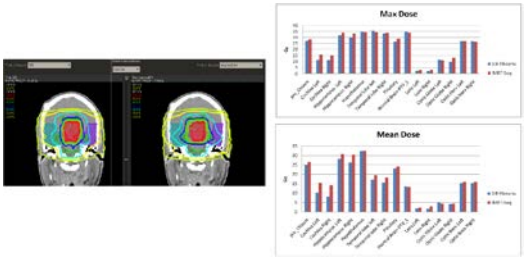

Figure 1.

PO052

LINAC-BASED VMAT RADIOSURGERY WITH A NON-COPLANAR MONO-ISOCENTER TECHNIQUE (HYPERARC (HA)) IN BRAIN METASTASES (BM): A SINGLE-INSTITUTION EXPERIENCE

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Aims: We reviewed toxicity and outcome data of our series of patients (pts) treated with HA technique for single or multiple BM.

Methods: Pts with BMs and good performance status treated with HA technique were enrolled in the study; they were retrospectively evaluated as to local progression-free survival (LPFS), defined as the time from the end of radiotherapy (RT) to the radiological progression of a treated lesion or the onset of new lesions, overall survival (OS) from the end of RT to the death or last follow-up, and toxicity.

Results: 40 pts (25 males, 15 females) accounting for 101 BM, treated at our institution from March 2019 to January 2021, were reviewed. 4 pts underwent a second HA treatment, after a time interval of 3, 3, 4, and 13 months from the first HA respectively; 3 pts had an onset of new BM with stable dimensions or reduction of the treated ones; 1 pt had increasing of the treated BM plus onset of new ones. The total number of HA courses was 44. Primary tumor histology was lung in 18 pts, melanoma in 5, kidney in 4, breast in 4, colon in 3, pancreas in 2, cardias in 1, thymic carcinoma in 1, testis germinoma in 1, parotid in 1. Median age at diagnosis of BM was 65 (range 24-83). The average number of BM in each HA course was 2.3 (range 1-9). A single BM was present in 23 of 44 HA courses, multiple BM in 21. The average diameter of the greatest lesion was 1.9 cm (range 0.2-5). GTV encompassed the macroscopic contrast enhancing lesion on T1-MRI. PTV was obtained from the GTV plus an isotropic margin of 2 mm. 27 Gy in 3 fractions or 21 Gy in single fraction were prescribed depending on lesion size or brain localization. 16 courses were 21-Gy single-fraction; average diameter of the greatest lesion was 0.9 cm (range 0.2-2). 28 courses were Gy in 3 fractions; average diameter of the greatest lesion was 2.5 cm (range 0.2-5). MRI at follow – up was available in 30 of 40 patients (69 BM; 34 HA courses); among these, after a median follow – up of 6.1 months (range 1.1-26), 10 pts had a stable disease or a reduction of the treated lesion, 5 pts an increasing size of at least 1 treated lesion, 12 pts the onset of new lesions, 3 pts both. LPFS was 3.2 months (range 1.1-18.1). 3-month and 6-month local control rates of the treated BM were 70% and 40%, respectively. In the whole series, median OS was 5.7 months (range 1.1-26). No G2/G3 toxicities were reported.

Conclusions: HA treatment proved to be safe in our patient population, even when repeated after a certain time interval.

PO053

TREATMENT OF PATIENTS AFFECTED BY GLIOBLASTOMA: UPDATE OF MONO-INSTITUTIONAL RETROSPECTIVE STUDY

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Aim: Optimal treatment for elderly patients (E-pts) with high grade glioblastoma (GBM) is not yet well defined. The standard approach involves Surgery + Radiotherapy +/ Chemotherapy + supportive care. The extent of tumor resection is considered controversial in this setting of pts. Benefit of CHT with Temozolomide (TMZ) is not consolidated, indications should be evaluated based on the presence of MGMT methylation, and on the comorbidity and performance status.

Materials and Methods: We conducted a retrospective analysis of 70 E-pts with diagnosis of GBM IV grade sec. WHO (44 men and 27 women) over the age of 70 (median age 75.5; range 70-84) from July 2011 to June 2021, and Karnofsky performance status score (KPS) variable 40-100. All patients underwent biopsy or total or subtotal surgical resection, (8pts biopsy, 23pts total resection, 47pts subtotal resection, 2 radiological diagnosis). 23pts (KPS >70) underwent RT treatment with concomitant TMZ and 47pts (KPS<70) received RT alone. Standard fractionation (SFRT) 60 Gy/30 fractions (fr) (27pts) and hypofractionation (HRT) 39.90 Gy/15 fr (41pts). Alternative treatment schedules were used for 2 pts: 54 Gy/1.8Gy fr, considering the location of the disease (thalamus, mesencephalus) and 42 Gy/3Gy fr (pts with synchronous lung cancer). 3D-CRT plan was generated using 3-5 beams (16pts) or 15-beams (25pts). IMRT plan was generated for 29pts (to increase compliance of E-pts).

Results: Treatment was well tolerated in most of pts, neurological symptoms (headache) have been reported, and treated with anti-edema therapy. During concomitant RT + CHT treatment, G1/G2 nausea and vomiting occurred. One pt experienced hematologic toxicity (thrombocytopenia) resulting in discontinuation of concomitant treatment; one pt experienced liver toxicity with interruption only of TMZ. 69pts were evaluated with MRI/VC pre-post intervention. (One pt did not perform MRI staging due to the presence of pacemaker (PM), 15pts did not underwent MRI re-evaluation (1 for PM, 14 for worsening clinical conditions); 55pts was evaluated with MRI/VC after 30/60 days from the end of RT; 25pts showed radiological stability of the disease (15pts /25 RT + TMZ); 20pts showed radiological progression (8pts /20 RT + TMZ).

Conclusions: Despite the prognosis of E-pts affected by GBM, different approaches can be considered. The extent of tumor resection and combined use of RT (better if HRT) + TMZ treatment could be a good approach in E-pts with a good KPS.

PO054

A COMBO-RADIOTHERAPY IN THE MANAGEMENT OF ATYPICAL GRADE II MENINGIOMAS

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Aims: The role of adjuvant radiation therapy (RT) in surgically treated Atypical Meningiomas (AMs) patients is not clearly defined, particularly after a gross total tumor resection (GTR). When a subtotal resection (STR) is obtained, post-surgical RT delivering 54-60Gy is a common practice. We examine clinical results using a "Combo-RT" approach using both Intensity Modulated Radiotherapy (IMRT) or Volumetric Arc Therapy (VMAT) and Fractionated Stereotactic Radiotherapy Boost (FSRT-Boost) in patients with Grade II AMs with a STR. In this observational study performed with prospectively intent we evaluate the effect of this kind of Combo-RT to identify the factors associated with progression free survival (PFS) and overall survival (OS).

Methods: Sixteen patients with Grade II AMs who underwent surgical treatment between November 2015 to January 2020 were enrolled in this study. Of these, eight (50%) a subtotal resection (STR) (Group A) and eight (50%) had a recurrent meningioma after STR (Group B). All patients received Combo-RT: IMRT or VMAT on surgical bed was delivered using a LinAc (Elekta Synergy Platform), and FSRT boost on residual meningioma was performed using a CyberKnife System (Accuray Incorporated, Sunnyvale, California). Biologically effective dose cumulative (BED Cum) was calculated according to the linear-quadratic model assuming an alpha/beta value of 4Gy. Univariate and multivariate analyses were performed to identify predictive factors for PFS and OS.

Results: There were 7 male and 9 female patients with a median age of 62 years (range, 31-80 years). 14/16 patients showed a Mib1-value >4%. For IMRT or VMAT, the median cumulative dose delivered was 46 Gy (range 44-57.5 Gy, using 1.8-2.3 Gy in 22-25 fractions). For FSRT, the median dose delivered was 15Gy in 3 fractions calculated at a median isodose line of 77% (range 70-80%). Actuarial 10- years OS in group A and B was respectively 100% and 66.6%, actuarial 3-years PFS was respectively 100% for the former group and 85.7% for the latter. In Patients who had a Mib 1>4%, a 3-years PFS of 85.71% was observed; the two patients who had a lower proliferative index showed a 100% 3-years PFS.

Conclusions: Combo-RT is an effective adjuvant treatment in patients with STR Grade II AMs. Our study showed that STR atypical meningiomas should be treated 1-2 months after surgery with this approach without waiting for relapses because our outcomes are better with respect to historical data.

PO055

PROTONTHERAPY IN PEDIATRIC PATIENTS WITH CENTRAL NERVOUS SYSTEM TUMORS: A SYSTEMATIC REVIEW

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Aims: Pediatric patients with central nervous system tumors may develop severe long-term complications after radiotherapy. Proton-therapy (PT) has theoretical advantages, over conventional photon-based radiotherapy, due to the theoretically reduced risk of long-term side-effects and second tumors. However, there are few data on actual toxicity after PT in this setting. In particular, randomized studies and literature reviews addressing this topic are lacking. Therefore, we performed a systematic review on toxicity and outcome after PT in pediatric central nervous system tumors.

Methods: A systematic search was performed in PubMed database using the following search strategy: ("brain"[MeSH Terms] OR "brain"[All Fields]) AND ("pediatrics"[MeSH Terms] OR "pediatrics"[All Fields] OR "pediatric"[All Fields]) AND ("protons"[MeSH Terms] OR "protons"). Only papers in English reporting PT-induced toxicity were included.

Results: Among 144 articles screened for relevance, 19 studies were deemed eligible (five prospective and 14 retrospective), including 2,.544 patients. Median follow-up ranged between 0.1 and 18.2 years (median 3.7 years). The most common late toxicities were neuroendocrine deficiency (6.0%), vasculopathy (2.9%), brainstem/brain necrosis (2.8%), ototoxicity (2.3%), radiological changes (1.5%), and visual symptoms (0.6%). Only 10 studies reported toxicity based on the CTCAE scale (G1: 5.9%, G2: 4.9%, G3: 2.0%, G4: 0.3%, and G5: 0.2%). Long-term outcomes were reported in 13 papers. Progression-free survival, reported as crude value, was 80% in one study, 48% as 2-year rate in one study, 76% as 3-year rate

in one study, 83%-89% (in the subgroup of Germ Cell Tumors)/ 82% (in others) as 5-year rate in four papers, and 83% as 8-year rate in one study. Local control, reported as 3-year rate was 85% and 91% in two studies, and 83%-89% (Germ Cell Tumors)/82%-77% (other) as 5-year rate in four studies. Two-year Overall Survival (OS) was 68%-91% as reported in two papers, 3-year OS was 90%-96% in three studies, 5-year OS was 87%-100% (Germ Cell Tumors)/82%-83% (other) in five papers, 7-year OS was 80% in one paper, and 8-year OS was 100% in one study.

Conclusions: Although high-level evidence is lacking, this review confirms a relatively low risk of toxicity after PT in this setting. In terms of outcomes, the results are similar to the ones recorded with photon-based radiotherapy. Prospective controlled trials are needed to confirm these data.

PO056

LOW-DOSE FRACTIONATED RADIOTHERAPY WITH CONCOMITANT TEMOZOLOMIDE IN GLIOBLASTOMA MULTIFORME WITH PSEUDOPROGRESSION: A MONO-INSTITUTIONAL EXPERIENCE

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Aims: Pseudoprogression is still a challenging issue in clinical practice, occurring in about 20% of high-grade glioma patients treated with adjuvant radiation plus temozolomide (TMZ).1 Pathological confirmation is the gold standard for the diagnosis of pseudoprogression but it is not often applicable, and it may take several months before pseudoprogression can be clearly distinguished from early tumor progression on follow-up imaging. The therapeutic approach is usually to continue with the adjuvant TMZ. According to our institutional experience in taking advantage of chemosensitive effect of low dose fractionated radiotherapy in Glioblastoma Multiforme (GBM)2-3-4 at recurrence or at diagnosis with poor prognosis, we explored the safety and efficacy of low-dose radiotherapy plus temozolomide in patients with GBM with evidence of pseudoprogression after radiochemotherapy.

Methods: Patients affected by GBM previously treated by primary radiochemotherapy with evidence of pseudoprogression during adiuvant chemotherapy with temozolomide were enrolled. Radiologically, pseudoprogression was defined as a new or enlarging area(s) of contrast agent enhancement, in the absence of true tumor growth. Low dose radiotherapy (0.60Gy twice daily over 5 days, every 28 days) with concurrent temozolomide for two cycles was administered. Primary endpoints were toxicity, progression free survival (PFS) and overall survival (OS).

Results: A total of twenty-seven patients were enrolled from January 2018 to August 2020. Acute hematologic toxicity G1-G2 was observed in 6 patients (22.2%) and G3 in 1 patient (3.7%). No acute neurological toxicity was detected. Two patients (7.4%) had partial response after low-dose radiotherapy while stable disease was registered in 10 patients (37%) for at least 8 weeks. Fifteen patients experienced progressive disease (55.6%). With a median FUP of 20 months (range 4-35 months), the median OS was 15 months with a 1-year OS of 61.3%, while the median PFS was 9 months with a 1-year PFS rate of 36%.

Conclusions: Low-dose radiotherapy with concomitant temozolomide was well tolerated and could be useful in continuing the use of the first-line chemotherapy in patients with pseudoprogression, reserving the shift to a second line of chemotherapy only for those patients with a progression disease.

PO057

RE – IRRADIATION (RERT) FOR RECURRENT GLIOBLASTOMA (RGBM): UPDATED RESULTS

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Aim: ReRT for rGBM remains controversial, although several studies have suggested a dose of 36 Gy as standard in the re-treatment setting. We evaluated outcomes and toxicity following reRT for rGBM, in some cases to higher than 36 Gy.

Methods: Between December 2017 and April 2021, 15 patients with rGBM were re-irradiated at recurrence. Patients' data, 5 males and 10 females (median age at time of re-irradiation 58 years, range 37-72), were analysed. Eight had reRT after second surgery, the remaining underwent re-irradiation alone. GTV was defined by MRI T1-weighted contrast-enhancing lesion. PTV was defined by GTV plus a 1-cm margin. Maximum cumulative dose for optic chiasm, optic nerves and brain stem was extracted from DVHs. CTCAE v4.0 was used to define toxicity.

Results: Primary treatment doses were 60 Gy in 30 fractions in 14 patients and 40.05 Gy in 15 fractions in 1. The mean interval between first and second treatment was 12 months (range 5.6-20 months). All patients under-

went Stupp protocol (concomitant – adjuvant Temozolomide (TMZ)). ReRT doses were 54 Gy, 46 Gy, 40 Gy, 36 Gy in 27, 23, 20, 18 fractions in 3, 1, 4, and 6 patients, respectively. One patient underwent a hypo-fractionated reRT (30 Gy in 6 fractions). VMAT was used in 12 patients and Tomotherapy in 3. 11 patients had an in-field relapse, 2 a marginal relapse and 2 an out-field relapse. The mean cumulative dose to chiasm was 42.1 Gy (range 3.1-76.4), to right optic nerve 28.1 Gy (range 1.8-66.7), to left optic nerve 30.4 Gy (range 1.8-61), and to brain stem 61.3 Gy (range 5.8-99.6). No treatment related grade 3 or 4 toxicities were experienced. One patient had a disease progression immediately at the end of reRT, with dramatic worsening of clinical conditions. Fotemustine, as second-line chemotherapy after reRT, was administered in 11 patients and TMZ in 3, while 2 patients received no second-line chemotherapy. Median overall survival from the end of reRT was 5.5 months (range 0.5 – 18.9). Currently, three patients are still alive after the completion of reRT, one in progression of disease at MRI, two in stable disease; average time from the onset of relapse to last follow – up was 8.1 months (range 4.2 – 11.6); average time from the end of adjuvant TMZ to last follow – up was 22.3 months (range 19 – 24.2).

Conclusions: ReRT even at doses greather than 36 Gy was safe, well tolerated, and completed in all patients. Further studies are needed to define efficacy and dose constraints.

PO058

RE-IRRADIATION IN GLIOBLASTOMA: IS IT POSSIBLE? IS IT FEASIBLE?

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Aim: Radiotherapy (RT) is already performed to treat primary brain tumors; however, the effect of repeated RT for recurrent tumors has not been fully explored. The aim of this study is to determine the efficacy of re-irradiation in recurrent glioblastoma.

Methods: Between November 2019 and May 2021, 17 patients with recurrent glioblastoma were included and treated with re-RT. Stereotactic radiosurgery (SRS) and hypo-fractionated stereotactic radiotherapy (HSRT) were performed using Volumetric Modulated Arc Technique (VMAT).

Results: Twentyfour SRS-HSRT treatment sessions were performed, median age was 52 years, (range 37-70), 3 patients were female and 14 male. SRS with a median dose of 25 Gy (range 20-30 Gy) in 1-5 fractions were performed. There were 3 treatment-related grade 3 adverse events (headache). Five patients out of 17 were dead for progression of the disease. With a median FU of 6 months the median overall survival (OS) was not reached and 6-months OS rate after re-irradiation was 60%. The median progression free survival (PFS) and 6-month PFS rate after re-irradiation were 3 months and 30%, respectively. No relevant clinical deteriorations in term of performance status were described.

Conclusion: Re-irradiation for patients affected by recurrent glioblastomas should be considered for its safety and feasibility. In this setting of patients with a poor prognosis, a gain, even if modest, in term of OS and PFS, without affecting the patient's quality of life, it could be favourable. An evaluation in a larger number of patients is needed to obtain more solid data.

PO059

CAN SILIBININ ASSOCIATED WITH RADIOTHERAPY PLAY A ROLE IN PATIENTS WITH BRAIN METASTASES?

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Aims: The occurrence of Brain Metastases (BMs) is increasing given the availability of a more accurate radiological imaging such as Magnetic Resonance Imaging (MRI) for detecting also small brain lesions and the most effective systemic therapy able to control extra-cranial disease. An estimated 20% of patients with cancer will develop BMs. Although, target therapy, immunotherapy, new radiotherapy (RT) techniques as radiosurgery (SRS) or Hypofractionated Stereotactic Radiosurgery (HSRS) has proven to be effective on brain metastasis, median overall survival was 6 months. A better understanding of the molecular and cellular mechanisms underlying brain metastasis might lead improvements in overall survival rate. In brain microenvironment, reactive astrocytes are key components. Brain metastatic cells induce and maintain the co-option of a pro-metastatic program driven by signal transducer and activator of transcription 3 (STAT3) in reactive astrocytes surrounding metastatic lesions. In patients, active STAT3 in reactive astrocytes correlates with reduced survival from diagnosis of intracranial metastases. Blocking STAT3 signaling reduces experimental brain metastasis from different primary tumor. Silibinin, a natural polyphenolic flavonoid, has been shown to impair STAT3 activation. Aim of this study is evaluated role of Silibinin in terms of toxicity reduction and brain control.

Methods: An oral supplement containing Silibinin and Vit B1 was prescribed to patients with brain metastases before radiotherapy or during the follow-up. The supplement was administrated twice a day per one month

than once a day.

Results: From January 2021 we prescribed an oral supplement containing Silibinin in 21 patients with multiple BMs receiving RT. Primary tumor was lung adenocarcinoma, melanoma or breast cancer in 13, 5 and 3, respectively. Eight, 9 and 4 patients were previously treated with radiosurgery, HSRS and whole brain radiotherapy (WBRT), respectively. In 3 cases Silibinin was prescribed before radiotherapy, in other patients during the follow up for radiological (19%) or symptomatic radionecrosis (43%). Silibinin was well tolerated and clinical status remained stable or increased. The majority of patients dismissed or reduced corticosteroids, only ones didn't interrupt steroid.

Conclusions: In our initial experience, Silibinin is well tolerated and allowed us to reduce corticosteroids dosage. Disease response in terms of local control is under evaluation.

PO060

IS HYPOFRACTIONATED RADIATION THERAPY AN OPTION ALSO FOR NON-ELDERLY GLIOBLASTOMA PATIENTS?

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Purpose: Hypofractionated radiation therapy (HRT) (40 Gy/15 fractions) represents an alternative to conventional fractionation radiation therapy (CRT) (60 Gy/30 fractions) for elderly glioblastoma patients. The aim of this study was to assess if HRT could provide adequate rates of overall survival (OS) in poor prognosis patients.

Methods: Between 2014 to 2020, we retrospectively reviewed the medical reports of 177 patients treated with either HRT or CRT for GBM at the Radiation Oncology Department of the Spedali Civili (Brescia, Italy). When clinically feasible, patients underwent concomitant and adjuvant treatment with temozolomide (TMZ) according to Stupp protocol.

Results: 81 patients underwent HRT and 96 CRT. Median age at presentation was 71 years and 63 years, respectively. Patients had gross or partial resection in 47% and in 92% of the cases whereas TMZ was administered in 63% and in 96% of the patients, respectively. No acute grade 3-5 toxicity was reported. Median OS for the entire cohort was 11.3 months. Median OS for the HRT subgroup was 8.2 months; median OS for the CRT subgroup was 15.6 months (p=.000). For the HRT subgroup, only surgery and TMZ positively influenced OS. Patients who underwent partial or gross total resection reached median OS of 11.3 months. Patients who did not undergo surgery (except for biopsies) reported OS of 7.1 months (p=.001). Administration of TMZ prolonged OS from 5.5 months to 10.5 months (p=.000). At multivariate analysis, extent of surgery and administration of chemotherapy confirmed their positive influence on OS.

Conclusions: Our data are in line with literature and support the hypothesis that HRT could be offered to poor prognosis patients. Hopefully, these results could provide the basis for a larger prospective randomized trial.

PO061

IMPACT OF RECURRENCE PATTERN IN PATIENTS UNDERGOING A SECOND SURGERY FOR RECURRENT GLIOBLASTOMA

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Aims: The impact of different patterns of glioblastoma (GBM) recurrence has not yet been fully established in patients suitable for a second surgery. Through the present observational study we aimed to examine the impact of different patterns of GBM failure on patients' survival and second surgery outcomes.

Methods: Overall survival was assessed according to clinical characteristics, including pattern of recurrence, in a prospective cohort of recurrent GBM patients. Survival curves were calculated using the Kaplan-Meier method and the log-rank test was applied to evaluate the differences between curves.

Results: Contact with ventricles, a second surgery and meningeal spread had a statistically impact on patient survival after the diagnosis of GBM recurrence (p=0.032, p=0.019 and p<0.01, respectively). Patients with local recurrence had better survival than patients with non-local ones, 24.1 versus 18.2 months, respectively (p=0.015, HR=1.856 (1.130-3.050). Considering the cohort as a whole, the second surgery conferred an advantage in recurrent survival respect to non-operated patients. However, this advantage was more evident in patients with local recurrence (p=0.002 with HR 0.212 (95% CI 0.081- 0.552) and p=0.029 with HR=0.522 (95% CI 0.291-0.936), respectively).

Conclusions: The local recurrence pattern could be a promising field of interest for patients with recurrent GBM suitable for a second surgery.

PO062

LONG-TERM OUTCOMES OF PATIENTS DIAGNOSED WITH GANGLIOGLIOMA: A SINGLE-CENTRE RETROSPECTIVE EXPERIENCE

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Aims: Gangliogliomas are rare, slow-growing tumors of the central nervous system (CNS). They are usually low-grade tumors (WHO grade I), characterized by the presence of both neuronal and glial neoplastic cells. We performed a retrospective analysis with the aim to evaluate treatment outcomes.

Methods: Data of patients diagnosed with pathologically confirmed intracranial ganglioglioma treated at our institution from January 1990 to December 2020 were retrospectively collected and analyzed.

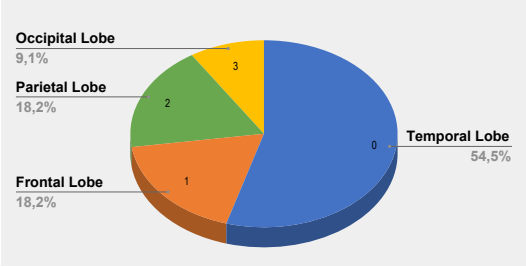

Figure 1.

Results: Data of 11 patients, including 9 males and 2 females, were analyzed. Mean age was 29.5 years (range 13-54). The majority of patients underwent radical surgery (90.9%), biopsy was performed in only 1 patient. Histopathological diagnosis was WHO grade I ganglioglioma in 4 patients, grade II in 4, and anaplastic ganglioglioma (grade III) in 3 patients. Temporal lobe localization was the most common (54.4%), followed by parietal lobe (36.4%) and frontal lobe (36.4%) [Figure 1]. Six patients received adjuvant radiation therapy (RT): 2 patients were treated with 3D-conformal radiation therapy (3DCRT) and 3 with intensity-modulated radiation therapy (IMRT) for a mean dose of 51,8Gy (range 50,4-54 Gy), one patient was treated with single fraction stereotactic radiosurgery SRS (16 Gy). No patients received concomitant chemotherapy. During follow-up, disease recurrence was diagnosed in 2 patients. In one case, a repeated SRS was performed with a dose of 15Gy. The second patient received systemic therapy with temozolomide (3 cycles). Both recurrences were observed in patients with temporal lobe localization. At the time of analysis, 5 patients are currently alive with stable disease, while 4 patients are without evidence of disease (NED). One patient died from disease progression, another patient died for another cause. Mean PFS was 104 months (range 11-243); mean OS was 106.8 months (range 11-266). No recurrences were observed for grade I lesions.

Conclusions: In our cohort of patients diagnosed with ganglioglioma, WHO grade confirms its impact on patients outcomes. A higher frequency of temporal lobe localization was observed in our series compared to other lobes, as reported in literature.

PO063

USE OF DEXAMETHASONE AS SUPPORTIVE THERAPY IN ADJUVANT STEREOTACTIC RADIATION THERAPY: INSTITUTIONAL EXPERIENCE

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Aims: our experience with dexamethasone in pills as prophylactic supportive therapy in adjuvant stereotactic fractionated radiotherapy in resected brain metastases.

Methods: from 2019 to 2021, 21 patients who underwent surgical resection of a cerebral metastasis followed by fractionated stereotactic radiotherapy were identified. The patients were selected for: age, Karnofsky Performance Status, extent of extracranial disease, the number and size of cerebral metastases, extent of resection. All patients were treated within 30 days of surgery. The whole surgical cavities were treated with 27 Gy in 3 fractions. Dexamethasone were given in the immediate preoperative period and then rapidly tapered postoperatively. We prescribed dexamethasone tablets 2mg/qid or 4mg/qid as prophylactic supportive therapy to start one week before fractionated stereotactic radiotherapy to reduce neurological sympthoms. We doubled the initial dose the day of fractionated stereotactic radiotherapy. Doses were reduced with a 8 mg reduction at 4 mg and 2 mg and a 4 mg reduction at 2 mg, thereafter to a maintenance dose of 2 mg, continued until clinic review.

Results: At 1 month, n 18 patients remained on corticosteroids, at 3 months 9 patients, at 6 months n 3 patient, and at 12 months no patients remained on corticosteroid therapy. Some patients were maintained on corticosteroid treatment for a longer time due to peritumoral edema, or worsening neurological symptoms upon wean.

Complications related to corticosteroid therapy were seen in 20% of patients: hyperglycemia. Insomnia occurred in n. 7 patients. One patients suffered of steroid myopathy. All patients declared that the use of tablets was easier than intramuscular injection or counting a lot of drops. In the four elder patients, the oral therapy was administered by themseleves without care giver helps.

Conclusions: Our corticosteroid protocol has proven to be very useful in weaning patients from this therapy. The overall prevalence of side effects in this study was low. The incidence of specific side effects such as hyperglycemia, steroid myopathy or insomnia was in line with the data of literature. We not reported any Cushing's syndromes or steroid psychosis. The use of tabs was an helpful choice for our patients showing very high compliance with therapy. Our results demonstrate that tailoring therapy could maximize the benefit to reducing corticosteroid dependence and, in the same way, long-term and serious complications.

PO064

RETROSPECTIVE ANALYSIS OF MENINGIOMA PATIENTS TREATED WITH SURGERY AND RADIOTHERAPY

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Purpose: This study aimed to retrospectively assess prognostic factors and outcome in patients with benign (grade I) and atypical (grade II) meningioma treated with surgery and radiotherapy.

Methods: Patients with a histological diagnosis of meningioma underwent to radiotherapy treatment after surgical resection (total or subtotal) or for recurrence. Radiotherapy was administered as 25Gy/5fx (stereotactic) or 54Gy/27fx (standard dose) and 50,4Gy/28fx for cervical spine localization. Progressive Disease (PD) was recorded and evaluated along with size, grading and tumor localization, type of resection, timing RT and toxicity.

Results: Between March 2017 and March 2021, 24 patients with meningioma (median age 65) referred to our centre for evaluation (12 male and 12 female): 22 patients were treated with surgery (7 total and 15 subtotal resection) and two with definitive radiotherapy. 5 patients were Meningioma grade I, 17 grade II (atypical) and 2 had no histological diagnosis. Seven patients had complete resection (2 received adjuvant RT), 15 partial (10 received postoperative RT, 4 received RT for recurrence and 1 no RT). At 36 months NED (not evident disease) patients were 77%. Progressive desease (PD) was recorded only in patients who underwent subtotal resection with a median of 22 months. All grade I and 68% of grade II did not progress at 36 months.

Conclusion: We have recorded an advantage in terms of local control at 36 months in meningioma patients treated with radical or postoperative radiotherapy.

PO065

RESPONSE TO BEVACIZUMAB TREATMENT IN A PATIENT WITH GLIOBLASTOMA RELAPSE

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Aims: This case illustrates a significant response, assessed by imaging, in a patient with High Grade Glioma (HGG) treated with Bevacizumab 5 mg/kg q14 as a third line chemotherapy (CT).

Materials and methods: In March 2017 a 74-year-old woman underwent surgical resection of a frontal lesion resulting in GBM grade IV WHO, GFAP +, p53 +/-, MIB-1 23%, met MGMT 15%, IDH1-IDH2 wt, without 1p/19q co-deletion. According to STUPP protocol the patient was treated with post-operative radio-chemotherapy, followed by 12 cycles of sequential CT with Temozolomide 200mg/mq concluded in July 2018. Since then, the patient was evaluated every three months with Magnetic Resonance Imaging (MRI) which confirmed stable disease. In August 2020 an MRI revealed signs of progressive disease, for which the patient received Fotemustine 75 mg/mq q21 (3 cycles) as second-line chemotherapy. In December 2020 MRI showed further progression as an increase of the neoplastic mass with greater infiltration of the anterior commissural structures. For this reason the patient was administered third-line chemotherapy with Bevacizumab 5 mg/kg q 14. After 4 cycles of Bevacizumab, in March 2021 MRI showed considerable reduction of the volume and extent of the disease, together with reduction of edema surrounding the lesion. Furthermore, the positive radiological response was associated with a modest clinical improvement.

Results: Our heavily pretreated patient showed remarkable response to Bevacizumab, assessed by MRI, after having maintained progressive disease during previous lines of treatment.

Conclusion: In selected patients the administration of Beva can be associated to improved survival, as it reduces tumor angiogenesis by neutralizing the biological activity of VEGF, thereby inhibiting tumor growth and vasogenic brain edema.

PO066

RADIOTHERAPY IN FRAGILE ELDERLY HEAD AND NECK CANCER PATIENTS: TOXICITY, COMPLIANCE AND RESPONSE

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Aims: To assess and analyze factors which could influence toxicity, compliance and treatment response in elderly patients (pts) with head and neck cancer (HNCC) and multiple comorbidities.

Methods: We selected HNCC pts ≥75 years, treated with 3D-CRT, IMRT or VMAT from 2004 to 2019. Patients' frailness was assessed by Geriatric-8 tool (G8) test.

Results: We included 80 consecutive patients, 61 males and 19 females, with a median age of 80 (range: 76-83.5). All pts were discussed in a multidisciplinary meeting. No surgery or chemotherapy indication was given. According to AJCC staging, 30 pts (37.5%) were classified as stage I-II, while 50 pts (62.5%) as stage III-IV (locally advanced). All pts were defined as frail according to G8 score. Radiotherapy with curative intent was performed in 85% of the cases with a median prescribed dose of 66 Gy (range: 60-70). Twelve pts were treated with palliative intent (15%) with a median prescribed dose of 46,5 Gy (range: 33.37-50). Ten pts required preventive percutaneous endoscopic gastrostomy to ensure adequate nutrition. According to RTOG acute toxicity scale, G2 mucositis was the most frequent (43.8%), followed by G1 (42.5%) and G3 (13.7%). We observed a significant correlation between mucositis and hypertension (p 0.0122) and CTV dimension (p-value 0.0005). Pts developed mainly G1 skin toxicity (42.5%), followed by G2 (38.75%) and G3 (18.75%). In our sample, male manifested significantly higher skin toxicity (p 0.0089). Eight pts temporary stopped the treatment (median: 10 days, range: 5-11.5). The median follow-up was 348 days (range: 102-810) for pts who received treatment with curative intent, complete response was achieved in 37 pts (54.4%), while disease progression was reported in 31 (22.1%). No clinical or radiological progression was observed during radiotherapy or in the first 12 months after the end of the treatment.

Conclusions: In our series, radiotherapy was an appropriate treatment option for elderly pts. Chronological age should not be considered as the only factor capable of not addressing elderly patient to definitive treatment. Our results are promising in terms of efficacy and tolerance, achieving a good treatment toxicity profile. We also demonstrated that exclusive radiotherapy with curative intent enabled a durable response over time.

PO067

PROGNOSTIC NUTRITIONAL INDEX PREDICTS WEIGHT LOSS IN HEAD AND NECK CANCER PATIENTS TREATED WITH DEFINITIVE CHEMO-RADIOTHERAPY

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Background: The Prognostic Nutritional Index (PNI) is a parameter of nutritional and inflammation status related to toxicity in cancer treatment. Since data for head and neck cancer are scanty, this study aims to investigate the association between PNI and acute and late toxicity for this malignancy.

Table 1. Odds ratio (OR) and 95% confidence interval (CI)a for acute G3-G4 toxicity according to nutritional factors.

Acute toxicity	events	PNI		Albumin (g/dL)		Lymphocytes/mm³	
		≥50	<50	≥4.1	<4.1	≥1780	<1780
		Ref.	OR (95% CI)	Ref.	OR (95% CI)	Ref.	OR (95% CI)
All	120	1	1.17 (0.61-2.25)	1	1.12 (0.58-2.16)	1	1.00 (0.51-1.98)
Mucositis	84	1	0.70 (0.38-1.31)	1	0.72 (0.39-1.35)	1	1.00 (0.53-1.90)
Weight loss> 10%	27	1	4.84 (1.73-13.53)	1	2.96 (1.16-7.57)	1	1.53 (0.61-3.85)
Dermatitis	26	1	1.77 (0.72-4.34)	1	1.62 (0.66-3.94)	1	1.04 (0.42-2.57)

[a]Estimated though logistic regression model, adjusting for gender, age, cancer site, performance status, TNM stage, BMI, and ever smoking.

Methods: A retrospective cohort of 179 head and neck cancer patients treated with definitive radiotherapy with induction/concurrent chemotherapy was followed-up (median follow-up: 38 months) for toxicity and vital status between 2010 and 2017. PNI was calculated according to Onodera formula and low/high PNI levels were defined according to median value. Odds ratio (OR) for acute toxicity were calculated through logistic regression model; hazard ratios (HR) for late toxicity and survival were calculated through the Cox proportional hazards model.

Results: median PNI was 50.0 (interquartile range: 45.5-53.5). Low PNI was associated with higher risk of weight loss > 10% during treatment (OR = 4.84, 95% CI: 1.73-13.53 for PNI < 50 versus PNI ≥ 50), which was in turn significantly associated with worse overall survival, and higher risk of late mucositis (HR = 1.84; 95% CI:1.09-3.12). PNI predicts acute weight loss >10% and late mucositis.

Conclusions: PNI could help clinicians to identify

patients undergoing radiotherapy who are at high risk of acute and late toxicity.

PO068

THE ROLE OF RADIOTHERAPY TO THE SALIVARY GLANDS IN THE MANAGEMENT OF REFRACTORY SIALORRHEA IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS: RESULTS IN SIX CONSECUTIVE CASES

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Aims: Amyotrophic lateral sclerosis (ALS) is a degenerative disease of the central nervous system. The management of affected patients (pts) requiring dedicated facilities and staffing. A joint clinical program was started between our Radiotherapy (RT) Unit and the Unit treating this disease at our Hospital. The aim was to optimize the management of sialorrhea, a complication of ALS, using RT in pts not responding to the drugs (amitriptyline, atropine, scopolamine) and injections of botulinum toxins into the salivary glands (SG). In this report we describe our experience with RT in 6 consecutive pts.

Methods: From 2019 we have treated 6 pts with ASL and refractory sialorrhea. 4 were male and two female, median age was 64 years old (range 44-73). All pts were refractory to conventional therapies. CTV include the submandibular (SG) and the parotid glands (PG). Based on literature data we selected as our standard regimen the treatment of both SGs and the lower 2/3 of both PGs with a prescription dose of 12 Gy in 2 fractions. All pts received 3D-conformal RT and were treated with 6-10MV photons. All pts were actively monitored during all treatment sessions for the detection of vital signs. A favourable response was defined as a complete or partial regression of sialorrhea. Median follow up was 17 months.

Results: 4 cases received the standard regimen. A fifth pt requested further treatment due to persistent sialorrhea, so we delivered a third fraction of 6 Gy to the PG bilaterally. In the last pt for the same reason we added to the standard regimen two further treatments, delivering total doses of 24 Gy to the left PG, 12 Gy to the right PG, 16 Gy to the right SG and 6 Gy to the left SG. This pt is currently being planned for a further treatment due to persistent sialorrhea. A favorable response was observed in 5 out of 6 pts (83.3%). 3 pts had a partial regression of the symptom and 2 pts had a complete regression. One pt did not respond even to repeated treatments. In 5 pts no acute or chronic side effects related to RT were observed. One pt developed xerostomia 17 months after RT.

Conclusions: In our experience RT is a safe and effective treatment for refractory sialorrhea in pts with ASL. In most cases an adequate compromise between efficacy and toxicity was achieved with a regimen of 12 Gy in 2 fractions delivered to both SGs and to a subvolume of both PGs. In some pts further treatment may be needed and may be effective in achieving adequate relief from the symptom

PO069

HEMODYNAMIC EVALUATION OF RT-INDUCED CAROTID ARTERIES INJURIES BY USING COLOR-DOPPLER US IN ASYMPTOMATIC PATIENTS WITH HEAD AND NECK CANCERS AFTER RT ALONE AND RT-CT: PRELIMINARY RESULTS

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Aims: Radiotherapy alone or radio-chemotherapy are the cornerstone in the treatment of head and neck tumors. Despite the advances of technology, treatment planning and delivery of modern radiation therapy, it is not possible to avoid completely carotid arteries from high dose radiation fields. The radiation effect on vessels could trigger the degeneration process of the vascular wall with progressive thickening and increased probability of vascular accidents. The aim of our study was to select asymptomatic patients at risk for vascular accidents.

Methods: In order to evaluate the radiation-induced carotid arteries injuries in this cohort of patients we performed a color-doppler US in different moments of the treatment course: before starting radiation (baseline), 1, 6 months, 1 and 2 years after the end of treatment. The color-doppler US provided to measure the intima-media thickness (IMT) and to evaluate the blood flow efficiency through the artery. The analysis has been performed on per-protocol population.

Results: In February 2020 we started the accrual of all head and neck cancer patients referring to our Radiotherapy Department. Limitations and optimisation of health resources imposed during SARS-CoV-2 pandemic did not allow us to reach a large number of patients but the enrollement is still open and we are now presenting preliminary results. Until April 2021 we enrolled 22 patients. To date none of the patients achieved 2 years US control while 6 and 13 patients achieved 1 year and 6 months control of IMT, respectively. 11 of these patients received an VMAT-IGRT, 2 patients received a 3D-CRT.

6 patients underwent to concomitant radio-chemotherapy, the others underwent to RT alone. Analyzing the difference of IMT between 6 months after completing RT and baseline we observed an average thickening of 0,7 mm; at 1 year the observed average thickening was 1,45 mm. No vascular accident occured in our cohort of patients.

Conclusions: Our preliminary results are consistent with literature data. We observed a progressive thickening of IMT, despite the limited follow up. This preliminary analysis underlines the importance of monitoring asymptomatic patients at risk for vascular accidents who underwent to radiation therapy, to allow early intervention measures.

PO070

SARCOPENIA IS PREDICTIVE OF RADIATION INDUCED DYSPHAGIA IN POSTOPERATIVE LSCC PATIENTS UNDERGOING ADJUVANT RADIO(CHEMO)THERAPY

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Objectives: Skeletal Muscle Loss (SML) and Systemic Inflammation can increase radiotherapy-induced toxicity and chemotherapy dose-limiting adverse events. The aim of this study is to evaluate their role in patients with advanced-stage laryngeal squamous cell carcinoma (LSCC) receiving postoperative radio(chemo) therapy.

Methods: Patients with stage III-IVB LSCC who underwent total/partial laryngectomy and adjuvant radio(chemo)therapy at our institution between 2018 and 2019 were reviewed. Using a predefined, double blind protocol, we contoured, on simulation CT, the Cross-Sectional Muscle Area (CSMA) at the level of third cervical vertebra (C3), which demonstrated to be a reliable surrogate of total body Skeletal Muscle Mass (SMM) in previous clinical trials. Pre-radiotherapy Neutrophil to Lymphocyte Ratio (NLR) value was used as a marker of systemic inflammation. We correlated CSMA and NLR with radiation-induced toxicity during adjuvant treatment and after six and twelve months calculated according to NCI-CTCAE v.4.3 scale, and with chemotherapy dose-limiting toxicity. Chi-square method was applied to assess the endpoint.

Results: We included 74 patients, with a median age of 64 years (range: 48-84 years). Patients were treated by VMAT with simultaneous integrated boost (SIB) technique. A dose of 60-66Gy to the tumor bed with the involved nodal region and a prophylactic dose of 54–60 Gy to the elective neck nodal region, delivered in 30-33 fractions (5 fractions per week), were administered. Chemotherapy consisted of Cisplatin at a dose of 100 mg/m^2, every 3 weeks. Our results showed that Dysphagia (≥G2) (p: 0,003) and Xerostomia (≥G1) (p:0,007) measured at the end of treatment, significantly correlated with CSMA . No significant association was found with late toxicity. NLR had no significant effect on the treatment-related toxicity.

Conclusions: CSMA could represent an independent prognostic factor for treatment related toxicity in advanced-stage LSCC patients receiving postoperative radio(chemo)therapy and deserves further investigations.

PO071

ABSTRACT WITHDRAWN

PO072

WEEKLY HYPOFRACTIONATED PALLIATIVE RADIOTHERAPY IN POOR PERFORMANTS STATUS WITH HEAD AND NECK CANCER UNFIT OF STANDARD RADIOTHERAPY TREATMENT; SURVIVAL, ACUTE AND LATE TOXICITY OUTCOMES

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Purpose: Aim of this study was to evaluate survival rates, acute and late toxicity after hypofractionated palliative radiotherapy (RT) in patients (pts) with head and neck (H&N) cancer unfit of standard RT treatment.

Methods and materials: Between December 2010 and June 2020, 65 pts with advanced H&N cancer underwent hypofractionated palliative RT treatment. The prescribed dose was 36,75-42 Gy in 7-8 fractions (ff) given 1 fraction of 5,25 Gy weekly. All pts underwent CT simulation and as immobilization system we utilized a head thermoplastic mask. CTV often coincided with GTV and PTV was obtained by GTV-CTV + a margin of 3-5 mm. A VMAT or IMRT technique was used in 23 pts (35,4%) and a 3DCRT technique in 42 pts (64,5%). Concomitant chemotherapy was administered in only 4 pts (6%).

Results: At analysis 36 patients (55,4%) were male and 29 (45,6%) were female. The mean age was 79 years old (range 42-100 years) and the median KPS was 60 (range 40-90). After a mean follow-up of 9 months the

mean OS was 10 months (median of 6 months), median PFS 4 months. Overall, 60% of pts completed RT at the prescribed dose and 40% interrupt it due to PD, clinical worsening or lost motivation. A clinical or radiological examination response was observed in 54% of pts; CR 23%, PR 31%, SD 6%, PD 19% and in reaming 21% (lost at follow up) was not possible to evaluate the response. In pts receiving prescribed dose the response rate was 79%, of them 34,2% had a CR. Also, pts receiving the prescribed had a higher survival rate compared to patients which interrupt RT treatment (8 mths *vs* 2 mths; p-value 0,0001). In patients receiving 42 Gy in 8 ff the median OS was 11 months. Moreover, KPS > 70, PTV < 400 cc, and clinical or radiological response were prognostic factors regarding OS (p<0,05). G2 acute or late toxicity was observed in 29% pts (36% in pts treated with IMRT-VMAT; 38% in pts receiving 3DCRT). G3 or higher acute or late toxicity was observed in 4,5% pts (G3 1,5%; G4 1,5% and 1,5% G5); all cases with ≥ G3 toxicity were treated with 3DCRT technique .

Conclusion: Weekly palliative hypofractionated RT appears feasible in H&N cancer unfit of other treatment strategy, with a response rate of 79%. Total dose, KPS>70, PTV<400 cc resulted prognostic factors regarding OS. Particular attention must be paid regarding late toxicity in this subset of pts. IMRT-VMAT technique is recommended to be used due to reduce G2 or higher toxicity.

PO073

SINGLE-CENTER EXPERIENCE ON PATIENTS WITH RECURRENT OR METASTATIC HEAD AND NECK SQUAMOUS CELL CARCINOMA TREATED WITH NIVOLUMAB

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Aims: The anti-PD-1 monoclonal antibody Nivolumab represents a safe and effective new therapeutic option in patients with recurrent or metastatic (R/M) Head and Neck Squamous cell carcinoma (HNSCC) progressing after platinum-based therapy. We retrospectively analyzed a series of 44 patients treated in our center, evaluating the efficacy and the toxicity profile of Nivolumab.

Methods: From September 2018 to May 2021, 44 consecutive patients underwent systemic therapy with Nivolumab after local or distant progression of disease. Toxicity was assessed by the Common Terminology Criteria for Adverse Events toxicity scale (CTCAE v.4.03). We included patients with diagnosis of R/M HNSCC, independently from HPV status, progressing after platinum-based chemotherapy. Our endpoints were PFS and OS and toxicity.

Results: Among 44 patients with a median age of 70 years (48-88 years), treated with Nivolumab in our center, 37 (84%) patients had received at least one or more prior lines of systemic therapy and 37 (84%) had a performance status of 0 or 1 at the time of the start of the treatment. All subsites of disease were represented, with the oropharynx site (27% of the patients) being the most frequent one, followed by oral cavity site (18%). HPV status was tested only in 16 patients: 50% patients were HPV positive. At a median follow-up of 4.5 months (1-31 months), patients were able to complete a median of 12 cycles of Nivolumab. OS recorder was 5 months and PFS was 3 months. 25 patients (57%) experienced progression of disease, while 19 patients (43%) were still on treatment at the time of the analysis. The most common treatment-related adverse events recorded were G2 hypothyroidism (7 patients) and G3 fatigue in 5 patients (11%). None of the patients discontinued Nivolumab for immune-related toxicity.

Conclusions: Our mono-institutional experience confirmed that Nivolumab represents an effective and well tolerated drug for patients with diagnosis of recurrent or metastatic squamous cell carcinoma of the head and neck, that progressed within 6 months after platinum-based chemotherapy or received one or more lines of systemic therapy.

PO074

OBESITY POTENTIAL BIOMARKER FOR PREDICTION OF OVERALL SURVIVAL IN HEAD AND NECK PATIENTS TREATED WITH RADIO-CHEMOTHERAPY

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Objectives: The prognosis of head and neck cancer patients is traditionally determined using several different clinical characteristics such age, stage, high alcohol consumption and cigarette smoking. The purpose of this study was to evaluate the prognostic relevance obesity (BMI> 29.9 Kg/m^2) head and neck cancer (HNC) patients treated with radio-chemotherapy (RT/CT).

Methods: BMI was retrospectively assessed in 134 HNC locally advanced patients (median age 63,5,range 20-84,M:F 4:1) treated between January 2015 to June 2020. The following were the inclusion criteria. All patients (> 18 years old) with locally advanced squamous cell carcinoma underwent adjuvant or exclusive radiotherapy concomitant with cisplatin, BMI was calculated before the beginning of RT/CT. For the present study, overall survival (OS) and progression free survival (PFS) were defined as days between the end of the treatment and death or progression date of last follow-up.

Results: Patients with a BMI above 29.9 Kg/m^2 showed a favorable trend regarding the overall survival

(p= 0,086; HR 0.489, IC 0.211-1,082) in univariate analysis. Instead BMI was not corralated with PFS (p= 0,644; HR 0.802, IC 0.211-1,082).

Conclusion: In our study we have shown that obesity is a potential biomarker for patients with locally advanced HNC treated wih radiotherapy concomitant with cisplatin. The role of obesity and BMI remain controverse in literature. These findings can be explained with a better nutritional status before the beginning of the therapy compared with normal and underweight population. More prospective studies with larger population are required.

PO075

MUSCLE MASS VARIATION AND NUTRITIONAL SUPPORT IN HNSCC PATIENTS: A PRELIMINARY ANALYSIS

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Aims: To analyze the pattern of muscle mass variation in head and neck squamous cell carcinoma (HNSCC) patients treated with radiotherapy (RT) or radiochemotherapy (RT-CHT).

Methods: From 2016 to 2020, 78 consecutive HNSCC patients treated by VMAT RT or RT-CHT with definitive or adjuvant purpose have been identified. A preliminary data analysis of 61 patients has been performed. Computer tomography (CT) scans at baseline and at 3 months after the end of treatment were used for each patient to obtain the Skeletal Muscle Index (SMI) at the C3 vertebral level. The SMI pre-treatment and post-treatment and the body mass index (BMI) pre-treatment and post-treatment have been calculated. The nutritional status of the patient has been assessed and supported by the nutrition department of our hospital during the treatment and the follow-up. Patients' burden of comorbidities has been assessed by Charlson Score.

Results: The median follow-up was 16 months. Seventeen patients (27,7%) experienced recurrence with the median time of 7 months from the time of the end of treatment. In our preliminary data analysis, changes in SMI were weakly correlated to changes in BMI (ρ=0,387; p=0.011). Furthermore, SMI loss at the 3 months CT, taken place in 10 patients (6,1%), is weakly correlated to disease recurrence or progression (ρ=0.230; p=0.143). Cutaneous acute toxicity and mucous acute toxicity (score > 2 in RTOG toxicity scale) has been experienced by 14 patients with no apparent correlation to SMI loss or disease recurrence or progression. Charlson Score (median value: 4), instead, seems to be correlated to the SMI loss (ρ=0,411; p=0.007). A preliminary logistic regression was performed to assess the role of glutamine supplementation, received by 37 patients, showing that who underwent recurrence or progression was more likely not to have been performed supplementation.

Conclusions: Our study shows that SMI loss weakly correlates to BMI loss, making the change of muscle mass subtle and difficult to be assessed in routine treatments. Patients' burden of disease could be a predictor of an increased SMI loss during treatment. Further analysis should be performed to assess the role of glutamine supplementation in HNSCC patients undergoing RT or RT-CHT.

PO076

EFFICACY OF ORBITAL RADIOTHERAPY IN LONG-LASTING GRAVES' ORBITOPATHY

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Introduction: Graves Orbitopathy (GO) is an insidious disease requiring frequent and prolonged access to cures with not always successful outcomes and causing a severe decrease in QoL. Currently available therapeutic spectrum ranges from medical and surgical therapy to radiant orbital therapy. Here we present a case of successfully treated GO which required several therapeutic approaches and a close follow up for almost 4 years.

Case description: A 52 y old woman smoker, first presented to our outpatient care with a 2 year history of monolateral GO (right eye) which started with progressive diplopia in euthyroid autoimmune thyroiditis. The patient had already been treated elsewhere with parenteral glucocorticoid (GC) therapy (4,5g methylprednisolone, 6-MP) and strabismus surgery. After one year she developed hyperthyroidism and underwent total thyroidectomy. In the meantime, the worsening of the orbital disease (severe exophtalmos and CAS persistently >4) brought the patient to our hospital, where she was examined in a multidisciplinary setting. At first she was treated with a course of parenteral GC therapy (4,5g 6-MP) and, as she reached a low TRAb titer and CAS<3, she underwent orbital decompression surgery of the right eye with significant proptosis reduction. After 6 months she was also treated with strabismus surgery, with resolution of diplopia. Nevertheless, during follow up, the patient again showed signs of active GO (CAS=3) with mildly elevated TRAb titer, suggesting that the eye disease was likely to recur after 3 years of non-stop treatment. After multidisciplinary discussion, with the involvement of a radiother-

apist, we decided for a radiotherapy approach, possibly representing a medium-long term solution. The patient underwent 10 radiotherapy sessions (2Gy each session) distributed over 2 weeks. The radiation treatment was administered by X photons and advanced VMAT –IGRT technique which guarantees extreme precision in the radiation delivery. Orbital Radiotherapy (OR) was associated with a new course of parenteral GC (total dose= 2g 6-MP) split into four administrations, two the week before and two after OR. Despite the development of slight diplopia 1 week after OR, the patient experienced prompt resolution of signs and symptoms related to GO activity (CAS=0) as well as 3 slight reduction in proptosis and significant improvement in QoL. Such improvement remained stable at the 3 and 6 months follow up.

Conclusions: In this case the application of a combined medical, surgical and radiation therapeutic protocol enabled the resolution of a long-lasting eye disease (4 years), which had already been unsuccessfully treated several times with both medical and surgical approaches. The persistence of slight diplopia after OR might be related to muscle fibrosis which was already present at the time of OR but did not require any surgical treatment. This case displays the importance of a tailored-therapy in GO and that OR might be considered as an option in patients with recurrent and long-lasting disease.

PO077

RADIOTHERAPY IN PATIENTS WITH CARDIAC IMPLANTABLE ELECTRONIC DEVICES: THE VALUE OF *IN VIVO* DOSIMETRY

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Aims: Evaluate the importance of block the irradiation beams on the 5 mm expansion of the cardiac implantable pacemaker (ICP) volume contour, PRV, to assure that its received dose was lower than the one planned because of a set-up error. In vivo dosimetry was used to measure dose distribution for head and neck cancer patients treated with TomoTherapy.

Methods: For the planning a complete block on the entry and the exit of the beams was used for the device for Patient A and for the device PRV for Patient B. For both patients the device was outside the treatment area. The distance of ICP from the target volume was 4.5 cm for Patient B and 0.5 cm for Patient A. In vivo measurements were performed for both patients. The plans were optimized to have the best target coverage, sparing of the OARs and a cumulative dose <2 Gy on the device. During some treatment sessions TLDs and EBT3 films were located on all ICPs area to measure maximum punctual dose or to acquire the dose map distributions, see Figure 1.

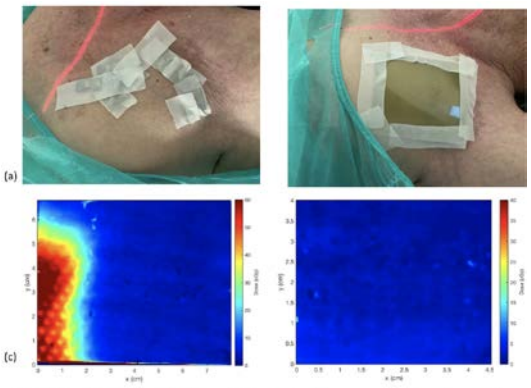

FIG1: (a) The EBT3 films and the TLDs used for the punctual dose measurements on the pacemaker during the treatment; (b) the EBT3 film used for the dose distribution measurement on the pacemaker; (c) dose map distribution of an irradiated EBT3 film placed on the pacemaker during the first treatment fraction for Patient A; (d) dose map distribution of an irradiated EBT3 film placed on the pacemaker during the first treatment fraction for Patient B

Figure 1.

Results: For Patient A, the 60 cGy isodose reported by the film had the same shape and size than the one evaluated by the TPS and it was also very close to the device. The highest punctual dose read out was 63.6±1.97 cGy for EBT3 and 102.3±10.225 cGy for the TLD (with the TLD in the upper part of the device volume, very close to the treatment field). These doses are linked to a single delivery event; taking into account the number of all the treatment fractions, the maximum dose received by the device will surely be significantly higher than the planned one and this patient will be a higher risk patient. For Patient B, the films recorded doses lower than 10 cGy while the maximum dose values estimated by TPS for the device and its PRV for the whole treatment were 99 cGy and 175 cGy, respectively. The maximum punctual dose values recorded by EBT3 film and the TLDs were 6.11±0.21 cGy and 5.2±0.8 cGy, respectively. For Patient B the measured dose values confirm that, also taking into account the number of all the treatment fractions, the maximum dose on the device will be lower than the planned one.

Conclusions: It can be deduced that the complete block on the entry and the exit of the beams applied to the ICP is not enough to reduce the dose received by the device. It is necessary to block the irradiation beams on the device PRV to reduce the maximum dose to ICP and to assure that the device would not receive a higher dose than the one planned because of a set-up error.

PO078

EFFECT OF PAROTIDS AND SUBMANDIBULAR GLANDS-SPARING IN IRRADIATION WITH IMRT/VMAT TECHNIQUE ON GRADE OF XEROSTOMY IN HEAD AND NECK CANCER PATIENTS

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Aims: The submandibular glands produce most of the unstimulated saliva output and are involved in radiation-related xerostomia. We retrospectively review data on patients with the head and neck cancer who underwent to radiation treatment, in order to evaluate the correlation between submandibular glands irradiation and xerostomia.

Methods: All patients with stage pT2-T4 N0/+ or cT1 N+ head and neck cancer treated with bilateral neck IMRT or VMAT from 2017-2021 at our institution were included. Selected patients with favorable primary tumor characteristics and no controlateral neck disease were treated with parotids and/or SMGs-sparing IMRT/VMAT. The patients were clinically evaluated at 1-2 weeks, 1 month for the first 6 months and then every 6 months for the years following the end of treatment. Xerostomia as a side effect was evaluated with the Common Terminology Criteria for Adverse Event version 5.0.

Results: Thirty patients underwent post-operative radiotherapy with IMRT or VMAT technique with sparing of the parotids and submandibular glands. The mean parotid dose was less than 30 Gy in 30/30 patients (100%) and the mean submandibular glands dose was less than 40 Gy in 25/30 patients (83%). In patients whose average dose to the parotids and sub-mandibular glands was found to be within the limits of constraints dose, xerostomia was found to be equal to G0 according to the CTCAE version 5.0 (Common Terminology Criteria for Adverse Event version 5.0) without the need to resort to pharmacological or replacement therapies.

Conclusions: Our study confirms the need to adapt the therapeutic strategy in terms of radiotherapy technique in the patient with head and neck cancer. The winning choice falls on the IMRT or VMAT technique with absolute respect for the dose constraints on the parotids and submandibular glands. All this in order to prevent xerostomia as a side effect, long-term disabling effect for this category of patients.

PO079

HYPOFRACTIONATED RADIOTHERAPY IN OLDER PATIENTS WITH HEAD AND NECK CANCER: A FEASIBILITY AND SAFETY SYSTEMATIC REVIEW FOR CLINICIAN

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Objective: Radiotherapy (RT) in the head and neck (H&N) site are undoubtedly the most challenging treatments for patients (pts). Older and frail pts are not always able to tolerate it and there are still no clear guidelines on the type of treatments to be preferred for them. The recommendations for Risk-Adapted H&N Cancer Radiation Therapy during the COVID-19 Pandemic provided by the ASTRO-ESTRO consensus statement achieved a strong agreement about Hypofractionated RT (HFRT). A systematic literature review was conducted in order to evaluate the feasibility and safety of HFRT for older pts affected by H&N malignancies.

Materials And 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, case series and case reports describing the use of HFRT in pts with mean age ≥65 years were included. The analysis was based on the type of study, number of pts, mean age, tumor site, histology, performance status (PS), RT details, concomitant chemotherapy (CT) and described clinical outcomes. All the reported doses have been calculated in Equivalent dose in 2Gy fractions (EQD2) and Biologically Effective Dose (BED) using α/β=10 Gy or α/β=12Gy.

Results: We selected 17 papers that met the inclusion criteria and divided them in 4 categories. 6 articles analyzed HFRT performed twice daily in repeated cycles, 3 once a day in repeated cycles, 4 in alternative days and the last 4 in consecutive days.

Conclusions: HFRT seems to be a good treatment with an acceptable prolonged disease control. In older patients fit for radical treatments a 55 Gy in 20 fractions regimen can be proposed as a valid alternative to the standard fractionated RT.

P0080

THE IMPACT OF PATIENT PREFERENCE IN THE TREATMENT ALGORITHM FOR RECURRENT/METASTATIC HEAD AND NECK SQUAMOUS CELL CARCINOMA: A CASE REPORT AND MINI-LITERATURE REVIEW

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Aims: The purpose of this study is to highlight the relevance of patience preferences on the strategy of care of the head and neck squamous cell carcinoma (HNSCC) as a variable outcome in addition to survival, recurrence or physical impairment. Our work is about a case report and a mini literature review.

Methods: We report a clinical case of a 73 years old patient with diagnosis of recurrent-metastatic laryngeal squamous cell carcinoma (RM-HNSCC) and heavy symptom burden treated with Pembrolizumab monotherapy after refusing chemotherapy or any other intensive treatment approach.

Results: One month after the first drug administration, the patient obtained a partial remission of symptoms with no voice impairment. Radiologic assessment showed stability of disease after the first 3 cycles. He maintained an unchanged ECOG-PS 0, mild hoarseness and no voice dysfunction, with optimal treatment tolerability. Due to the persistence of laryngeal disease, we proposed radiotherapy to the larynx while continuing immunotherapy. The patient decided to refuse local treatment and continue exclusively pembrolizumab monotherapy. Currently, the patient has received 6 cycles of pembrolizumab with unaffected well-being and clinical stability of disease. Recently some authors focused their effort on analysing the subset of head and neck patients who are inclined to refuse treatment. We selected and analyzed some published studies where the attention was focused on Quality of Life (QoL) and patience preference on the choice between "being cured of my cancer" or "living as long as possible" as their top expectations. We found that the percentage of patients with HNSCC who refused surgical- and/or radiotherapy-based definitive therapy were older and had more advanced stages of tumor than patients who accepted the treatment proposal. In addition, it was identified the advanced age, worse socioeconomic status and lip and oral cavity tumor as the main risk factors related to patient refusal of care.

Conclusions: A specific questionnaire for assessing patients' preferences in the RM setting is not available nowadays and in our opinion it should be developed and recommended as it may allow to fully integrate also the RM-HNSCC patients' priorities in the medical decision, where the heterogeneity of the disease burden, personality trait, symptomatic presentation and differential tolerability profile of treatment options available can be of great impact in the clinical outcome.

P0081

LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER: OUTCOME, TOXICITY AND PREDICTIVE FACTORS IN FRAIL PATIENTS TREATED WITH EXCLUSIVE HYPOFRACTIONATED RADIOTHERAPY

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Aims: The aim of this study was to evaluate outcome, toxicity and predictive factors of recurrence and mortality in a cohort of patients treated with exclusive hypofractionated radiotherapy (RT) for locally advanced non-small cell lung cancer (LA-NSCLC).

Table 1.

Patients characteristic	N° (%)
Age	
Median	77 years
Range	47-93 years
≤70	16 (16.5%)
>70	81 (83.5%)
PS ECOG	
0-1	75 (77.3%)
2-3	22 (22.7%)
Smoke	
Yes	21 (21.6%)
No	7 (7.2%)
Previous	69 (71.1%)
Cardiological comorbidities	
Yes	79 (81.4%)
No	18 (18.5%)
Pulmonary comorbidities	
Yes	36 (37%)
No	61 (63%)
Charlson Comorbidity Index	
≤6	32 (33%)
>6	65 (67%)
G8 Score	
>12	41 (42.3%)
≤12	56 (57.7%)
Histology	
Adenocarcinoma	36 (37.1%)
Squamous cells	45 (46.4%)
Other	6 (6.2%)
Not available	10 (10.3%)
TNM (VIII ed)	
II (A-B)	27 (27.8%)
III (A-B-C)	66 (68%)
IVA	4 (4.2%)
PTV volume	350 cc (range 56-1004 cc)
Total Dose	
50 Gy	35 (36.2%)
55 Gy	39 (40.2%)
56 Gy	21 (21.6%)
60 Gy	2 (2%)

Methods: Inclusion criteria were: age > 18 years, LA-NSCLC (stage II-IV) not suitable for systemic therapy. RT was delivered in 20 fractions for a total dose of 50-60 Gy. All treatments were performed with VMAT technique. Acute and late toxicities were recorded according to CTCAE v5.0. The statistical analysis was performed using Stata 14. The Kaplan Meier analysis was applied to assess local control (LC), distant metastasis free survival (DMFS), progression-free survival (PFS) and overall survival (OS). Univariate analysis was used to correlate outcomes to prognostic factors.

Results: Between 2011 and 2019, 97 patients were treated with exclusive RT. Patients' characteristics are summarized in Table 1. After a median follow up of 21.3 months (range 2–89 months), 37 patients (38%) had a local progression and 59 patients (60.8%) had a distant progression. At the time of analysis 85 patients (87.6%) died. One, 2 and 5-year OS rate were respectively 67.8% (95% CI 57.5-76.1), 30% (95% CI 21-39.2) and 11.6% (95% CI 6-20). One, 2 and 5-year PFS rate were respectively 50.7% (95% CI 40-60), 21% (95% CI 13-30.7) and 15% (95% CI 7-25). One, 2 and 5-year LC rate were respectively 76% (95% CI 64.6-84), 46.6% (95% CI 33.3–59) and 40% (95% CI 26-53.5). One, 2 and 5-year DMFS rate were respectively 56.2% (95% CI 45.3-65.7), 35.3% (95% CI 25-46) and 26.7% (95% CI 15.3-39.4). At univariate analysis for PFS, TNM stage emerged as prognostic factor (HR1.43, 95% CI 1.09-1.87, p=0.008). Adenocarcinoma correlated with a better PFS (HR0.7, 95% CI 0.56-0-93, p=0.014) and DMFS (HR0.72, 95% CI 0.54–0.98, p=0.03). PTV volume as a continuous variable correlated with OS (HR1.00, 95% CI 1.001-1.00, p=0.00), PFS (HR1.00, 95% CI 1.00–1.00, p=0.004) and DMFS (HR 1.00, 95% CI 1.00–1.00, p=0.007). The most common acute and late toxicities are reported in Figure 1 and 2.

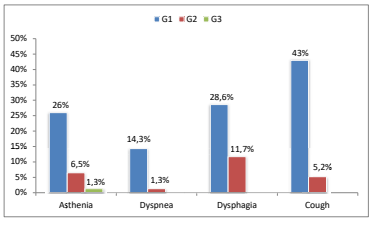

Figure 1. Acute toxicity

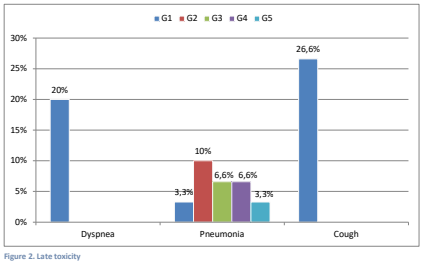

Figure 2. Late toxicity

Figures 1 and 2.

Conclusions: Exclusive hypofractionated RT represents an effective and safe choice in patients with locally advanced NSCLC, not undergoing systemic therapy. PTV volume correlated with OS, PFS and DMFS. Adenocarcinoma histology was associated to a better PFS and DMFS.

PO082

SEQUENTIAL CHEMO-RADIOTHERAPY WITH HYPOFRACTIONATION IN PATIENTS AFFECTED BY STAGE IIB-IV NON-SMALL CELL LUNG CANCER (NSCLC): OUTCOME, TOXICITIES AND PREDICTIVE FACTORS

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Aim: Describe clinical outcome and predictive factors in terms of OS and PFS in a cohort of patients affected by stage IIB-IV non-small cell lung cancer (NSCLC), treated with sequential chemo-radiotherapy with hypofractionation.

Table 1,

Sex		
Male	87	79%
Female	26	21%
Smoking habits		
Never	7	6%
Pregressive	63	56%
Active	41	36%
Cardiological comorbidity		
none	58	51%
one comorbidity only	40	35%
multiple comorbidity	15	13%
Pneumological comorbidity		
none	91	81%
COPD	19	17%
others	3	3%
Performance status		
0	44	39%
1	64	57%
2	5	4%
Histology		
Adenocarcinoma	59	52%
Squamous cell	49	43%
Large cell	1	1%
Unspecified	5	4%
Stage (AJACC VIII ed.)		
IIB	7	6%
IIIA	28	25%
IIIB	49	43%
IIIC	5	4%
IVA	20	18%
IVB	4	4%
Distant Metastasis		
M0	88	78%
M1a	9	8%
M1b	11	10%
M1c	3	3%
Not avaiable	2	2%

Chemotherapy regimens	n	%
Cisplatin + Gemcitabine	31	27%
Carboplatin + Gemcitbine	25	22%
Cisplatin+ Pemetrexed	19	17%
Carboplatin+ Pemetrexed	10	9%
Carboplatin + Vinorelbine	9	8%
Gemcitabine only	6	5%
Cisplatin + Vinorelbine	3	3%
Carboplatin + Paclitaxel	2	2%
Cisplatin- Etoposide	2	2%
others	6	5%

Radiotherapy schedule	**Gy/fr**	**n.**	**%**
55 Gy /20 fr	2,75	50	44%
50 Gy / 20 fr	2,5	36	32%
55 Gy /22 fr	2,5	13	12%
56 Gy / 20 fr	2,8	9	8%
60 Gy / 20 fr	3	2	2%
45 Gy / 15 fr	3	1	1%
45 Gy / 18 fr	2,5	1	1%
interrupted		1	1%

Methods: The study included patients affected by unresectable stage IIB-IV treated with sequential CT-RT. Hypofractionated RT was delivered by VMAT technique, with doses ranging 45 to 60 Gy in 2,5-2,7-3 Gy per frac-

tions, 5 days a week. Acute and late toxicities were recorded according to CTCAE v5.0. Univariate analysis was performed by Stata14 to correlate outcomes to prognostic factors. Kaplan Meier analysis was applied to assess distant metastasis free survival, local control, progression free survival and overall survival

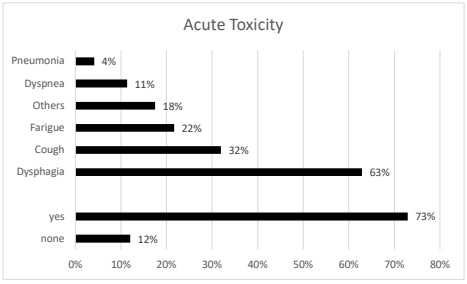

Figure 1

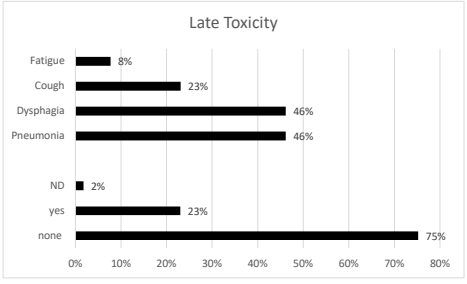

Figure 2

Figures 1 and 2.

Results: From June 2010 to September 2019, 113 patients were enrolled. Median age at the time of diagnosis was 67,5 y.o (from 43 to 83). Demographic and treatment characteristics are summarized in Table 1. CT-RT was well tolerated: all but one of the patients completed the treatment without interruption. Acute toxicity was recorded in 73% of the patients, late toxicity in 23% of cases.Toxicity profiles are shown in Figures 1 and 2. After a median follow up of 16,1 months (1-93.7months) OS at 1, 2 and 5 years was 61%[CI 0.52–0.70], 41%[CI 0.32-0.50] and 27%[CI 0.18-0.36] respectively. None of the analyzed variables was predictive for OS at univariate analysis. PFS was 36% at 1 year[CI 0.27-0.45], and 14% at 5 years[CI 0.08-0.23]. Factors related to a shorter PFS included advanced stages of the disease[HR 1,22; 95%CI 1.04-1.45; p=0.01], PTV volume [HR 1.00, 95%CI 1.00003-1.00141 p=0.04]and mean esophageal radiation dose [HR 1.03; 95%CI 1.00-1.06, p=0,01]. After 1, 2 and 5 years from the treatment, local failure rate was 29% [95%CI 0.61-0.79]; 38% [95%CI 0.5-0.7]and 46% [95%CI 0.4-0.6] respectively. Large PTV resulted associated with local recurrence [HR 1.00, p=0.007, CI 1.0003-1.002]. Almost 44% of our patients develop metastasis 1 year after the diagnosis [95%CI 0.34-0.53]. Distant progression rate at 2 and 5 years was 32%[CI 0.23-0.41] and 23%[CI 0.14-0.43] respectively. Disease stage correlated with distant progression[HR 1.30, p=0.004, 95%CI 1.08-1.57].

Conclusion: Chemo radiotherapy is an effective and well-tolerated treatment. In our study PTV volume, mean esophageal radiation dose and advanced stages of the disease increase the risk of a poor prognosis in patient with stage IIB-IV NSCLC treated with sequential CT-RT

PO083

THE IMPACT OF POST-OPERATIVE RADIATION THERAPY (PORT) IN PATIENTS WITH THYMOMAS AND THYMIC CARCINOMAS: MONOINSTITUTIONAL EXPERIENCE

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Methods: We retrospectively analysed 27 consecutive patients (17 thymomas, 8 thymic carcinomas) who underwent surgery with a curative intent and PORT to the mediastinal surgical bed and microscopic/macroscopic disease, if present, from 2006 to 2020 at our institution. Eight patients received neo-adjuvant chemotherapy prior to surgery. Surgical margins status was reported as follow: R0 resection (microscopic negative margin) was achieved in 14 patients, R1 (microscopic positive margin) in 11 patients and R2 (macroscopic positive margin) in 2 patients. According to Masaoka-Koga staging system 4, 6, 13 and 4 patients were stage I, II, III and IV of disease, respectively. Acute toxicities were graded according to the RTOG/EORTC scor¬ing system and late toxicities where scored according to the SOMA (symptoms, objective, management, analytic) scoring system. The Kaplan Meier method was used to assess overall survival (OS), relapse-free survival (RFS) and metastases-free survival (MFS). Sub-group analysis was performed stratifying patients with R0 *vs* R1-2 resection margins, patients staged I-II *vs* III-IV stages and patients with A-AB-B1 *vs* B2-B3-0 histologies.

Results: PORT was administered with 3-dimesional conformal radiotherapy in 23 patients while 4 patients were treated with intensity-modulated radiotherapy. The median planning target volume (PTV) was 250cc (range 60-610). Median dose was 54 Gy delivered using conventional fractionation (2 Gy daily). Median follow-up was 54 months. OS at 1- and 5-years was 96.3% and 89%. One- and 5-year RFS was 100% and 83%. MFS at 1- and 5-years was 92% and 67%. Patients with stages III-IV had worst 5-yers OS and MFS compared to stages III-IV, 83 *vs* 100% (CI 95%: 1.16-2.06; p 0.03) and 45 *vs* 100% (CI 95%: 1.42-2.8; p 0.01). WHO histologies B2-B3-0 showed worst 5-years OS and MFS compared to A-AB-

B1 group, 82.6 *vs* 100% (CI 95%: 1.27-2.2; p 0.02) and 46.6 *vs* 100% (CI 95%: 1.2-2.6; p 0.02) . No acute nor late G3-4 toxicities were observed.

Conclusions: PORT in patients with thymic malignancies achieved good local control and a safe toxicity profile. Patients with III and IV Masaoka stage and WHO B2-B3-0 histology had significant worst OS and MFS.

PO084

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

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Aims: Several real world experiences have been reported about 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 Durvalumab following sequential ChT-hypofractionated RT. In this prospective trial we report safety and effectiveness of stereotactic ablative radiotherapy (SABR) in LA-NSCLC patients treated with radical-intent based on PACIFIC trial.

Methods: Unresectable and unfit to concurrent ChT-RT LA-NSCLC patients were enrolled in a phase II trial of SABR. Neoadjuvant ChT was prescribed only in fit patients. Patients who had not progression of disease after neoadjuvant ChT and SABR, received Durvalumab as consolidation therapy every two weeks for up to 24 cycles or until progression or unacceptable toxicity in patients enrolled in expanded access program (EAP). The gross tumor volume (GTV) included primary tumor (GTV-T) and CT-PET positive node/s (GTV-N).

Results: Between June 2015 and February 2021, 73 unresectable and unfit to concurrent ChT-RT LA-NSCLC patients were enrolled, of these 46 (63%) received neoadjuvant ChT. 10 (14%) LA-NSCLC patients treated with radical-intent based on PACIFIC trial are reported. Cancer stage was IIIA and IIIB in 6 and 4 patients, respectively; 6 and 4 had adenocarcinoma (ADK) and squamous cell carcinoma (SCC). All cases had PTV overlapping the major airways. Median prescribed dose was 45 Gy (range, 40-55) and 40 Gy (35-45) in 5 fractions to T and N, respectively. Median follow-up achieved 20 months (range, 4-42). Today, 3 (30%) patients are still in treatment and 4 (40%) have completed 24 cycles of immunotherapy. Two and 1 patient had experienced local recurrence (LR) and brain metastasis during consolidation therapy and discontinued Durvalumab after a median time of 9 months (range, 8-10) after SABR. One (EAP) developed LR 30 months after completing treatment. At last follow-up all patients were alive. The median duration of Durvalumab was 10 months (range, 4-42) for all patients and 12 months (range, 4-42) for patients who had not disease progression. No adverse events of ≥G3 grade was recorded. No patients discontinued Durvalumab due to toxicity and/or incompliance.

Conclusions: PACIFIC trial has revolutionized the management of LA-NSCLC. SABR and immunotherapy can be the backbone of patients unfit to concurrent ChT-RT.

PO085

STEREOTACTIC ABLATIVE RADIOTHERAPY IN LOCALLY-ADVANCED NON-SMALL-CELL LUNG CANCER: A PHASE II TRIAL

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Purpose: To assess local control (LC) and safety of stereotactic ablative radiotherapy (SABR) in unresectable locally advanced non-small cell lung cancer (LA-NSCLC) patients enrolled in a phase II trial.

Methods and materials: All patients were unfit for concurrent chemo-radiotherapy (ChT-cRT). Neoadjuvant ChT was prescribed only in fit patients. The tumor volume included primary tumor (T) and CT-PET positive node/s (N). A simultaneous integrated boost (SIB) was optimized to differentiate the dose to primary tumor (T) and lymph-node/s (N).

Results: 73 LA-NSCLC patients were recruited. The median age was 73 years (range,45-89) and 51 (70%) were male. Histology was adenocarcinoma (ADK) and squamous cell carcinoma (SCC) in 56% and 44%, respectively. The stage was IIB, IIA, IIIB and oligometastatic IV in 12 (16%), 34 (47%), 18 (25%) and 9 (12%), respectively. 60 (82%) had ultra-central tumor with PTV overlapping the major airways. 43 (59%) received neoadjuvant ChT and 10 (14%) adjuvant Durvalumab. In 35 (48%) cases T and N were separately treated using SIB technique to administer a higher dose to T. Median prescribed dose was 45 Gy (range, 35-55) and 40 Gy (35-45) in 5 fractions to T and N, respectively. During a median follow-up of 20 months (range, 4-71), 20 (20%) patients had experienced local recurrence (LR) at a median time of 16 months (range, 4-30) and 24 had thoracic nodal-recurrence at a median time of 16 months (range, 4-28). 25 (34%) developed distant metastases 13 months after SABR (range, 4-26). At last follow-up, 57 (78%) patients were alive, 27 (37%) without radiological evidence of disease. No patients developed ≥ G3 acute and late toxicities. The treatment compliance was 100%.

Conclusions: LA-NSCLC patients treated with

SABR had optimal LC and promising overall survival in absence of ≥G3 toxicity. Our prospective results provide an attraction to evaluate this approach in selected LA-NSCLC patients unfit to concurrent ChT-cRT.

PO086

MRI GUIDED STEREOTATIC RADIOSURGERY BOOST OF BRAIN METASTASES IN SCLC: A CASE REPORT

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Aims: Whole brain radiotherapy (WBRT) is recommended as a standard treatment for Brain Metastases (BMs) in patients with Small Cell Lung Cancer (SCLC), but stereotactic radiosurgery (SRS) is a potential treatment option for carefully selected SCLC patients with a small number of BMs. We report the case of a 66-year-old long surviving woman affected by SCLC and brain metastases (BMs) treated with Chemo-Radiotherapy and WBRT plus an additional SRS boost .

Methods: A 66-year old woman with SCLC limited disease,cT2aN2M0 (stage IIIA) according to the 7th edition of TNM system, was treated with four courses of cisplatin (80 mg/m^2) and etoposide (100 mg/m2×3) combined with concurrent hyperfractionated Radiotherapy (45 Gy delivered in 30 fractions-twice daily). At the end of ChemoRadiotherapy, brain MRI revealed a 7mm diameter brain metastatic lesion in the temporal lobe. We planned a WBRT with a dose of 30 Gy in 10 fractions, followed by a sequential SRS boost (21Gy in 3 fractions) on the temporal BM resulting in a cumulative effective biological dose (BED10) of 74.7Gy. After 15 months, a follow-up brain MRI revealed the presence of a new BM in the occipital lobe measuring 9 mm in diameter. Therefore, we decided to treat the new brain lesion with an SRS treatment consisting of 21Gy Gy in 3 fractions. The patient underwent regular follow-up every 6 months consisting of brain MRI and total body CT scans. The Response to treatment was Assessed by means of T1 gadolinium enhancing disease, T2 and FLAIR changes, the appearance of new lesions, corticosteroid requirement, and clinical status.

Results: No acute effects related to both treatments were observed in our patient. After two year of follow-up, there was no neurocognitive impairment without systemic and local progression. The brain MRI showed complete response for both the lesions.

Conclusions: Due to the SCLC-derived intracranial dissemination and with the aim of improving intracranial control, focal radiation boost combined with adjuvant WBRT may be a preferred strategy for SCLC patients with brain metastases, which is safe, effective and well tolerated.

PO087

MONO-INSTITUTIONAL EXPERIENCE OF STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR T1–T2 LUNG CANCER: RESULTS IN A RETROSPECTIVE SERIES OF 21 PATIENTS (PTS)

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Aims: To evaluate outcomes of stereotactic body radiotherapy (SBRT) for primary T1-T2 early stage lung cancer in a retrospective series of 21 pts.

Materials and Methods: Between September 2013 and December 2020, a single-institution cohort of 21 patients with early-stage lung cancer (T1-T2N0M0) received lung SBRT. Median age was 76 years (range:58-89), median Karnofsky Performance Status was 90 (range:60-100), median Charlson Index was 6 (range:2-9). Histology was NSCLC in 16 pts, SCLC in 1 pt, in 4 pts histology was not assessed and tumor was confirmed by sole imaging findings (PET scan-directed SABR strategy: >85% probability of malignancy). All pts underwent a pre-treatment FDG-PET scan and baseline respiratory function tests. In our series of 21 pts we performed 23 treatments for T1 (n=20) and T2 (n=3), central (n=3) and peripheral (n=20) primary lung tumor lesions. The prescribed dose ranged from 48Gy to 60Gy in 3 to 8 fractions. Most patients (56%) were treated with 50Gy in 5 fractions; median BED was 103Gy [α/β=10], range:76.8 Gy-180 Gy. Seventeen pts (80%) received ablative doses of ≥100Gy, range: 100Gy-180Gy. Fractionation choice was dependent on tumor size and location. 4DCT scans were done in all pts and used to delineate target volumes. Routine follow-up of all pts was performed at 3 to 6 months with CT-scan and/or PET-CT; respiratory function tests were repeated when clinically indicated. Toxicity was assessed according to CTCAE scoring system v4.03.

Results: Early side effects, occurring within 6 weeks of treatment, were uncommon: only one case of G1 acute pulmonary reaction (4%) was recorded. Late toxicity, at 6 months from SBRT was as follows: pulmonary G1 reactions in 14 pts (66%), pulmonary G2 in 1 pt (4%), chest wall G1 in 1 pt (4%). No Grade 3–4 acute and late reactions were recorded. Median follow-up was 25 months (range:6-35 months) and median survival for all pts was

not reached. According to Kaplan- Meier analysis: actuarial 2- and 3-year Local Control of irradiated lesions (n23) was 95% and 86%, respectively; actuarial 2 and 3-year Overall Survival for the 21 pts was 81% and 53%, respectively; actuarial 2 and 3-year Cancer Specific Survival for the whole series of pts was 92% and 67%, respectively (Figure 1).

Conclusion: Our experience confirms that SBRT can be considered a safe, well tolerated and effective treatment option for early stage lung cancer, with excellent results both in terms of disease local control and survival rates.

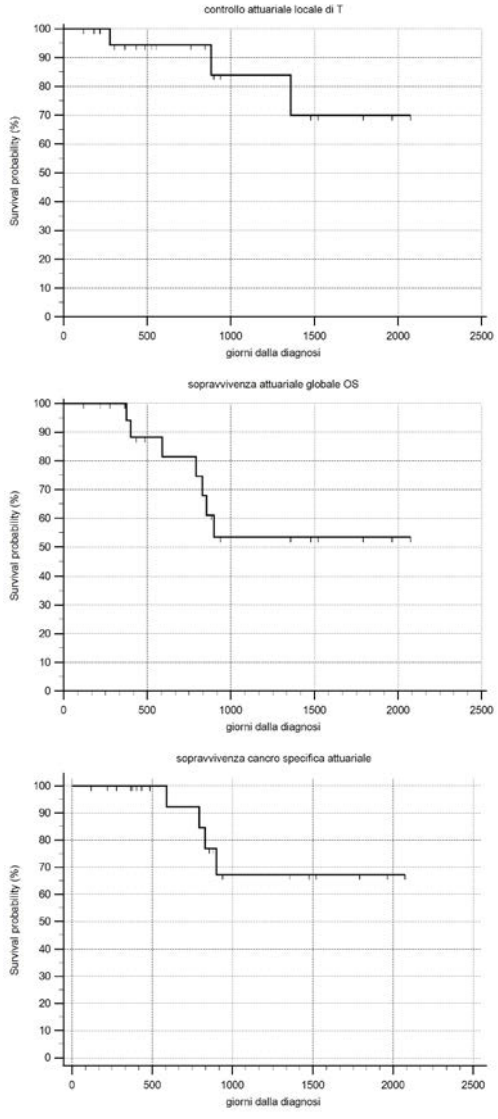

Figure 1.

PO088

RADIOTHERAPY FOR LUNG CANCER IN COVID-19 PATIENT: A CASE REPORT

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Background: COVID-19 pandemic has upset the standard of care in oncology. The lack of specific guidelines for SARS-CoV-2 positive patients made therapeutic choices extremely difficult, notably in thoracic oncology.

Methods: We described our experience of radiotherapy during COVID-19 infection in a patient with local relapse of non small cell lung cancer (NSCLC) previously operated. The tumor board decided to treat the patient with exclusive radiotherapy. We prescribed 60 Gy in 30 fractions to isocenter with conventional fractionation with one volumetric modulated arc technique (VMAT). An image guided radiotherapy with daily cone beam CT (IGRT) was also performed. Thirteen of the 30 scheduled fractions were administered during SARS-CoV-2 positivity. A detailed and specific procedure was put in place to avoid the contagion among radiotherapy staff and other patients.

Results: The patient was carefully monitored and no specific symptoms emerged and successfully completed the scheduled treatment. During RT, an improved O2 saturation, as well as a reduction of dyspnoea and cough, were detected. Two weeks after the end of the RT course was diagnosed contralateral pneumonia; probably due to a mycotic infection, resolved with steroid therapy, broad-spectrum antibiotics and antifungal therapy.

Conclusions: Lung radiotherapy for NSCLC in asymptomatic COVID-19 patients is feasible; safety measures are mandatory to minimize the risk of spread. These data must be confirmed in a large number of patients.

PO089

STEREOTACTIC BODY RADIOTHERAPY (SBRT) OF PRIMARY AND METASTATIC PULMONARY LESIONS FROM OTHER NEOPLASIA: THE CLINICAL EXPERIENCE OF PIACENZA HOSPITAL

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Aims: The aim was to evaluate the effectiveness and safety of SBRT in the treatment of early stage inoperable primary lung tumors, relapses and locoregional metastases from primary lung and pulmonary oligometastases from other solid neoplasms.

Methods: From 01/09/2013 to 30/04/2021 100 patients (pts) were treated with SBRT, of which 89 with lung cancer and 11 with lung oligometastases from another solid neoplasm (Table 1). Of the 89 pts with pulmonary neoplasia, 67 treatments with stereotaxic technique were performed on early stage inoperable primary pulmonary nodules (67 pts), 26 on pulmonary metastatic nodules (14 pts) and 8 on nodules referable to pulmonary recurrence in previously radiotreated patients received more than one stereotaxic treatment (8 pts). Regarding the 11 pts with lung oligometastases from another solid neoplasm, 20 stereotaxic treatments were provided and 3 pts (27%) underwent radiotherapy on more than one pulmonary nodule. The total dose (range 24-60 Gy) was prescribed based on the location (central or peripheral) and volume of the tumor, taking into account the dose limits of the organs at risk (Table 2).

Table 1. Patient and tumor characteristics.

Sex	Male/female	73/27
Age (years)	Median (range)	75 (51-89)
Histology		
Cancer lung (89 pts)		
Primary nodules (67 pts)	Lung cancer AD/SCC/NSCLC*	20/15/32*
Metastasis (14 pts)	Lung SCC/lung AD/lung unknown	2/4/2
LR Nodules (8 pts), *(Not rebiopsy)*	Lung SCC/lung AD, (primary lung cancer)	2/8
Metastasis (11 pts)	colorectal CA/oral cavity SCC/uterine CA/esophageal CA/skin melanoma/soft tissue sarcoma/cervical CA/ breast CA	2/2/2/1/1 1/1/1
T stage (NSCLC): *Primary nodules (n°67)* *Metastasis nodules (n°26)* *LR nodules (n°8)* *oligometastatic nodules (n°20)*	T1/T2 ≤3 cm/ >3 cm - ≤ 5 cm " " " "	50/17 21/5 8/0 17/3
Location (n° Tot 121 nodules treated)	Peripheral/Central	89/32

AD adenocarcinoma, SCC squamous cell carcinoma, *NSCLC non-small-cell lung cancer (not biopsy), CA cancer, LR local recurrence

Table 2. SBRT (lung dose fractionation).

Stereotactic body radiotherapy (SBRT)
From 01/09/2013 to 30/04/2021

	Dose fraction/cGy Total Dose										
SBRT pts lung CA	750cGyx8 **60 Gy**	800cGyx3 **24Gy**	800cGyx4 **36Gy**	800cGyx5 **40Gy**	1000cGyx4 **40Gy**	1000cGyx5 **50 Gy**	1100cGyx5 **55Gy**	1200cGyx3 **36Gy**	1200cGyx4 **48Gy**	1800cGyx3 **54 Gy**	**TOT**
Primitive Nodules	1	7	1	1	1	20	5	2	14	15	67
Metastasis Nodules	0	5	1	0	0	11	0	0	4	5	26
LR Nodules	0	2	0	1	1	1	1	0	2	0	8
Oligomts	0	0	0	1	0	10	0	0	0	9	20
TOT	1	14	2	3	2	42	6	2	20	29	121

LR (Local Recurrence), PTS (Patients), OLIGOMTS (Oligometastasis), CA (Cancer)

Results: Median follow-up after SBRT was 17 months (range 3-72 months) and was assessed by quarterly chest-abdomen CT and 18FDG-PET CT if further investigation required. Local tumor response was assessed according to RECIST criteria. In our experience, SBRT in the lungs ensured overall survival and local control of 31% and 50% respectively at 3 years. In 4 pts with lung oligometastases from other solid neoplasm (36%) SBRT allowed to delay the administration of systemic therapies. The available data on the prognostic role of SBRT are rather heterogeneous and inconclusive. Acute and chronic toxicities, assessed according to the RTOG/EORTC criteria, were found to be mild. Only 3 patients (3%) reported acute G1 toxicity (dry cough and chest pain in the absence of a rib fracture three months after the end of radiotherapy).

Conclusions: SBRT represents a widely used treatment modality due to its high efficacy rate in terms of local disease control, its non-invasiveness and negligible toxicity. The most important predictor for local disease control is dose fractionation.

PO090

CHEST RE-IRRADIATION CHALLENGE: A PATIENT WITH LOCAL RECURRENCE OF SMALL CELL LUNG CANCER.

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Aim: Re-irradiation of local recurrence of small cell lung cancer (SCLC) after chemo and radiotherapy is challenging. To date, there is a lack of common consensus and specific guidelines for prescribing reirradiation dose and dose limits for organs at risk (OAR). In this report, we describe a case of locoregional relapse after chemoradiotherapy in SCLC.

Method: A 61-year-old male patient with limited chest SCLC in March 2018 underwent chemo-radiotherapy: 60 Gy in 30 fractions on primary tumor and stations with pathological lymph nodes, using volumetric modulated arc therapy (VMAT) daily guided by cone-beam CT (CBCT). During treatment the patient reported coughing, dysphagia, and asthenia, then he was treated with steroids, proton pump inhibitors, and sucralfate. A good response was observed during follow-up, but an increase in a para-esophageal node occurred on CT in October 2019. The patient underwent chemotherapy again, but the lesion progressed and therapy with Nivolumab was started. However, the disease continued to progress, and the node reached a size of 50x31 mm. We performed a simulation CT, with a customized immobilization system as similar as possible to the previous one. The slices are 2 mm thick, and the images were matched to diagnostic images with intravenous contrast. We define a GTV represented by the recurring node, with an expansion of 2 mm to define a PTV. The prescription dose for VMAT treatment CBCT-guided was 54 Gy @ 2 Gy. The experience reported by Meijneke et al. was used to set OAR treatment goals. In particular, an attempt was made to keep the maximum accumulated doses of Heart, Esophagus, and Trachea below 115 Gy, 85 Gy, and 89 Gy, respectively.

Result: The patient reported no toxicity during retreatment. At the first follow up in November 2020 the lesion was in partial response (35x21 mm *vs.* 50x31 mm), in February 2021 the node was stable in size, but a new CT acquisition in April 2021 revealed a new increase (43x32 mm) with the appearance of a satellite pulmonary nodule. The patient shows no chronic toxicity. The resulting maximum accumulated doses of Heart, Esophagus

and Trachea were 15 Gy, 82 Gy, and 86 Gy, respectively.

Conclusion: Chest reirradiation is currently a challenge that can be successful in selected patients with relapsing SCLC. The maintenance of the accumulated dose on OAR is of fundamental importance for the absence of acute toxicity. Chest reirradiation has been shown to have good performance for local disease control.

PO091

EFFICACY OF ABLATIVE STEREOTACTIC BODY RADIATION THERAPY (SBRT) IN PRIMARY LUNG CANCER PATIENTS: A 10-YEAR MONO-INSTITUTIONAL EXPERIENCE

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Aims: to evaluate outcome rates and safety after ablative Stereotactic Body Radiation Therapy (SBRT) in inoperable primary lung cancer.

Methods: patients with primary lung cancer treated with ablative radiotherapy were included in this retrospective analysis. Inclusion criteria were: primary lung cancer in stage I-II, exclusion of surgery due to comorbidities or refusal of the patient to undergo surgical treatment. All lesions were contoured on a 3 mm CT-scan using abdominal compression to reduce tumor motion. A FDG-PET/CT-scan fusion was used if available. Radiotherapy was delivered with fractionated SBRT using 3D-conformal technique. A median total dose of 36 Gy (range: 24-50) in 3-5 daily fractions was delivered to the isodose 65%. Instrumental reevaluation (CT-scan and/or FDG-PET/CT) were performed every 3-6 months after the treatment.

Results: from January 2010 to December 2020 a total of 85 patients were treated [M/F=62/23; median age: 80 years (range: 53-89 years); tumor site: right (50.6%) and left lung (49.4%) with majority of lesions sited at superior lobe (55.3%); stage I (94.4%), and stage II (5.6%); histology: adenocarcinoma (35.3%), squamous cell carcinoma (20.0%), not specified carcinoma (9.4%), and poorly differentiated (1.2%). 34.1% of patients had radiological lung lesions not histologically typed. Nineteen patients (22.3%) were lost to follow-up. With a median follow-up time of 24 months (range: 3-58 months), 72.8% of patients showed a radiological overall response (36.4% CR, 36.4% PR), 15.1% of patients presented a PD, and 12.1% a SD. No patients showed ≥ G3 acute and late toxicities. One-year follow-up showed 90.9% of radiological overall response (51.5% CR, 39.4% PR), 6.1% of patients presented a PD, 3.0% a SD, with no ≥ G3 acute and late toxicities.

Conclusions: ablative SBRT treatment showed a favorable and promising results in terms of local efficacy and safety in primary lung cancer patients.

PO092

A CASE OF BILATERAL INTERSTITIAL PNEUMONIAE AFTER THE FIRST ADMINISTRATION OF DURVALUMAB

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Aims: We report the case of a bilateral immune-related pneumonia in a Stage IIIA Non Small Cell Lung Cancer (NSCLC) elderly patient after the first administration of Durvalumab subsequent to a primary radiochemotherapy treatment.

Materials and methods: A 81-year-old patient with an history of previous smoking, hypertension and emphysema, ECOG 0 was diagnosed a NSCLC Stage cT3N2M0 (Stage IIIA). Staging exams (CT and PET/CT) revealed a primary ascessualised tumor mass located in the lower lobe of the left lung together with two gross mediastinal adenopathy of the 7 (subcarinal) and 8 (paraesophageal) mediastinum level. The case was discussed within the multidisciplinary tumor board that decided the patient would undergo primary surgical removal of the ascessualised lung lesion followed by a radiotherapy-based treatment on mediastinal lymph nodes.

Results: Patient underwent to an atypical resection of lower left lobe (Histology: Adenocarcinoma G3 PDL-1 60%) followed by an involved field RT on PET+ lymphnodes. RT was delivered by using a VMAT/IGRT technique at a conventional fractionation with a total dose of 66Gy combined with 7 administration of weekly Carboplatin AUC 2. The treatment was well tolerated and the patient experienced a radiological partial response >50% at the first evaluation 1 month after the end of treatment. Then, we started Durvalumab at 10mg/Kg as consolidation therapy. After two days patient experienced a grade 4 dyspnea, fever 39° C and type 1 respiratory failure assessed by arterial gas analysis. CT scan showed a bilateral intertstitial lung disease that was consistent with an immune-related pneumonia. Thus, the patient was hospitalized and treated with corticosteroids and high-flux oxygen. Despite therapy the patient's clinical and radiological conditions declined, developing severe respiratory failure associated with bilateral interstitial pneumonia, pneumothorax and pneumomediastinum. The patient eventually died after two weeks due to cardiopulmonary failure.

Conclusion: This case shows how Durvalumab-therapy can potentially be fatal, even in patients with good PS without specific risk factors at the beginning of the treatment.

PO093

STEREOTACTIC ABLATIVE RADIOTHERAPY TO PRIMARY BREAST CANCER IN DE NOVO IV STAGE DISEASE: PRELIMINARY RESULTS OF A DOSE ESCALATION STUDY

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Aims: Approximately 5-10% of women present de novo metastatic breast cancer (MBC). Even if literature data do not support loco-regional treatment in all patients, some of the study results suggest that there is a subset of patients who might benefit from local treatment especially those who have improved survival with the new effective target agents. Advantages of stereotactic ablative radiotherapy (SABRT) in treating breast primary tumor in metastatic breast cancer relies on the radio-biological advantage, on the possibility of continuing systemic treatment without interruption and of treating symptomatic lesions. We developed a prospective dose escalation trial to evaluate the maximum tolerated dose (MTD) of SABRT to primary breast cancer.

Methods: Patients with histologically confirmed diagnosis of invasive breast carcinoma (luminal and/or HER2 positive) and distant metastatic disease not progressing after 6 months of systemic therapy with a tumor CT or 5FDG-PET detectable were deemed eligible. The starting dose was 40 Gy in 5 fractions (level 1) because this dose proved to be safe in dose-escalation trial on adjuvant SABRT. The maximum dose level was chosen as 45 Gy in 5 fractions. Dose limiting toxicity (DLT) was any grade 3 or worse toxicity according to CTCAE v.4. Time-to-event Keyboard (TITE-Keyboard) design (Lin and Yuan, Biostatistics 2019) was used to find the MTD. MTD was the dose of radiotherapy associated with a ≤ 20% rate pre-specified treatment-related DLT.

Results: To date 10 patients have been treated at the starting dose level. Median age was 80 years (range 53-89). 8 patients had a luminal disease while 2 patients had an HER2 positive disease. No protocol defined DLTs were observed. When examining AEs, grade 2 skin toxicity occurred in 3 patients with diseases located next to the skin and showing clinical retraction. Eight patients with a minimum follow-up of 6 months were evaluable for response: 4 achieved a complete response and 4 achieved a partial response. The mean reduction in the sum of the largest diameters of target lesions was of 61.4% (DS=17.0%). In all patients with a skin retraction, retraction disappeared after treatment. Only one patient had local failure to treated breast lesion 20 months after treatment, with systemic disease progression.

Conclusions: SABR to primary breast cancer seems feasible and associated with symptoms reduction. Continued accrual to this study is needed to confirm the safety and assess the MTD.

PO094

THE ROLE OF TIMING OF 3D BOOST IN BREAST CONSERVATIVE TREATED PATIENTS: DOSIMETRIC COMPARISON AND ACUTE TOXICITY IN CONCOMITANT ONE VERSUS SEQUENTIAL

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Aims: To evaluate dosimetric equivalence and impact on acute toxicity of concomitant boost (CB) versus sequential boost (SB) in patients with breast cancer (BC) submitted to conservative surgery in view of growing evidence that concomitant one provides superior tumor coverage and normal tissue sparing.

Methods: Ninety women treated with 3D radiotherapy (RT) with boost from January 2020 to May 2021 were selected. All of these were low-risk, Luminal A or B, early stage invasive BC, stage pT1-2(R0), pN0-1mi and were treated with conservative surgery. Forty-five of these were submitted to 3D hypofractionated RT with field-in-field CB, other 45 with hypofractionated RT too, but boost was administered sequentially. EQD2 dose to the surgical bed with CB was 59.52 Gy (0.50 Gy/fraction for 15 fractions plus 2.70 Gy/fraction on entire breast) instead of 60 Gy of the SB (16 fractions of 2.75 Gy entire breast and 9 Gy/3 fractions of boost). Clinical and toxicity data according to CTCAE classification v5.0 were recorded. A dosimetric comparison was performed, including the planning tumor volume (PTV) coverage with 95% of the prescription dose (PD), conformity index (CI), homogeneity index (HI). The maximum dose (D_{max}) to the skin profile normalized to the PD, lung V_{16Gy}, heart V_{5Gy} and mean dose (for left-sided tumours) were also evaluated.

Results: Table 1 summarizes patients layering. Clinical findings were substantially homogeneous between the two groups. There were no differences in PTV coverage (median 96% for both CB and SB groups, interquartile range (IQR) 2 and 3, respectively; p=0.912). Median lung V_{16Gy} was 11% (IQR 6) for CB, 10% (IQR 4) for SB, respectively (p=0.155); heart V_{5Gy} and mean dose were equally 2% (IQR 4; p= 0.768), and 1 Gy (IQR 1; p=0.944), respectively. SB patients experienced skin toxicity grading G2-3 in 42.2% of cases, compared to the 15.6% of G2 and no G3 dermal impairment for CB (p=0.0003). Median CI was 0.96 for CB, and 0.98 for SB

(p=0.044); median HI was 0.27 for CB, and 0.29 for SB (p=0.0007). Correlation between the skin D_{max} and skin toxicity rates/cosmesis is ongoing.

Conclusions: Tumor bed field-in-field CB is cost-effective, may improve outcomes of breast-conserving RT with easy implementation, ensures a more homogeneous target volume dose distribution and lower toxicity profile than SB, with shortened overall treatment time. The analyses completion on skin dosimetry and cosmetic results will further clarify our promising findings.

Table 1.

Table 1. Characteristics of the population in study (patients layered for concomitant or sequential boost)

Parameters	N° (%) CB group 45 patients	N° (%) SB group 45 patients	*p* value (<0.05)
Age (years)			
Median	65	62	0.806
Range	46-86	44-84	
Breast side			
Right	27 (60.0)	29 (64.4)	0.668
Left	18 (40.0)	16 (35.6)	
Site of breast tumor			
Upper outer quadrant	25 (55.6)	34 (75.6)	
Lower outer quadrant	11 (24.4)	3 (6.7)	
Upper inner quadrant	6 (13.3)	3 (6.7)	0.426
Lower inner quadrant	2 (4.4)	4 (8.9)	
Retroareolar	1 (2.2)	1 (2.2)	
Histology			
Invasive carcinoma of NST	38 (84.4)	41 (91.1)	
Invasive lobular carcinoma	4 (8.9)	4 (8.9)	0.127
Mixed IDC and ILC	1 (2.2)	0 (0.0)	
Other	2 (4.4)	0 (0.0)	
Tumor grading			
G1	9 (20.0)	3 (6.7)	
G2	36 (80.0)	39 (86.7)	0.016
G3	0 (0.0)	3 (6.7)	
Luminal phenotype			
Luminal A	44 (97.8)	42 (93.3)	0.312
Luminal B	1 (2.2)	3 (6.7)	
T stage			
pT1	43 (95.6)	43 (95.6)	0.316
pT2	2 (4.4)	2 (4.4)	
N stage			
pN0	43 (95.6)	44 (97.8)	0.562
pN1mi	2 (4.4)	1 (2.2)	
Endocrine therapy (AIs or TAM)			
Yes	39 (86.7)	42 (93.3)	0.297
No	6 (13.3)	3 (6.7)	
Acute skin toxicity			
G0	**14 (31.1)**	4 (8.9)	
G1	**24 (53.3)**	**22 (48.9)**	**0.0003**
G2	7 (15.6)	**15 (33.3)**	
≥G3	0 (0.0)	**4 (8.9)**	

CB=concomitant boost; SB=sequential boost; NST=no special type; IDC=invasive ductal carcinoma; ILC=invasive lobular carcinoma; AIs=Aromatase inhibitors; TAM=Tamoxifen

PO095

POSTOPERATIVE RADIOTHERAPY IN BREAST CANCER PATIENTS TREATED WITH NEOADJUVANT CHEMOTHERAPY

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Aims: The use of neoadjuvant chemotherapy (NAC) in early stage (triple-negative and HER2-positive patients), locally advanced and inflammatory breast cancer has been rising in the last few decades. Patients with pathological complete response (pCR) have been shown to have better outcome, while patients either less or not responsive to NAC may benefit of alternative adjuvant therapies. The purpose of this study was to investigate recurrence and survival outcomes in patients with breast cancer treated with NAC, radical surgery and local-locoregional RT.

Methods: Seventy-nine patients treated with NAC, surgery, and adjuvant RT at our institute between April 2004 and May 2020 were enrolled. Adjuvant RT delivered 45-50 Gy in 20-25 fractions to the chest wall or whole breast, treating once daily, five times per week. Axillary, supraclavicular, internal mammary lymph node chains and/or boost RT to the tumor cavity were administrated if indicated. pCR is defined as absence of residual invasive cancer on pathological evaluation of resected breast and lymph nodes specimens after NAC.

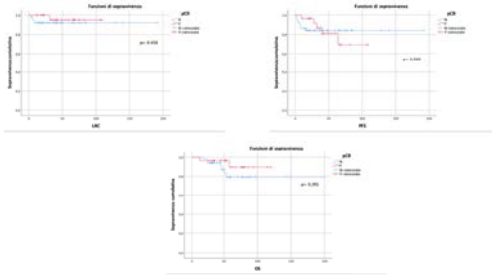

Figure 1. Outcomes for patients stratified by pCR. a) Locoregional control b) Progression free survival c) Overall survival

Figure 1.

Results: At a median follow-up of 40 months (range 4-192), 70 patients (89%) were alive. Thirty-three patients (42%) were stage III, forty-six stage II (58%). Most of the patients (86%) received NAC including taxane and anthracyline. According to molecular subtypes, luminal A accounts for 24 patients (30%), luminal B for 38 (48%), Her2-enriched for 10 (13%), triple negative for 7 (9%). There were 13 patients (16.5%) who experienced disease recurrence. Four patients (5%) had LRR only, 8 patients (10%) distant metastases only, while 1 patient (1%) had both locoregional recurrence and distant metastasis. Actuarial rates of locoregional control (LRC), progression-free survival (PFS), and overall survival (OS) were 92.9%, 78.2%, and 83.4% at 5 years, respectively. Regarding pCR, no significant differences were seen in LRC rates (p=0.4), and PFS (p=0.9) Although 5-year OS rates were 79.2% in patients that did not achieve a pCR

and 89.5% in patients that achieved pCR (Figure 1) this expected difference resulted not significant (p = 0.3), may be due to the low number of cases examined. No difference was also found in radioinduced toxicity profile between patients treated with NAC and those treated with adjuvant chemotherapy.

Conclusions: NAC, surgery and postoperative RT are an effective and well tolerated treatment in patients with high-risk breast cancer.

PO096

POST-OPERATIVE RADIATION THERAPY AFTER NEOADJUVANT CHEMOTHERAPY AND SURGERY IN BREAST CANCER PATIENTS

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Aim: The aim of this study is to evaluate the therapeutic effectiveness of adjuvant radiotherapy for breast cancer (BC) patients treated with neoadjuvant chemotherapy (NAC) and surgery (S).

Methods: We performed a retrospective analysis of clinical and pathological records of BC patients treated with NAC and S, with (RT group) or without (NoRT Group) adjuvant radiation therapy at Policlinico Tor Vergata (Rome), between October 2005 and December 2020. Adjuvant RT was delivered with 50 Gy in 25 fractions to the chest wall/whole breast. Regional node irradiation and boost RT to tumour bed cavity were left to discretion of treating radiation oncologist. Primary endpoints were locoregional control (LRC) and overall survival (OS). All time-to-event endpoints had the date of surgery as the start date. Multivariate analysis was performed using Cox proportional hazards regression modelling.

Results: A total of 131 BC patients were included. 67 pts (51%) received adjuvant RT and 64 pts (49%) were treated with NAC and S alone. The indication of RT was guided by pre-NAC tumour characteristics (cN2-N3 disease at diagnosis, p=0.034), by the type of surgery performed (Breast Conserving Surgery, p=0.011), as well as the response of the tumour to NAC (absence of complete response p=0.043). Median age at diagnosis was 48 years. Pts and clinical features are shown in Table 1. After a mean follow-up of 60.3 months, we identified 12 locoregional recurrences: 4 in the RT group and 8 in the NoRT group. The mean time to LRR was 4.7 years. Twenty-three pts (17.56%) developed distant metastases with no significant difference between the two groups. Mean LRR-FS was 60.1 months and mean PFS was 33.8 months. Multivariate analysis revealed that two factors independently predicted for LC: adjuvant RT (RR 0.18 95%CI 0.03-0.97 p=0.046) and the achievement of pCR post-NAC, defined as the absence of residual invasive carcinoma at surgery. The association between RT and OS was not statistically significant, otherwise molecular pattern showed a significant association with OS (RR 2.71 95% CI 1.19-6.13 p=0.016).

Conclusions: Adjuvant RT was found to improve LC in BC patients treated with NAC followed by S, but no effects on OS were observed. Molecular pattern could help in NAC setting to select the best pts for adjuvant RT post NAC+S.

Table 1.

	NO-RT Group	RT Group
	64 (49%)	67 (61%)
Age at diagnosis		
• ≤ 40 years	11 (17.3%)	8 (11.9%)
• 41-50 years	32 (50%)	28 (41.8%)
• 51-60 years	16 (25%)	18 (26.9%)
• >61 years	5 (7.7%)	13 (19.4%)
Histology		
• CDI	55 (86%)	45(67.2%)
• CLI	2 (3.1%)	8 (11.9%)
• Infiltr. carcinomatosis	7 (10.9%)	14 (20.9%)
Molecular Pattern*		
• LLA	8 (12.5%)	5 (7.5%)
• LLB	31 (48.4%)	34 (50.7%)
• TN	8 (12.5%)	7 (10.4%)
• Her2 +	17 (26.6%)	21 (31.4%)
Clinical T at diagnosis		
• cT1	6 (9.4%)	4 (5.9%)
• cT2	34 (53.1%)	30 (44.8%)
• cT3	7 (10.9%)	10 (14.9%)
• cT4	17 (26.6%)	23 (34.3%)
Clinical N at diagnosis		
• cN0	34 (53.1%)	20 (29.8%)
• cN1	23 (36%)	33 (49.2%)
• cN2	7 (10.9%)	12 (17.9%)
• cN3	0 (0%)	2 (3%)
Surgery		
• Mastectomy	56 (87.5%)	42 (62.7%)
• BCS	8 (12.5%)	25 (37.3%)
Axillary dissection		
• Yes	48 (75%)	51 (76.1%)
• No	16 (25%)	16 (23.9%)
pCR		
• Yes	19 (29.7%)	10 (14.9%)
• No	45 (70.3%)	57 (85.1%)

PO097

SKIN LATE TOXICITY EVOLUTION IN BREAST CANCER PATIENTS TREATED WITH HYPOFRACTIONATED RADIOTHERAPY WITHOUT BOOST

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Aims: To report late skin toxicity evolution in 998 of early-stage breast cancer (BCA) patients (pts) treated with hypofractionated whole breast adjuvant radiotherapy (HWBRT) without boost.

Methods and Materials: From 02/2009-07/2016, 998 consecutive BCA pts treated with HWBRT to a total dose of 40.05 Gy/15 fractions delivered in 3 weeks, without boost, who had at least 42 months (mts) of follow-up were included in this analysis. Median age was 62.01 (IQR:51.60-70.02) years. Right sided were 47.5% and left sided 52.5%. Histology was in situ for 84 (8.4%) of pts and invasive in 91.6%. Chemotherapy was prescribed in 27.6% of pts, hormonal therapy in 80% and monoclonal antibodies in 8.3%. Late toxicity was evaluated with SOMA-LENT scale.

Results: Median follow up was 83.67 (IQR: 59.67-107.67) months. Late toxicity ≥G1 was divided into edema and hyperpigmentation (EH), observed in 32.2% of pts (28.2% G1, 3.9% G2, 0.1% G3), and atrophy, fibrosis, telangiectasia, and pain (FATP), observed in 18.3% of pts (14.2% G1, 3.1% G2, 0.9% G3 and 0.1% G4). E-H were present mainly at six-month follow-up and decreased over time. The proportion of pts with G0 toxicity increased from 68.1% at six mts to 96.8% at 42 mts; the proportion of patients with G1 toxicity decreased from 28% to 3%, and G2 toxicity from 3.8% to 0.2%. G3 toxicity disappeared within 18 mts (Figure 1a). The evolution of FATP toxicity was opposite. Even though improvements over time were registered for some pts, an overall worsening trend for toxicity FATP over time was observed. For those pts showing at least G1 FATP toxicity overall, the first occurrence of toxicity was registered at 6 mts for 37.4% of the pts. For the same patients the median time to first occurrence of toxicity was 18 mts.

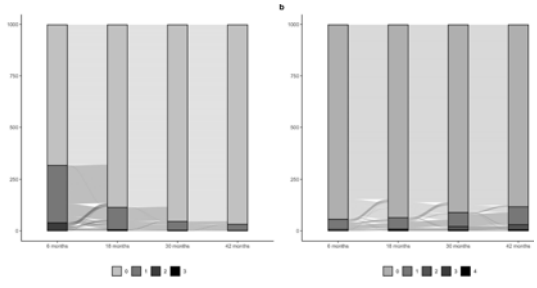

Figure 1.

The proportion of pts with G0 toxicity decreased from 94.4% at 6 mts to 88.3% at 42 mts, while the proportion of pts with G1 toxicity increased from 4.9% to 8.7%, and G2 toxicity from 0.7% to 2.4%. G3 toxicity was registered for the first time at 18 mts after radiotherapy, increasing from 0.3 to 0.5% at 42 mts, while the sole G4 toxicity registered at 18 mts follow-up remained unchanged at 42 mts (see Figure 1b). Few pts worsened thereafter, but one new G1 toxicity was registered even at the 9th-year of follow-up.

Conclusions: While EH improves over time, almost disappearing at 18 mts, FATP increases over time, but the worst grades occur between 18-42 mts after the end of HWBRT.

PO098

MACHINE LEARNING APPLICATIONS FOR NODAL STATUS PREDICTION IN BREAST CANCER PATIENTS WITH POSITIVE SENTINEL LYMPH-NODE BIOPSY AFTER NEOADJUVANT THERAPY

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Aims: The management of the axilla in breast cancer patients treated with neoadjuvant systemic therapy (NAST) following positive sentinel lymph node (SNLD) dissection is controversial, and more refined strategies are warranted to weight the cost/benefit ratio of local treatments (i.e. axillary node dissection, target axillary volumes). This study aims to explore the potentials of machine learning (ML) in this clinical setting, as a tool to inform clinical decisions.

Methods: Two-hundred sixty-five patients who had received NAST and had a positive SLN biopsy followed by axillary dissection at the European Institute of Oncology IRCCS between 2001 and 2018 were considered eligible. Least absolute shrinkage and selection operator (LASSO) and random forest (RF) models were selected and implemented by both train-validation-split procedure and cross-validation (CV), respectively. Models were trained using clinically-relevant variables (i.e. Radiotherapy after primary Chemotherapy Criteria (Rapchem criteria), age, clinical tumour stage at presentation (cT), clinical nodal stage at presentation (cN), ratio between positive sentinel lymph node and total sentinel lymph node (ratio), extracapsular extension (ECE) and vascular invasion). Performance was assessed by accuracy and area under the receiver operating characteristic curve (AUC-ROC).

Results: The best performances were achieved using a train-validation-split procedure, getting an AUC of 0.721 (Figure 1A) with an accuracy of 72.8% for RF and by using 5 folds cross-validation, obtaining an AUC of 0.724 and an accuracy of 70.2% for LASSO (Figure 1B)

Overall, LASSO and RF performances were comparable. For both models the most relevant features for the prediction of further nodal involvement were Rapchem criteria, Age, Ratio and ECE (Figure 1C). One evident difference between the models is that LASSO also considered cN and NAT response to be significant.

Conclusions: The application of ML models in clinical practice is a promising decision-making tool. The weight given to the individual variables by the models is an interesting cue from a clinical point of view to pave the way for the consideration of new biomarkers (i.e., ECE) for the prediction of further axillary involvement. In order to obtain widely applicable models, training models with larger database and performing validation on external cohorts could improve the reliability and generalizability of previsions.

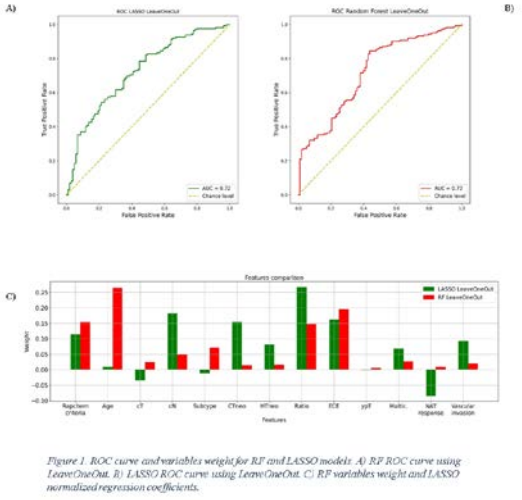

Figure 1. ROC curve and variables weight for RF and LASSO models. A) RF ROC curve using LeaveOneOut. B) LASSO ROC curve using LeaveOneOut. C) RF variables weight and LASSO normalized regression coefficients.

Figure 1.

PO099

SERENITY TRIAL: SECOND LINE ERIBULIN FOR LOCALLY ADVANCED OR METASTATIC BREAST CANCER. FOCUS ON NEUROPATHY AND OVERALL TOXICITY

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Aims: Eribulin mesylate is widely used as second line therapy in patients affected by locally advanced or metastatic breast cancer (LA/MBC). In this setting, patients are usually pretreated with taxanes as adjuvant, neoadjuvant or metastatic treatment, so neuropathy frequently occurs. This symptom leads to drug delays, dose reductions and discontinuations in addition to a potential detrimental impact on health-related quality of life (HRQoL). SERENITY is a longitudinal, prospective, observational study aiming to assess HRQoL and neuropathy-related toxicity profile of eribulin used as second line chemotherapy in a in real life cohort of pretreated HER2 negative LA/MBC.

Methods: Patients with LA/MBC with disease progression to a first line chemotherapy regimen were enrolled at the beginning of eribulin treatment at two different institutions. Neuropathy and pain were evaluated before the first and every 3 cycles of eribulin during clinical examination. With the same time points, patients were required to fill out EORTC quality of life questionnaires (QLQ-C30, QLQ-BR23, QLQ-CIPN20).

Results: We report preliminary results about the first 8 patients treated in 2 different oncologic centers from August 2018 to December 2020. Median age at diagnosis was 55.5 years. Sixty-two percent of patients underwent adjuvant chemotherapy while 38% neoadjuvant; 37.5% received adjuvant endocrine therapy (ET). Fifty percent of patients received taxanes as previous adjuvant or neoadjuvant therapy, and 50% as first line treatment for metastatic disease. After a median follow up of 23 months, the mean progression free survival (PFS) with eribulin was 7.5 months (range 2-20). Motor neuropathy (evaluated according to NCI-CTCAE v 5.0) was grade 1 in all patients and grade 1 sensory neuropathy was found in 75% of patients with grade 2 in 25% at baseline. We did not report a significant deterioration of neurological symptoms during the course of therapy and not evidenced a significant worsening of pain evaluated in accordance with the Visual Analog Pain Scale (VAS). Global health status (GHS) score, derived from QLQC30, was not worsened after 3 cycles of eribulin compared to baseline in 7 patients (87.5%).

Conclusions: Our analysis showed that eribulin does not significantly impact pain and neuropathy when used in LA/MBC patients pretreated with taxanes, without affecting HRQoL. However, further evidence from larger samples is needed to confirm these findings.

PO100

TANGENTIAL FIELDS WHOLE BREAST RADIOTHERAPY IN CT1-2 CN0 BREAST CANCER PATIENTS WITH PATHOLOGICAL SENTINEL LYMPH NODE: OUTCOMES COMPARISON WITH OR WITHOUT AXILLARY DISSECTION

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Aims: In the past, axillary dissection (ALND) was performed for tumour staging and to improve local control (LC). Axillary management in cN0 breast cancer (BC) patients with positive sentinel lymph node (SLN) is unclear in case of ALND omission. The ACOSOG Z0011, comparing patients treated with or without ALND in cN0 and SLN+, demonstrated ALND safely omission, although criticized for radiotherapy (RT) fields non-uniformity. We previously conducted the LISEN trial in cN0 patients and SLN+ with ALND omission, treated with whole breast RT (WBRT) without high tangent or nodal RT. Currently, to validate ALND omission safety, we compared 2 groups with similar pathological characteristics and same RT fields: LISEN patients and patients who underwent ALND.

Methods: We analysed female patients with histologically proven BC, cT1-2cN0 submitted to conservative surgery and SLN biopsy with (group 1) or without (group 2) ALND, without neoadjuvant therapy. In both groups, adjuvant systemic therapy was prescribed according to staging and tumor biology; tangential fields WBRT was planned. Clinical outcomes, as local recurrence (LR), regional recurrence (RR), loco-regional recurrence (LRR), distant metastases (DM), disease-free survival (DFS) and overall survival (OS), were analysed, measured from surgery until first event.

Table 1. Patients and tumor characteristics in209 breast cancer patients with positive Sentinel Lymph Nodetreated with ALND (Group 1) and SLN biopsy only (Group 2).

Group 1	76	Group 2	133
	n (%)		n (%)
Age (years)range	34-76	Age (years)range	35-83
Pathological Stage		Pathological Stage	
Tis	1 (1.3)	Tis	1(0.8)
T1a	1 (1.3)	T1a	1(0.8)
T1b	8 (10.6)	T1b	28(21.0)
T1c	47 (61.8)	T1c	80(60.1)
T2	19 (25)	T2	23 (17.3)
Histological type		Histological type	
Ductal	61 (80.3)	Ductal	109 (81.9)
Lobular	9 (11.8)	Lobular	10 (7.6)
Other	6 (7.9)	Other	14 (10.5)
Grade		Grade	
1	31 (40.8)	1	71 (53.4)
2	39 (51.3)	2	54 (40.6)
3	6 (7.9)	3	8(6.0)
Molecular subtypes		Molecular subtypes	
Luminal A	47 (61.8)	Luminal A	88 (66.1)
Luminal B (HER2 negative)	11 (14.5)	Luminal B (HER2 negative)	30 (22.5)
Luminal B (HER2 positive)	13 (17.1)	Luminal B (HER2 positive)	10 (7.6)
HER2+	2 (2.6)	HER2+	1(0.8)
Basal-like	3 (4.0)	Basal-like	4 (3.0)
Adjuvant Chemotherapy		Adjuvant Chemotherapy	
Yes	43 (56.6)	Yes	57 (42.9)
No	33 (43.4)	No	76 (57.1)
Adjuvant Hormonal Therapy		Adjuvant Hormonal Therapy	
Yes	72 (94.7)	Yes	126 (94.7)
No	4 (5.3)	No	7 (5.3)

Results: We analysed 209 patients (76: group 1, 133: group 2). Patients, tumour and treatment characteristics are reported in Table 1. The median number of histologically positive nodes were one in both groups. In group 1 all patients underwent WBRT with conventional fractionation (50 Gy, 25 fractions). In group 2, 126 (94.7%) received a conventional fractionation and 7 (5.3%) hypofractionation (40-40.05 Gy, 16-15 fractions). The median follow-up was 92 months (range= 21-131) for group 1 and 50 months (range= 5-91) for group 2. The 5-year LR, RR, LRR, DM, DFS and OS were: 1.3%, 1.3%, 0%, 2.6%, 96.1% and 94.7% respectively for group 1 and 3.2%, 1.5%, 1.5%, 6.7%, 93.6% and 96.9%, respectively for group 2. For group 1 the 9-year LR and DFS were 2.6% and 94.7%. Comparing both groups, LR occurred in 2 and 4 patients, RR in 1 and 1, DM in 2 and 5 and death in 4 and 1 in group 1 and 2, respectively.

Conclusions: Similar outcomes were reported in both groups. Although ALND seems to improve LC, its omission has not a worse impact on DFS and OS, sparing axillary morbidities. We are waiting for a longer follow-up to confirm these results.

PO101

FIVE-FRACTION ONCE-WEEKLY HYPOFRACTIONATED ADJUVANT WHOLE BREAST RADIOTHERAPY IN OLDER PATIENTS. MONO-INSTITUTIONAL EXPERIENCE

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Aim: Moderate hypofractionation is now the standard of care for adjuvant whole-breast radiotherapy after breast-conserving surgery for breast cancer. According to recently published 10-year results from the FAST trial, this study retrospectively analysed toxicity profiles and clinical outcomes of five-fraction once-weekly hypofractionated whole-breast radiotherapy for early stage breast cancer in older patients.

Methods: A total of 179 patients were treated with WBRT from August 2016 to December 2019. Patients were given 5.7 Gy in 5 weekly fractions for a 28.5 Gy total dose over 5 weeks. A concomitant tumour bed boost (0.5 Gy per fraction) was given in 39 patients (22%), from 28.5 Gy to 31 Gy total dose. Clinical end-points were acute and late toxicity, local control (LC), disease-free (DFS) and overall survival (OS).

Results: Median follow-up was 37 months (range, 17-60 months). The mean age was 78 years. Most patients had pT1(68%), cN0-pN0 (78%), ductal infiltrative tumors (87%), G1-G2 (89%), with no in situ component (75%). Tumors were mainly hormone-sensitive (92%), with low proliferation index (70%), c-erb-B2 negative (95%), luminal A (54%), luminal B (38%). Surgical resection margins were in the major percentage negative (94%). Patients received adjuvant hormonal therapy (78%), and adjuvant chemotherapy was given in only 3%. The 3-year LC, DFS and OS rates were 99.5%, 94% and 95% respectively. Maximum detected acute skin toxicity was G0 in 73% of patients, G1 in 24%, G2 in 3%, and no G3-G4 toxicity was reported. Late toxicity in terms of

fibrosis was observed G1 in 28% of patients, G2 in 4%, and G3 in less then 2%. Grade1 breast edema was observed in 8% of patients and G2 in 3%. Grade 1 hyperpigmentation was registered in 7% of patients, G2 in 2%. Pain was reported as G1 in 15% and G2 in 3%.

Conclusions: Our retrospective analysis confirms the published 10-year FAST trial findings that a once-weekly hypofractionated whole-breast radiotherapy appears to be feasible and effective especially for a selected population of old breast cancer patients with mainly low-risk features. This schedule allow frail patients to receive breast conservative surgery and adjuvant whole breast radiotherapy limiting hospital accesses and increasing treatments tolerability.

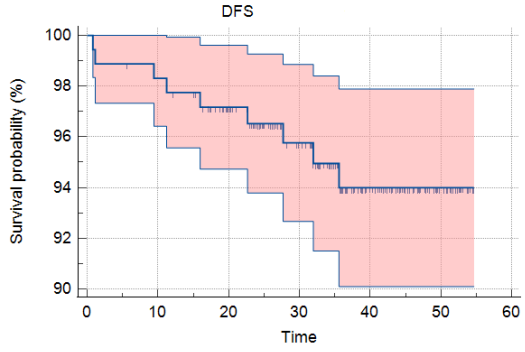

Figure 1.

PO102

HYPOFRACTIONATION AND CONCOMITANT BOOST IN DUCTAL CARCINOMA IN SITU (DCIS): ANALYSIS OF A PROSPECTIVE CASE SERIES WITH LONG TERM RESULTS

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Aims: We previously published in 2014 a subgroup analysis of 103 patients affected by DCIS treated with breast conservative surgery (BCS) and hypofractionated whole breast radiotherapy (WBRT) with concomitant boost (CB) with a median follow up of 48 months. Here we present long-term results on clinical outcome and toxicity with a median follow up of 11,2 years.

Methods: Between 2005 and 2012, 82 patients with DCIS after BCS received hypofractionated adjuvant radiotherapy with concomitant boost at our Hospital. All patients received the same fractionation schedule: prescription doses of 45 Gy / 20 fractions and 50 Gy / 20 fractions, respectively planned on whole breast and tumor bed.

Results: After a median follow-up of 11,2 years (range 5-15 years) 9 patients (11%) developed local recurrence (LR), of seven of which were invasive disease (77,8%) and 2 DCIS (22,2%). Median time to recurrence was 7,07 years (range 2.42-12.70 years). The LR rates at 5 and 10 years were 2.4% and 8,2%, respectively. Of the 9 patients who experienced a LR, 7 underwent a unilateral mastectomy, two a conservative surgery. The 5- and 10-year overall survival were 98,8% and 91,6%, respectively. The 5- and 10-year breast cancer specific survival were 100% and 99%, respectively. Maximum detected acute skin toxicity was as follows: grade G0 in 40% of patients, G1 in 50%, G2 in 9% and G3 in 1%. Late skin and subcutaneous toxicity were generally mild with only 1% of patients experiencing G3 events. No major lung and heart toxicity were detected. Cosmetic results were excellent in 50% of patients, good in 40%, fair in 8% and poor in 2%.

Conclusions: Hypofractionation is a frequently employed strategy to perform WBRT after BCS in DCIS. Our long-term data demonstrate safety, efficacy and tolerability. Our experience suggests that HF and CB might be a feasible option for DCIS.

PO103

DOSIMETRIC IMPACT OF MEAN HEART DOSE CONSTRAINT IN VMAT PLANNING OF ADJUVANT HYPOFRACTIONATED RADIOTHERAPY WITH SIMULTANEOUS INTEGRATED BOOST FOR EARLY BREAST CANCER

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Aims: In early stage breast cancer, long term toxicity represents an important issue. Is well known that late cardiac toxicity is influenced by the RT dose. We present data from a phase II institutional trial for adjuvant hypofractionated radiotherapy with simultaneous integrated boost, using VMAT technology, with particular interest for heart dosimetry.

Methods: Patients affected by early-stage breast cancer, treated with breast conserving-surgery, have been enrolled in this phase II trial. Any systemic therapy was allowed either in neoadjuvant or adjuvant setting. All patients underwent VMAT-SIB technique to irradiate the whole breast with concomitant boost irradiation of the tumor bed. Doses to whole breast and surgical bed were 40.5 Gy and 48 Gy respectively, delivered in 15 fractions. We introduced the mean heart dose (MHD) < 4 Gy as additional dosimetric goal, in order to minimized the heart dose.

Results: Between August 2010 and August 2014, 450

patients were enrolled. Median age was 60 years old (range 27-88). The median follow-up was 77 months (range 23-116). After 5 years, chronic skin toxicity was G1 in 3.2% and G2 in 1.3% of patients; no G3 or higher toxicities were reported. Cosmetic outcome was good/excellent in 98.4% of patients. Breast pain was declared by 12.7% of patients. After the introduction of the MHD as additional dosimetric goal, the dose to that structure has been reduced: the average MHD was 5.83±1.58 Gy before the amendment, lowered to 4.19±0.97 Gy after the amendment (Figure 1). We reported 2 patients, both treated to the left breast, with ischemic cardiopathy: for one patient it occurred after 3.5 years and the MHD was 5.94 Gy, for another patient at 7 years from treatment and the MHD was 6.75 Gy; in both cases the heart volume receiving more than 18 Gy was less than 0.5%.

Conclusions: Hypofractionated Radiation Therapy with simultaneous integrated boost is a valid option for adjuvant treatment in patients affected early stage breast cancer, assuring low recurrence rates, low toxicity rate and good cosmetic outcome. With the requirement of a MHD < 4 Gy in the optimization of RT plans for protocol patients, the dose received by heart significantly reduced, achieving a better plan optimization.

PO104

A RISK ADAPTED STRATEGY FOR HEART SPARING IMRT IN LEFT SIDE BREAST CANCER

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Aims: Radiation induced heart toxicity in left breast cancer is dependent on mean heart dose (MHD), age and cardiovascular risk factors (CRF). The aim of the present study was to evaluate how MHD reduction obtained by intensity modulated radiotherapy (IMRT) in free breathing (FB) and in deep inspiration breath hold (DIBH) affects the risk of radiation induced cardiotoxicity.

Methods: A preliminary analysis was conducted on 20 consecutive left breast cancer patients. Two IMRT plans, one in FB and one in DIBH, were generated for every patient. MHD obtained in FB-IMRT and in DIBH-IMRT was used on a model to calculate the 10ys-cumulative excess risk due to radiotherapy (10ys-CER). The variation of 10ys-CER were simulated in presence or absence of CRF and at every age between 30 and 79. Results obtained with this preliminary analysis was used to identified patients candidate to FB-IMRT or to DIBH-IMRT. To validate the findings obtained by preliminary analysis, 244 patients with left side breast cancer treated with FB-IMRT or DIBH-IMRT were studied prospectively. For every patient 10ys-CER was calculated and results provided by FB-IMRT and DIBH-IMRT were compared.

Results: Preliminary analysis: in absence of CRF, the mean 10ys-CER ranged between 0.008% an 0.54% in FB-IMRT and between 0.005% and 0.35% in DIBH-IMRT (p=NS). 10ys-CER was below 1% for all patients, both in FB as in DIBH. In presence of CRF the mean 10ys-CER ranged between 0.05% an 3.01% in FB-IMRT and between 0.03% and 2.03% in DIBH-IMRT (p=0.007). Based on this preliminary findings patients with or without CRF were selected for DIBH-IMRT and for FB-IMRT respectively. Validation analysis: 244 patients were divided in 3 groups: patients with CRF treated with DIBH-IMRT (Group A, N°=134), patients with CRF non compliant with DIBH and treated with FB-IMRT (Group B, N°=34) and patients without CRF treated with FB-IMRT (Group C, N°=76). 10ys-CER was higher in Group B compared with Group A (p=0.0027) and Group C (p=0.00024). If a cut-off of 10ys-CER=1% was considered clinically significant, the number of patients that exceed this cut-off were 1%, 47% and 0% for Group A, B an C respectively. Elderly population mainly benefit from DIBH-IMRT. Figure 1 showed 10ys-CER distribution in function of age.

Conclusion: Heart sparing obtained with FB-IMRT is adequate in absence of CRF, while in presence of CRF a DIBH-IMRT technique should be preferred, especially in elderly population.

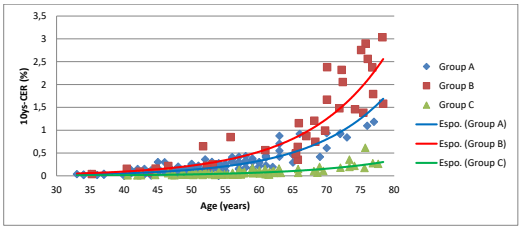

Figure 1: 10ys-CER distribution in function of age for Group A (DIBH-IMRT and cardiovascular risk), Group B (FB-IMRT and cardiovascular risk) and Group C (FB-IMRT, no cardiovascular risk)

Figure 1.

PO105

HALFMOON CONTOURING: CAVEATS AND PITFALLS IN A REAL-LIFE SERIE. THE IEO EXPERIENCE

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Aims: The increasing use of immediate breast reconstruction (IBR) after mastectomy and its interaction with post-mastectomy radiotherapy (PMRT) has become a subject of great interest. In fact, besides the potential impact of RT on the cosmetic results, the reconstructed breast may affect the ideal target coverage and the optimal OARs sparing. The present study aims to report the European Institute if Oncology IRCSS (IEO) experience with implant-sparing RT using the HALFMOON (Helical ALtered Fractionation for iMplant partial OmissiON) technique.

Methods: Halfmoon treatment was delivered using TomoTherapy® Hi-Art System (Tomotherapy Inc., Madison, WI) in helical modality (TomoHelical) at the IEO between January 2020 and May 2021. Contouring was based on ESTRO/ACROP guidelines for PMRT after implant-based IBR. The exclusion criteria were: (i) pT4, (ii) pectoral muscle invasion, (iii) breast recurrence, (iv) atypical reconstruction, (v) presence of a breast cancer gene mutation, (vi) age < 40 years. For the two latter criteria, direct Tomotherapy is preferred over TomoHelical. The adverse tumor factors were: (i) extensive peritumoral vascular invasion (ii) tumors close to the dorsal fascia. The chest wall CTV is composed of ventral part (between the skin and the implant); in case of adverse tumor factors, the partial dorsal part (between the implant and the rib wall) is added to ventral CTV. Dose volume constraints for prostethics-PTV were for D30% < 28 Gy, D50% < 24 Gy, D70% < 20 Gy and Dmean < 25 Gy.

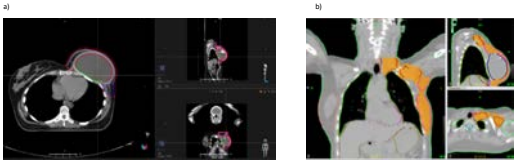

Figure 1. Example of Halfmoon technique: target volumes delineation (a) and dose distribution (b).

Results: A total of 76 patients were considered for Halfmoon treatment. Among those, 22 were excluded; 14/22 (64%) were excluded for anatomy issues (e.g. absence of space between tissue expander and skin), 2/22 (9%) were excluded for a peri-prosthetic fluid collections and 6/22 (27%) for other issues. A total of 18/54 patients underwent primary systemic therapy with 4 pathological complete responses. Tumor stage was: T0 for 4/54 (7%), T1 for 17/54 (32%), T2 for 25/54 (46%), T3 for 8/54 (15%), N0 for 11/54 (20%), N1 for 15/54 (28%), N2 for 15/54 (28%), and N3 for 13/54 (24%). The partial dorsal part was contoured in 15/54 patients, mostly for extended limphovascular invasion (12/15). An example of Halfmoon technique is shown in Figure 1.

Conclusions: From the reported experience implant sparing RT using Halfmoon tecnique is technically feasible and should be administered in carefully selected patients. Data concerning toxicities and oncological outcomes are being retrieved.

PO106

CARDIOLOGICAL MONITORING AND SAFETY OF ULTRA-HYPOFRACTIONATED WHOLE BREAST IRRADIATION AFTER BREAST-CONSERVING SURGERY FOR PATIENTS AFFECTED BY BREAST CANCER: AN OBSERVATIONAL PROSPECTIVE COHORT STUDY (SAFE-FORWARD)

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Background: The recently published FAST-Forward trial showed that, in selected breast cancer (BC) patients, a five-fraction regimen of radiotherapy (RT) delivered in 1 week to the whole breast is non-inferior if compared to a standard 3-week regimen in terms of local control and toxicity at 5 years. An overview of trials from the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) showed that breast RT was associated with an increased risk of heart disease and cardiovascular death. Many of the studies included in this review involved older treatment techniques, which probably delivered a higher dose to the heart. Recently, there has been an effort in developing new techniques in order to minimize the risk of side effects. The introduction of the modern CT-based three-dimensional conformal treatments and breathing-adapted RT represents an innovation in the treatment of BC. Most of the available literature concerning heart toxicity considered normal or moderate hypofractionation schedules. This prospective cohort study aims to assess heart toxicity using a 1-week radiation schedule regimen of 26 Gy in five daily fractions.

Methods: Patient population includes both invasive and ductal carcinoma in situ receiving ultra-hypofractionated whole breast irradiation (26 Gy in 5 fractions) after BCS. Adjuvant endocrine therapy as per local policy is allowed. Main exclusion criteria are mastectomy, chemotherapy, and needs for a tumor bed radiation boost. All patients will be monitored for 12 months, receiving a cardiological assessment before RT (baseline), and at 2-, 6-, and 12-month after RT end. Both acute- and early-late toxicity, will be scored according to EORTC/RTOG and CTCAE (v.5) scales. Patients will undergo six-monthly follow-up clinical visits for the first 5 years and annual follow-up visits thereafter up to 10 years. Breast cosmesis will be evaluated through the BCCT.core tool and

through the EORTC QLQ-C30 and BR45 module questionnaires at baseline, at the end of RT treatment, at 2- and 6-month.

Results: The enrollment started in November 2020. All patients will be treated with ultra-hypofractionated whole breast irradiation (26 Gy in 5 fractions) after breast conserving surgery. Still today the median age is 68 years; all patients are females.

Conclusions: The aim of this observational prospective cohort study is to assess heart toxicity in patients treated with 1-week radiation schedule regimen of 26 Gy in five daily fractions after BCS.

PO107

SURFACE GUIDED ADJUVANT RADIOTHERAPY TATTOO-FREE FOR BREAST CANCER

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Aim: To test inter-fraction and intra-fraction variability of patients' position in women with breast cancer (BC) that received radiation therapy (RT) using a tattoo-free treatment approach guided by a system of Surface Guided RT (SGRT).

Method: Patients with BC received lumpectomy + adjuvant hypofractionated whole breast RT with simultaneous integrated boost on tumor bed for a total dose respectively of 40.5Gy and 48Gy in 15 fractions. During simulation procedures, all patients were immobilized in a supine position and underwent to a planning CT (2 mm slide thickness) without skin tattoo using a system of SGRT (Optical Surface Monitor System AlignRT®) to register and verify patients' position. An expansion of 6mm in the transverse direction and 8mm in cranial–caudal direction was applied from CTV to PTV. The treatment was delivered using an FFF-VMAT technique. For each treatment session, match values of all 3 translational and 3 rotational axes were recorded. To evaluate inter-fraction variability, daily portal images were performed, revising setup treatment position, and acquiring data. To evaluate intra-fraction variations, SGRT was applied, acquiring data regarding final patient's position at the end of RT. Data regarding acute side effects were collected weekly during RT and at the end of treatment according to RTOG radiation morbidity scoring system.

Result: Between 01/2021-04/2021, a total of 375 treatment sessions were analyzed in 25 women. Clinical data were summarized in Table 1. Inter-fraction mean values (±SD) (IC95%) were as follow: longitudinally 2.2mm (±1.6) (2-2.4), laterally 1.4mm (±1.1) (1.2-1.5), vertically 1.8mm (±1.5) (1.6-1,9), roll 0.0° (±0.3) (0.03-0.1), pitch 0.8° (±0.6°) (0.8-0.9), yaw 0.67° (±0.53°) (0.6-0.7). Intra-fraction mean values (±SD) (IC95%) were: longitudinally 0.12mm (±0.11mm) (0.1-0.13), laterally 0.07mm (±0.07mm) (0.06-0.08), vertically 0.12mm (±0.12mm) (0.1-0.13), roll 0.33° (±0.34°) (0.28-0.37), pitch 0.43° (±0.49°) (0.36-0.49), yaw 0.35° (±0.44°) (0.29-0.4). All patients completed their treatment. G0 acute skin toxicity was recorded in 13 (52%) cases and G1 in 12 (48%) cases. No skin toxicity≥2 was observed or other types of side effects.

Conclusion: The analysis shows that the SGRT-guided tattoo-free approach in breast RT is a reproducible and safe treatment suggesting that radiological imaging could be reduced to verify treatment patients' position.

Table 1. Main characteristics of study population.

Total treatment session	375
Total patients	25
Median age (range)	58 years (43-80)
Disease Laterality	
Left Breast	14 (56%)
Right Breast	11 (44%)
Surgery	
Lumpectomy	25 (100%)
Sentinel Lymph node Biopsy	20 (80%)
Axillary dissection	5 (20%)
Disease Stage	
IA-IB	17 (68%)
IIA	3 (12%)
IIB	4 (16%)
IIIA	1 (4%)
Histology	
CDI	16 (64%)
CDI + Cis	5 (20%)
CLI	4 (16%)
Grading	
1-2	17 (68%)
3	8 (32%)
Bio-molecular disease profile	
Luminal A	15 (60%)
Luminal B HER 2-negative	5 (20%)
Luminal B HER 2-positive	3 (12%)
Triple Negative	2 (8%)
Systemic Therapy	
Hormonal Therapy	23 (92%)
Adjuvant Chemotherapy	5 (20%)
Target Therapy	3 (12%)
Radiation Treatment (RT)	
Whole Breast hypofractionated RT	25 (100%)
Simultaneous Integrated Boost	22 (80%)
Whole Breast PTV Volume (range)	700 cc (500-1100)
Boost PTV Volume (range)	60 cc (40-90)
Median overall treatment time	5 minutes (range 3-7 minutes)

PO108

DOSIMETRIC COMPARISON OF DEEP INSPIRATION BREATH HOLD VERSUS FREE BREATHING WITH IMRT TECNIQUE FOR LEFT- SIDED BREAST CANCER AFTER BREAST CONSERVATIVE SURGERY

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Aims: Patients with left- sided breast cancer (LSBC) undergoing adjuvant radiotherapy after conservative surgery (BSC), are at high risk of long term cardiac morbidity, which is correlated with dose to the heart. This study aims to evaluate the potential of DIBH method in the respiratory motion management for these patients; the main goal is to spare the heart, the left anterior descending coronary artery (LAD) and omolateral lung.

Methods: Between January 2020 and February 2021, 24 patients with LSBC after conservative surgery were analyzed retrospectively. Whole breast were irradiated with IMRT technique in DIBH; the respiratory motion management was performed with the AlignRT® technology, a surface guided radiation therapy (SGRT) system, using a 3-mm treatment gate window. During the TC simulation without contrast enhancing, 2 scans are acquired, one in free-breathing (FB) and one in deep inspiration (DIBH) and both are outlined. One plan for each scan was optimized in order to do a dosimetric plan comparison and to have a backup plan in case of patient compliance loss during treatment. Dose prescription was 42,5 Gy in 16 fractions in 5 patients and 50 Gy in 25 fractions in 19 patients. Boost to tumor bed, 10 Gy in 5 fractions was used in 8 patients. We compared dose to the heart, lung, LAD between plans in DIBH and FB.

Results: Compared to FB, DIBH resulted in a significant reduction in mean heart dose (46%), in mean lung dose (22%) and mean LAD dose (31%). We evaluated, in both plans, the distance between organ at risks (OAR)-PTV in cm and we got: heart-PTV was 9,0 cm *vs* 9,9 cm; lung-PTV was 7,6 cm *vs* 8,1 cm; LAD-PTV was 6,1 cm *vs* 7,3 cm. Mean PTV coverage (V95%) was 93,5% in DIBH *vs* 95% in FB.

Conclusions: The use of the DIBH technique in left-sided breast cancer irradiation effectively reduces the radiation doses to the LAD region, heart and lungs, even if the target coverage in DIBH is slightly worse than in FB. This latest result is related to the need for shorter treatment time in DIBH and consequently the choice of simpler beams geometry adopted. The large dose reductions seen in the LAD and HEART could potentially translate into clinical benefit of reduced cardiac toxicity, as these structures have been previously shown to receive the highest doses which are associated with radiation-induced injury.

PO109

THE FAST PROTOCOL IN ADJUVANT BREAST CANCER RADIOTHERAPY: CORRELATION BETWEEN ACUTE SKIN TOXICITY, DOSIMETRIC RESULTS, AND PATIENTS' ANTHROPOMETRIC PARAMETERS

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Aim: Hypofractionated radiotherapy is not widespread, although recent studies have proven its non-inferiority after primary surgery for early-stage breast cancer (BC). This study analysed the preliminary data and factors influencing acute skin toxicity in BC patients, treated according to the radiotherapy FAST protocol.

Methods: Early-BC patients were treated with 28.5 Gy in 5 fractions once a week (FAST protocol) using the 3D-CRT field-in-field (FIF) technique at a single Institution. Clinical target volumes (CTVs), dosimetric parameters, and tumour characteristics were recorded and analysed. The parameters measured to assess the breast size are the cup size, the nipple-to-pectoral muscle distance (NPD), and the maximum medio-lateral thickness (MLT) along tangential fields. Adverse skin reactions were assessed according to CTCAE v. 5.0 at the end of treatment and after one month.

Results: Between December 2020 and May 2021, 21 early-BC patients (median age 67 years, 51–80) were enrolled, of whom 6 underwent forced deep-inspiration breath-hold. 67% of patients had fair skin (skin phototype I/II according to the Fitzpatrick scale). The median CTV volume was 374.5 cm^3 (60.3-684.2) with a median NPD of 4.5 cm (1.7-6.4) and a median MLT of 21.9 cm (14.3-26.6). The 10%, 38%, 29%, and 24% of patients wore an A, B, C, and D bra cup-size, respectively. CTVs registered a median V95% of 99.6% (96.6-100.0) and a median V105% of 0.0% (0.0-4.7). The median 105% isodose was 1.3 cm^3 (0.0-48.0) of whom 0.3 cm^3 (0.0-5.2) in the first centimetre below the skin surface. Lung and heart dose constraints were never exceeded. Only 2 patients, out of 21, showed a grade 1 (G1) erythema and no instance of grade 2 (G2) skin toxicity was documented.

Conclusions: Our findings confirmed the safety of the FAST regimen also in BC patients with fair skin and large breast volume. The use of FIF technique helped in mitigating the acute skin reactions, minimizing the target dose inhomogeneity and hot spots usually associated to a higher risk of acute adverse events and suboptimal final cosmetic outcomes. A longer follow-up and a larger patients' population are required to confirm these results.

PO110

EXPERIENCE OF HYPOFRACTIONATED POST-MASTECTOMY IRRADIATION (PMRT) TO REDUCE WOMEN'S EXPOSURE TO THE VIRUS DURING LOCKDOWN. THE COVID-19 PANDEMIC AND ITS CONSEQUENCES ON RADIOTHERAPY PRACTICE IN THE YEARS 2020 AND 2021

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Aims: In March 2020, with the first lockdown due to the COVID-19 pandemic, the San Giovanni Addolorata Hospital in Rome guaranteed life-saving cancer treatments but, as recommended by scientific societies, introduced unusual hypofractionation schemes even if already described in the literature.

Methods: From March 2020 to May 2021, 29 women with indication for PMRT performed the scheduled hypofractionated therapy with 6MV photons and VMAT technique with a dose of 42.56 Gy in 16 fractions of 2.66 Gy each, both on the chest wall and on the drains lymphatics not removed (III and IV level) and in 1 cases also for bilateral disease (Figure 1). In the presence of polyurethane breast implants, the jokingly called "donut" technique was introduced, with dosimetric saving of the central part of the prosthesis to improve the already low contracture rate of the polyurethane (1).

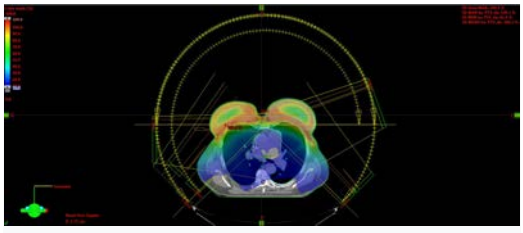

Fig.1 5-arch treatment plan with bilateral prosthetic saving (double donut)

Figure 1.

Results: All women completed PMRT and none developed infection with the SARS-COVID 19 virus, also thanks to the nursing triage done at the entrance to the ward. The techniques used are tomotherapy and the multiple arch VMAT (Rapidarc) after volumetric contouring of targets and organs at risk. To avoid prosthetic contracture and subsequent removal, the donut dosimetric technique made it possible to irradiate the chest wall without involving the central part of the prosthesis in the irradiation. None of the prostheses to date have been removed due to contracture.[1] Most of the patients experienced only itchy skin rash (G1-G2), especially in the reconstructions with larger prostheses. To date, no effects have yet been found on the brachial plexus, as well as on the ipsilateral pulmonary level and on the heart, but a longer follow-up is required.

Conclusions: Hypofractionated PMRT introduced into clinical practice during the COVID-19 pandemic offered mastectomised women the opportunity to dedicate 3 weeks instead of 5 to radiotherapy, quickly returning to normal. The further advantages found are the reduction of the waiting list and health costs. An opportunity has arisen from a global problem such as the pandemic, given the good tolerance also in women undergoing adjuvant and neoadjuvant chemotherapy.

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PO111

NEW FRACTIONATIONS IN BREAST CANCER: VMAT VERSUS 3D-CRT, A DOSIMETRIC STUDY

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Aims: Adjuvant Radiotherapy (RT) following primary surgery in women with early breast cancers (EBC) plays a central role in reducing local recurrences and mortality. The FAST FORWARD trial demonstrated that hypofractionated 1-week adjuvant RT is non-inferior to standard schedule in terms of local relapse, cosmetic outcomes and side-effects. Aim of this in silico study was to evaluate the dosimetric aspects of 1-week RT course, administered with volumetric modulated arc therapy (VMAT) technique, compared to 3D-CRT tangential fields traditional irradiation technique.

Methods: Left side EBC patients undergoing adjuvant RT were selected. 3D-CRT tangential fields and VMAT plans were generated for each patient. ESTRO guidelines for the Clinical Target Volume (CTV) delineation and FAST-Forward protocol for CTV to Planning Target Volume (PTV) margin definition were used. Total prescribed dose was 26 Gy in 5 fractions. The homogeneity index (HI) and the global conformity index (GCI) were used in order to evaluate dose distribution reliability and to perform planning techniques.

Results: The analysis included 21 patients with left EBC treated with adjuvant RT following conservative surgery. PTV coverage comparison between 3D-CRT and

VMAT plans showed significant difference for GCI; no statistically significant differences regarding HI were observed. For organs at risks (OAR), a statistically significant difference was observed in terms of skin V103%, Heart V5% and ipsilateral Lung V30%.

Conclusions: In the frame of 1-week hypofractionated treatment of left EBC, this in silico study showed that both 3D-CRT and VMAT are feasible techniques in terms of dosimetric outcomes.

PO112

HYPOFRACTIONATED WHOLE BREAST RADIOTHERAPY IN LARGE BREAST SIZE PATIENTS: IS REALLY A RESOLVED ISSUE?

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Purpose: The purpose of this study was to evaluate the impact of breast size on acute and late side effects in breast cancer (BC) patients treated with hypofractionated radiotherapy (Hypo-RT).

Materials and Methods: In this study we analyzed patients over 55 years with a diagnosis of early BC, candidate to Hypo-RT after conservative surgery. The treatment consisted in 42.40Gy in 16 Fractions to the whole breast±a boost of 10-16Gy in 4-8 Fractions to the tumor bed. Acute and late skin toxicities were evaluated in accordance with the RTOG scale. Multivariable logistic analysis was performed using dosimetric/anatomical factors resulted associated with toxicity outcome in univariable analysis.

Results: Among patients treated between 2009 and 2015, 425 had at least 5 years of follow-up. At RT end, acute skin toxicity ≥G2 and oedema ≥G2 occurred in 88 (20.7%) and 4 (0.9%) patients, respectively. The multivariable analysis showed association of skin toxicity with boost administration ($p<0.01$), treated skin area receiving more than 20 Gy (TSA) ($p=0.027$) and breast Volume receiving 105% (V105%) of the prescription dose ($p=0.016$), but not breast size. At 5 years after RT, fibrosis ≥G1 occurred in 89 (20.9%) patients; ≥G2 toxicity occurred in 17 (4.0%) patients. Oedema ≥G1 was registered in 36 (8.5%) patients. At a multivariable analysis, fibrosis resulted associated with breast volume≥1000 cm3 ($p=0.04$), breast V105%>450 cm3 and hypertension ($p=0.04$). As for oedema, multivariable logistic was related with hypertension and age's logarithm, but not with boost administration; breast volume had an unclear impact ($p=0.055$).

Conclusions: A recurrent association was found between the acute toxicities and breast V105%, which is correlated with breast size. Late toxicity was associated to breast size and breast V105%, but it is impossible to say which variable is the most prognostic. This may suggest that a more homogenous RT technique may be preferred for patients with larger breast size.

PO113

STEREOTACTIC RADIOSURGERY WITH CYBERKNIFE FOR HER2-BREAST CANCER BRAIN METASTASIS: LOCAL CONTROL AND OVERALL SURVIVAL IN 32 PATIENTS WITH 82 LESIONS

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Aims: Outcomes of patients with HER2-breast cancer brain metastasis (BCBM) remain suboptimal. To evaluate the effectiveness of local therapy (stereotactic radiosurgery [SRS]) we analyzed local control (LC), distant intra-cranial control (DBC) and overall survival (OS) in patients with metachronous HER2-BCBM.

Methods: Data of consecutive patients who underwent SRS with CyberKnife (Accuray, USA) from February 2012 to November 2020 were retrospectively analysed. Parameters included demographics, histology and primary tumour characteristics, presence and control of extracranial disease, number of lesions, single and total gross target volume (GTV). Preliminary results of OS, LC and DBC at the last follow up were evaluated. This retrospective study was notified to our Ethical Committee (IEO N93/11).

Results: Thirty-two consecutive patients for a total of 82 metachronous HER2- BCBM treated with CyberKnife were included in this preliminary analysis. Median follow up from primary surgery and SRS was 113 months (range 42-241) and 17 months (range 0-101). Median time to brain-progression from initial diagnosis of breast cancer was 78 months (range: 15-215) with 17/32 (53%) patients with both cranial and controlled-extracranial disease at the time of of SRS. Patients were treated for all brain lesions they presented, with a median of 2 lesions for each patient (range, 1- 9). Total median SRS dose was 21 Gy (range, 18-24 Gy) given in 1 to 3 fractions, in alter-

nate days. Median single lesion GTV was 0.29 cm3 (range, 0.02-13.22). At the last follow up available, 17/32 patients were alive (OS=53%; 16 patients with both cranial and extracranial disease). LC was reported in 56 of the 82 treated lesions (68%; 1 and 3-years LC : 65% and 45%, respectively-Figure 1), while DBC (no appearance of any new intracranial lesions) was observed in 10/32 patients (31%). Univariate and multivariate analysis for correlation with demographics, tumour and treatment characteristics are ongoing. No patients experienced severe neurotoxicity (Grade 4-5 in the Common Terminology Criteria for Adverse Events) with only 5 asymptomatic radionecrosis recorded.

Conclusions: Our results showed OS in line with literature and a satisfactory 1 and 3-years LC rates with almost one third of our patients alive with no appearance of any new intracranial lesions after SRS and no severe neurotoxicity in the entire population. Ongoing-statistically analysis are needed to correlate outcome with prognostic factors.

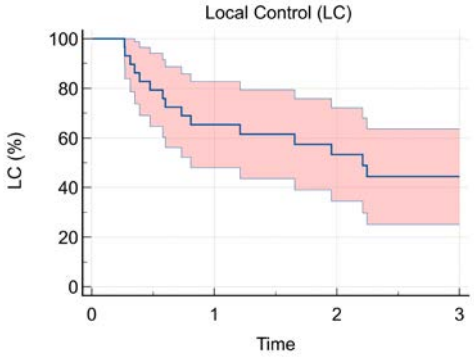

Figure 1.

PO114

ACUTE TOXICITY OF HYPOFRACTIONATED LOCOREGIONAL RADIOTHERAPY IN ADVANCED BREAST CANCER

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Aim: Hypofractionated whole breast radiotherapy is becoming the standard after conservative surgery for breast cancer (BCa), but the interest in hypofractionation is growing even for locoregional treatments, involving not only breast/chest wall, but also lymph nodal (LN) areas. We report acute toxicity in patients with advanced BCa treated with hypofractionated radiotherapy (HRT) to breast/chest wall and regional LN in our Institute.

Methods: From 03/2018 to 05/2021 131 advanced BCa pts (98% female, 2% male) underwent locoregional HRT after conservative surgery (58%) or mastectomy (40.5%), and 3 pts received radical RT (1.5%). Two pts had bilateral BCa (133 irradiated breasts). Median age was 52 (26-86) years. Molecular subtypes were: Luminal A 29%, Luminal B Her2- 28.5%, Luminal B Her+ 19%, HR negative Her2+ 13% and Triple negative 10.5%. Neoadjuvant chemotherapy was prescribed in 55% of pts, adjuvant in 55%, and concomitant in 11%. Adjuvant hormonal therapy was prescribed in 76% of pts (IA or TMX -/+ LH-RH analogue). Thirty-three% of pts underwent HER2-targeted therapy. Treatments were delivered with 3DCRT (11%), VMAT (30%) or Tomotherapy (59%, TomoDirect or TomoHelical), to a total dose of 40.05 Gy in 15 fractions, delivered in 3 weeks, to breast/chest wall and regional LNs. A simultaneous integrated boost (SIB) up to 48 Gy to the tumor bed was delivered for pts with high-risk local relapse. The target was: whole breast in 60% (46% right, 54% left), chest wall in 40% (40% right, 60% left), supraclavicular LN in 100%, axillary LN in 34.4%, and internal mammary chain in 13.5% of cases, respectively. A SIB to the tumor bed was delivered in 34.5% of pts. Acute toxicity was registered according to CTCAE v 4.0.

Results: Acute toxicity is summarized in table 1. No patient experienced ≥G3 acute toxicity. No significant differences in toxicity were found between the different RT techniques. G2 skin toxicity was experienced in 13% of pts with SIB and 8% without SIB.

Conclusions: Locoregional HRT is feasible with low acute toxicity, without significant differences between the different RT techniques. Longer follow-up is needed to evaluate late toxicity and local control.

Table 1.

Toxicity	G0			G1			G2		
	3DCRT	VMAT	Tomo	3DCRT	VMAT	Tomo	3DCRT	VMAT	Tomo
Breast/chest wall erythema	14%	8%	19%	73%	82%	71%	13%	10%	9%
Axillary/supra-clavicular erythema	28%	20%	41%	66%	75%	40%	6%	5%	7%
Dysphagia	28%	30%	31%	66%	50%	54%	6%	20%	15%

PO115

ULTRAHYPOFRACTIONATED RADIOTHERAPY, IN BREAST CANCER, IN THE COVID-19 ERA

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Aim: To reduce treatment time in patients with early

breast cancer in recent COVID-19 pandemic period. Radiation oncology's community suggested to minimize hospital access in order to guarantee treatment, reducing the risks related to the pandemic.

Materials and Methods: From June 2020 to July 2021, we recruited 23 women ≥60 years old, with early stage breast carcinoma, undergoing subjectedbreast-conserving surgery (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 end esthetic outcomes. Secondary end points were impact on quality of life 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 toxicity was assessed with the RTOG score. In order to evaluate esthetic outcomes, two photos were taken for each patient, (antero lateral and antero medial), at the beginning, at the end of the tratment, and then at 3, 6 and 9 months follow up.

Results: We enrolled 23 patients with mean age of 76 years (range 66-84). The median follow-up was 6 months (range 0-9). Skin erythema and edema were the most common acute adverse events. With the limit of the short follow-up, no one developed recurrence and not significant esthetic changes were found. Acute toxicity evaluated was not greater than G2, with 20 patients (86,9%) with G0-1. The most frequent adverse event was fibrosis, which in 2 cases (8.6%) was associated with low breast shrinkage. Only 1 patient (4.3%) had a 9-month follow-up and presented a G1 toxicity (slight fibrosis). All patients had a high level of satisfaction and among all patients, who reported acute or chronic tossicity, only 2 (8.6%) had a low impact on QoL. The ultrahypofractionated regimen reduces treatment sessions by 66.6% compared to the standard hypofractionated treatment, with an obvious impact on waiting time list. Furthermore, in this period, the risks of spreading COVID-19 it is also reduced.

Conclusions: Once□weekly hypofractionated radiotherapy is a feasible and well tollerated alternative for early breast cancer adjuvant management with low acute toxicity and accetable cosmetic outcomes, reducing the risks of spreading COVID-19 and waiting time list.

PO116

CLINICAL AND TECHNICAL PROTOCOL OF ACCELERATED PARTIAL BREAST IRRADIATION SHARED BY THE INTERDISCIPLINARY GROUP OF ONCOLOGICAL CARE OF AN EUSOMA BREAST CENTER

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Aims: Several studies investigated radiotherapy accelerated partial breast irradiation (APBI) instead of whole breast radiotherapy (RT), after conservative surgery for low-risk breast cancer (BC). ASTRO recommendations suggest APBI suitability in selected patients: age>50 years, T1 or Tis, G1-G2, size ≤2,5 cm, negative margins. We describe our internal clinical and technical protocol of APBI supported by the multidisciplinary team of our Breast Center.

Methods: APBI protocol was drafted by radiation oncologists dedicated to BC of our center and then approved by Interdisciplinary Group of Oncological Care (GICO) of the EUSOMA Breast Center. Each specialist provides its contribution by suggesting the best management within his discipline for the senological path of patients suitable of APBI. At the end of this process the protocol was validated and published in local and regional official institutional documents.

Table 1. Inclusion and exclusion criteria.

INCLUSION CRITERIA	EXCLUSION CRITERIA
Age ≥70 years	Age < 70 years
Invasive ductal carcinoma	invasive lobular carcinoma, carcinoma in situ
pT1	pT>1
cN0 and pN0	N+
Conservative surgery	Oncoplastic surgery
Luminal A-like	Luminal B-like and/or Her2-overexpressing
Surgical margins negative	Surgical margins positive
Unifocal presentation	Multifocal presentation
BRCA negative	BRCA positive
Absence of lymphovascular invasion	Presence of lymphovascular invasion
Any tumor grade if pT< 10 mm, Low-intermediate Grade for pT>11mm and <20 mm	High grade for pT>11 mm
Absence of metastasis	Clinical evidence of metastasis at baseline
No Neoadjuvant systemic therapy	Neoadjuvant systemic therapy
Informed consent	Clinical and/or technical contraindications to RT

Results: Patients potentially eligible for APBI should be identified during pre-surgical multidisciplinary meeting (MDM) according to age, clinical-radiological presentation, histotype and immunohistochemistry. Inclusion and exclusion criteria are reported in table 1. Radiologist supplies morphological concerns regarding unifocal presentation and surgical bed, implying eventual magnetic resonance upon completion of diagnostic iter. During surgery tumor bed is defined by 4-6 clips. Eligibility of patients is confirmed on the basis of definitive histologic report during post-operative MDM. Feasibility of APBI is confirmed during the initial RT consultation. Clinical tar-

get volume (CTV) should comprehend surgical scar, whole visible surgical bed bounded by surgical clips, with regards to pre-operative imaging. Planning Target Volume is obtained by isotropic expansion of 1 cm of CTV. Organs at risk and dose constraints follow the current scientific literature. RT techniques adopted are 3D conformal or intensity modulated; schedules preferred are 30 Gy (5 Gy/daily or on alternate days), 27 Gy (5,4 Gy/daily), 38,5 Gy (3,85 Gy/ daily).

Conclusions: APBI is supported by robust evidence showing no difference in local recurrence or overall survival. It is a treatment approach able not only to shorten course of RT, but also to reduce the irradiation of organs at risk. The elaboration of clinical and technical protocols on modern techniques such as APBI determines an impact in terms of quality assurance and behavioral uniformity in clinical practice.

PO117

PATTERN OF LOCAL RECURRENCE ACROSS THE MOLECULAR SUBTYPES AFTER HYPOFRACTIONATED RADIOTHERAPY FOR BREAST CANCER

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Aim: To evaluate the impact of molecular subtypes on outcome in a series of breast cancer (BC) patients treated with hypofractionated whole breast irradiation (HWBI) and intraoperative electron boost.

Methods and Materials: Women aged≤ 48 with pt1-2N0-1 BC who received 12- Gy IOERT boost followed by 3-dimensional conformal HWBI in 13 fractions (2.85 Gy/die) were categorized by molecular subtypes. Local relapses (LR) and survival (disease-free, DFS; specific, BCSS; overall, OS) were analyzed.

Results: 518 consecutive BC patients (median age 43) were treated between 2004 and 2014. The classification of molecular subtypes BC were as follows: 42% Luminal A, 31.5% Luminal B HER2 -, 11.2% Luminal B HER2+, 2.3% negative hormonal receptors HER2+, 13% Triple Negative. Younger women (<40 years) were less likely to have Luminal A tumors. Systemic treatments consisted in endocrinotherapy (HT) in 61%, chemotherapy (CT) in 13.6%, combined CT-HT in 23% (2.4% refusal or data missing). Trastuzumab was given to 55/71 HER2+ patients. Ten-year LR cumulative incidence was 3.4% (95%CI, 2.0-5.3) (21 lrs, of which 8 "true"). At 10 years, the incidence of LR was 3.8% for Luminal A, 2.5% for Luminal B HER 2-, 1.7% for Luminal B HER2+, 18.8% for negative hormonal receptors HER2+ and 1.5% for Triple Negative. At univariate analysis, molecular subtypes was not a predictor for LR. Over time, local control rate decreased for Luminal A and for negative hormonal receptors HER2+, while remained steady for Triple Negative. At 10 years, OS and BCCS were higher for Luminal A (more than 98%) and statistically significantly decreased from Luminal B HER2+ (around 96%) to Triple Negative and negative hormonal receptors HER2+ (around 92%). The 10-year DFS was the lowest (70%) for Luminal B HER2- negative group, which was affected the most by distant metastases (DM), and the highest for Luminal B HER2+ group (12% at 10 years, p <0.001). Over time, the largest increment of DM occurred in Luminal A tumors, where the incidence increased from 0.9% at 5 years to 3.7% at 10 years. The occurrence of DM for Triple Negative and HER2+ remained steady through 5 to 10 years (8.3% and 6%, respectively).

Conclusions: No impact of molecular subtypes on local control was observed. HWBI proved to be effective in achieving a good local control which was comparable and lower than that reported by the landmark trials.

PO118

DOSE REDUCTION TO NORMAL TISSUES (NT) WITH HALFMOON TECNIQUE (HT) IN BREAST CANCER (BC) IRRADIATION AFTER POSTMASTECTOMY IMPLANT RECONSTRUCTION (PIR)

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Aim: HT is a technique for BC irradiation after PIR and has been developed in order to avoid implant irradiation preserving coverage of clinical target volume(CTV)and maintainig low doses to NT. Aim of this study is to evaluate HT plans in terms of implant dose and NT exposure.

Materials and Methods: Between December 2020 and June 2021,10 pts with retropectoral PIR were treated in our Centre, with 50 Gy to chest wall(CW) with intensity modulated treatment (IMRT) and 46 Gy to regional nodes with 3 D CRT.Computed tomography scan in a supin position with 3 mm slices thickness was performed. Recently,the European Society of Radiation Oncology and Advisory Committee Practice(ESTRO-ACROP) introduced new guidelines for CTV delineation after IR. The committee recommended CTV delineation for the CW after pre and retro pectoral implantation. Our CTV

involved skin, subcutaneous tissues and pectoralis major muscle, excluding the implant, CW and rib plane. Organ at risk contoured were the controlateral breast(CB), left anterior coronary artery(LDCA),heart, thyroid, esophagus, spinal cord, ipsilateral lung(IL),controlateral lung(CL) and implant.The planning target volume(PTV) was CTV+3mm and included the skin.

Results: All HT plans were generated using 6MV photons and were normalized so that at least 95% of CTV received 95% of the prescribed dose. The maximum dose(MD) to any point was limited to 107%. NT constrains were as follows: mean dose(mD) to implant<8Gy, MD and mD of the CB were<5 and 2Gy, respectively; heart mD<5Gy; MD and mD of LDCA<12Gy and 5Gy; IL volume receiving 10 and 20Gy were limited to 35% and 20%,respectively; mD of CL<2-3Gy; esophagus MD<50Gy and thyroid mD<20Gy. All pts were regularly followed by the physician once a week. The potential complications associated with this treatment include acute toxicity(AT), such as radiodermitis (RD) and chronic toxicity (CT), such as fibrosis/contracture of the implant. RD grade 1 was identified in 4/10 pts. The site of most desquamation was frequently observed in anterior axillary fold. Dysphagia moderate grade 1-2 was identified in 2/10 pts. All AT were graded according to the Common terminology of Criteria for adverse effects(CTCAEv4.0). No pts developed severe RD or subacute fibrosis/contracture of the implant.

Conclusion.HT in PIR significantly reduced dose to implant and was well tolerated. Long term follow up with larger number of pts are needed to wide implementation of this technique.

PO119

VMAT BOOST IN HYBRID PLAN WITH TANGENTIAL BEAMS FOR WHOLE BREAST TREATMENT: A DOSIMETRIC STUDY

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Aim: Whole breast radiation therapy (WBRT) with a boost to the tumor bed following conservative primary surgery in women with breast cancer (BC) plays a central role in reducing local recurrences and mortality. Volumetric modulated arc therapy (VMAT) technique has been shown to allow better dose conformation with low dose levels to organs at risk (OARs), compared to static fields three dimensional Conformal Radiotherapy (3D-CRT). Aim of this study was to evaluate the feasibility and dosimetric advantages of sequential boost (SB), administered with VMAT technique in hybrid plans with tangential beams for whole breast treatment.

Methods: BC patients undergoing adjuvant RT from June to October 2020 were selected. ESTRO guidelines for the Clinical Target Volume (CTV) delineation were used. Total delivered dose was 60-66 Gy; 50 Gy in 2 Gy daily fractions for whole breast and 10-16 in 2 Gy daily fractions Gy to tumor bed was 10-16 Gy in 2 Gy daily fractions.

Results: The analysis included 31 patients with BC treated with adjuvant RT following conservative surgery. Hybrid treatment plans characterized by a 3D-CRT plan using tangential mediolateral and lateromedial fields for the irradiation of the whole breast Planning Target Volume (PTV) and a sequential VMAT plan with 2 coplanar arches for boost PTV irradiation were generated. As regarding to organs at risks (OARs), contralateral breast, ipsi- and contro-lateral lung and heart costraints values were analysed.

Conclusions: In the frame BC RT, this dosimetric study showed that hybrid plans performed with 3D-CRT and VMAT techniques are feasible in terms of dosimetric outcomes.

PO120

PEMPHIGOID AND RADIOTHERAPY: CASE REPORT AND LITERATURE REVIEW UPDATE

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Aim: Bullous pemphigoid (BP) is a common autoimmune bullous disease generally occurring in elderly patients. Itchy and tense blisters on normal skin or erythematous and edematous lesions on the trunk and extremities usually characterize BP. Trigger factors are still unclear while several case reports suggest a potential role of radiotherapy (RT) as BP trigger for disease onset or recrudescence. A review was performed in order to provide an update of literature. A case report of a patient affected by BP undergoing two radiotherapy courses for a primary breast cancer was also reported.

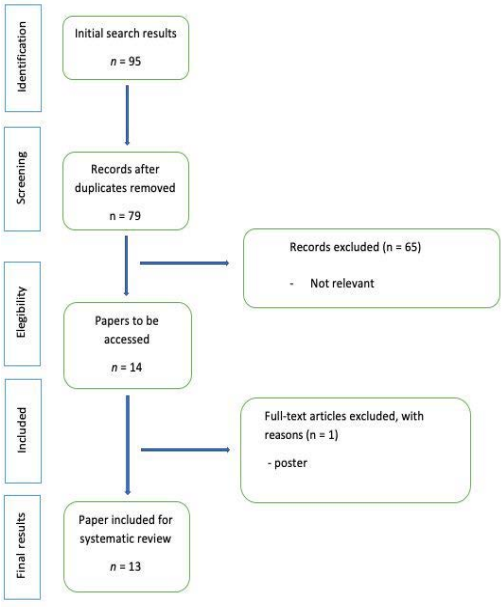
Methods: A comprehensive review of the published literature was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The review included studies describing BP and its relationships with RT treatments.

Results: A total of 13 articles were reviewed. Studies characteristics analysis resulted in eleven case reports, one case series and one large-scale case–control study.

Conclusions: Literature update confirms the exis-

tence of a reasonable connection between RT and BP. Case report showed that a multidisciplinary management seems to assure the feasibility of RT in patients affected by BP, not depriving them of standard therapeutic opportunities.

Table 1. Inclusion and exclusion criteria.



PO121

EXPERIENCE ON USE OF SURFACE-GUIDED RADIOTHERAPY FOR BREAST CANCER PATIENTS SET UP

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Aims: Surface-guided radiotherapy(SGRT) is a valid technique to add precision and accuracy to radiotherapy. Commonly breast cancer positioning is a Laser Based Set up (LBS) PortalVision (PV)-verified; in this study we present data about LBS compared to LBS plus Surface Based Set up (SBS) using AlignRT System (Vision RT, London, UK), verified by PV as well, in our small patients (pts) cohort.

Methods: From June to November 2020, 23 pts affected by breast cancer receiving hypofractionated radiotherapy, were selected for a mixed set up protocol (MSP) of LBS+SBS based on:

- Manual alignment driven by tattoos
- Shifts according to treatment plan
- Shifts adjustments driven by SBS and residual shifts (Δ) registration
- PV acquisition for first 3 RT-days

In case of shifts agreement between SBS and PV:

- Calculation and application of SBS average shifts, PV acquisition, capture of new reference surface on 4th RT day
- Daily SBS using the new reference surface, PV confirm just for shift > 3mm
- PV at 7th and 11th RT day's

In case of persistent disagree between SBS and PV, from 4th day, pts shifted to standard LBS extended no action level (ENAL) protocol (PV at 9th RT day). First three days of protocols were overlapping. 13/23 pts followed the MSP, 10 pts were shifted to LBS ENAL protocol. We analyzed the data of these 13 pts and compared them with other 13 pts, with the same tumor characteristics treated with the LBS ENAL protocol. Data on 3dimensional shifts (vertical, longitudinal, lateral) of each pts were registered; for MSP we recorded SBS PV-verified shifts, daily SBS shifts, eventual Δ after SBS; for ENAL protocol LBS PV-verified shifts were included. The vector offset (VO) as Δvert2+Δlong2+Δlat2 of both protocols was evaluated.

Results: The mean and median VO were 3.8 mm and 4.3 mm (range 1.9-5.5mm) for SBS and 3.6mm and 4.2 mm (range 0-5.4 mm) for LBS, difference was not statistically significant; instead the residual SBS VO was 1.5mm, significant when compared with LBS shifts ($p<0.01$). The cumulative probability to positioning pts within 5mm from isocenter is equal for LBS as for SBS (80%) but the probability to positioning pts within 3.6mm from isocenter increases to 99.5% in case of SBS use.

Conclusions: For selected pts daily SBS improves set up RT precision without additional dose adding daily set up control. SBS shows significative PV-shifts decrease ($p<0.01$) when used for fine isocenter positioning, permitting reduction of PV and RT dose.

PO122

DOSIMETRICAL COMPARISON BETWEEN DEEP INSPIRATION BREATH HOLD AND FREE BREATHING TECHNIQUE RADIOTHERAPY IN LEFT BREAST CANCER PATIENTS

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Aims: Adjuvant radiotherapy (RT) after breast-conserving surgery (BCS) for breast cancer (BC) is a standard treatment. The adoption of Deep inspiration breath hold (DIBH) technique increased in the last years, especially to treat patients (pts) on the left side. This modality decreases cardiac structures dose, especially to radio-sensitive structures like the left anterior descending artery (LAD) where any additional dose increases the risk of coronary artery disease and risk of ischemic heart disease. The aim of this study was to evaluate the reduction of dose to heart, LAD and ipsilateral lung (IPSL) between DIBH and free breathing (FB) techniques in left breast irradiation.

Methods: We enrolled twentyfour pts with diagnosis of left BC in our institutional DIBH protocol. Treatment schedules were 50 Gy in 25 fractions (conventional schedule) or 40.05 Gy in 15 fractions (hypofractionated schedule), with or without sequential boost to tumor bed. The patients were monitored by a respiratory gating system. We compared dose to the heart, LAD and ipsilateral lung (IL) between plans in DIBH and FB using standard defined parameters: mean dose (Dmean) to the heart and heart volume receiving < 13 Gy (V13); mean dose to IL and IL volume receiving < 20 (V20); mean dose to LAD.

Results: DIBH was associated with a significant reduction in all studied parameters for the heart, the LAD and the IPLS maintaining an equal coverage of planning target volume (PTV). The median heart V13 was 2,83Gy in DIBH and 2,94 Gy in FB. All pts treated with DIBH reported a reduction in mean dose to the heart of about 33%. All pts treated with DIBH reported a reduction to the LAD in mean dose of about 30%. The average Dmean reported to IL and the average IL (V20) between DIBH and FB was similar. DIBH was associated with a reduction in all studied parameters for the heart, the LAD and the IPLS

Conclusions: DIBH technique could be easily incorporated into daily routine permitting dose reduction to the heart, the LAD and IPLS in left breast cancer irradiated patients.

PO123

HYPOFRACTIONATED RADIATION THERAPY IN PATIENTS WITH A LEFT BREAST CANCER USING THE DEEP INSPIRATION BREATH-HOLD (DIBH) TECHNIQUE: UN UPDATE

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Aims: An increased risk of potential adverse cardiovascular injury has been associated with adjuvant radiotherapy for patients with left-sided (pts) breast cancer. Thanks to the DIBH technique, delayed cardiac toxicity is minimized. Our aim is to update and analyze the case histories of patients treated with the "CatalystTM / SentinelTM system" (C-RAD AB, Uppsala, Sweden) and the hypofractionated intensity-modulated radiotherapy.

Methods: Between May 2019 and May 2021, eighty-seven patients were treated with adjuvant radiotherapy for the left breast cancer staged as T1 or T2 N0 M0. The mean age was 52 (ranging from 39 to 68). All pts underwent a breath control assessment and 90.8% met the DIBH criteria (BH capacity for 30 s). Excluded patients received hypofractionated treatment with free breathing technique (FB). The treatment involved a dose of 40.05 Gy / 15 fractions in 79 patients and 42.5 Gy / 16 fractions in 8 patients. In 38 pts a boost of 8.01 Gy / 2.67 fractions was delivered. We have analyzed retrospectively the mean and the maximum dose to the heart (MHD), the mean homolateral lung dose, contralateral breast and planning target volume coverage.

Results: The mean and the maximum dose to the heart (MHD) were 0.71 Gy (0.48-0.94) and 19.75 Gy (15.1-24.4) respectively; the mean ipsilateral lung dose was 4.3 Gy (3.4-5.2 Gy) and V20< 10.8 Gy (9.34-12.15). The maximum heart distance to the anterior cardiac contour crossing over the posterior edge of the tangential fields was 1.34 cm (0.94-1.74). The mean PTV coverage of the 95% of the prescribed dose were 97.2% (96.7-97.8%).

Conclusions: DIBH and hypofractionated IMRT is an increasingly consolidated treatment in clinical practice, feasible and safe in terms of target coverage and toxicity, as well as enthusiastically accepted by patients (pts).

PO124

SYNCHRONOUS BILATERAL BREAST CANCER IRRADIATION USING VMAT WITH A SINGLE ISOCENTER: A DOSIMETRIC EVALUATION

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Aims: Radiotherapy for synchronous bilateral breast cancer (SBBC) is still challenging due to many issues among which the lack of standard guidelines, large target volumes treated and, overall, the necessity of limiting doses to heart and lungs. 3D-CRT suffer from several limitations when applied to SBBC, while volumetric-modulated arc therapy (VMAT), using different plan settings, has been applied with good results. Aim of this study was a dosimetric evaluation of SBBC irradiation using VMAT with a single isocenter.

Methods: This study included 10 patients with SBBC. The clinical target volume (CTV) was contoured accord-

ing to the Radiation Therapy Oncology Group contouring atlas group. Treatment planning was obtained with VMAT, single isocenter, two pairs of partial arcs (each associated to a single breast) and optimized with 2.5 cm skin flash. The prescribed dose was 50 Gy at 2 Gy per fraction to the CTVs and the primary aim in RT planning was to deliver at least 95% of the prescribed dose in 95% of the CTV. Quantec constraints and recent studies published in literature were considered to evaluate the dose distribution to Organs at Risk (OARS): lungs, heart, and left anterior descending artery (LAD). Plans were evaluated by dose-volume histogram (DVH) analysis. For all patients, Conformity Index (CI) and Homogeneity Index (HI) were calculated according to literature. Mean percentage target coverage and mean OAR doses across patients were evaluated.

Results: By means of SBBC irradiation using VMAT with a single isocenter we obtained the following results (mean±SD): dose to CTV was 50.2±0.3 Gy, V95% was 98.2±0.2 and V105% was 1±0.9. For target volume CI was 0.98±0.09 and HI was 0.01±0.02. For left lung Dmean was 6.72±0.9 Gy and V20, V10, V5 were 8.93±2.4%, 17.90±3.1%, 33.99±6.5%, respectively. For Lung Right Dmean was 7.74±1 Gy, and V20, V10, V5 were 11.03±2.7%, 20.88±2.6%, 38.42±5.2%, respectively. The average dose to heart was 4.16±0.8 Gy and V25 was 0.08±0.02%. For ADA the average dose was 7.32±1.4 Gy while dose max 14.2±2.4 Gy.

Conclusion: In conclusion, for SBBC, the use of VMAT with a single isocenter provided excellent results improving target coverage and limiting cardiopulmonary exposure. Moreover, in our study V105% to target is relatively low.

PO125

ANALYSIS OF PROGNOSTICS FACTORS IN RECURRENT BREAST CANCER: OUR EXPERIENCE AT TOR VERGATA UNIVERSITY

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Aims: In this observative retrospective study we aimed to evaluate the role of prognostic factors in women with local recurrence of breast cancer.

Methods: Patients with histologically confirmed recurrent breast cancer (BC) have been evaluated. Mean time and anatomic zone of local recurrence were recorded and evaluated along with the principal prognostic factors like the molecular profile, the dose distribution of first treatment, and systemic therapy.

Results: From December 2000 to February 2021 16 women with recurrent BC and median age of 66 years were observed and treated at our institution. Among these 16 patients, 5 were Luminal like A (31%), 4 Luminal like B (25%), 3 triple negative (19%) and 4 HER 2 + (25%). Nine patients (56%) had infiltrating ductal carcinoma (CDI), 3 (19%) infiltrating lobular carcinoma (CLI) and 4 (25%) ductal carcinoma in situ (CDIS.) Grade 4 was recorded in 4 pts (25%), G2 in 5 pts (31%), G1 in 2 pts (12%). For 5 it was not possible to determine the grading (31%). All pts received adjuvant RT at first diagnosis: 11 pts hypofractionated RT (69%), and 3 pts received also a tumor bed boost (19%). Fourteen patients underwent breast conservative surgery (BCS) (87%), 2 mastectomy (13%); 4 were treated with neoadjuvant CHT (25%) and 8 with CHT adjuvant (50%). The mean time to local recurrence was 6 years, but patients with the worst prognostic molecular profile (HER 2+ and Triple negative) relapsed earlier (mean time to relapse 3 y) compared to luminal one's (mean time to relapse 6 y). All patients had local recurrence in the same quadrant of the previous tumor, and 2 (13%) presented with skin involvement too. Previous treatment plan demonstrated optimal coverage of the PTV dose (95-105%). Finally, 14 women (87%) relapsed with the same molecular profile, 2 pts (13%) developed a tumor with poorer prognosis immunohistochemistry.

Conclusions: This cohort confirmed the results that immunohistochemical profiles with poor prognosis such as HER 2+ and triple neg recur in less time and with more aggressive clinical presentation. Despite the adequate coverage of the target, the time to relapse is influenced by the molecular pattern.

PO126

RE-IRRADIATION OF NODAL RECURRENCE IN BREAST CANCER WITH HELICAL TOMOTHERAPY OR VMAT: WHICH ONE OF THESE DOES MAKE THE DIFFERENCE?

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Aim: Helical Tomotherapy (HT) and VMAT are two techniques suitable to re-irradiate breast cancer (BC) recurrences. Herein we report a comparison of these two techniques in three reirradiation scenarios for nodal BC recurrences after whole breast 3D postoperative RT

Methods: Treatment planning was performed with matching of simulation CT with previous RT treatment CT plan to assess dose to ipsilateral lung (iL), heart (H) as organs at risk (OAR's). Plans with HT and VMAT were carried out with TPS (Raystation® v10A) and then compared in terms of PTVs coverage, dose to OAR's and delivery time (DT). Patient (pt) A relapsed in right supraclavicular nodes and axillary III level. Pt B relapsed in the

irradiated 50 Gy left breast and axilla. She underwent salvage mastectomy and nodal dissection. Pt C had a massive nodal recurrence in the right supraclavicular fossa and whole axilla. In all 3 cases IMRT–SIB in 25-30 fractions (frs) was prescribed not overpassing a cumulative dose of 100- 110 Gy on the irradiated sites. CTVs1 included the primary sites of recurrence and prophylactic nodal areas. The Prescription Dose (PD) was 45 Gy-54 Gy in 1.8 Gy/2 Gy/frs. CTVs 2 consisted of the positive nodes on CT/PET receiving a boost of 63 Gy, 2.10 Gy/frs. In HT plans a directional blocking dictates were given to respect OAR's already irradiated. In VMAT dual arches irradiation were applied.

Results: Target volume coverage was defined as the volume of PTV receiving at least 98% (V98) and 107% (V107) of the PD. In pt A, for HT and VMAT plans V98 was 98% and 100% respectively. V107 was 0% in both cases. For iL, V5, V10 were similar (17.8% *vs* 18%; 14% *vs* 12%). MLD was 4 Gy *vs* 12 Gy. For heart, MHD was 22 cGy *vs* 8 cGy. DT was 148 sec. *vs* 120 sec. In pt B, PTVs V98, V107 values were similar (100% *vs* 99%;0% in both). For iL, V5, V10 and MLD were 56%, 27%, 9 Gy *vs* 67%, 47% and 14 Gy respectively. For MHD a dose of 4.6 Gy *vs* 4.1 Gy was found. DT was 561 sec *vs* 150 sec. In pt C, PTVs V98 of 99.5% was found in both cases; the mean V107 nearly 0% in both. For iL, V5, V10 and MLD values of 37%, 32%, 9,5 Gy *vs* 35%, 32% and 9,5 Gy were observed. MHD was 3.3 Gy *vs* 3.2 Gy. DT was 181 sec *vs* 140 sec. No statistically significant differences were recorded (p=0.022) in PTVs coverage and OAR's dose constraints.

Conclusions: Re-irradiation for nodal recurrent breast cancer is feasible as in HT as in VMAT: no substantial differences have been found. Delivery time could make the difference.

PO127

LOCALLY ADVANCED BREAST CANCER: VMAT TECHNIQUE ON THE CLAVICULAR REGION

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Aims: The purpose of the study was to evaluate the acute side effects of skin, the cosmetic results and disease control in patients, with locally advanced breast cancer, who received adjuvant radiotherapy on the breast or chest wall and on the clavicular lymph nodes.

Methods: By October 2018 to April 2021, in our center, were treated 38 women with locally advanced breast cancer. 20 patients underwent conservative surgery, 18 underwent mastectomy and all patients underwent axillary dissection. The median age was 56 (range 29-88). 30 patients were treated with field in field step and shoot technique on the breast or chest wall, 8 were treated with VMAT technique on the breast or chest wall. All women were treated with VMAT technique on the clavicular region. On the clavicular region the total radiotherapy dose was 50 Gy whit 2 Gy fraction dose. On the breast or chest wall the total radiotherapy dose was 50 Gy whit 2 Gy fraction dose. On the breast the integrated or concomitant boost was 0.33 Gy for fraction. 95% of the target dose was contained in 95% of the volume and all organ dose constraints have been respected.

Results: All women completed radiotherapy. 31 patients (82%) presented acute toxicity of skin of grade 1, mild erythema was observed in 26 patient and dry flaking was observed in 5 patient. 5 patients (13%) presented acute toxicity of skin of grade 2, moderate erythema was observed in 4 patients and wet flaking was observed in 1 patient. In a 12.7 months average (range 2-25) follow-up was observed in 2 patients (5%) distant recurrence and no local disease was observed in any patient. 4 patients (10%) presented loss of skin elasticity.

Conclusions: In our study the VMAT technique, in particular on the clavicular region, allowed not to have high degrees of acute skin toxicity. The low degree of skin toxicity allowed a satisfactory cosmetic result. The radiotherapy, on the clavicular region, whit VMAT technique has been proved to be an appropriate treatment choose for control disease. However a longer follow-up and a larger number of patients are needed to confirm these results.

PO128

1-WEEK HYPOFRACTIONATED ADJUVANT WHOLE-BREAST RADIOTHERAPY: A SINGLE-CENTRE PRELIMINARY EXPERIENCE

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Aims: In line with principles of hypofractionation for adjuvant radiotherapy (RT) of early breast cancer (EBC), the 5-year results of FAST-Forward trial confirmed the non-inferiority of 1-week schedule with respect to the standard 3-week or 5-week regimens in terms of treatment safety and tumor local control. Here, we report our preliminary clinical experience testing the feasibility and tolerance of 1-week regimen.

Methods: From December 2020 to March 2021, seven EBC patients (age ≥79 years and/or affected by comorbidities) were treated at our Institute with 1-week hypofractionated adjuvant whole-breast RT. The whole breast, including the soft tissues from 5 mm below the skin surface to the deep fascia, was contoured as CTV. RTOG skin toxicity was evaluated during treatment and after 6 months of follow up.

Results: Right breast was irradiated for 5 patients, while a bilateral breast irradiation was performed for a 84-years old patient. A total dose of 27 Gy in 5 daily fraction was prescribed to the PTV in 3 cases, while a total dose of 26 Gy was delivered in 5 fractions for patients ≥ 82 years and affected by left/bilateral BC. All treatments were delivered with VMAT technique and daily IGRT with Surface-Guided Radiotherapy without tatoo references. Excellent target coverage and respect of OARs dose contraints (Heart: V1.5<30%, V7<5%; omolateral lung: V8<15%) were obtained for all plans. No RT-related local cutaneous toxicity (RTOG score 0) was observed during treatment. Only one patient had a 6-months follow up: RTOG grade 2 skin oedema is reported; instrumental and clinical examination confirm tumor local control.

Conclusions: Our preliminary experience confirms published data on feasibility, early good tolerance and effectiveness of adjuvant RT with 1-week hypofractionated regimen. Further evaluations with randomized trials enrolling larger populations of selected patients, as well as prolonged follow up periods, are necessary to compare this regimen to the standard-of-care. In selected cases (*e.g.* elderly patients with comorbidities limiting the adherence to standard therapies), this approach could be safetly 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.

PO129

THE IMPACT OF YOUNG AND VERY YOUNG AGE ON OUTCOME AFTER HYPOFRACTIONATED RADIOTHERAPY FOR BREAST CANCER.

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Aim: To investigate the impact of young and very young age on local control and survival after hypofractionated whole breast irradiation (HWBI) for adjuvant radiotherapy for breast cancer (BC) including of intraoperative electron boost (IOERT)

Methods and Materials: Premenopausal women , who received 12- Gy IOERT boost at the time of conservative surgery followed by 3-dimensional conformal HWBI in 13 fractions (2.85 Gy/die) as part of breast conservative treatment, were grouped according to age <40 and 40-48. Local relapses (LR) and survival (disease-free, DFS; specific, BCSS; overall, OS) were analyzed.

Results: 518 consecutive BC patients with median age of 43 were treated between 2004 and 2014.Of them, 163 were <40 and 355 were 40-48. Clinical and histologic characteristics were well balanced except for statistically significantly higher nodal positivity, which lead to higher rate of axillary dissection and chemotherapy prescription, larger tumor size, greater incidence Grade 3 and lower rate of luminal A subtype in the group <40. Median follow-up was 118 months. No difference by age was found for OS and BCCS: in both the age groups survival outcomes were 100% at 5 years and around 98% at 10 years. Likewise, no difference by age was seen for DFS: in the groups <40 and 40-48 years of age, DFS was 85.3% and 90.4% at 5 years and 74.1% and 79.9% at 10 years, (p=0.14), respectively. The rate of distant metastases was similar, regardless of age. Statistically significantly difference was observed regarding local recurrence between the two age groups: in the groups <40 and 40-48 years of age LR was 1.8% and 1.4% at 5 years and 5.2% and 2.5% at 10 years, (p=0.04), respectively. In the group younger than 40 there was 12 events/1526PY= 0.79 events x 100 PY versus 9 events/3232 PY=0,28 events x 100 PY in the older age group. Using the lower age threshold of 35 (n=56), no difference was observed compared to the older counterparts (p=0.25).

Conclusions: In a population of young premenopausal patients of 48 or under, younger women (<40) presented more aggressive tumor stages and tumor subtypes and suffered from higher incidence of local relapse. No difference was observed for any survival outcomes, underlining the efficacy of salvage treatments. Patients under 40 confirmed to be at increased risk of recurrence and should be candidate to dose escalation strategy.

PO130

SEQUENTIAL PHOTON BOOST AFTER BREAST CONSERVING SURGERY

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Aims: To evaluate target coverage, dose to organs at risk, acute toxicity, and cosmesis in patients treated with whole breast irradiation (WBI) and sequential photon boost to the lumpectomy area, after breast conserving surgery (BCS).

Methods: Between February 2020 to March 2021, twenty-two patients whit early stage breast cancer have been treated with radiotherapy after conservative surgery. The dose prescription to the residual breast was 50 Gy in 25 fractions of 2 Gy. The sequential photon boost of 10-16 Gy (2Gy/fraction) on tumor bed was delivered, defined in based on the visualization of surgical clips.

Radiotherapy was performed with 3D-conformational technique by means of 2 tangent fields to irradiate the breast as a whole and 2 oblique fields for the sequential boost. Acute toxicity was evaluated using RTOG criteria.

Results: All patients completed the radiation treatment without interruption. Median follow-up was 5 months (range, 3-12 months). Grade 3-4 acute toxicity was not seen, and grade 2 toxicity was very low. Planning target volume (PTV) coverage, Organs at risk (OAR) dosimetry and cosmetic outcome were optimal.

Conclusions: Acute toxicity after whole breast irradiation (WBI) and sequential photon boost is acceptable. Although further evaluations are necessary to assess late toxicity and tumor control. Furthermore a comparison electron and the photon boost techiniques will be done.

PO131

MANAGEMENT OF MALIGNANT PHYLLODES TUMOR OF THE BREAST WITH LIPOSARCOMATOUS DIFFERENTIATION: A CASE REPORT

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Aim: To investigate the role of adjuvant radiotherapy (RT) in malignant Phyllodes tumor of the breast (MPTB).MPTB are rare neoplasms that account for 2.5% of all fibroepithelial lesions, and 10%-20% exhibit malignant transformation. Malignant transformation often occurs in the form of stroma, and usually shows fibrosarcomatous differentiation. Liposarcomatous differentiation is a rare, developed stromal component of phyllodes tumors.

Methods: A 56-year-old woman presented with a one-year history of a palpable mass in the right breast. The patient reported that it had increased in size. Physical examination revealed a bulky and fixed mass in the external quadrant of right breast. Standard mammography revealed a bulky benign mass on the right (maximum diameter 5 cm). Ultrasound imaging revealed, in correspondence with the clinically palpable swelling, three rounded formations with regular contours and a liquid echo structure with fine internal echoes with a maximum diameter of 28, 12 and 10 mm respectively. In terms of echogenicity there was a suspected dysplastic cystic areas. New physical examination revealed volume increase (maximum diameter 20 cm) of the firm and fixed mass in the right breast. Ultrasound-guided 14-gauge core biopsy revealed a stromal overgrowth with nuclear atypia and some lipoblasts. Subsequent simply mastectomy was performed and the specimen showed a well-demarcated round tumor (14 cm max diameter) that was a mesenchymal neoplasm mainly with spindle cells with moderate to high pleomorphism, rich vascularization, areas of necrosis, high mitotic index, presence of liposarcomatous component. The presence of a glandular component leads to the diagnosis of malignant philloid tumor with stromal overgrowth. The patient has been treated with adjuvant radiation therapy to chest wall with total fraction dose: 50 Gy in 25 fraction.

Results: At 12 months follow up after radiotherapy was performed PET TC and TC tb showing absence of local recurrence and distant secondaryism.

Conclusion: The association of phyllodes tumour and liposarcomatous differentiation is rare, with few previously reported cases in literature. The role of adjuvant radiotherapy remains uncertain, but consideration can be given for his use in cases of malignant phyllodes tumours.

PO132

A SINGLE SKIN METASTASIS FROM BREAST CANCER: A CASE REPORT

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Aims: To report a rare case of breast carcinoma with single distant skin metastasis.

Methods: A 51 years old female had a history of left breast cancer in 2019, she underwent left mastectomy with the axillary dissection. The histology report revealed invasive lobular carcinoma of the breast, grade 2, with positive estrogen receptors (90%) and positive progesterone receptors (90%), HER-2 negative (score 0), Ki 67: 12%, associated to ductal carcinoma *in situ* and with 2 positive lymph nodes of 17 examined, staged as cT2cN2. No distant metastasis was detected by whole body CT scan. And she started hormone therapy with tamoxifene. She came to our attention in January 2021 for an excised skin lesion, of 0.5 cm, in the right suprascapular region, that the pathology report described as a recurrent metastatic breast adenocarcinoma with the immunophenotype compatible to the precipue primary. Both whole body CT scan e PET/CT scan were negative.

Results: The patient was discussed in our multidisciplinary team's meeting, the skin metastasis report was also confirmed by the review of the histological preparations and we proposed an adjuvant radiotherapy on the surgical scar, stop tamoxifene and started letrozole. A dose of 45 Gy in 15 daily fractions was administered.

Conclusions: To date the patient is in excellent clinical condition and there aren't suspected signs of disease recurrence. This case report highlights the importance of considering cutaneous metastasis as a possibility in patients with prior history of primary internal malignancy.

P0133

OUTCOME AND TOXICITY PROFILE OF ADJUVANT HYPOFRACTIONATED IMAGE-GUIDED RADIOTHERAPY IN PATIENTS WITH BILIARY TRACT CARCINOMA

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Aims: Adjuvant radiochemotherapy is controversial in patients (pts) with biliary tract carcinoma (BTC). We report our results of toxicity and outcome using adjuvant hypofractionated RT in BTC.

Methods: After surgery pts with BTC underwent contrast-enhanced computed tomography (c-e-CT) or CTPET simulation, CTV included surgical bed and regional LNs considering tumor site. PTV was defined adding 1, 1, 1.5 cm to CTV. Prescription dose was 40-44.25 Gy in 15 frs with SIB up to 50 Gy to R1 or CTPET +. RT was delivered with VMAT or tomotherapy (TT) concomitant to capecitabine (cape).

Results: From 05/2009 to 07/2020, 57 pts (32 M; 25 F) were treated. Median age: 68 years (45-86). Characteristics of pts and treatment are reported in table. CTPET simulation was performed in 26 pts (14 pts were PET +). The average PTV was 387 cc (110-861) and the average PTV of SIB was 49 cc (28.5- 80). At a median follow up of 21 months (2-118), median Overall survival (OS) was 31 months and 53 pts were evaluable for acute and late toxicity. G1-G2 acute toxicity occurred in 36 pts. No acute G3 or G4 toxicity showed. G1-G2 late toxicity occurred in 8 pts. Main toxicity was gastrointestinal. Only 5 pts had G3 late toxicity (1 gastric ulcer, 2 stenosis, 2 cholangitis). There was no difference in terms of toxicity between TT and VMAT. Median time to local progression (TTLP) and time to distant progression (TTDP) were 26 months for both. One, 3 and 5 years OS were 91%, 44% and 23%, respectively. One, 3 and 5 years local failure for survival (LFFS) were 84%, 32% and 11%, respectively. Grading was a significant prognostic factor for OS (G1-G2: 33 m *vs* G3: 20 m; p=0.038), a trend in favour of G1-G2 was shown for TTLP (G1-G2: 28 m *vs* G3: 18 m; p=0.08) and TTDP (G1-G2: 27 m *vs* G3: 19 m; p=0.065). Margin status showed a trend in favour of R0 in term of TTDP (R0: 31 m *vs* R1: 20 m; p=0.061) and OS (R0: 38 m *vs* R1: 27 m; p=0.081), no difference in term of TTLP (R0: 31 m *vs* R1: 22 m; p=0.12). No significant difference in term of OS, TTLP and TTDP between pT1-T2/pT3-T4 and pN0/pN+.

Conclusions: Adjuvant hypofractionated RT concomitant to cape in pts with BTC is feasible with a good toxicity profile despite the large volumes of PTV and the high RT dose of SIB when used. Grading and margin status were the main predicting outcome factors. Adjuvant ChT can explain the outcome between pT1-T2/pT3-T4 and pN0/pN+. The trend in favour of R0 in term of TTDP and OS while the no difference in term of TTLP suggests to consider neoadjuvant RT to improve R0.

Table 1. Characteristics of patients and chemoradiotherapy treatment.

Gender	**Number (n) of pts: 57 (%)**
Male	32 (56%)
Female	25 (44%)
Site of Tumor	**n (%)**
Klatskin tumor	26 (46)
Common or distal bile duct	17 (30)
Intrahepatic	7 (12)
Gallbladder carcinoma	7 (12)
Pathological stage	**n (%)**
T1-T2	30 (53)
T3-T4	27 (47)
N0	28 (49)
N+	25 (44)
Nx	4 (5)
Margin status	**n (%)**
R1	38 (67)
R0	19 (33)
Grading	**n (%)**
G1	5 (9)
G2	36 (63)
G3	16 (28)
Chemotherapy	**Number (n) of pts (%)**
Neoadjuvant ChT	**5 (9)**
GEMCITABINE+CDDP	5 (9)
Adjuvant ChT	**22 (39)**
CDDP+GEMCITABINE	11 (50)
PEXG	2 (9)
GEMOX	2 (9)
GEMCITABINE	1 (4.5)
CAPECITABINE	1 (4.5)
Concomitant ChT	**43 (75)**
CAPECITABINE	43 (75)
Radiotherapy	**Number (n) of pts (%)**
Tomotherapy	35 (61)
VMAT	22 (39)

P0134

ESOPHAGEAL CANCER TREATED WITH INDUCTION CHEMOTHERAPY FOLLOWED BY NEOADJUVANT CHEMO-RADIOTHERAPY: INCIDENCE AND PATTERN OF LOCO-REGIONAL RECURRENCE

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Aims: To evaluate the incidence and pattern of failure and to define a dosimetric map of loco-regional recurrence (LRR) for patients (pts) with locally advanced esophageal cancer (EC) treated with induction chemotherapy, followed by neoadjuvant chemo-radiotherapy, and surgery.

Methods: We retrospectively reviewed ECs treated with trimodality therapy between 2008 and 2019 at our Institution. The site of first failure was documented as distant, LRR or combined (distant and LRR). LRR included anastomotic/perianastomotic failure (AR) and regional lymph node recurrence (NR). A dosimetric

analysis was performed to correlate LRRs to radiation target volumes, using both rigid (RIR) and deformable image registration (DIR) to better compare computed tomography (CT) anatomy. A cause specific hazard model was used to evaluate prognostic factors for recurrence.

Results: 126 EC pts (78 adenocarcinoma, 48 squamous cell carcinoma; 115 cT3/4; 110 cN+; median age 63 years) were eligible for the analysis. The neoadjuvant chemo-radiotherapy (nCRT) schedule consisted of an induction phase of weekly administered docetaxel, cisplatin, and 5-fluorouracil (TCF) for 3 weeks (94.4% of cases, or weekly paclitaxel and carboplatin (PC) in 5.6%), followed by a concomitant phase of weekly TCF (93.7% of cases, PC in 6.3%) for 5 weeks with concurrent radiotherapy (50-50.4 Gy in 25-28 fractions). Conformal (3D-CRT) and intensity modulated (IMRT) radiation techniques were adopted in 55.6% and 44.4% of cases, respectively. At the time of surgery, pCR was achieved in 49.2% of pts, with a 98.4% of R0 resection rate. With a median follow-up of 64 months (95% CI: 56-72.7), median overall survival (OS) and progression free survival (PFS) were 97.4 months (95% CI: 57.5-NE) and 47.5 months (95% CI: 29.5-117), respectively. 56 (44.4%) pts experienced recurrent disease, with a distant, combined, and isolated LRR pattern in 37 (66.1%), 11 (19.6%), and 8 (14.3%) cases, respectively. Concerning the 19 (15.1%) LRRs, 12 (63.2%) pts had NR, 6 (31.6%) AR, and 1 (5.2%) NR+AR. The dosimetric evaluation showed that 4 LRRs occurred as in-field (mean recurrence Dmean 27.8±23.1 Gy/Dmax 50.8±0.6 Gy), 2 as marginal (Dmean 3.7±4.0 Gy/Dmax 33.2±16.8 Gy), and 13 as out-of-field failure. The 5-years cumulative incidence of LRR was 9% in pathological complete response (pCR) vs 21.5% in non-pCR (HR 0.24, p=0.0078), 31.9% in pN+ vs 9.6% in pN0 (HR 6.82, p=< 0.0001), and 9.3% in ≥ 60 years vs 27% in < 60 years (HR 0.32, p=0.0155), 0.0% in cT1/2 vs 16.8% in cT3/4 (NE) and 0.0% in female vs 18.5% in male pts (NE).

Conclusions: LRR represents an uncommon event in ECs treated with trimodality therapy, suggesting a pivotal role of preoperative radiotherapy in reducing the risk of loco-regional failure. pCR, pN0, age > 60 years, cT1/2 and female gender were associated with lower rate of LRR.

P0135

CHEMORADIATION FOR THE TREATMENT OF SQUAMOUS CELL CARCINOMA OF ANAL CANCER: LONG-TERM DISEASE OUTCOME AND A PRELIMINARY INTEGRATION WITH PRE-TREATMENT MRI-BASED TOOLS

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Aims: Chemoradiation (CRT) is the standard of care in squamous cell carcinoma (SCC) of the anal canal. We retrospectively analyzed outcomes and toxicity of a series of consecutive patients (pts) treated at our Center in the last decade. Particular interest was reserved to organ preservation, evolution of treatment's patterns and possible predictive role of MRI imaging.

Methods: Inclusion criteria were: histologically proven, stage I-III SCC of the anal canal, MRI or endoscopic ultrasound for local staging and whole-body CT scan-CT/PET for systemic staging. CRT schedule were mainly two: - 45 Gy to anal canal, mesorectum, pelvic and inguinal nodes (elective volume) and boost up to 59.4 Gy to tumor and positive nodes (gross disease); - 46.2 Gy to the elective volume and simultaneous integrated boost to gross disease up to 56 Gy. For each patient GTVs were defined on diagnostic T2-, DWI-weighted MRI and ADC maps (ROI). These ROIs were used to extract radiomic features from the images; these features are going to be correlated to tumor response. Primary endpoints were freedom from loco-regional recurrence (FFLR), freedom from salvage (FFS), freedom from colostomy (FFC). Secondary endpoints were acute/late toxicities, and overall survival (OS). Survival was estimated using Kaplan-Meier method; univariate analysis, using log-rank test, identified variables with impact on endpoints. SPSS®v.23 was used for statistical analysis.

Results: 130 pts were included in the analysis. Majority of pts had stage IIIA (22.6%) disease. Median dose was 59.4 Gy to gross disease. Regarding chemotherapy, 54 pts received CDDP+5FU, 42 pts Mitomycin+5FU. With median follow-up of 47 months, median FFLR was 170 months, median FFS and FFC were not reached. 2- and 5-year OS were 87.1% and 69.6%, respectively. Treatment interruption and local progression were associated with worse OS (p=.004 and p<.001, respectively). 5-year FFLR was lower in male (p<.001), tumor fistulization (p=.008) and HIV+ pts (p=.025). Main acute toxicity was G3 perianal skin radiodermitis (60% of pts). G2 fecal incontinence experienced in less than 5% of pts. Pre-treatment MRI-based tool, predicting disease response, is still ongoing.

Conclusions: CRT in SCC anal canal guarantees fair loco-regional control preserving organ function. Predictive biomarkers to select patients for risk adapted strategies are lacking, pre-treatment MRI-based tools need to be explored to identify parameters related to treatment response.

PO136

RISK ADAPTED ABLATIVE RADIOTHERAPY (RADAR) APPROACH FOR LOCALLY ADVANCED PANCREATIC CANCER (LAPC), AFTER INTENSIVE CHEMOTHERAPY

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Aims: To assess the efficacy of a Risk Adapted Ablative Radiotherapy (RAdAR) approach in patients with unresectable locally advanced pancreatic cancer (LAPC), after intensive induction chemotherapy.

Methods: This observational study includes patients with LAPC who received RAdAR following induction chemotherapy from January 2017 to December 2019. Patients were treated using a simultaneous integrated boost (SIB)-based dose prescription strategy. If feasible, 5-fraction stereotactic ablative radiation therapy (SAbR) was used, administering 30 Gy to the planned target volume (PTVt) and 50 Gy SIB to the tumour–vessel interface (TVI). Alternatively, a hypofractionated ablative radiotherapy (HART) schedule (50.4 Gy in 28 fractions to the PTVt, with a TVI SIB of 78.4 Gy) was adopted. Primary endpoints were freedom from local progression (FFLP), overall survival (OS) and progression-free survival (PFS).

Results: A total of 64 patients were included. Induction chemotherapy consisted of gemcitabine nab-paclitaxel in 60.9% and FOLFIRINOX in 39.1% of cases. SAbR was used in 52 (81.2%) patients and HART in 12 (18.8%). After radiotherapy, surgery was performed in 17 (26.6%) patients. Median follow-up was 16.1 months (range 3.1-47.0 months). Overall local control (LC) rate was 78.1%, with no difference between resected and non-resected patients (2-year FFLP 81.6% vs.56.4%; p=0.112). Median OS and PFS were 36.9 months (95% CI 32.5-39.7) and 13.9 months (95% CI 10-17.9), respectively. Resected patients had a better OS (53.4 versus 29.1 months; p=0.0001) and PFS (29 versus 7.8 months; p<0.0001) compared to non-resected patients (Figure 1). In non-resected patients, no significant difference was found between SAbR and HART for median FFLP (28.1 versus 18.5 months; p=0.614), OS (29.7 versus 25.4 months; p=0.624), and PFS (8.2 versus 6.2 months; p=0.478). One patient (1.6%) experienced an acute grade 4 gastro-intestinal bleeding. No other acute or late grade ≥ 3 toxicities were registered.

Conclusions: The RAdAR approach for selected LAPC patients after intensive induction chemotherapy, is an effective radiation treatment strategy and a promising therapeutic option in a multimodality treatment regimen.

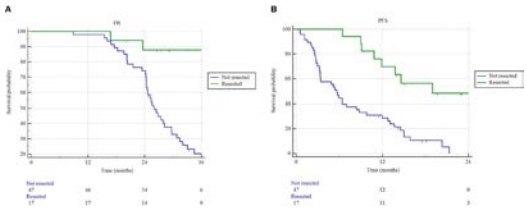

Figure 1.

PO137

STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR UNRESECTABLE PANCREATIC CANCER

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Aims: To report our experience with SBRT in patients with unresectable or locally recurrent pancreatic cancer after primary surgery.

Methods: Between August 2015 and December 2020, 35 patients (pts) with unresectable or recurrent pancreatic cancer underwent exclusive SBRT. Patients were submitted to SBRT with micro-multileafs collimator or to volumetric modulated arc therapy (V-MAT) with image guided technique. We evaluated clinical and radiological response, local control (LC) was considered with partial response and stable disease. Toxicities were graded according to CTCAE version 5, statistical analysis was performed with Kaplan-Meier method.

Results: Median age was 70 years (range, 46-92 years), median KPS 90% (range, 80-90%), 3 pts had only radiological diagnosis, 3 were neuroendocrine cancer and 29 were adenocarcinoma, respectively. Five pts had recurrent cancer after surgery, the other 30 pts were unresectable due to locally advanced disease in 21 pts, age and comorbidity or metastatic disease in 2 and 7 pts, respectively.

Chemotherapy was given in 74% of pts in various schedules and timing before SBRT. Median radiation dose was 30 Gy (range, 20-40 Gy) delivered in 5 fractions. Median PTV was 130 cc (range, 19-313cc). Simultaneous integrated boost with median dose of 35 Gy was given to median GTV of 59,6 cc (range, 22-97cc) in 3 pts. After median follow-up of 10 months (range, 1-40 months) local control was 74% (+/- 11%) at 1-year and 63% (+/- 14%) at 2-years. Particularly, 14 pts (40%) had radiological stable disease, 7 (20%) partial response, 14 (40%) progression disease, respectively. Median overall survival was 11 months, 47% (+/- 8%) at 1 year and 27% (+/- 8%) at 2 years. No difference in LC were found for subsequent parameters: dose, recurrent disease, histology,

type of radiological response. Abdominal pain was present before SBRT in 19 pts (54%) and a clinical response was obtained in 10 of 19 (52%) cases. Acute G1-2 gastrointestinal toxicities were registered in 6 (17%) and 4 pts (11%), respectively, no late toxicities was found.

Conclusions: in our small series SBRT is a safe and effective option for unresectable or locally recurrent pancreatic cancer obtaining a good local palliation. However, SBRT can be considered in the multimodality treatment of advanced pancreatic cancer.

PO138

STATISTICAL DEPENDENCE OF THE CLINICAL AND PATHOLOGICAL RESPONSE ON THE INITIAL TUMOR VOLUME AFTER NEOADJUVANT TREATMENT

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Aims: Neoadjuvant chemoradiation followed by total mesorectal excision is the mainstay of treatment of locally advanced rectal cancer. The purpose of this study is to verify if clinical and pathological response to neoadjuvant treatment is statistically dependent to the initial tumor volume.

Methods: Patients submitted to neoadjuvant chemoradiation were the object of this retrospective analysis. Prior to treatment all patients were submitted to a staging lower-abdomen MRI. GTV (gross tumor volumes) were delineated on that imaging under supervision of an expert Radiologist. The clinical target volume (CTV) included the whole mesorectal space and elective lymph nodes. Radiotherapy treatment plan was based on simulation CT-scan and image registration of the staging MRI. Radiotherapy was delivered with VMAT technology and associated with Capecitabine. The clinical response to neoadjuvant treatment was assessed on restaging MRI performed 4-6 weeks after the end of chemoradiation. Total mesorectal excision was planned after further 2-4 weeks.

Results: From 2016 to 2020 96 patients were submitted to preoperative chemoradiation for locally advanced rectal adenocarcinoma. Their median age was 61 years, 56 patients were male, 40 female. All patients received a prescribed dose of 50 Gy delivered in 25 fractions to the whole mesorectal space and elective lymphnodes. Fourty-seven patients (49%) also received a simultaneous integrated boost (SIB) on GTV and corresponding mesorectum to a total dose of 55 Gy. The median GTV was 23.1 cc (range 604.4-3.2 cc) without significant differences between the two groups. At the restaging MRI complete response (CR) was observed in 19 patients (19.8%), while a partial response was observed in all the remaining patients (no. 77, 80.2%). All the patients were submitted to total mesorectal excision after 6-8 weeks from the end of chemoradiation. After surgery an optimal pathological response (Dworak tumoral regression scale 3-4) was reported in 77 cases. Logistic regression showed that the clinical response after neadjuvant treatment was statistically correlated to tumor volume mesaured at the staging MRI, regardless of the total dose (OR=1.04, CI=1.003-1.089, p=0.004). Pathological response did not show the same correlation (OR=1.00, CI=0.99-1.00, p=0.96)

Conclusions: In patients with locally advanced rectal cancer a complete pathological regression after preoperative chemoradiation was not correlated to the initial tumor volume.

PO139

INTENSITY-MODULATED RADIATION THERAPY (IMRT) FOR THE TREATMENT OF LOCALLY ADVANCED ANAL CARCINOMA: OUTCOMES OF A 10-YEARS CLINICAL EXPERIENCE

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Aims: To describe the results of a series of squamous cell anal carcinoma (SCAC) patients receiving definitive chemoradiotherapy (CRT) delivered with IMRT.

Methods: We retrospectively reviewed the data of SCAC patients treated between 2011 and May 2021 with IMRT and concomitant chemotherapy (CT) according to doses and volumes currently used at our institution. Depending on tumor response and initial staging a sequential boost was planned. Collected data were patients and treatment characteristics, tumor control, acute-late toxicity and overall survival. Survival endpoints were estimated by Kaplan-Meier method and prognostic factors were assessed via Cox regression analysis (SPSS software v.23).

Results: 110 patients were analysed: 80 females (73%), median age 64.3 years, 61% staged T3-4 and 71% N positive. All but 2 patients received CT, 92% with FUMIR. Median dose to the primary tumor was 55 Gy (range 41.8-61.2), of which 89% delivered by simultaneous integrated boost. Median treatment time was 37 days. 68% of patients received a sequential RT boost mainly by brachytherapy (53 of 74) with a median dose of 8 Gy (range 3.5-26). Median total EQD2 dose to primary site was 59.3 Gy (range 50-73.6). Median follow-up was 35.4 months. 35% of patients experienced ≥G3 acute toxicity;

G2 late toxicity was reported in 24% of cases, only 4 patients experienced ≥G3 late toxicity. In a median time of 5.8 months 82.7% of patients achieved complete response (CR); locoregional recurrence (LRR) was reported in 20.9% of cases at median interval from treatment start of 9.7 months. 15 patients (14%) underwent abdomino-perineal resection due to persistent or recurrent disease, 3 others underwent minor surgery. Overall, 23.6% patients had a colostomy at time of follow-up, of which 54% placed before treatment. There were 13 deaths at time of analysis (11.8%), of which 9 cancer related. 3-year-overall survival (OS), disease-free survival (DFS) and colostomy-free survival (CFS) were 92% (95% CI 89.2-95%), 71.7% (95% CI 66.9-76.5%) and 84% (95% CI 80.3-88%) respectively (Figure 1). 3-year-local control was 87% (95% CI 83.4-90.6). N stage was associated with poorer CR (aHR=0.45, p=0.002) and higher LRR (aHR=1.6, p=0.029).

Conclusions: Our results on a big cohort of patients, mainly with locally advanced SCAC and long follow-up time, confirmed that IMRT allows high local control with manageable toxicity. Studies on dose individualization to optimize CR and reduce late toxicity are warranted.

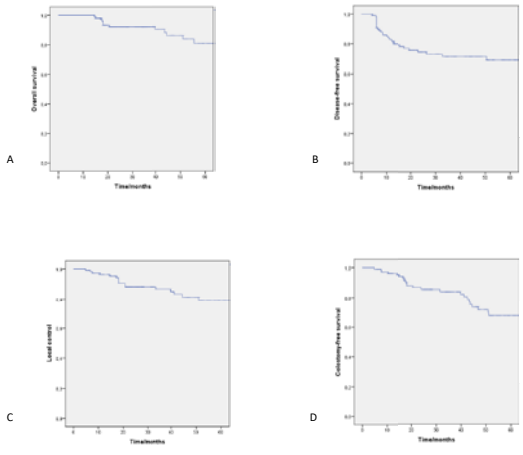

Figure 1. Kaplan Meier survival curves. A: Overall survival. B: Disease-free survival. C: Local control. D: Colostomy-free survival.

Figure 1.

PO140

TOTAL NEOADIUVANT THERAPY (TNT) AND SIMULTANEOUS INTEGRATED BOOST IN LARC PATIENTS WITH LPLN

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Aims: Between 11 to 14% of patients with locally advanced rectal cancer (LARC) have positive lateral pelvic lymph nodes (LPLN) at the diagnosis, related to a worse prognosis with a 5-year survival rate between 30 to 40%. The best treatment choice for this group of patients is still a challenge. The optimal radiotherapy (RT) dose for LPLN patients has been investigated.

Methods: We retrospectively collected data from LARC patients with LPLN at the primary staging MRI, treated in our center from March 2003 to December 2020. Patients underwent a neoadjuvant concomitant CTRT treatment on T, mesorectum and pelvic nodes, associated with a fluoride-based chemotherapy. The total reached dose was 45Gy at 1.8Gy/fr on the elective sites and 55Gy at 2.2Gy/fr on the disease and mesorectum. Patients were divided in two groups based on whether they received a simultaneous integrated RT boost on the LPLN or not. Local control (LC), overall survival (OS), disease free survival (DFS) and metastasis free survival (MFS) were evaluated in the whole group and then compared between the two groups.

Results: A total of 257 patients were evaluated:125 were included in the RT boost group and 132 in the non-RT boost group. The median follow-up period was 48.6 months. LC resulted in 92.6% of the whole populations but not to be affected by the RT boost on the LPLN. Considering DFS, OS and MFS they resulted in 73%, 81% and 86.4%, respectively in the entire population. From the comparison of the two groups, there was a favorable trend towards the RT boost group even though the results were still not significant (0.1, 0.06 and 0.07, respectively).

Conclusions: TNT has shown to be beneficial on the survival outcomes (OS; DFS, MFR and LC) in patients with LARC and LPLN. Furthermore, simultaneous integrated RT boost on LPLN seems to affect MFS and OS with a favorable trend. Additional analysis should be completed to evaluate the real contribution of a RT boost.

PO141

NEOADJUVANT RADIOTHERAPY DOSE ESCALATION FOR LOCALLY ADVANCED RECTAL CANCER IN THE NEW ERA OF RADIOTHERAPY; A REVIEW OF LITERATURE

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Aim: To analyze the role of neoadjuvant radiotherapy dose escalation for LARC using innovative radiotherapy techniques.

Material and methods: In December 2020 we conducted a comprehensive literature search of the following electronic databases: PubMed, Web of Science, Scopus and Cochrane library. The limit period of research included articles published from January 2009 to December 2020.Screening by title and abstract was carried out to identifying only studies using radiation doses EQD2 ≥54 Gy and VMAT, IMRT or IGRT techniques. The authors' searches generated a total of 2287 results and, according to PRISMA Group (2009) screening process, 21 publications fulfil selection criteria and were included for the review.

Results: The main radiotherapy technique used consisted in VMAT and IGRT modality (74.12 %). The mainly dose prescription was 55 Gy to high risk volume and 45 Gy as prophylactic volume in 25 fractions given with SIB technique (42.85 %).The mean pCR was 28,2 % with no correlation between dose prescribed and response rates (P = >0.5). The R0 margins and sphincter preservation rate were 98.88 % and 76.03, respectively. After a mean follow-up of 35 months local control was 92,29 %. A ≥ G3 toxicity was 11,06 % with no correlation between dose prescription and toxicities. Patients receiving EQD2 dose > 58.9 Gy and BED > 70.7 Gy had higher surgical complications rates compared to other group (p-value= 0.047).

Conclusions: Dose escalation neoadjuvant radiotherapy using innovative techniques is safe for LARC achieving higher rates of pCR. EQD2 doses > 58,9 Gy is associated with higher rate of surgical complications.

PO142

THE TREATMENT 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: 25 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.

PO143

IN-SILICO STUDY OF DOSE ESCALATION USING INHOMOGENEOUS DOSE PRESCRIPTION IN PANCREATIC SBRT: FEASIBILITY AND PROGNOSTIC FACTOR

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Aims: Stereotactic Body Radiotherapy (SBRT) has been proposed to improve outcome following chemotherapy in non-resectable locally advanced pancreatic cancer (LAPC). However, prescription of more intensive schedules has been traditionally limited by risk of severe injury to nearby organs at risk (OARs), particularly in case of substantial overlap between planning volume and critical structures. To achieve higher tumor control, a biologically effective dose (BED) of 100 Gy10 , corresponding to a dose 50 Gy in 5 fractions of 10 Gy assuming $\alpha/\beta=10$, is desirable. The aim of our *in silico* study is to assess the feasibility of dose escalation using inhomogeneous dose prescription for pancreatic SBRT and to determine which patients may be eligible for this strategy based on anatomical proximity between target volumes and OARS.

Methods: We collected data from 14 LAPC patients treated at our Institution. For each patient, a CyberKnife (CK) treatment plan was optimized for Synchrony fiducial-guided pancreatic SBRT to a planned dose of 50 Gy and 40 Gy in 5 fractions to the gross tumor volume (GTV) and the planning target volume (PTV), respectively. PTV was created by 5 mm GTV isotropic expansion. Acceptable target coverages were: a dose of 50 Gy and 47.5 Gy to at least 90% and 95% of the GTV, and a dose of 40 Gy to 95% of the PTV. Planned doses to the target regions and OARs were evaluated and statistically analyzed. For each plan, the intersection volume between the PTV and OARs expanded by 5 mm was defined as Expansion-Intersection Volume (EIV).

Results: Median GTV and PTV volumes were 40.8 (range 22.3-205.3) cc and 73.7 (range 36.1-266.7) cc , respectively. In all cases V35 to duodenum, stomach and bowel was maintained below 0.5 cc. Median EIV was 12.9 (3.9-25.1) cc. Median V50 and V47.5 for GTV was 91.0% (range 82.4%-97.8%) and 96.8% (range 92.5%-99.9%), respectively: GTV coverage was acceptable in 10/14 cases. Median V40Gy for PTV was 96.8% (range 90.0%-99.8%): PTV coverage was acceptable in 11/14 cases. Spearman correlation showed a significant association between EIV and V47.5Gyfor GTV (rho -0,77228, $p<0.001$) and V40Gyfor PTV (rho -0,68352, $p<0.001$), respectively.

Conclusion: Inhomogeneous dose escalated prescription using fiducial-based SBRT with Cyberknife respiratory tracking is a feasible strategy in selected patients with LAPC. EIV is significantly correlated with target coverage and may identify patients eligible for dose escalation.

PO144

SIMULTANEOUS INTEGRATED BOOST (SIB) IN NEOADJUVANT CHEMORADIATIONTHERAPY FOR RECTAL CANCER RESULTS IN A BETTER CLINICAL RESPONSE ON THE MRI: A RETROSPECTIVE ANALYSIS

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Aims: In the last year 13.326 new cases of rectal cancer were diagnosed in Italy, more than half of them were locally advanced and needed to be treated with multimodality approaches (radiotherapy, chemotherapy, surgery) to reach high rates of cure. Aim of the present study was to compare the responses and toxicity of the two radiotherapy treatment schedules used in our center in the last 5 years trying to identify the optimal personalized dose prescription.

Methods: Patients affected by locally advanced rectal cancer, submitted in our Center to neoadjuvant chemoradiation over the past 5 years were the object of this study. All patients followed a highly standardized care path which included staging with colonoscopy, chest-abdomen CT and pelvic MRI with contrast, case discussion on multidisciplinary board, neoadjuvant radiochemotherapy with capecitabine, restaging with colonoscopy and pelvic MRI at 4-8 weeks, followed by surgery. All rectal lesions were contoured on MRI with the supervision of an expert radiologist.

Results: We identified a total of 96 patients treated with 50 Gy on the whole mesorectum and pelvic drainage lymph nodes in a total of 25 daily fractions delivered by VMAT. Forty-five of them also received a 5 Gy simultaneous integrated boost on the rectal lesion and corresponding mesorectum. The median tumor size was 22.6 cc (range 3.2-604.4) without significant difference in the 2 groups. Acute toxicity was similar in the higher dose group compared to the standard group, with Grade ≥ 3 GI toxicity being registered in 2 (2.1%) *vs* 4 (4.2%) patients respectively ($p=0.33$). At the clinical pre-operative restaging, a higher rate of clinical complete responses was observed among patients submitted to SIB radiotherapy (14 *vs* 4). This difference was not confirmed at the pathological examination after surgery, which was radical in all cases.

Conclusions: In our experience, in patients undergoing neoadjuvant CTRT for rectal cancer, a total dose of 55 Gy delivered to the rectal lesions and corresponding mesorectum does not lead to worse tolerance and result in a better clinical response to treatment. Subsequent follow-up analysis will clarify the role of the additional radiotherapy dose on local control of the disease.

PO145

CORRELATION OF ACUTE HEMATOLOGIC TOXICITY AND IRRADIATION OF PELVIC BONE MARROW AFTER CONCURRENT CHEMORADIATION IN ANAL CANCER PATIENTS

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Aims: To evaluate a dosimetric correlation between the dose received by pelvic bone marrow (BM) and the hematologic toxicity (HT) in patients (pts) undergoing chemoradiation (CRT) for anal cancer. Indeed, HT represents one of the major causes of treatment interruption, leading to an increase of overall treatment time.

Methods: We retrospectively selected 65 pts treated with CRT for anal cancer from 2011 to 2020. Pts underwent pelvic intensity-modulate radiotherapy (IMRT) or volumetric-modulated-arc radiotherapy (VMAT) to a total dose of 45 Gy to prophylactic nodes and 50.4 Gy to intermediate risk volume, with a boost up to 59.4 Gy to gross tumor volume. Pts underwent concomitant chemotherapy for 2 cycles. We identified 4 sub-volumes in the pelvic bones to assess a correlation between dosimetric parameters (mean dose, V5, V10, V15, V20, V30, V40, V45) of BM and HT: iliac crests (IC), lumbar sacral BM (LSBM), lower pelvis (LP), composed by bilateral pube + ischia + acetabula + femur heads, and the sum of all subsites defined as total pelvic BM (TPBM). HT was evaluated according to RTOG scale. Endpoints included white blood-cells count (WBC), neutrophil-count (NC), hemoglobin (Hb) and platelet (PTL) nadirs.

Results: 70.7% of pts were women; 4.6% were HIV positive. Clinical stage was as follow: 27,7% T2, 41.5% T3 and 24.6% T4; 67.7% of pts had positive nodes. CRT was interrupted for more than 3 days in 10 pts due to HT. 40% of pts showed G3 HT: 27.7% WBC, 23.1% NC and 10.8% PTL. A multivariate linear regression model assessed a statistically significant correlation between the HT and the following dosimetric parameters: V40 LSBM (p=0.01); V45 LSBM (p=0.008); V40 TPBM (p=0.03); V45 TPBM (p=0.047). These correlations were confirmed by non-parametric analysis for V45 TPBM (p=0.0001). A statistically significant correlation between V45 TPBM and the risk of HT > G3 was found at the logistic regression (p=0.006). The ROC curve analysis showed that V45 TPBM was the best classifier for toxicity in this patient cohort. V45 TPBM > 17% resulted to predict HT > grade 3 with a sensitivity of 100%.

Conclusions: Highly conformal techniques, such as IMRT and VMAT, allows for low-dose to pelvic BM but could also ensure a better treatment modelling which spares BM with consequent reduction of HT. From our analysis, V45 TPBM dosimetric parameter could be capable of predicting HT > grade 3 (V45 TPBM > 17%). This parameter could be used to improve toxicity profile by treatment optimization.

PO146

EFFICACY OF DEFINITIVE CONCOMITANT CHEMO-RADIOTHERAPY IN ANAL CANCER PATIENTS: A MONO-INSTITUTIONAL EXPERIENCE

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Aims: To evaluate outcomes rates and toxicity after definitive chemo-radiotherapy (CT-RT) with volumetric arc therapy (VMAT) and simoultaneous integrated boost (SIB) in anal cancer patients (pts).

Methods: Pts with anal cancer treated consecutively with definitive CT-RT with VMAT-SIB technique from June 2015 to December 2020 were included in this retrospective analysis. Inclusion criteria were: anal cancer in stage I-III or oligometastatic stage IV, all histologies, and performance status ECOG 0-3. All pts were treated with radical intent in concomitant to systemic therapy. All lesions were contoured on 2,5-5 mm CT-scan with contrast enhancement if available. A MRI and/or FDG-PET/CT-scan fusion was used for contouring. RT was delivered with VMAT-SIB technique. Clinical and instrumental revaluation (EUS, CT-scan, MRI and/or FDG-PET/CT) were performed every 4-6 months after the treatment. Acute and late toxicities were assessed with CTCAE v. 4.03 and EORTC-RTOG scales, respectively.

Results: A total of 52 pts were treated [M/F=8/44; median age: 65 years (range: 35-83 years); histology: SCC (96.2%), ADK (3.8%); stage I (5.8%), II (53.8%), III (38.5%), IV (1.9%). All pts (100%) were treated with SIB-VMAT technique to a dose of 55.5-55.8 Gy to T and positive lymph node and 45 Gy to pelvis in 30-31 fx (1.8/1.85 Gy/fx). All pts (100%) underwent CT in concomitant to RT: 5FU + mitomycin (92.3%), capecitabine (5.8%), and 5FU (1.9%). Two pts (3.8%) were not able to end RT, and stopped CT after the 1st cycle (Nigro scheme) due to treatment toxicity. Only 1 patient (1.9%) temporarily suspended treatment due to acute toxicity. Two pts (3.8%) were lost to follow-up. With a median follow-up time of 24 months (range: 3-73 months), 80.0% of pts showed a clinical and radiological overall response (74.0% CR, 6.0% PR), and 20.0% a PD. Of the latter, only two pts (4.0%) showed distant metastases as well locoregional recurrence, while 8 pts (16%) presented only locoregional relapse. Five pts with PD (10.0%) underwent to salvage abdominoperineal surgery, four pts (8.0%) were dead with disease progression, and 1 (1.9%) continues systemic therapy. Only 5.8% of pts presented G3 acute toxicity (bleeding, epitheliolysis, and proctitis).

No pts showed >G3 acute toxicities, and >G2 late toxicity.

Conclusions: Definitive CT-RT treatment with VMAT and SIB showed a favorable and promising results in terms of local efficacy and toxicity in anal cancer pts.

PO147

NEOADJUVANT RADIOTHERAPY DOSE ESCALATION FOR LOCALLY ADVANCED RECTAL CANCER (LARC); PRELIMINARY RESULTS OF A MONO ISTITUTIONAL CENTRE

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Aims: The aim of this study was to evaluate pathological response, survival rate and toxicities in patients (pts) affected by LARC underwent neoadjuvant RT dose escalation in association with Capecitabin 1650 mg/mq/day.

Methods: From June 2015 to Decembre2020, 40 pts affected by LARC underwent neoadjuvant RT-CT followed by surgery. The dose prescription was 52,5-55 Gy in 25 fractions (45 Gy to the pelvis and 52,5-55 Gy to the T, N+ and mesorectum) delivered by VMAT- SIB technique 5 daily fractions; 27 pts (67,5%) received 55 Gy in 25 ff and 13 pts were treated with total doses of 52,5 Gy in 25 ff. In association of RT treatment Capecitabin 1650 mg/mq/day was given. We evaluated survival outcomes and clinico pathological characteristics of Tumour (T), Nodal (N), margins, N-down-staging and T-down-staging. According to CTCAE *vs* 5 scale acute and late toxicity was evaluated. OS, PFS and LC were calculated using SPSS 22 version software.

Results: At the analysis 23 pts were male (57,5%) and 17 female (42,5%). The median age was 65 years old (range 27- 79 years old). After a median follow-up of 27 months (range 3-67 months) the estimate Kaplan-Meier OS was 88%, PFS 85% and LC 96%. A complete response (CR) as ypT0N0 was obtained in 25% of pts ; 30,4% in pts receiving 55 Gy in 25 ff and 23,07 in patients receiving 52,5 Gy in 25 ff. At histological examination a T-CR was observed in 27,2% of pts and a N-CR in 72,8% of pts. A R0 margins was obtained in all pts (100%). Moreover, a T down-staging was observed in 75% of pts and a N-down staging in 78% of pts. Overall 4 pts (10%) had progression disease; of them 1 pt had local and distant metastases and 3 pts had distant metastases. All pts underwent systemic treatment. GI and GU G3 acute toxicity was observed in 1 pts (2,5%), G2 in 10% and G1 in 57%. There was not G4 or higher acute or late toxicity. Post-surgical complications were observed in 11 pts (27,5%) and consisted in wound dehiscence in 4 pts, fluid collection in 3 pts, infections in 3 and fistula in 1 patient.

Conclusions: Neoadjuvant RT dose escalation 52,5-55 Gy/25ff with VMAT-SIB technique was effective with high rate of CR, T and N – down staging. We found low rates of G3, G2 toxicity. Randomized trials with higher number of pts and longer follow-up are needed to define optimal interval time between RT and surgery, toxicity and identify pts candidate of wait-and see strategy.

PO148

DEFINITIVE RADIO-CHEMOTHERAPY IN VERY ELDERLY PATIENTS WITH LOCALLY ADVANCED RECTAL CANCER: FEASIBILITY AND EFFICACY

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Aims: To evaluate safety and efficacy of definitive chemo-radiotherapy (CRT) in very elderly patients (≥80 years) with locally advanced rectal cancer, unfit for surgery.

Methods: Between 2018 and 2021, 12 patients with locally advanced rectal (cT3-4 N0-1) cancer were treated in our center with definitive radio-chemotherapy. All of them were over 80 years (very elderly) (range 80-96 y/o) and were considered unfit for surgery. We estimated Comorbidity (Charlson comorbidity index) and Performance status (KPS and ECOG score). Toxicity treatment's compliance and overall survival were studied. The study subjects underwent dihydropyrimidine dehydrogenase (DYPD) gene deficiency testing and all of them were wild-type. All patients were treated with concomitant Radio-Chemotherapy; 5 pts with continuous infusion of 5-fluorouracil (5-FU) at 200 mg/mq/day for five days/w; 4 pts with 5-FU 200 mg/mq daily, 2 pts with De Gramont and 1 pts with FOLFOX every 14 days. 7 patients were treated with IMRT, 5 pts with 3DCRT. Target volume includes primary lesion and locoregional mesorectal spread, without prophylactic lymphnodes irradiation, to a total dose of dose 54-64 Gy with conventional fractionation. All patients during the treatment were evaluated with IGRT with cone-beam CT. Probiotics and nutritional supplementations were administrated to prevent acute radiation-induced diarrhea.

Results: After a median follow-up of 24 months (range 4-43 months), a G1-2 enteritis with diarrhea was developed in 4 patients, spontaneously reduced after few days. 10 pts showed G2 erythema, while GU toxicity (cystitis and urgency and nocturia) occurred in 2 pts.

None of them had severe G3-4 toxicity that lead to treatment drop-off, with the exception of 1 pts with G3 diarrhea. 10 pts are still alive (median OS of 27 months), 1 died for disease progression and 1 for age-related problems.

Conclusions: Some elderly patients with locally advanced rectal cancer may have long-term disease control when treated with a non-surgical approach. Definitive Radio-chemotherapy was feasible and should be considered as a treatment option for carefully selected very elderly patients.

P0149

TOXICITY AND LONG-TERM OUTCOMES OF RADIO-CHEMOTHERAPY IN ANAL CANCER: A MONOCENTRIC RETROSPECTIVE STUDY

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Aims: To evaluate efficacy and tolerance of curative radiotherapy (RT) concomitant to chemotherapy (CHT) unless contraindicated on 25 patients (pts) with anal cancer, in terms of acute and early late toxicity, overall survival (OS), progression-free survival (PFS), local recurrence-free survival (LRFS) and metastasis-free survival (MFS).

Methods: Twenty-five pts affected by anal tumour were treated from 2012 to 2019, including 72% (18 pts) with a diagnosis of squamous cell carcinoma and 28% (7 pts) with other histological type. Fifteen pts had stage I (60%), 1 IIA(4%), 2 IIA(8%), 5 IIIB(20%) and 2 IIIC(8%). Twenty-four pts underwent Intensity Modulated Radiotherapy (IMRT), while 1 pt Volumetric Modulated Arc Therapy (VMAT) technique, with a total dose of 55 Gy in 25 fractions to the tumor and to positive lymph-nodes and 45 Gy in 25 fractions to pelvis and inguinal stations; in 88% (22 pts) was administered CHT concurrent. Toxicity assessment has been considered in acute and in early-late (up to 12 months post RT completion) for gastrointestinal (GI), genitourinary (GU), cutaneous (CU) and haematological (HT) districts, according to Radiation Therapy Oncology Group (RTOG) scoring system. Survival outcomes were calculated through Kaplan-Meier curves.

Results: Acute CU G1 toxicity was recorded in 7 pts (28%), G2 in 10 pts (40%), G3 in 3 pts (12%). Acute GI G1 toxicity was registered in 9 pts (36%), G2 in 11 pts (44%), G3 and G4 in 1 (4%) and 1 (4%) pt respectively. Acute GU G1 toxicity was recorded in 9 pts (36%), G2 in 5 pts (20%). Acute HT G1-G2 toxicity in 2 (8%) and 2 (8%) pts respectively. Regarding early-late toxicity: CU G1 toxicity was observed in 2 pts (8%) and G2 in 1 pt (4%), GI G1 toxicity was recorded in 11 pts (44%), G2 in 3 pts (12%) and G4 in 1 pt (4%). GU G1 toxicity was observed in 5 pts (20%) and G2 in 2 pts (8%). No early-late HT toxicity was reported. Early-late dyspareunia was recorded in 1 pt. Median follow-up time was 47.3 months (range, 5.5-104.9 months). At 1-, 2- and 5-years survival probability were as follows: OS 96%, 92% and 81.1%, PFS 91.8%, 79.1% and 79.1%, LRFS 91.8%, 83.3% and 83.3%, MFS 96%, 87.3% and 87.3% respectively. Median survivals were not reached.

Conclusions: Our retrospective study shows a good profile toxicity. After 5 years, radio-chemotherapy combined showed to be effective and safe in this population.

P0150

PREDICTIVE AND PROGNOSTIC FACTORS IN ESOPHAGEAL CARCINOMAS TREATED WITH MULTIMODAL THERAPY: THE ROLE OF 18F-FDG PET TC

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Aims: [18F] fluorodeoxyglucose positron emission tomography/computed tomography ([18F] FDG-PET/CT) is used for tumour staging, response assessment and prognosis prediction in different tumours, but its role in oesophageal cancer is still debated. The aim of the present study was to evaluate the role of semiquantitatve PET parameters as possible prognostic and predictive factors in a series of oesophageal carcinomas treated with combined modality treatment.

Methods: A series of 43 patients affected with oesophageal carcinoma and treated with chemo-radiotherapy (CRT) followed by surgery in 20 cases, underwent pre-treatment 18F-FDG PET/CT. Semiquantitaive PET parameters were evaluated including Standardized Uptake Value (SUVmax e SUVmean), Metabolic Tumour Volume (MTV) and Total Lesion Glycolysis (TLG) with isocontour of 41% and 50%. Further variables analysed were gender, primary tumour site, histological type, use of surgery, achievement of a radical resection and chemotherapy regimen. The correlation of all variables with treatment response, loco-regional control (LR control) Overall (OS) and Disease Free (DFS) Survival was evaluated with log-rank, Student's t- and Chi-squared tests.

Results: As possible predictive factors, pre-treatment PET parameters did not show significant differences between responders and non-responders ($p \geq 0.10$). In terms of prognostic factors, MTV correlated with better OS: patients with MTV41 <11.32 cm^3 and MTV50

<8.07cm^3 (both p-value=0.04) showed better 3-year survival rates (33% *vs.* 20%). Further factors predicting for better prognosis were the use of surgery and radical resection (R0) (both p-value <0.01). Of note, there was no correlation between MTV and surgery (p=0.1).

Conclusions: The present study shows that, among pre-treatment PET parameters, MTV values resulted to be significant prognostic factors for OS, together with the use of surgery and undergoing R0 resection.

P0151

PRE-OPERATIVE INTENSITY MODULATED RADIATION THERAPY WITH SIMULTANEOUS INTEGRATED BOOST IN LOCALLY ADVANCE RECTAL CANCER: A MONO-INSTITUTIONAL EXPERIENCE

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Aim: Preoperative chemoradiotherapy as multimodal approach is a standard of care for locally advance rectal cancer (LARC). Intensity modulated radiation therapy (IMRT) with simultaneous integrated boost (SIB) is promising in terms of toxicity profile and compliance to therapy, especially in elderly patients (E-pts) where organ preservation could be the main objective. We carried out an analysis of our series where RT-dose intensification was applied in preoperative treatment of LARC

Materials and Methods: Pts who were treated with preoperative IMRT-SIB and concurrent capecitabine (CAPE) for LARC from August 2018 to March 2021 were retrospectively enrolled. All pts underwent routine staging: TB scan, pelvic MRI, biopsy, and colonoscopy: 32pts (47%) underwent transrectal ETG and 12pts (18%) PET scans. Planning scan was performed in prone position with a full bladder and belly bord support. Target volume and organ at risk (OAR) were contoured according to RTOG atlas. We prescribed 45Gy to the pelvic nodes and mesorectum with 55Gy SIB to the gross tumor and corresponding mesorectum in 25 fractions. Constraints score card was created according to literature and implemented in the planning process to respect goals for planning target volumes and OAR (Figure 1). We used CTC-AE v5.0 to evaluate acute toxicity and tumor regression grade (TRG) Dworak system and pathologic complete response (pCR) to assess treatment response

Results: We identified 68pts (12% II stage and 88% III stage of disease). Pts and tumor demographics are described in table. All pts completed RT without interruption; 7% received reduced-dose CAPE and 95% received full-dose. Ten pts (14%) developed grade (G) 2 gastrointestinal (GI) acute toxicity (diarrhea, tenesmus); 3pts (4%) developed G2 genitourinary acute toxicity (dysuria). No G3–4 acute toxicity was observed. Between E-pts (41% of the sample, median age 77) only 4pts (7%) developed G2 GI-GU acute toxicity. After combined treatment we were able to evaluate response in 40pts out of overall 68: 9pts (23%) achieved radiologic and histologic CR (median age 72) and were sent to wait and see, and 31pts underwent surgery. Tumor and nodal downstaging were observed in 23pts (74%) and 20pts (65%) respectively; 5 pts (16%) obtain pCR. TRG 3-4 was obtained in 13 pts (42%)

Conclusions: IMRT-SIB and concurrent CAPE for LARC show excellent pts compliance and acceptable acute toxicity especially for E-pts with promising results in term of organ preservation

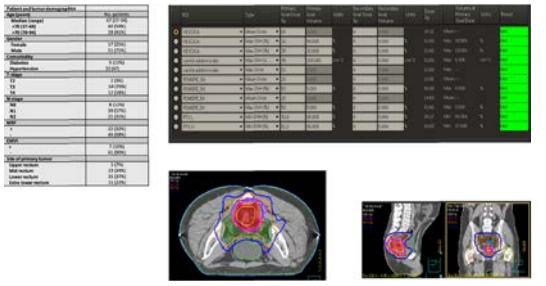

Figure 1.

P0152

LIFTING AND FIXATION OF INTESTINAL LOOPS TO MAINTAIN SAFE DOSE CONSTRAINTS FOR INTENSITY-MODULATED RADIATION THERAPY (IMRT) OF AN ANAL CANCER: A CASE REPORT

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Aims: Combination of chemotherapy and radiotherapy (CRT) is the treatment of choice for anal canal squamous cell carcinoma (ASCC) because of its effectiveness in preserving the anal sphincter. Highly conformal irradiation techniques, such as intensity-modulated radiation therapy (IMRT), help to reduce RT dose to normal tissues and nowadays represent the optimal RT option for ASCC. Despite the latest technological advances, some anatomical presentation can still represent a challenge for RT planning. Below, we introduce a surgical method to remove intestinal loops from the treatment field based on laparoscopic lifting and fixation of bowel loops.

Methods: A 66 years-old woman affected by III stage ASCC, with a history of glaucoma and hysterectomy for

fibrosis, was prescribed a concomitant CRT with IMRT planning. The bowel loops were fixed in the pelvis, because of fibrosis and adhesions due to previous surgery, exposing the patient to an increased radiation enteritis (RE) risk, despite the use of a modern technique such as IMRT that allows to sculpt the RT dose on the target while sparing the surrounding healthy organs. No other set up solution has provided optimal loop savings according to constraints. Thus, a laparoscopic lifting and fixation of intestinal loops with resorbable sutures was performed, in order to remove them from the treatment field. Subsequently, the patient underwent a further CT-scan simulation to confirm the suspension of the small bowel from the pelvis. The procedure significantly displaced the bowel loops outside the high-dose radiotherapy field, allowing a safe delivery of the planned RT, in terms of both dose and volume.

Results: After the surgical procedure, a separation of at least 3 cm of loops from the PTV1 was achieved. (Figure 1). Dmax to the loops in the pelvis was 49.7 Gy before and 38 Gy after procedure. The patient could start new RT planning within 3 days post-procedure and was able to complete the scheduled radiotherapy, without developing acute RE or other gastrointestinal toxicity. IGRT with daily Cone-beam CT confirmed the removal of the loop from high dose radiotherapy region.

Conclusions: Laparoscopic lifting can be an effective technique to displace ectopic small bowel loops. It can help to prevent excessive bowel irradiation and facilitate curative chemoradiation.

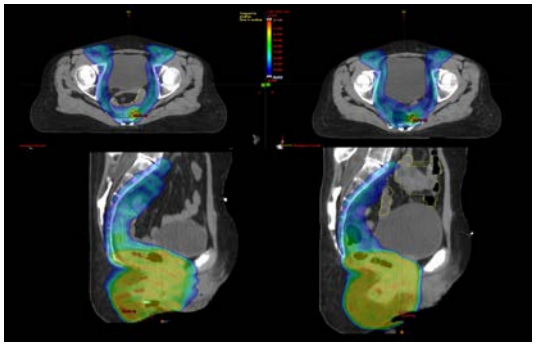

Figure 1.

PO153

CURATIVE CHEMORADIOTHERAPY FOR ANAL CANCER: OUR EXPERIENCE

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Aims: Anal cancer is a rare malignancy. The mainstay of curative treatment for stage II-III anal cancer is concurrent chemoradiotherapy. Intensity modulated radiotherapy (IMRT) has proven to reduce severe acute and late toxicities. For patients who develop metastatic disease, survival is poor. The aim of this investigation is to analyze the efficacy and toxicity of chemoradiotherapy in a small group of patients.

Methods: From January 2016 to December 2020, 29 patients affected by anal cancer referred to our Department: 7 of them had palliative treatment and 22 patients underwent radical chemoradiotherapy.

Patients characteristics were: 17 females and 5 males, and mean and median age 64 and 65 years, respectively (range 39-90 years). All pts had good PS (0-1), squamous cell carcinoma histology, and stage II-III (TNM/UICC 2017). 19 pts received curative radiochemotherapy, while 3 patients had radiotherapy alone. Concurrent chemotherapy included a combination of Mitomicyn, 5FU, Capecitabine, or Cisplatin. Radiotherapy treatment was performed in all pts with volumetric arc therapy (VMAT) techniques with a dose of 45 Gy in 1,8 Gy fractions over 5 weeks to elective nodes and simultaneous integrated boost (SIB) plan prescribing 55 Gy in 2,2 Gy fractions to the primary tumor and positive nodes in 25 fractions. Mean and median follow-up were 22,4 and 17,4 months respectively.

Results: At time of analysis 16 pts were alive with no-evidence of disease (NED), 2 pts are alive with metastatic disease and 4 pts died: 2 of these for distant metastasis (lung and lymph node involvement) and 2 pts died for non oncologic cause. No treatment interruption was observed. Grade 2 hematologic toxicity and grade 2-3 gastrointestinal tract and dermatologic toxicity were observed. The most common non hematologic acute toxicity include desquamation, proctitis, cystitis, and diarrhea. The 2-years local control (LC) rate was 85%; 3/20 patients (15%) developed local recurrence, and in these patients mean relapse-free survival was 10 months. Mean and median survival (OS) were 24 and 19 months respectively (range 2,4-62,7 months)

Conclusions: Concurrent curative chemoradiotherapy represents standard treatment for stage II-III anal cancer patients. Highly conformal radiation dose, such as IMRT decreases acute toxicity to normal tissue and improves treatment compliance. Although this examined a small number of patients, radical radiochemotherapy with IMRT planning is feasible and effective in anal cancer patients.

PO154

FINDING SAFE DOSE-VOLUME CONSTRAINTS FOR SBRT RE-IRRADIATION (SALVAGE SBRT) OF INTRAPROSTATIC PROSTATE CANCER RELAPSE: THE IEO EXPERIENCE

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Aims: Consensus for the optimal management of isolated prostate cancer (PCa) recurrence following external beam radiotherapy (RT) (EBRT) is lacking. The primary aim of this study is to provide preliminary indications for safe constraints of rectum and bladder in patients re-irradiated with stereotactic body RT (SBRT).

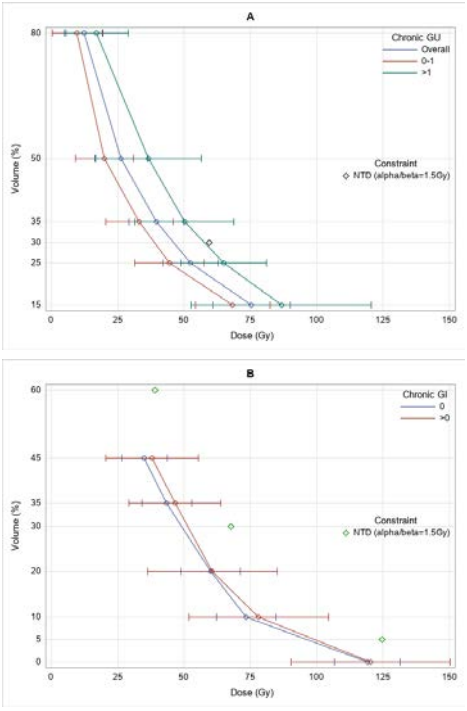
Methods: Data from patients treated for PCa and intraprostatic relapse, from 1998 to 2016, were retrospectively collected. First RT course was delivered with 3D conformal RT techniques, SBRT or volumetric modulated arc therapy (VMAT). All patients underwent re-irradiation with SBRT with heavy hypofractionated schedules. Cumulative dose volume values to organs at risk (OARs) were computed and possible correlation with developed toxicities was investigated.

Results: Twenty-six patients were included in the analysis. Median age at re-irradiation was 75 years, and mean interval between the two RT courses was 5.6 years and the median follow-up was 4 years. The median follow-up after salvage SBRT was 47.7 months (13.4-114.3 months). First and second RT courses characteristics are reported in Table 1. After re-irradiation, 18 (69%) and 12 (46%) patients were free from any grade (G) acute and chronic GU/GI toxicity, respectively. On the other hand, while only three patients (12%) experienced acute GU G2 events, 12 patients (46%) developed chronic GU/GI G2/G3 toxicity. Regarding late GU toxicities, if patients are divided into G0-1 and G>1 groups, Dbladder30% parameter will be much below the dose-volume limit in the former group but very close to this point in the latter (Figure 1A). After analysing GI events, no statically significant associations were found neither between the cumulative dose and chronic toxicities, nor between risk category and toxicities (Figure 1B). No statically significant associations were found neither between the median cumulative dose and toxicities nor between risk category and toxicities: but, of note, 56% of the HR patients developed GU/GI toxicity while only the 25% of the LR ones did (odds ratio 3.75, p value 0.16).

Conclusions: On the basis of the very few rectal/intestinal major toxicity events registered, the median values of the patients' dose-volume points can represent a safe rectum dose volume histogram. Regarding bladder, D30 could represent an important parameter to consider to prevent late GU toxicity. Finally, patients' comorbidities status should be considered.

Table 1. First and second RT courses characteristics.

RT Course	Year	# pts	Technique	System	Total dose [EQD_2], median (min, max)	Total dose (1^{st} + 2^{nd}) [EQD_2], median (min, max)
1^{st} RT	1998 - 2008	16	3D conformal	--	78.0 (60.5-85.0)	
	2011 - 2014	10	SBRT / VMAT	Cyberknife / VERO		130.6 (116.4-159.3)
2^{nd} RT	--	26	SBRT / VMAT	Cyberknife / VERO	64.3 (37.1-85.0)	



Abbreviations: **GI** = gastrointestinal; **GU** = genitourinary; **NTD** = normalized total dose.

Figure 1. Chronic GU (A) and GI (B) toxicities.

PO155

LONG-TERM OUTCOMES OF PET GUIDED EXTENSIVE NODAL RADIOTHERAPY FOR PROSTATE CANCER LYMPH-NODAL RELAPSE

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Aims: Although replaced in recent years by PSMA PET/CT 11Carbon- and 18Fluoro-Choline were the first PET/CT tracers used to identify prostate cancer (PCa) relapses after surgery +/- adjuvant/salvage radiotherapy (ART/SRT), anticipating diagnosis of bone and lymph-nodal (LN) metastases and changing therapeutic strategy. We report long term outcomes of salvage extended–nodal radiotherapy (ENRT) in PCa pts presenting positive (+) LN at Choline PET/CT.

Methods: From 02/2005-11/2020, 175 PCa pts were treated for LN relapses with ENRT at a median total dose (TD)= 51,8 Gy/28 fr, and Choline PET/CT guided simultaneous integrated boost (SIB) to a median TD= 65,5 Gy. Primary GS score was 3 in 58, 4 in 85, 5 in 23, and not available in 9 pts. Median iPSA=12 (2.4-541) ng/ml. The majority of pts (162) were previously treated with surgery and 88 with ART/SRT. Median age at relapse was 69.5 (50.2-87.4) years. Median PSA was 2.16 (0,18-187) ng/ml. Median number of PET + LN was 2 (1-20). Androgen Deprivation Therapy was used in 95 pts for a median of 26 (3-64) months, not prescribed in 38, and 42 were castration–resistant.

Results: With a median follow up of 58 (0-159,2) mts, acute RTOG upper gastro-enteric (uGE) toxicity was 26.3% Grading (G)1 and 8.6% G2, rectal toxicity (GI) was 12.6% G1 and 4% G2, genito-urinary (GU) toxicity was 14.3% G1, 3.4% G2 and 2.3% G3. Late toxicities were: uGE G1 2.3%, GI G1 0.6%, G2 2.9% and G3 1.1%, and GU G1 10.9%, G2 6.3%, G3 6.9% and G4 0.6% (1 cystectomy due to previous prostate bed irradiation).

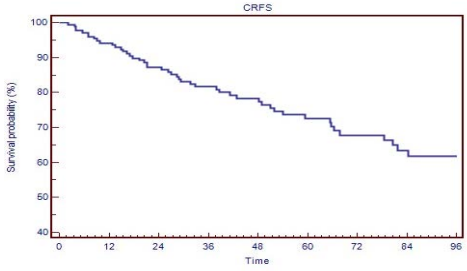

Figure 1.

Median PSA at the last follow-up was 0,730 (0,00-4350,00) ng/ml. 62.9% of pts presented a biochemical relapse, 28.6% a clinical relapse in bone (13.7%), LN (10.9%), bone and LN (0.6%), bone and lung (0.6%), lung (1.7%), pleural and mediastinum (0.6%) and prostate bed (0.6%). Only 4 relapses (2.3%) were in the field of salvage radiotherapy, and another one in field and distant (0.6%). At the last follow-up 66 pts were dead (37.7%), but only 18.3% because of disease progression. Median biochemical relapse free survival (bRFS) was 33.8 months, clinical relapse free survival (CRFS) was 137.5 months, cancer specific survival (CSS) was 147.7 months, and overall survival (OS) was 110.4 months. 5-year Kaplan Meier estimates were: bRFS 35.3%, CRFS 75.1% (Figure 1), CSS 82%, OS 67.3%.

Conclusions: ENRT with PET guided SIB for PCa LN relapses determines good CRFS and CSS. Only 5 of 175 patients presented in field LN relapses.

PO156

INDEPENDENT ROLE OF DOSE-ESCALATION AND PROPHYLACTIC WPRT IN SALVAGE RT AFTER RADICAL PROSTATECTOMY

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Aims: The role of both RT dose-escalation and prophylactic whole-pelvis irradiation (WPRT) in the setting of salvage RT (SRT) after radical prostatectomy are still highly debated. Aim of this analysis was to investigate the independent role of both in a large cohort of men treated with high-dose SRT.

Matherial and Methods: A merged database comprising men treated with SRT in six Institutes was analyzed. Only pts with a minimum (if alive) follow-up of 5 years and a PSA ≤2 ng/mL at SRT start were considered. This resulted in a cohort of 725 men treated with a median 2-Gy equivalent dose (EQD2) of 72 Gy (IQR 70-72.85). Radiotherapy was delivered to prostatic bed (PB) only in 455 men, to PB+WPRT in 270. Adjuvant androgen deprivation therapy (ADT) was given to 38% for a median of 14 months.

Results: The median follow-up was 102 months (IQR 78-140), median PSA at SRT 0.43 ng/mL (IQR 0.24-0.80). Two Receiver Operating Characteristics (ROC) curve analyses indicated an EQD2 dose ≤72 Gy as the most informative cut-off with respect to the risk of both biochemical and clinical relapse (p≤0.0003). The 8-year biochemical relapse-free (bRFS) and clinical disease-free survival (cDFS) in patients treated at EQD2 doses ≤72, >72 and ≤74 or >74 Gy were 57%, 78% and 75% (p<0.0001, Figure 1) and 81%, 89% and 89% (p=0.002), respectively. The 8-year bRFS and cDFS in men treated with PB only (median dose to PB 70 Gy, median PSA at SRT 0.42) or PB+WPRT (median dose to PB 72.58 Gy, to WPRT 48.38 Gy, median PSA at SRT 0.43) were 62% *vs* 73% (HR 0.61, p=0.0003) and 87% *vs* 83% (HR 0.70, p=0.054). SRT doses >72 Gy, WPRT and adjuvant ADT emerged as independent predictors of improved post-SRT bRFS, while WPRT was the sole treatment-related factor

significantly improving cDFS. The overall 8-year risk of Grade ≥3 toxicity was 5% *vs* 14% in men treated at EQD2 doses ≤72 *vs* >72 Gy (p=0.002), being however almost identical (4.9% *vs* 5.1%) in the cohort receiving conventionally-fractionated RT (Table1).

Conclusions: Both EQD2 doses >72 (but not >74 Gy) and WPRT, as well as ADT, significantly improved bRFS, while only WPRT, but not the sole dose-escalation, significantly reduced the risk of clinical recurrence. Further analyses will address which pts subsets can safely be spared such treatment intensification.

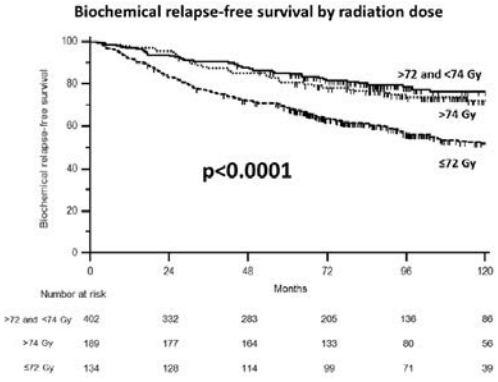

Figure 1.

PO157

EVALUATION OF ORGAN MOTION EFFECT ON DOSE IN SBRT TREATMENTS FOR OLIGOCURRENT PROSTATE CANCER

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Aims: Geometric and anatomical variations have a major impact on SBRT treatments, where high gradient dose in few fractions and small fields are applied, so better accuracy of the delivery treatment is required. The purpose of this research is to evaluate the OARs displacement by simulating inter-fraction variability in SBRT treatments.

Methods: Patients with lymph nodes oligorecurrent PCa treated with SBRT between 2012 and 2015 on the VERO system and planned with Iplannet (v4.5.3 by BrainLab®) were included in the study. To evaluate inter-fraction variability, OARs were delineated both on planning CT and on rigidly co-registered CBCTs using RayStation (RaySearch) and the union volume for each one was computed (VU). For each OAR, a new contour was created by sequentially applying a margin of 3, 5, 8, 10, 15, 20 mm (VE) and the percentage volume (V%) of the intersection between VE and VU with respect to VU was computed. The evaluation of organ motion or deformation between the OARs contoured on planning CT and on CBCTs was performed on RayStation using Dice similarity coefficient (DSC) and maximum distance to agreement (Max_DA).

Results: Thirty-nine patients were included in the study. The highest agreement was reported for the femoral head (DSC = 0.79; Max_DA = 0.9 cm) and the lowest for colon (DSC = 0.37 and Max_DA = 1.6). All the other OARs showed an intermediate behaviour (Table 1). The minimum value of margin, in mm, which ensured a V% > 95%, for femoral head, cauda, bladder, ileum, colon and rectum was 3 (97.2%), 3 (97.5%), 8 (97.0%), 10 (95.9%), 15 (96.6%) and 8 (95.4%), respectively.

Table 1.

OAR	DSC	Maximum DA (cm)
Femur	0.79	0.9
Cauda	0.72	0.64
Bladder	0.70	1.5
Rectum	0.68	1.3
Ileum	0.50	1.6
Colon	0.37	1.6

Conclusion: Colon and ileum resulted the most critical OARs as, considering the V%, they need a margin of 15 and 8 mm respectively to reach the 95% threshold. This can be ascribed not only to organ motion but also to the different shape of the organs, as showed by the lower DSC. The median maximum dose variation is due to motion of the two OARs, with the colon showing a more pronounced median Dmax with respect to the ileum. Anatomical differences concerning bladder and rectum can be mainly related to their filling status and hence to patient's preparation. Future prospective foreseen the plans to be recalculated with higher dose prescription per fraction to evaluate constrains compliance. The present study is an ancillary study of RADIOSA clinical trial (AIRC IG-22159) and will be used as a benchmark for analyzing prospective results from the trial.

PO158

SALVAGE STEREOTACTIC BODY RADIOTHERAPY TO PROSTATE BED FOR RELAPSED PROSTATE CANCER: A MONO-INSTITUTIONAL PRELIMINARY EXPERIENCE AND LITERATURE REVIEW

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Aims: To investigate the feasibility, efficacy and safety of Salvage Stereotactic Body Radiotherapy (S-SBRT) to prostatic bed for local relapsed prostate cancer (LRPC) after radical prostatectomy with or without following adjuvant/salvage radiotherapy (RT).

Methods: A literature search via PICO in MEDLINE/PubMed database was conducted in May 2021 using the following keywords: (P) Prostate cancer relapse (I) Prostatic bed stereotactic body radiotherapy. In this work the preliminary experience on LINAC-based S-SBRT performed at our Institute is also reported: between December 2020 and May 2021, 5 patients with RM- or PET-confirmed prostate cancer local recurrence after radical prostatectomy (mean age 79.5 years, PSA in the range 0.2-2.7 ng/ml) were treated with a total dose of 30 Gy in 5 fractions to prostatic bed using daily IGRT. Dosimetric parameters for OARs were defined according TG 101 criteria. None of patients underwent previous adjuvant/salvage RT; no simultaneous androgen deprivation therapy (ADT) was administered.

Results: Among the 21 papers identified with our literature search, 10 studies (enrolling a total a 304 patients) reported good disease-control and toxicity outcomes after S-SBRT to prostatic bed or macroscopic prostate bed recurrence delivered with Cyberknife or LINAC. In 9 studies, the prescribed total dose ranged between 25 and 45 Gy in 5 fractions, according to previous prostate bed irradiation; in a single study (with Cyberknife) 12 patients were treated with a total dose of 36 Gy in 6 fractions to macroscopic recurrence. All S-SBRT treatments performed at our Institute were well tolerated (G0-G1 RTOG urinary and rectal toxicity); all followed up patients obtained a reduction of PSA value under 0.2 ng/ml.

Conclusions: S-SBRT seems to be a feasible, effective and safe option for LRPC, even in the setting of re-irradiation. Nowadays, taking into account these advantages and a patient-specific multidisciplinary evaluation, ADT delay could be proposed. Confirms on long-term treatment effectiveness and tolerance are expected in prolonged follow up periods. The integration of modern imaging information will support the optimal therapeutic strategy.

PO159

PREDICTORS OF URINARY INCONTINENCE 2 YEARS AFTER RT WITH DIFFERENT INTENTS FOR PROSTATE CANCER

F. Munoz[1], G. Sanguineti[2], V. Vavassori[3], E. Garibaldi[4], B. Avuzzi[5], D. Cante[6], J.M. Waskiewicz[7], A. Magli[8], L. Ferella[1], A. Faiella[2], E. Villa[3], M. Gatti[4], B. Noris Chiorda[5], E. Moretti[8], T. Rancati[5], F. Badenchini[9], R. Valdagni[5], N. Di Muzio[9], C. Fiorino[9], C. Cozzarini[9]

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Aims: To identify predictors of patient-reported urinary incontinence (PRUI) two years after radical, adjuvant or salvage RT (RAD, ADV, SALV) for prostate cancer (PCa).

Methods: A prospective cohort of 407 men enrolled in a multi-Institutional, observational registered study investigating radiation-induced toxicity, with complete ICIQ-SF questionnaire at baseline and 2 years after RT start, was analyzed. Patient characteristics: RAD n=141, cT1/T2/T3a/T3b 19/37/33/11%, median 2-Gy equivalent dose (mEQD2) 80 Gy; ADV n=104, pT2/pT3a/pT3b 8/36/56%, mEQD2 70.41 Gy, median time to RT (mTTRT) from prostatectomy 3.9 months; SALV n=162, pT2/pT3a/pT3b 45/33/22%, mEQD2 74 Gy, mTTRT 19.1 months. ADT was given to 95%, 56% and 37% of pts treated with RAD, ADV and SALV intent, respectively, for a median of 24 months. Frequency and amount of urine leakage and their impact on self-perceived QoL (ICIQ-SF3, 4 and 5, respectively) were analyzed, as well as the overall ICIQTOT score. The 75th percentiles of ICIQ-SF3, 4, 5 and TOTAL worsening at 2 years with respect to the baseline were considered as end-points. Severe PRUI (ICIQTOT≥13 points) at two years was also analyzed. The association between these end-points and many clinical and dosimetric variables, including 2-Gy equivalent RT doses (EQD2), RT intent, use of concomitant ADT, comorbidities, patient personality as measured by the EPQR questionnaire, baseline Bowel, Emotional, Social and Systemic Domains as evaluated by the IBDQ questionnaire, was investigated by univariable (UVA) analyses. Variables with a è-value <0.20 at UVA were entered into a multivariable backward logistic regression analysis (MVA).

Results: No role emerged (even at UVA) for EQD2. Only baseline ICIQTOT (OR 1.32, p>0.0001) and SALV intent (OR 3.143, p=0.004) independently predicted an ICIQTOT score at 2 years ≥13 points. A summary of the predictors of PRUI worsening is shown in Table 1, including the performance of the resulting models in terms of area under curve (AUC) and goodness of fit

(Hosmer-Lemeshow test).

Conclusions: Baseline urinary incontinence status and RT intent are the major factors predicting 2-year patient-reported urinary incontinence. The impact of RT intent (ADV/SALV *vs* RAD) is stronger for the "objective" (frequency and amount) PRUI symptoms. Both psychoticism and lie personality trait (a measure of social acquiescence) significantly reduce patient perception of the detrimental effect of PRUI on their QoL

Table 1.

Factors Independently Predictive of 2-Year Significant Worsening (≥75° percentile with respect to baseline) of PRUI – Multivariable Analysis

	Δ ICIQ3 ≥1	Δ ICIQ4 ≥2	Δ ICIQ5 ≥2	Δ ICIQ TOTAL ≥5
Bowel Domain Baseline	OR 0.56, p=0.049			
Emotion Domain Baseline		OR 0.69, p=0.04		
Hypertension				OR 2.05, p=0.02
RT Intent	RAD=Reference ADV OR 4.07, p=0.003 SALV OR 5.91, p<0.0001	RAD=Reference ADV OR 3.27, p=0.005 SALV OR 4.25, p=0.0002		RAD=Reference ADV OR 2.09, p=0.004 SALV OR 2.72, p=0.002
ICIQ-SF 3 Baseline	OR 0.39, p<0.0001		OR 2.38, p=0.0005	
ICIQ-SF 4 Baseline		OR 0.50, p<0.0001		
ICIQ-SF 5 Baseline				OR 0.84, p=0.03
ICIQ-SF TOTAL Baseline				
IPSS1 (Incomplete Emptyng) Baseline		OR 1.80, p=0.02		
IPSS7 (Nocturia) Baseline			OR 0.74, p=0.03	
Psycoticism			OR 0.70, p=0.05	0.69, p=0.02
Lie			OR 0.76, p=0.02	
Area Under Curve	0.75	0.74	0.69	0.70
Hosmer & Lemeshow test	p=0.14	p=0.79	p=0.89	p=0.88

PO160

SALVAGE STEREOTACTIC BODY RADIATION THERAPY (SBRT) RE-IRRADIATION FOR LOCAL RECURRENCE OF PROSTATE CANCER: A MONO-INSTITUTIONAL RETROSPECTIVE ANALYSIS OF 20 PATIENTS

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Aims: The aim of this study was to evaluate the outcomes and toxicities of local re-irradiation with stereotactic body radiation therapy (SBRT) in patients with local recurrence of prostate cancer after curative radiotherapy.

Methods: Twenty patients were treated with SBRT between December 2010 and March 2020. All patients had clinical/radiological local relapse in the prostate and no distant metastasis. Fourteen patients (70%) received 30 Gy in 5 fractions/3w, 3 (15%) received 25 Gy in 5 fractions/3w, 2 (10%) received 23 Gy in single fraction and 1 (5%) 37.5 Gy in 5 fractions/3w. All patients underwent image-guided radiotherapy (IGRT) using cone-beam computed tomography (CBCT) system as daily pre-treatment imaging. Seven out of 20 patients (35%) received also hormonal deprivation therapy. Toxicity was evaluated using the Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer Criteria. Biochemical control was assessed according to the Phoenix definition (NADIR + 2 ng ml (-1)).

Results: Median follow-up was 36 months (range 2-85 months). Median age was 78 years (range 65-89 years), median pre-SBRT prostate specific antigen (PSA) was 3.3 ng ml (range 0.24-18.3 ng/ml). The median planning target volume (PTV) was 65 cm^3 (range 8-148.7 cm3). The median overall survival (OS) was 57 months (95% i.c. 23.5-90.8) and the actuarial 2-year and 5-year OS was 89% and 40% respectively. Two-year and 5-year Biochemical free survival (BFS) was 55% and 47%, respectively. Local control (LC) at 2-year and 5-year was 73% and 62%, respectively. Disease free survival (DFS) at 2-year and 5-year was 67% and 57%, respectively. Median BFS, LC and DFS were not reached. Six patients (30%) experienced grade 1-2 acute urinary toxicities. Grade 1-2 late urinary toxicities were reported in 13 patients (65%).

Conclusions: SBRT re-irradiation for locally recurrent prostate cancer offers a satisfactory tumor control and shows a low toxicity profile.

PO161

ARTO (NCT03449719), QUALITY OF LIFE MONOCENTRIC REPORT AFTER STEREOTACTIC TREATMENT AND ABIRATERONE

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Aims: ARTO-NCT03449719 is a multicenter, randomized phase II trial including oligometastatic Castrate Resistant Prostate Cancer (CRPC). To explore the Quality of Life (QoL) impact of radiotherapy, we report preliminary analysis of patients with at least 6 months of follow-up.

Methods: Twenty nine patients enrolled at the trial promoting institute were included in the analysis. All patients had oligometastatic CRPC and were randomized 1:1 to receive either Abiraterone Acetate alone (16 patients as control arm) or associated with stereotactic body radiation therapy (SBRT) on all sites of disease (13 patients as treatment arm). QoL evalutation by EORTC QLQ-C30 was performed at 3 and 6 months after randomization. Differences among baseline, 3 and 6 months evaluations and between control and treatment arm were considered clinically significant if exceeding 10 points for global health status (GHS). Regarding other EORTC QLQ-C30 questionnaire items, differences exceeding Minimal Clinically Important Difference (MCID) reported in literature were considered significant.

Results: After 3 months, an average decrease of 13 points in terms of GHS was reported for the overall population. Difference between average values of decrease reported in control and treatment arm (11 *vs* 16 points, respectively) did not exceed minimal clinically important difference (MCID). However, complete recovery in terms of GHS was noticed at 6 months, with average improvement of 2 points on overall population, 3 points on control and 1 point on treatment arm. Physical, role, emotional, cognitive and social functioning were stable at 3 and 6 months. SBRT significantly influenced only social functioning, with a 10 points difference between control and treatment arm at 3 months (MCID 8.4). However, 6 months recovery was reported, with a difference lower than MCID at last evaluation (2.08 increase in the control and 2.8 decrease in treatment arm). At 3 months, appetite was significantly increased in both arms (11 points), but this difference, compared to baseline, was recovered at 6 months evaluation.

Conclusion: In oligometastatic CRPC undergoing abiraterone treatment, GHS significantly decreased after 3 months, but recovered at last follow up. No impact of SBRT was reported on the analyzed items, except for social functioning at 3 months, however, complete recovery at 6 months was reported.

PO162

SIMULTANEOUS INTEGRATED BOOST INTENSITY MODULATED RADIATION THERAPY (SIB-IMRT) IN PROSTATE CANCER: ANALYSIS OF OUTCOMES

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U.O.C. Radioterapia - ASP 7

Aims: We presented our outcomes to evaluate acute and late toxicity, Overall survival and Freedom from biochemical recurrence in patients with localized high risk (cN0) and pelvic node-positive (cN1) prostate cancer, undergoing moderately hypofractionated IMRT-SIB, combined with androgen deprivation therapy (ADT).

Methods: From April 2014 to May 2021, 61 patients with high risk-localized prostate cancer and with pelvic node-positive prostate cancer were treated by Whole Pelvis SIB-IMRT. The median age of patients was 66 years old (range: 42-80). All patients received 50 Gy (2.0 Gy/fr) to the pelvic lymph nodes chains and a SIB to a dose of 67.5 Gy (2.7 Gy/fr) to the prostatic volume, in 25 fractions, with concurrent ADT. A SIB to a dose of 57 Gy (2.28 Gy/fr) was delivered to the involved lymph node regions in 21 patients with pelvic lymph node metastases, diagnosed clinically N1 by 11C-Choline CT/PET. Specific diet during Radiotherapy such as lactose, fat and fibre-restriction and reduced intake of motility stimulants have been suggested. Toxicity was scored using CTCAE 5.0 and IPSS score.

Results: All patients finished the treatment as planned. The incidence of grade 1 acute Gastro-Intestinal (GI) toxicity was 15. The incidence of grade 2 and 3 acute GI toxicity was 6% and 2%, respectively. Grade 1 acute Genito-Urinary (GU) side effects were observed in 24% of the patients; Grade 2 and 3 acute GU side effects were observed in 12% and 4% of the patients respectively. No increased toxicity was observed in the 21 lymph node-positive patients receiving a simultaneous pelvic nodal Boost. A decline in prostate-specific antigen (PSA) level was observed in all cases after SIB-IMRT. Rates of late GI toxicity were 5%, 2% and 2% for grade 1, 2 and 3, respectively; while rate of late GU toxicity grade 1, 2 and 3 were 2%. No patient experienced grade >3 acute or late GI and GU toxicity. The actuarial 6-years Overall survival and Freedom from biochemical failure were 96.7% and 90.2%, respectively. Distant metastases were observed in 3 patients.

Conclusions: Moderate hypofractionation of localized-high risk prostate cancer and pelvic lymph node-positive prostate cancer with SIB-IMRT has a satisfactory results in terms of toxici-ty and good efficacy.

PO163

ANALYSIS OF INTER-FRACTION ERRORS IN RELATION TO RECTAL AND BLADDER VOLUMES VARIATIONS USING CONE-BEAM COMPUTED TOMOGRAPHY IN VMAT RADIOTHERAPY FOR PROSTATE CANCER PATIENTS

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Aims: Set-up errors and pelvic organ motions can vary prostate position between planned Computed Tomography (CT) and Cone Beam CT (CBCT) performed during radiotherapy (RT) in prostate cancer (PC) patients. The aim of this study is to evaluate inter-fraction prostate motion, in empty rectum and controlled bladder filling, on planned-CT and CBCT.

Methods: In 33 PC patients we performed a daily CBCT in the first four days of RT, calculated the average shifts in the three axes and then repeated CBCT once a week after the correction of these prostate shifts. We estimated rectum and bladder volumes on each planned-CT and CBCT for each patient. We calculated the median shift variations on all 3 axes and rectum and bladder filling variations between planned-CT and CBCTs on the first 4 CBCTs, on the following weekly CBCTs and for the total of CBCTs. Linear regression mixed models taking into account the random effect of repeated measures

were employed, to identify correlation between median prostate shifts and rectum and bladder filling variations.

Results: A total of 443 CBCTs were analyzed. Table 1 reported results of median shifts and rectum and bladder filling variations on the first 4 CBCTs, on the following weekly CBCTs and for the total of CBCTs.

Table 1. Analyses of median prostate shifts in x, y and z axes, rectum and bladder filling variations and correlations between median prostate shifts and rectum and bladder filling variations.

		First 4 days CBCTs (IQR)	CBCTs after systematic correction (IQR)		All CBCTs (IQR)	
Median shifts	x (cm)	0.2 (-0.1, 0.4)	-0.0 (-0.2, 0.1)		0.03 (-0.16 to 0.22)	
	y (cm)	-0.0 (-0.2, 0.2)	0.0 (-0.2, 0.2)		-0.10 (-0.24 to 0.23)	
	z (cm)	-0.2 (-0.4, 0.1)	-0.1 (-0.4, 0.2)		-0.10 (-0.39 to 0.19)	
Filling variations	Rectum	2.7 (-23.6, 30.5) %	-14.9 (-33.3, 7.1) %		-10.3 (-31.1, 16.6) %	
	Bladder	-2.2 (-12.4, 8.2) %	0.8 (-9.5, 8.8) %		-0.0 (-10.3, 8.7) %	
			Bladder filling variation (p-value)	Rectum filling variation (p-value)	Bladder filling variation (p-value)	Rectum filling variation (p-value)
Axis	x	/	0.211	**0.035**	0.967	**0.036**
	y	/	**0.013**	0.098	0.860	0.467
	z	/	**0.045**	0.443	0.057	**0.039**

CBCT: Cone Beam Computed Tomography; IQR: Interquartile range.
p-value significance in bold

For all CBCTs median prostate displacements along the three axes (x, y and z) averaged over all patients were: 0.03 (IQR: -0.16 to 0.22) cm in x, -0.10 (IQR: -0.24 to 0.23) cm in y and -0.10 (IQR: -0.39 to 0.19) cm in z, and median rectum and bladder filling variation were -0.0 cc (-10.3, 8.7) and -27.3 cc (-109.5, 44.7), respectively. The analyses of all CBCTs for relationship between prostate shift along all axes and rectum and bladder filling variations demonstrated a statistically significant correlation in x and z axes (p=0.036 and p=0.039, respectively) only for rectum. Furthermore, correlations analyses in CBCTs obtained after systematic set up correction resulted statistically significant in y and z axes (p=0.013 and p=0.045, respectively) for bladder and in x (p=0.035) for rectum filling variations.

Conclusions: Our results seem to validate our set up protocol for rectum and bladder preparations in correlation to small prostate shifts.

PO164

TOMOTHERAPY-BASED MODERATE HYPOFRACTIONATION FOR LOCALIZED PROSTATE CANCER

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Purpose: Moderate hypofractionated radiotherapy is widely used in the treatment of localized prostate cancer (PCa). To date, only few studies have been published on hypofractionated radiotherapy delivered with image-guided helical tomotherapy (HT) in localized PCa. We retrospectively analyzed outcome and toxicity after HT-based moderate hypofractionated radiotherapy in patients with localized PCa.

Materials and Methods: 76 patients were enrolled in the study. Disease was stratified according to D'Amico classification: 16 (21%) low-risk, 34 (44.5%) favorable intermediate risk, 8 (10.5%) unfavorable intermediate-risk, and 18 (24%) high-risk. Androgen deprivation therapy was prescribed in 43 cases. Clinical target volume (CTV) included the prostate in the low-risk group and the prostate plus 2/3 of the seminal vesicles in intermediate and high-risk groups. A total dose of 60 Gy (20 x 3 Gy) or 67.5 Gy (25 x 2.7 Gy) was prescribed. The χ^2 test was used to analyze associations between toxicity and dosimetric and clinical parameters. The Cox proportional hazard regression model was used for multivariate analysis. Kaplan-Meier method was used for survival analysis.

Results: Median follow-up was 42.26 months (interquartile [IQR], 23-76). At 4-year, overall survival (OS) and metastasis-free survival (MFS) were 91% and 89%, respectively. At log-rank test, high-risk disease and International Society of Urological Pathology (ISUP) class 4-5 were associated with a worse MFS. Eventually, smoking habitude negatively affect MFS (p=0.001). In multivariate model, only smoking habitude emerged as independent, significant variable (HR 7.32, 95%CI 1.57-34.16, p=0.011). Acute and late grade ≥ 2 gastro-intestinal (GI) toxicity was observed in 6.5% and 2.6% of patients, respectively. Acute and late grade ≥ 2 genito-urinary (GU) toxicity were 31.5% and 3.9%. Four-year late GI and GU grade ≥ 2 toxicity were 3% and 7%, respectively. Acute GI toxicity was associated with statins medication (p=0.04) and androgen deprivation therapy (p=0.013). Acute GU toxicity was associated with the use of anticoagulants (p=0.029) and antiaggregants (p=0.013).

Conclusions: HT-based moderate hypofractionation was associated with a very low rates of toxicity. Respecting planning dose-constraints, it seems that baseline clinical features, individual factors such as co-morbidities, lifestyle choices and use of medications have an impact on radiation-induced toxicity and on the risk of disease progression.

PO165

STEREOTACTIC BODY RADIOTHERAPY IN OLIGOMETASTATIC PROSTATE CANCER PATIENTS: AN APPROACH TO IMPROVE DISEASE CONTROL

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Aims: Patients (pts) with oligometastatic prostate cancer (OMPC) increased over the years. Androgen deprivation therapy (ADT) represents the gold standard in pts with diagnosis of OMPC. Stereotactic body radiotherapy (SBRT) is emerging as an alternative option in order to improve efficacy of ADT, to delay starting ADT or the development of drug resistances. The aim of this study is to evaluate progression free-survival (PFS), treatment failure free-survival (TFFS) and ADT-free survival (ADTFS) in OMPC pts treated with SBRT.

Methods: From December 2019 to August 2020 40 pts were submitted to SBRT. Median age was 74,2 years (range 58-91). Pts were classified into three different cohorts: pts with *de novo* OMPC (24/40); pts who experienced oligo-recurrence during ADT therapy (10/40); ADT-untreated pts with a metachronous oligorecurrence (6/40). All pts with *de novo* OMPC underwent radiotherapy (RT) both on primary tumor and metastases (mts) with concomitant use of ADT. Pts who relapsed during ADT underwent RT on mts and continued ADT. ADT-naive pts underwent RT on mts delaying the start of systemic therapy. Delivered doses were 8-37,5 Gy in 1-5 fractions on the sites of metastases with SBRT technique in a daily schedule.

Results: Independently from specific cohorts, all pts enrolled reported a PSA response after SBRT. After a median 10-months follow-up (FU) (ranged 6-12 months), all patients showed a local response according to the different cohorts. In the de novo OMPC cohort 16 pts experienced a complete response (CR) and 8 pts reported a partial response (PR); median PFS was 10 months (4-12 months) and median TFFS was 12 (4-12 months). No pts reported acute and late side effects related to SBRT. CR was observed in all pts who experienced oligo-recurrence during ADT therapy; median TFFS was 6 months (5-12 months); no toxicity was recorded. In the ADT naive cohort all pts experienced CR; ADTFS was 10 months (range 5-12 months); no toxicity was recorded. Lower PSA levels and longer PFS predicts a better TFFS in pts with ADT and delay in the start of systemic therapy in ADT-naive pts.

Conclusions: In our study SBRT in OMPC was a safe and effective therapeutic option obtaining an excellent disease control rate and delaying the start of ADT in naive cohort pts.

PO166

ADJUVANT VERSUS SALVAGE RADIOTHERAPY AFTER RADICAL PROSTATECTOMY: A MONOISTITUTIONAL EXPERIENCE

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Aim: It remains unclear which is the optimal timing of radiotherapy after prostatectomy. We aimed to compare adjuvant radiotherapy (ART) versus observation followed by salvage radiotherapy (SRT) in a cohort of prostate cancer (PCa) patients.

Table 1.

	SRT (n= 52)	ART (n=56)
Age	**N (%)**	**N (%)**
• ≤ 59 years	6 (11.5)	13 (23.2)
• 60-69 years	23 (44.2)	29 (51.7)
• ≥ 70 years	23 (44.2)	14 (25)
Gleason Score		
• ≤6	10 (19.2)	2 (3.6)
• 7	26 (50)	28 (50)
• 8	9 (17.3)	10 (17.8)
• 9	7 (13.4)	16 (28.5)
ISUP		
• 1	10 (19.2)	2 (3.6)
• 2	15 (28.8)	10 (17.8)
• 3	11 (21.1)	18 (32.1)
• 4	9 (17.3)	10 (17.8)
• 5	7 (13.4)	16 (28.5)
D'Amico Risk Class		
• Low	10 (19.2)	2 (3.6)
• Favorable Intermediate	13 (25)	8 (14.2)
• Unfavorable Intermediate	11 (21.1)	16 (28.5)
• High	18 (34.6)	30 (53.5)
T stage		
• pT2	27 (51.9)	7 (13.4)
• pT3a	15 (28.8)	16 (30.7)
• pT3b	10 (19.2)	33 (63.4)
N stage		
• N0	42 (88.4)	35 (62.5)
• N1	2 (3.8)	9 (16)
• Nx	8 (15.3)	12 (21.4)
Margin Status		
• Positive	16 (30.7)	28 (50)
• Negative	36 (69.2)	28 (50)
Pelvis RT		
• Yes	9 (17.3)	10 (17.8)
• No	43 (82.7)	46 (86.1)
Concomitant ADT		
• Yes	20 (38.4)	23 (41)
• No	32 (61.5)	33 (59)

Materials and Methods: A restrospective analysis was carried out for PCa patients who underwent post-prostatectomy ART or SRT in our centre. We pooled data from patients with histologically confirmed prostate adenocarcinoma, stage ≥ pT2, N0-1 and R0-1. Time to Biochemical Relapse (BCR) and Metastasis Free Survival (MFS) were calculated from the end of the treatment to the last follow up, both were evaluated along with D'Amico Risk Class, age, Gleason score, ISUP, pelvic nodal RT, margin status, T stage, stage N, timing of post-operative radiotherapy and use of concomitant androgen deprivation therapy (ADT). The Cox proportional hazard regression analysis was applied in the multivariable models. Moreover, acute and late genitourinary (GU) and gastrointestinal (GI) toxicity were also compared, in according to CTCAE v5.0 criteria.

Results: Between June 2007 and May 2021, 108

patients were analyzed, 52 (48.1%) received SRT and 56 (51.8%) received ART. Patients were divided into risk groups according to D'Amico and most of them were over 60 years old. The clinical characteristics are summarized in Table 1. 36/108 (33%) BCR and 11/108 (10.2%) distant metastases occurred in both groups. In the multivariable analysis, no significant predictors of the Biochemical Relapse were found. On the other side, concomitant ADT (RR: 8.03, 95% CI: 1.10-58.8, p=0.04,) and pT stage (RR: 5, 95% CI: 1.18-21.3, p=0.02,) were significant for prediction of MFS. Acute GU toxicities occurred similarly in both group (44.7% in the SRT and 55.3% in ART). Of these, 79% were grade 1. Overall, 27.1% ≤3 grade acute GI toxic effects were found. None of the patients developed grade 4 GI or GU side effects.

Conclusions: Our study suggests that there are no differences between ART and SRt in terms of BCR and MFS. Acute and late toxicity were comparable between both groups. However, seems to be a statistically significant association between use of concomitant ADT, pT stage and MFS.

PO167

PATIENT-REPORTED ACUTE INTESTINAL TOXICITY AND IMPACT ON PATIENT QOL AFTER WPRT FOR PROSTATE CANCER

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Aims: An ongoing, registered, multi-Institute observational study is assessing the patient-reported (PRO)intestinal toxicity (IT) from IMRT whole-pelvis RT(WPRT) in the treatment, regardless of its intent. This analysis aims to describe the PRO acute IT and its detrimental effect on Emotional (EMOT), Social (SOC) and Systemic (SYST) Domains

Methods: The median EQD2 (α/β ratio 3 Gy) to the prostate, prostatic bed and lfn PTV was 80.03, 72.58 and 51.14 Gy, respectively. IT was measured by means (IBDQ), including 10 items evaluating the BOWEL Domain and 3 additional QoL scales analyzing the detrimental impact of IT on EMOT, SOC and SYST. In IBDQ scales (range 1-7), lower scores indicate worse situation. This analysis focused on 608 pts, enrolled from 2011-2020, with complete BOWEL scale at baseline, RT mid-point and end. The maximum decrease (=worsening, Δ worst) between baseline and RT mid-point or end of the ten BOWEL symptoms as well of EMOT, SOC and SYST Domains was assessed. In addition, the detrimental impact of a large number of clinical and treatment-related variables, including ADT, RT doses and intent, on the impairment of EMOT, SOC and SYST (n=597, 593 and 607, respectively), was investigated

Results: Overall, the RT-induced acute IT was mild, with only 4/10 BOWEL symptoms exhibiting a median Δ worst ≥-1 point: Loose Bowel Movement, Gas Passage and Urge to Defecate and Frequent Bowel Symptoms (IBDQ #1, Δ worst -2, Table 1a). The median Δworst of the remaining six BOWEL symptoms was zero. The corresponding median Δworst of EMOT, SOC and SYST were equally scanty, ranging from -0.25 to -0.60. The WPRT-induced increase of Gas Passage and Urge to Defecate, but also of Abdominal Pain, Rectal Bleeding and Nausea/Feeling Sick, whose WPRT-induced worsening was apparently only minimal, exerted an independent role on EMOT, SOC or SYST acute deterioration (Table 1).

Table 1.

	Emotion n=597	Social n=593	Systemic n=607
Volume of Lymph-Nodal PTV in cc	OR 1.001 – p=0.009	OR 1.001 – p=0.005	
No Adjuvant Hormonal Therapy Bicalutamide only LH-RH analogues or antagonist		Reference OR 2.66 – p=0.013 Non significant	
SOCIAL Domain Baseline		OR 1.95 – p=0.0001	
IBDQ1 Baseline	OR 0.84 – p=0.039		
IBDQ22 Baseline	OR 0.46 – p=0.02		
IBDQ1 Frequent Bowel Symptoms ΔWorst			OR 0.85 – p=0.015
IBDQ13 Abdominal Pain Δ Worst	OR 0.70 - p=0.003	OR 0.66 - p=0.0003	OR 0.61 – p=0.0001
ΔIBDQ17 Gas passage Δ Worst	OR 0.77 - p=0.015		OR 0.80 – p=0.03
ΔIBDQ22 Rectal Bleeding Δ Worst	OR 0.75 - p=0.026		OR 0.80 – p=0.04
IBDQ24 Urge to Defecate Δ Worst	OR 0.69 – p=0.002	OR 0.49 – p<0.0001	OR 0.80 – p=0.03
ΔIBDQ26 Accidental Soiling Δ Worst	OR 0.72 – p=0.006		
ΔIBDQ29 Feeling Sick Δ Worst		OR 0.71 – p=0.005	OR 0.70 – p=0.002
Area Under Curve	0.82	0.84	0.81
Hosmer & Lemeshow test	p=0.80	p=0.84	p=0.46

Conclusions: Opposite to that commonly believed, acute PRO IT deriving from WPRT delivered with modern IMRT techniques is minimal. Interestingly, the WPRT induced intestinal symptom most feared by the RO community, diarrhea, had an only negligible role in impairing the PRO QoL which was, quite unexpectedly, far more compromised by intestinal symptoms apparently only minimally affected by RT.

PO168

SEQUENTIAL STEREOTACTIC (SBRT) BOOST IN PATIENTS WITH MACROSCOPIC LOCAL RELAPSE AFTER RADICAL PROSTATECTOMY

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Aims: The purpose of our study is to evaluate, in patients with macroscopic local relapse after radical prostatectomy, the efficacy of salvage radiotherapy on the prostatic bed with a boost to the area of the recurrence on CSS (cancer specific survival), PFS (progression free survival) and OS (overall survival).

Methods: This study includes 17 patients (median age 67 years, range 52-75 years), with macroscopic local recurrence treated between 2014 and 2019 with radiotherapy on the surgical bed and sequential stereotactic (SBRT) boost +/- hormonal deprivation therapy (ADT). A macroscopic local recurrence was defined by a relapse in prostatic bed evidenced with choline PET and confirmed with multi-parametric MRI. The total dose applied to the prostate bed was 60 Gy in 30 fractions. Sequential boost dose was 16 Gy in 4 SBRT fractions. Three patients (17.6%) received also ADT.

Results: After a median follow-up of 70 months (range 32-90 months), 14 patients were alive and 3 died (1 for disease and 2 for causes not related with prostatic disease). The 5-year overall survival (OS) rate was 86.5%. The 5-year progression free survival (PFS) rate was 82.4%. Biochemical progression occurred in two patients (11.8%) and were treated with ADT. One patient (5.9%) developed single bone metastasis and one patient (5.9%) had lymph-node progression. No local recurrence was observed. The 5-year cancer specific survival (CSS) rate was 92.3%. The median of OS, PFS and CSS were not reached. No high grade (≥ 3) toxicity was reported.

Conclusions: Although limited, our experience showed that sequential SBRT boost in patients with macroscopic local relapse after radical prostatectomy was well tolerated and ensure a high rate of local control, OS, PFS and CSS.

PO169

BENEFITS OF USING STEREOTACTIC BODY RADIOTHERAPY FOR METACHRONOUS OLIGOMETASTASES IN CASTRATION SENSITIVE PROSTATE CANCER PATIENTS

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Aims: Metastases-directed therapy is an emerging, safe and efficient therapeutic approach for patients with oligometastatic/oligorecurrent/oligoprogressive metastases from prostate cancer (PCa) without showing major side effects. The aim of this retrospective analysis was to investigate the impact of Stereotactic body radiotherapy (SBRT) on the main clinical outcomes.

*Methods:*In our Institute 48 patients were treated by SBRT for oligometastatic recurrence (< 5 metastases) from hormone-sensitive PCa, detected by different radiological or biological imaging ([18F] FCH PET/CT, [68Ga] PSMA PET/CT, or CT plus bone scan) after biochemical recurrence (defined as for ASTRO Guidelines). The primary treatment was radical prostatectomy alone in 21 patients (44%), radical RT in 1 patients (2%), prostatectomy with adjuvant RT in 11 patients (23%), prostatectomy with salvage RT in 15 patients (31%). Primary endpoints of the analysis were overall survival (OS), local control (LC) and androgen deprivation therapy (ADT)-free survival in oligorecurrent PCa patients. All data were collected retrospectively.

Results: Patients' median age during SBRT was 69,3 years (range 47-81) and median PSA before being submitted to SBRT was 2,58 ng/ml (range 0.22-14,9 ng/ml). A total of 61 lesions were treated with SBRT, 52 lymph nodes and 9 bones. The dose delivered to the target ranged from 16 to 36 Gy in 3-7 fractions. Post-SBRT prostate-specific antigen (PSA) response was found in 29 (60.4%) of 48 patients. Patients were then followed using only serum PSA dosage every three months, while only patients with biochemical recurrence were completely restaged using imaging. LC rate was 96%, while median and 5-year OS were 24.9 months (range 3-83) and 92.9%±6.9ES, respectively. Data on ADT Free Survival will be available shortly. No grade II-IV adverse events were reported.

Conclusions: SBRT seems to be a very useful treatment and can be safely used together or as an alternative to ADT in appropriately selected patients with oligometastatic recurrence from PCa to control "oligo-progressive" lesions. Prospective randomized trials are on going and long term results will be very helpful to clarify the real clinical impact of metastasis directed therapy in this setting.

PO170

PROPHYLACTIC PELVIC NODAL RADIOTHERAPY COMPARATE TO ONLY PROSTATE BED IRRADIATION IN PATIENTS WITH PROSTATIC CANCER: A RETROSPECTIVE STUDY

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Aims: In patients with prostate cancer, a little known aspect in the post-operative setting is whether irradiating the lymph node chains instead of the prostate bed alone can confer an additional benefit in terms of disease recurrence. Purpose of our study was to demonstrate an improvement of biochemical control by post-operative nodal irradiation respect to prostate-only irradiation in patients with prostate cancer undergoing radical prostatectomy.

Methods: We evaluated 404 patients with prostate cancer treated with adjuvant or salvage RT from January 2011 to December 2011. All patients were treated using VMAT radiotherapy. ADT was administered to patients with high-risk prostate cancer in accordance with EAU guidelines. We studied biochemical progression free survival for each category of risk according to the NCCN classification. We did multivariate analysis of Progression Free Survival factors risk by step-wise method.

Results: Evaluating all patients with a median follow-up of 62 months, we did not found statistically significant advantage (p=0,77) by nodal radiotherapy; however, in the analysis of sub categories, we found a trend toward a significant advantage in prophylactic nodal irradiation in 140 patients with low and intermediate risk class (p=0,056).

Conclusions: Our study highlights how the whole pelvic nodal prophylactic radiation therapy does not offer an additional benefit in all patients, but only in selected patients with low-intermediate prostate cancer. Larger and prospective studies are needed to confirm our results.

PO171

PRELIMINARY RESULTS OF PHASE II MULTICENTER TRIAL ON CARBON-ION BOOST FOLLOWED BY IMRT FOR HIGH RISK PROSTATE CANCER

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Purpose: The definition of the optimal treatment for patients affected by high-risk prostate cancer (PCa) still represents a debated topic. Systemic- and radio-therapies (RTs) are subjected to resistance mechanisms developed by tumour cells and PCa is not an exception. In addition, carbon ion radiotherapy (CIRT) offers the advantage of a steep dose gradient due to the inverted profile of in-depth dose deposition compared to photons, which permits a greater sparing of organs at risk. The aim of this Phase II trial was to evaluate the feasibility, in terms of acute toxicity, of this mixed beam approach for patients with high-risk prostate cancer (PCa). The treatment consists of a CIRT boost followed by whole-pelvis intensity-modulated RT (IMRT).

Methods: Patients with localized high-risk PCa (NCCN classification) were enrolled at three different Cancer Centers. The primary endpoint was the evaluation of safety and feasibility with acute toxicity scored up to 1 month after the end of RT. Secondary endpoints were treatment early (3 months after the end of RT) and long-term tolerability, quality of life (QoL), and efficacy. At the end of RT, clinical assessment and prostate-specific antigen (PSA) measurements were performed every 3 months for at least 2 years and gastrointestinal (GI) and genitourinary (GU) toxicities were evaluated contextually. QoL of enrolled patients was assessed by IPSS, EORTC QLQ-C30, EORTC QLQ-PR25, and sexual activity by IIEF-5. Data on acute and late GI and GU toxicities were collected according to RTOG/EORTC grading system.

Results: Patients were treated with a CIRT boost of 16.6 Gy [RBE] in 4 fractions followed by whole-pelvis IMRT of 50 Gy in 25 fractions. From 10/2017 to 02/2021, 24 patients were enrolled in the study and 16 completed the whole RT course. All patients underwent concomitant long-term hormone therapy. Data of 15 patients were available for the preliminary analysis. Immediately after CIRT no patients experienced GU/ GI toxicity. At one and 3 months from the RT completion (CIRT followed by IMRT) no GI or GU toxicities greater than grade (G) 2 were observed. In details, considering acute GU toxicity, 8 patients have not reported any toxicity. Concerning GI 5 patients presented G1 acute toxicity and 2 of them G2. Longer follow up (12 months) was available for 7 patients, with one patient presenting GU toxicity classified as G1 and 1 patient presenting GU toxicity reported as G2. At the time of the writing all the patients have a biochemical control of disease.

Conclusion: At the current state, the mixed treatment schedule proposed by our study shows an optimal toxicity profile for both acute and chronic toxicity at one year from treatment. Such data instills confidence in the continuation of this mixed approach, whose long-term efficacy together with efficacy (in terms of biochemical control of disease) will be the object of additional analyses.

PO172

SALVAGE STEREOTACTIC BODY RADIOTHERAPY IN PATIENTS WITH LOCALLY RECURRENT PROSTATE CANCER

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Aims: This study investigates the use of salvage Stereotactic Body Radiotherapy (sSBRT) for prostate

cancer recurrences in patients previously underwent to a curative treatment: radical prostatectomy (RP), external beam radiotherapy (EBRT) or both.

Methods: This retrospective study included 11 patients (pts) with a median age of 82 years old (65-91 years) with biochemical failure confirmed clinically in 36% of pts by Magnetic Resonance Imaging (MRI) and 64% of pts by means of Positron Emission Tomography/ Computed Tomography (PET/CT). sSBRT was delivered with a daily image-guided radiation therapy (IGRT) and Volumetric Arc Modulated Therapy (VMAT).

Results: Between June 2019 and February 2021 we have recorded 11 pts: 18% of pts relapsed after RP and 64% of pts relapsed after EBRT; in 18% of pts we have reported a recurrence after both RP and EBRT. Pts have received sSBRT as follows: 36% in the whole prostatic gland, 27% in the prostatic bed, 27% in the right lobe, 10% in part of the prostatic bed. Median delivered dose was 30 Gy (25-37.5 Gy) in five alternate or consecutive days fractions with a mean calculated Biological Equivalent Dose (BED) value of 90 Gy (66,7-131,5 Gy) considering an alpha/beta of 3 Gy. Median time from previous treatment and biochemical recurrence was 96 months (47-183 months). Only G1 Genitourinary (G.U) acute toxicity was recorded (18% of the pts); 9% of pts experienced asthenia during the treatment. No acute GU toxicity ≥ G2 and gastrointestinal (G.I) toxicity was recorded. None of pts died. Median follow up (FU) was 12 months (3-23 months). After three months from the end of sSBRT 91% of pts had a biochemical response; only 9% had an increase of the PSA value. After 6 months 73% of pts had a reduction of the initial PSA value and only 9% had a PSA increase confirmed by imaging studies in non irradiated sites with a local complete response (RC) in irradiated sites. 18% of pts did not reach the 6 months FU.

Conclusions: In our study sSBRT for locally recurrent prostate cancer patients is a safe and feasible treatment having an excellent toxicity profile and an encouraging biochemical response.

P0173

VMAT-SIB ^{BOOST} TO THE DOMINANT INTRAPROSTATIC LESION IN LOW-INTERMEDIATE RISK PROSTATE CANCER: PRELIMINARY RESULTS OF A DOSE ESCALATION TRIAL

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Aim: To evaluate the safety and feasibility of stereotactic ablative radiotherapy (SABR) on prostate cancer patients treated with escalating doses to the dominant intraprostatic lesion (DIL).

Materials and Methods: This Phase I clinical trial enrolled low and intermediate – risk prostate carcinoma patients (NCCN risk classes), and American Urological Association (AUA) score ≤15. Rectal voiding, bladder filling and gold fiducials were mandatory for set-up. A Volumetric Modulated Arc with simultaneous integrated boost technique was used with progressively increased total dose to the DIL defined by magnetic resonance imaging (MRI). The prescribed dose to the prostate plus 3-mm margin (PTV2) was 35 Gy (7 Gy per fraction). The MRI enhancing lesion with 3-mm margin (PTV1) received the dose escalation in five fractions (planned dose levels: 40, 42.5, 45, 47.5, 50Gy (Table 1). Dose-limiting toxicity (DLT) was defined as any grade ≥ 3 gastrointestinal (GI) or genitourinary (GU) toxicity by Common Terminology Criteria of Adverse Events. Rectal sigmoidoscopy was performed in all patients 12 months after SABR. The Vienna Rectoscopy Score (VRS) was used to grade the 1 year-late rectal toxicity outcome.

Table 1.

Dose cohorts: VMAT-SIB dose escalation

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	-	3	35 Gy/7 Gy (70 Gy*, 117 Gy#)	45 Gy/9 Gy (108 Gy*, 180 Gy#)
3	-	4	35 Gy/7 Gy (70 Gy*, 117 Gy#)	47.5 Gy/9.5 Gy (118.8 Gy*, 197.9 Gy#)
3	-	5	35 Gy/7 Gy (70 Gy*, 117 Gy#)	50 Gy/10 Gy (130 Gy*, 216.7 Gy#)

Abbreviation: 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.

Table 1. Toxicity (CTC-AE v.4 scale)

		PTV1 Dose Levels	
Toxicity	Grade	I 40 Gy	II 42.5 Gy
Genitourinary	1	2	1
	2	1	1
	3-5	-	-
Gastrointestinal	1	1	-
	2	1	1
	3-5	-	-

Results: 13 patients (median age: 73 years, range:58-78) were enrolled between May 2014 and December 2020. All patients had cT2a-c N0 M0 clinical stage and/or a Gleason score of ≤ 7; 8 patients received 40Gy and 5 patients 42.5Gy. Prostate volumes ranged from 28.9 to 97.7 cc, with a median DIL volumes of 4.6 cc (range 1.4-

14.3). With a median follow-up of 28 months (range 2-72), no patients experienced dose-limiting toxicity (Table 1). Rectal bleeding (N=2) and pollachiuria (N=4) were reported as late toxicity, none higher than grade 2. 12/13 patients had a One-year VRS and grade 0, 1, 2, 3 were recorded in 3, 4, 3 and 2 patients, respectively. 10/13 patients (76.9%) underwent short course androgen deprivation therapy. Median PSA decreased from 5.4 ng/ml (range 4.2–9.6 ng/ml) (values at diagnosis) to 0.21 ng/ml (range 0.05–2.28ng/ml) (values at the last follow-up). According to Phoenix definition one biochemical failure was registered at the first dose level. One year-actuarial local control (defined as irradiated site progression-free) was 100%.

Conclusion: A SABR schedule of 35 Gy with a boost to the DIL up to 42.5 Gy in 5 fractions resulted to be safe and feasible in this setting. The maximum tolerable dose has not yet been reached and the study is actually ongoing.

PO174

GASTRO-INTESTINAL (GI) AND GENITO-URINARY (GU) TOXICITIES EVALUATION IN PROSTATE CANCER PATIENTS TREATED WITH INTENSITY-MODULATED RADIOTHERAPY (IMRT) MODERATE HYPOFRACTIONATION REGIMEN AND SIMOULTANEUS INTEGRATED BOOST (SIB)

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Aims: The aim of this study is to evaluate acute and late GU and GI toxicities in patients treated with pelvic intensity-modulated radiation therapy and Simoultaneus Integrated Boost for prostatic cancer.

Methods: We reclutated 60 patients affected by prostate cancer not operated treated from January 2017 from January 2021 in A.O.U Policlinico "G. Martino" and A.O. Papardo of Messina. All patients have been treated with IMRT with the same fractionation: 170 cGy in 29 fx on the pelvic lymph nodes, 190 cGy in 29 fx on prostate and seminal vesicles and 240 cGy in 29 fx with a SIB on the prostatic area. One patient was treated with a dose of 240 cGy in 12 fx on the pelvic lymph nodes, prostate and seminal vesicles. In three patients a SIB was delivered at a dose of 240 cGy in 29 fx and in one patient with a dose of 270 cGy in12 fx on PET positive lymph nodes. Toxicities were assessed with a telephone questionnaire using Radiation Therapy Oncology Group (RTOG scale).

Results: The median age was 78 years (range 64-88 years). The median V50 of the bladder was 13,49%, while the median V40 was 44,83%. 21 patients developed acute GU toxicities: G2 12 patients (57.1%), G3 8 patients (38.1%) and G4 1 patient (4.8%). 7 patients developed chronic GU toxicities: G2 6 patients (85.7%) and G4 1 patient (14.3%). A volume of 230 cc of the intestine absorbed a median dose of 34,54 Gy. Acute GI toxicities were reported by 32 patients: G1 20 patients (62.5%), G2 8 patients (25%) and G3 4 patients (12.5%). Chronic GI toxicities were reported by 12 patients: G1 6 patients (50%), G2 4 patients (33.3%) and G3 2 patients (16.7%).

Conclusions: Our experience seems to confirm a literature data on this issue. In particular, our study shows how the IMRT technique with moderate hypofractionation regimen in this setting of elderly patients have been excellent outcome and low profile of late toxicity.

PO175

LINAC-BASED STEREOTACTIC BODY RADIATION THERAPY (SBRT) IN ELDERLY PROSTATE CANCER PATIENTS

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Aim: An increasing number of literature data recommends SBRT in case of low-risk prostatic cancer (PC) patients. A Linac-based SBRT treatment with risk-adjusted prescription dose is usually proposed to elderly patients with PC. An update of data regarding patients treated in 22 months was performed to evaluate the safety and efficacy of SBRT.

Methods: Men aged ≥70 years affected by localized PC were treated with Linac-Based SBRT. The entire prostate was irradiated up to a dose of 35 Gy in 5 fractions. The dose was optimized to isodose line of 90% in low/favorable intermediate cases and 80% in unfavorable intermediate/high risk cases. A Volumetric Modulated Arc Therapy (VMAT) technique was used for planning and delivery. Treatment was delivered over 1 or 2 weeks based on PTV and pre-treatment urinary symptoms. Some patients also received androgen deprivation therapy (ADT) according to the risk group classification. Toxicity and quality of life (QoL) were assessed at baseline, after treatment and during follow-up (FU) using the Common Terminology Criteria for Adverse Events and International Prostatic Symptoms Score (IPSS). PSA values were recorded before treatment and during FU as biochemical response criteria.

Results: Between July 2019 and April 2021, 58 patients were treated. Median age was 76 years (range 61-88); 25 had low risk, 23 favorable/unfavorable intermediate risk and 10 high risk PC. Median pre-treatment PSA

was 5 ng/ml (range 0,61-25). ADT was prescribed in 16 (27%) patients. In cases in which dose was optimized to isodose 90%, Dmax was 38,9 Gy, whereas when optimizated to isodose 80%, Dmax was 43,8 Gy. Median PTV was 109,6 cc (range 75-157,7). Median baseline IPSS was 3 (range 0-6). At the end of the treatment, no >G1 acute toxicity was observed. Two-three weeks after SBRT, 10 (17%) patients reported G2 acute genitourinary toxicity (urinary frequency, urinary tract pain and urinary retention) and 7 patients (12%) presented rectal tenesmus. During FU, only 1 case of rectal bleeding in a patient who used anticoagulants was observed. No relevant deteriorations of QoL were described. At a median FU of 9 months (range 1-20), excellent biochemical disease control was achieved in all cases with a median PSA of 1,5 ng/ml (range 0,01- 7,3). No differences were observed between the two different prescription approaches.

Conclusions: Linac-based SBRT in patients affected by localized PC is feasible and well tolerated; excellent biochemical disease control is associated with high compliance of very elderly patients to treatment. Longer follow-up is needed to assess late toxicity profile and long-term results.

PO176

ADJUVANT, EARLY SALVAGE AND SALVAGE RADIOTHERAPY AFTER SURGERY IN PROSTATE CANCER: SURVIVAL OUTCOMES

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Aims: Endpoints of this retrospective study in terms of clinical outcomes were Overall Survival (OS), Biochemical-Free Survival (BFS) and Radiological Progression Free Survival (RPFS) of patients (pts) with histologically confirmed prostate cancer treated with post-operative radiotherapy after radical prostatectomy.

Methods: Our casistic involved 154 pts with a median age of 65 years (range 49-79), underwent adjuvant (36%), early-salvage (30%) and salvage radiotherapy (34%) between March 2011 and March 2020. RT was performed with Intensity Modulated Radiotherapy (IMRT)/ Volumetric Modulated Arc Therapy (VMAT) technique and dose varied from 62.5 to 70 Gy. Pts with a PSA value after surgery under 0.2 ng/dL and unfavorable histopathological characteristics (neoplastic invasion of seminal vesicles or extracapsular extension of neoplasm) were assigned to receive Adjuvant Radiotherapy (ART), pts with a PSA value between 0.2 and 0.5 ng/dL were treated with Early Salvage Radiotherapy (ESRT) and pts with a PSA value over 0.5 ng/dL or positive surgical margins received Salvage Radiotherapy (SRT). Univariate analysis (log rank) were assessed with Chi-square test and Kaplan-Meier method.

Results: Median follow-up was 70.3 months (range 11.3-121.4). OS at 5 and 8 years was 95.5% and 84.3% respectively for all pts included, with significant statistical difference (p=0.043) between pts treated with ESRT (OS at 5 and 8 ys = 97,7%) and SRT (OS at 5 ys = 95.5%; at 8 ys = 70.8%). BFS in the whole population was 71% at 5 years and 68,3% at 8 years, with a statistically significant difference (p=0,011) between pts treated with ART (BFS at 5 and 8 ys = 82.2%) and SRT (BFS at 5 ys = 61.3%; at 8 ys = 58.5%). RPFS was 85.7% at 5 years and 83.4% at 8 years: the same results were observed also in this case, with a statistically significant difference between pts treated with ESRT (RPFS at 5 and 8 ys = 95.7%) and SRT (RPFS at 5 ys = 73.3%; at 8 ys 67.3%; p=0.03).

Conclusions: Our analysis demonstrates that patients underwent Adjuvant RT have better survival outcome then patients treated with Salvage RT in terms of biochemical-free survival. A statistically significant difference is also demonstrated between patients treated with Early Salvage RT, that shows an improved overall survival and radiological progression-free survival, and Salvage RT.

PO177

OLIGOMETASTATIC PROSTATE CANCER: EVALUATION OF ACUTE TOXICITY AFTER VMAT-IGRT DIRECTED TREATMENT TO PRIMARY TUMOR AND METASTASES ASSOCIATED WITH ANDROGEN DEPRIVATION THERAPY

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Aims: Oligometastatic prostate cancer (OPC) is now being diagnosed more frequently as the result of improvements in diagnostic techniques such as functional imaging. It has been proposed that OPC patients may have a more indolent course and that the outcome may be further improved adding radiation therapy (RT) to systemic therapy. The aim of our analysis is to evaluate the feasability and tolerability of RT performed with a curative purpose.

Methods: We have analyzed 18 patients who were treated in our Radiation Department. 9 were affected by OPC at the time of diagnosis: 5 had node metastases and 4 had bone metastases. The other 9 patients had previously undergone to surgery and developed biochemical and clinical relapse: all the patients had nodal metastases. Radiation prescription doses were: 72 Gy and 63,6 Gy in 30 fractions to prostate gland and seminal vescicles

respectively, 54 Gy in 30 fr to prophylactic pelvic nodes, 60-66 Gy/30 fr to positive nodes, 66 Gy to bone metastases. RT was performed with Volumetric Modulated Arc Therapy with Integrated Simoultaneous Boost. 17 out of 18 patients were submitted to Androgen Deprivation (AD) during RT. We analyzed acute genito-urinary (GU) and gastro-intestinal (GI) toxicity assessed at the end of the treatment and during subsequent follow up, using RTOG scale. As secondary end point we reported also biochemical response and biochemical relapse free survival (BRFS).

Results: Follow up has been performed for 3-29 months. Toxicity was absolutely mild. At the end of the treatment 38,8% of patients had G1 GI and 61% had G0 GI toxicity, 11% had G2 GU, 44,5% G1 and 44 ,5% had G0 GU toxicity. At the last follow up only 1 patient had G3 GU toxicity and only 1 reported G2 GI toxicity. 6 patients have recently finished radiation treatment; among the other 12 patients 10 (83%) had biochemical response to radiation treatment in association to AD, in 9 (75%) of them PSA decreased to an undetectable level. In 8 (66,6%) PSA has not increased until the last follow up.

Conclusions: Our clinical case shows that VMAT-IGRT performed with curative purpose in OPC patient is absolutely well tollerated. Notable we observed only 1 case of G3 GU toxicity. Regarding biochemical response, even with a short follow up, the BRFS was 66,6% with a median follow up of 17,1 months. The limit of this study is that some patients have recently finished radiation courses and limited follow up is currently available.

PO178

A COMPARISON STUDY OF TOXICITIES OF TWO MODERATE HYPOFRACTIONATED TREATMENT SCHEDULES WITH TOMOTHERAPY AND VMAT FOR ELECTIVE PROSTATE CANCER RADIOTHERAPY: A MONOINSTITUTIONAL EXPERIENCE

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Aims: To compare genitourinary (GU) and Gastrointestinal (GI) toxicities in two different moderate hypofractionated schedules and techniques.

Methods: From February 2014 to November 2020, 271 patients with biopsy proven prostate cancer underwent elective radiotherapy in our Unit with two alternative moderate hypofractionated schedules: 170 patients received 70,2 Gy in 26 fractions of 2,7 Gy and 101 patients received 62 Gy in 20 fractions of 3.1 Gy. In 26 fractions group, 79 patients underwent Tomotherapy and 91 VMAT. In 20 fractions group, 5 patients received Tomotherapy and 96 VMAT. To evaluate toxicities by technique used, we compared 79 Tomo-patients to 91 VMAT-patient received 26 fractions. To evaluate toxicities by fractionation, we analyzed VMAT patients receiving different schedules: 91 (26 fractions) to 96 (20 fractions). The five patients irradiated with Arcangeli schedule and Tomotherapy, were excluded from data analysis as reported in Table 1. The acute and late urinary and rectal toxicities were evaluated by C.T.C.A.E. 4.02 and the SOMA-LENT modified Scales. Pearson X2 and exact Fisher test were used for statistical analysis.

Table 1. Number of patients treated for technique and fractionation.

Fractionation Schedule	Pts Tomo	Pts Linac	Pts tot
70,2 Gy (2.7 Gy x 26)	79	91	170
62 Gy (3.1 x 20)	5*	96	101
Tot	84	187	271

*: excluded from analysis

Table 2. Toxicitiy results for treatment schedule in VMAT. Statistical results (α = 0.05; statistically significant p-value <0.05).

Fractionation Schedule	Acute ≥ G2 GU % (n° pts)	Acute ≥ G2 GI % (n° pts)	Late ≥G2 GU % (n° pts)	Late ≥ G2 GI % (n° pts)
70,2 Gy (2.7 Gy x 26) (91 pts)	36% (33/91) 1 G3	9.9% (9/91)	7.7% (7/91)	1% (1/91)
62 Gy (3.1 x 20) (96 pts)	17.8% (19/96)	6.3% (6/96)	5.2% (5/96) 2 G3	1% (1/96) 1 G3
p-value (Pearson's X^2 test)	**0.01**	0.36	0.48	
p-value (exact Fisher's test)		0.43	0.55	1
Odds ratio	2.3	1.6	1.5	1.06

Table 3. Toxicitiy results for Technique used in 26 fractions. Statistical results (α = 0.05; statistically significant p<0.05).

Technique	Acute ≥ G2 GU % (n° pts)	Acute ≥ G2 GI % (n° pts)	Late ≥G2 GU % (n° pts)	Late ≥ G2 GI % (n° pts)
VMAT (91 pts)	36% (33/91) 1G3	9.9% (9/91)	7.7% (7/91)	1% (1/91)
Tomo (79 pts)	33% (26/79) 1G3	10% (8/79) 1 G3	7.6% (6/79) 2 G3, 2 G4	3.8% (3/79) 1 G3
p-value (Pearson's X^2 test)	0.65	0.98	0.96	
p-value (exact Fisher's test)		1	1	0.34
Odds ratio	1.16	1.01	0.97	0.28

Results: Comparing 26 fractions to 20 fractions, the acute and late ≥G2 GU and GI toxicities are in Table 2. In 26 fractions group, 1 patient, experienced acute G3 urethral stenosis. No G3 acute GI neither late GU and GI toxicities were found in this group. In 20 fractions group, no acute G3 GU or GI toxicities were experienced. For late effects, 2/5 patients with GU toxicity had G3 urethral stenosis and one of them experienced a late G3 GI toxicity: patient had

URC (Ulcerative Rectocolitis) disease in quiescent state during radiation therapy. Comparing Tomo to VMAT, acute and late ≥G2 GU and GI toxicities are reported in Table 3. In Tomo group 1 patient had acute G3 GU toxicity and 1 had an acute G3 GI toxicity. In VMAT group 1 patient had acute G3 GU toxicity. Late ≥G3 GU and GI were found in Tomo Group only: 2 patients experienced G3 GU toxicity (stenosis and hematuria) and 2 G4 (stenosis). One patient had late G3 GI proctitis. No late ≥G3 GU and GI toxicities were found in the VMAT group. Statistical results are reported in Table 4.

Conclusions: We can conclude that Tomotherapy and VMAT are both techniques available and safe in moderate hypofractionation for elective prostate cancer radiotherapy alternatively to each other. A worse acute urinary toxicity was found in 26 fractions group comparing treatment schedules in VMAT.

P0179

A MONOCENTRIC EXPERIENCE APPLYING THE HYPO-RT-PC TRIAL: ACUTE TOXICITY AND BIOCHEMICAL FREE SURVIVAL IN THE ULTRA-HYPOFRACTIONATED TREATMENT OF PROSTATE CANCER

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Aims: To register the acute and late urinary and rectal toxicities of 7 fraction ultra-hypofractionated radiotherapy for prostate cancer, and the biochemical recurrence after the treatment.

Methods: From September 2019 to April 2021 we have treated 27 patients with prostate cancer, using a scheme of 7 fractions in non-consecutive days for a total dose delivered of 42.7 Gy, according to the Hypo-RT-PC trial. The characteristics of the patients are summarized in the table below. We have registered the IPSS questionnaire during the first examination. The majority of the patients (89%) had fiducial markers implanted in the prostate; we used calcification in the gland as a substitute for the FM for the remaining 11% of patients. We also used pelvic MRIs acquired after the implants of FM for the contouring of the CTV,when available (78% of patients). Unlike the Swedish trial all treatments were planned using a VMAT technique with 6 or 10 MV with FFF, on Varian True Beam STX. We used IGRT with daily CBCT and triggering during the treatment. The CTV to PTV margins were 5 mm in all directions and 3 mm posteriorly. Before every treatment the patients had to get an enema and have a comfortably full bladder. We have set follow-ups at 1 month after the end of the radiotherapy and every 3 months after that.

Results: The acute toxicity (according to CTCAE 5.0) recorded on the last day of treatment was as follow: 20 patients had G0 rectal toxicity (74,1%), 6 had G1(22,2%), and only 1 had G2 toxicity (3,7%); regarding urinary toxicity 7 patients have nothing to report (25,9%), 17 of them had G1 toxicity (63%) and 3 had G2 (11,1%). At the 3 months FUP, the rectal toxicity (for 20 patients) was: 90% of G0 and 10% of G1; the urinary toxicity was 85% G0 and 15% G1. At 6 and 12 months we have observed an even lower toxicity except for two patients who experienced G2 rectal toxicity treated with topic treatments. The majority of our patients (89%) were intermediate risk as in the Swedish trial, 11% were high risk. Nevertheless we have registered a decrease in the PSA in all classes of risk during the FUP.

*Conclusions:*The toxicity of the treatment using a VMAT technique, fiducial markers and daily CBCT is very mild and almost nonexistent after 3 months. These precautions also allowed us to reduce the PTV margins used in the Hypo-RT-PC trial (5 mm and 3 mm posteriorly *vs* 7 mm isotropic margins) with an excellent PSA response. As for today we have not seen a biochemical recurrence.

Table 1.

PATIENTS CHARACTERISTICS		
AGE (years)	Median age	78
	Min	60
	Max	84
IPSS	Median	6
	Min	2
	Max	13
FIDUCIAL MARKERS	YES	24
	NO	3
ISUP GRADE	I	4
	II	11
	III	10
	IV	1
	V	1
PSA PRE-RT (ng/ml)	Mean PSA	8,95
	SD	6,11

P0180

POSTOPERATIVE MODERATELY HYPOFRACTIONATED RADIOTHERAPY IN PROSTATE CANCER: A MONO-INSTITUTIONAL PROPENSITY-SCORE MATCHING ANALYSIS BETWEEN ADJUVANT AND EARLY SALVAGE RADIOTHERAPY

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Aim: To evaluate the impact of moderately hypofractionated postoperative radiotherapy (RT) in prostate cancer (PCa).

Matherial and Methods: The data of 304 surgically resected PCa patients were analyzed. 105 patients underwent adjuvant RT (aRT), 77 early-savage RT (esRT), and 123 salvage RT (sRT). Biochemical relapse-free survival (BRFS), progression-free survival (PFS) and toxicity were analyzed. A propensity score matching (PSM) was performed to account for potential confounders between aRT and esRT groups.

Results: The median follow-up was 33 months. Three-year BRFS and PFS were 82 and 85.2%, respectively in the overall population. At the multivariate analysis, Gleason score and hormone therapy were factors independently correlated with BRFS and PFS. After PSM, there was no difference in BRFS and PFS between aRT and esRT patients. Severe toxicity was represented by grade 3 urinary incontinence (3.5%) and urgency (1%), and aRT correlated with increased any-grade acute toxicity. Severe grade 3 genitourinary late toxicity occurred in 1.3% of cases.

Conclusions: Postoperative moderately hypofractionated RT achieved acceptable disease control rate and demonstrated no increased or unexpected toxicity. Future prospective studies should evaluate the role of postoperative RT in patients with unfavorable disease characteristics.

PO181

INVESTIGATION OF CLINICAL OUTCOMES OF RADIOTHERAPY TREATMENTS

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Aims: Evaluate the effectiveness of different radiotherapy techniques for some of the cancers considered as big killer (prostate, breast and gynecological cancers) in terms of clinical outcome and economic costs of the treatment itself. This study is part of a project financed by "Bando Ricerca Salute 2018- Regione Toscana" grant.

Methods: For each treatment plan the target coverage and the dose parameters for organs at risk are evaluated with the use of DVH. Dose parameters for organs at risk are selected on the base of the functional organization of the organ and of the international literature. The doses will be converted to biologically weighted EQD2 doses if needed. Patients with the same cancer type and degree of malignancy are divided into groups according to the irradiation technique used for the treatments: 3DCRT, VMAT, TomoTherapy, interstitial high dose rate (HDR) breast brachytherapy and low dose rate (LDR) prostate brachytherapy with ^{125}I seeds. A database with all these dose parameters will be created for all the patients. The clinical outcome will be assessed on the basis of questionnaires based on Common Terminology Criteria for Adverse Events, administered to patients. The dosimetric parameters related to treatment with interstitial brachytherapy technique (HDR) versus those with external beams will be compared and the corresponding outcome will be evaluated above all in terms of local recurrences. In the case of prostate cancer, for low risk patient the treatments with external beams and brachytherapy with ^{125}I seeds will be compared both in terms of clinical outcome and dosimetric and economic evaluations.

Results: DVH Analytics software has been chosen for the extraction of the DVH dosimetric parameters and for the implementation of the database. The questionnaires have been grouped for the anatomical district. Up to date the plans of the patients treated with LDR brachytherapy have been analyzed: a database has been implemented and some of these patients have been seen for a follow up.

Conclusions: A complete database will be available to correlate dose distributions to clinical outcome for different radiotherapy techniques.

PO182

VIRTUAL BRACHYTHERPY WITH PROSTATE SBRT AND REAL-TIME ELECTROMAGNETIC TRACKING: TREATMENT COMPLIANCE AND PRELIMINARY FINDINGS

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Aims: To investigate treatment compliance and early gastrointestinal (GI) and genitourinary (GU) side effects in patients with organ confined prostate cancer following Virtual Brachytherapy (VB), meant as dose escalated prostate Stereotactic Body Radiation Therapy (SBRT), coupled with an electromagnetic (EM) tracking device for real-time intra-fraction organ motion.

Methods: Thirteen patients with organ confined prostate cancer were treated with VB in 4 or 5 fractions, in a single week, for a total dose of 38 Gy or 40 Gy, respectively. A volumetric modulated arc therapy (VMAT) was delivered on Linac platform with two 6FFF or 10FFF arcs optimized to have the 95% isodose covering at least 95% of the PTV (2 mm isotropic expansion of the CTV). After the daily CBCT, the EM tracking inter-

rupted the beam delivery whenever the prostate displacement exceeded 2 mm. Organ motion mitigation was obtained by a rectal micro-enema and a 100 cc bladder filling. International Prostate Symptom Score (IPSS) and acute toxicity with Common Terminology Criteria for Adverse Events version 5 (CTCAE_v5) scale were assessed.

Results: Median age was 77 years (range 63-81). Intermediate and high risk prostate cancer accounted for 70% and 30% respectively. Median PTV volume was 81.2 cc (range 48.9-128.5). Average total treatment time lasted 10.2 minutes (range 5.5-22.7), 6.7 minutes (range 2.7-17.8) for setup and 3.5 minutes (range 2.5-7.3) for beam delivery. In 45% of the monitored fractions, a new CBCT was mandated. The prostate was found within 1 mm from its initial position in 78% of the beam-on time, between 1 and 2 mm in 20%, and exceeds 2 mm only in 2%. All patients completed the treatment in the expected time and their compliance to the procedure was excellent. No clinically significant acute Grade 2 or higher GI (rectal) and GU toxicity was observed during treatment and at 3-months. Median IPSS score was 8 (range 2-14) at baseline and 6 (range 2-17) at 3-months. Median pre-treatment PSA level was 9,78 ng/ml (range 4,99-25) and dropped to 0,25 ng/ml (range <0,008-3,86) at 3-months.

Conclusions: Virtual Brachytherapy with VMAT-FFF technique coupled with daily image guidance including real-time EM tracking allowed dose-escalated treatment with negligible early side effects. The procedure was implemented rapidly and resulted well tolerated and less invasive than the surgically implanted transmitter. Fine tuning of the workflow may result in a further reduction in the number of treatment sessions.

P0183

A CASE OF URETHRAL METASTASIS IN A PATIENT WITH CASTRATION-RESISTANT PROSTATE CANCER: THE ROLE OF RADIOTHERAPY

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Aims: Distant urethral metastases of prostate cancer (PC) are very unusual. To our knowledge, in literature there are few cases of urethral metastases from PC treated with external beam radiation therapy (EBRT).

Methods: We reported a rare case of urethral castration-resistant PC metastasis in a 61-year-old man previously irradiated on the prostate with curative intent at the time of diagnosis. Urethral lesion was documented by means of Choline Positron Emission Tomography (CPET) and confirmed by the biopsy. Because of concomitant comorbidities patient was not submitted to surgery and was candidated to EBRT with cytoreductive and palliative intent. EBRT consisted of Volumetric Modulated Arc Therapy (VMAT) in a daily schedule.

Results: In our case we recorded an improvement on urinary symptoms and partial response delaying the start of a second systemic therapy line treatment.

Conclusions: To our knowledge, our experience is the first in literature that reported VMAT for urethral castration-resistant PC metastasis. Despite the short time of follow up, in the present case report, VMAT was a safe and effective option in this unusual clinical scenario.

P0184

EXTREME HYPOFRACTIONATION STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR CLINICALLY LOCALIZED PROSTATE CANCER: SPRINT PROTOCOL

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Aims: Extreme hypofractionation with stereotactic body radiation therapy (SBRT) has an emerging role as safe and effective alternative technique to deliver high-dose radiotherapy for low and intermediate risk prostate cancer. Enrolling in clinical trial is strongly encouraged. An institutional clinical protocol is proposed.

Methods: We reviewed the major clinical trials, retrospective studies and practice guidelines in this setting and analyzed the indications for prostate SBRT, inclusion criteria, practical treatment planning recommendations. A non-profit prospective mono-institutional non-pharmacological observational study was performed and approved by local Ethic Committee.

Results: Inclusion criteria are: histologically confirmed adenocarcinoma; low or intermediate risk class; prostate volume <90 cc; good urinary function sec. IPSS score. Among the exclusion criteria we identify: high risk class; clinical evidence lymphadenopathy or distant metastases at baseline; diseases contraindicating radiotherapy; previous prostatectomy, Trans-urethral resections, previous pelvic radiotherapy; Treatment plan cannot meet dose constraints. Target volumes are delineated in planning computed tomography co-registrated with diagnostic magnetic resonance imaging. Clinical target volume (CTV) is defined as prostate gland for low risk with inclusion of proximal part of seminal vesicles for intermediate risk. Planning at risk volume (PTV) is obtained from CTV plus 5 mm (3 mm posteriorly) . We considered as organs at risk: anal-rectum, posterior rectal wall, bladder, urethra, femoral heads, penile bulb, small intestine. The prescribed dose at the PTV is 36.25 Gy in

5 fractions of 7.25 Gy. An online positioning correction protocol is applied using Cone-Beam CT (CBCT) acquired before each therapy session. The primary end-points are biochemical progression free survival and clinical progression free survival. The secondary end-points are local control, overall survival, acute and late toxicity, quality of life.

Conclusions: Based on a comprehensive literature review, a clinical and technical protocol for SBRT in low and intermediate risk prostate cancer has been implemented, approved by local Ethic Committee and used in clinical practice according to clinical indication.

P0185

IMPROVING RECTAL DOSIMETRY FOR PATIENTS WITH LOW-INTERMEDIATE AND HIGH-RISK PROSTATE CANCER UNDERGOING EXTERNAL BEAM RADIOTHERAPY WITH BIOPROTECT/ PROSPACE BALLOON SYSTEM

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Purpose: In Intensity modulate radiotherapy(IMRT-SIB) of the prostate, the rectum is the dose-limiting organ at risk. The sparing of the anterior rectal wall is a prerequisite for safe delivery of doses beyond 70Gy. Spatial sparing of the rectum can be achieved by introducing a BioProtect-ProSpace-Balloon-System(BS) into the retroprostatic space. Once the balloon is in situ, it is inflated with sterile saline to reach the desired final configuration.This retrospective study examined the clinical safety and efficacy of BS between the prostate and rectum To report on-rectal dosimetric and toxicity outcomes

Material and Methods: Between 2019 and 2020, 9 patients (pt) with low-intermediate-high risk prostate cancer were enrolled, treated with IMRT-SIB technique in Hypofractionated, 70 Gy in 28 sessions. All patients underwent simulation CT and MRI pelvis pre and post Space placement. An evaluation of rival plans and the evaluation of dose and rectum volume was performed. The reduction in rectal dose upon use of the BS is highlighted when comparing the pre-implant and post-implant rectal DVHs. BS safety, the dosimetric effects on organs at risk were evaluated.

Results: The median follow up was 12 months, acute toxicity was assessed during the first 6 months. BS creates a space of up to 2 cm in the region of the treatment area. The median prostate-rectal separation achieved with BS was 12mm. The potential dose reduction on the rectum due to the enlarged distance between prostate and ventral rectal wall, was calculated by determining the differences in V30%,V40%,V50%,V60%,V70%,V75%, V80%, V90% and V100% at the prescribed dose level of 70 Gy. Rectal wall volume data were compared by using D2 ml and D0.1 ml. In 5 pt had acute G1 genitourinary toxicity. In 2 pt presented with late G1 genitourinary toxicity. In 2 pt had acute gastrointestinal toxicity (rectal tenesmus). No late gastrointestinal toxicities were observed.

Conclusions: Insertion of the Ballon spacer in prostate cancer patients receiving IMRT is safe, is clinically proven and biodegrades within six months of deployment, so no need for surgical removal. This effect has resulted in a significant radiation dose reduction to the rectum, resulting in acute and late significantly less GI toxicity. Further prospective clinical investigations on a larger number of patients will be necessary to define the clinical advantage of the BS.

Tables 1, 2, 3, 4.

Table n.1

	V30%	V40%	V50%	V60%	V70%	V75%	V80%	V90%
Δ mean	-5,0	-5,2	-5,0	-14,0	-15,1	-15,2	-15,0	-9,4
SD	5,3	4,6	7,1	6,8	3,9	2,6	1,8	1,4

Table n.2

	V50 Gy	V60 Gy	V70 Gy	V75 Gy
Δ mean (%)	-11,2	-9,1	-9,1	-4,9
SD	4,7	1,9	1,9	0,8

Table n.3

	D 2ml	D 0.1 ml
Δ mean (ml)	-7,9	-4,0
SD	2,4	3,2

Tab. N.4

Toxicity	Toxicity Grade	N. 9 PZ
Genitourinary		
Acute (1-6 MONTH)	G1	6
	G2	0
	G3	0
Late (6-12 MONTH)	G1	3
	G2	0
	G3	0
Gastrointestinal		
Acute (1-6 MONTH)	G1	2
	G2	0
	G3	0
Late (6-12 MONTH)		
	G1	0
	G2	0
	G3	0

PO186

PROSTATIC CANCER METASTATIC TO THE LYMPH NODES OF THE NECK: A REPORT OF THREE CASES

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Aims: Laterocervical metastases from prostate cancer are rare. We describe 3 cases treated in our center.

Methods: 1) 79-y-o man in 2008 underwent radical prostatectomy (RP) for an adenocarcinoma of the prostate. In 2013 patient (pt) underwent salvage radiotherapy (RT) to pelvis and prostatic lodge (74 Gy) and on 2014 a SBRT on an iliac lymph node (LN) for 40 Gy. In 2020 PSA was 1.24ng/ml and Choline C11 PET (CPET) scan showed accumulation at left sopraclavicular level. An otolaryngologist examination was negative. The case was discussed in the head and neck (H&N) multidisciplinary team. The pt made an exclusive RT on the adenopathy (54 Gy /18 fr) with CR to a subsequent CPET. 2) 78-y-o man in 2009 underwent RP and pelvic LN dissection for an adenocarcinoma of the prostate. In 2014 pt underwent salvage RT to pelvis (50 Gy). In 2015 pt performed lumboaortic RT (50Gy). In 2017 pt performed an ultrasound of the neck that showed suspicious LN in the left neck. The fibroscopic examination was negative. A FNAB of the laterocervical LN was positive for malignant tumor cells. Pt underwent surgical exeresis of the adenopathy. The histological report was: LN site of carcinoma metastases compatible with prostate cancer. Pt undergoing to functional laterocervical LN emptyng: no metastatic LNs were found. 7 months later another adenopathy in sopraclavicular area on the left was diagnosed. A FNAB resulted positive for malignant tumor cells. The tumor board of H&N group decided on exclusive RT. 54 Gy in 18 fractions was erogated on the neck and on the sopraclavicular area. Systemic disease was in the subsequent follow up. 3) 63-y-o man in 2013 underwent to RP and pelvic LN dissection for an adenocarcinoma of the prostate. Pt started adjuvant RT on the pelvis and prostate lodge (50,4/64,4 Gy). On 2021 PSMA PET described a pathological uptake in the left retroclavicular area. The tumor board of H&N group decided for RT (48 Gy/16 fr).

Results: Three pts with nodal neck localization from prostate cancer were treated in our Division. All pts received a multidisciplinary evaluation in H&N tumor board and diagnosis and RT planning were guided by functional imaging (PET).

Conclusions: Despite the overall high incidence of prostate adenocarcinoma and its propensity for metastatic spread, involvement of lymph nodes in the regions of the neck is relatively rare: the hematogenous spread of this disease via the vertebral venous system named Batson's plexus can justify such a finding.

PO187

A RARE LOCALLY ADVANCED ADENOMA MALIGNUM OF CERVIX: A CASE REPORT

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Aims: Adenoma malignum, or minimal deviation adenocarcinoma of the uterine cervix (MDA), is a rare variant of adenocarcinoma (1-3% of all cervical cancer). MDA is considered a human papilloma virus (HPV) independent neoplasm, well differentiated subtype of the gastric adenocarcinoma (GAS). There is no standard treatment for the rarity of this disease and for the difficult diagnosis due to MDA histological features, similar to cervical glands. Typical symptoms are vaginal discharge or bleeding. These carcinomas are also well known for their aggressive behaviour, chemotherapy resistance and poor prognosis. In early-stage, surgical approach includes radical hysterectomy, bilateral pelvic lymphadenectomy and salpingo-oophorectomy; the treatment of advanced stage is based on concomitant chemo-radiotherapy (CCRT).

Methods: In January 2018, a 51 years old female came in our Institution, with watery vaginal discharges. At clinical examination, the cervix appared subverted and stiff. Magnetic resonance imaging (MRI) scan showed a lesion of 40 mm in diameter, which extended to isthmus, vagina and parametrium; the patient had hydronefrosis. A biopsy of the lesion was performed and resulted in adenocarcinoma mucinosus, subtype minimal deviation (MDA), CK7+, CEAM reduct, Ca 125 -, p16 -, ER -, PgR -, Ki 67 10%, LSVI -, III B FIGO stage. Due the locally advanced disease, the patient underwent chemotherapy dose dense (carboplatin AUC 2 and taxol 80 mg/m^2) for 6 weekly cycles, followed by chemo-radiotherapy (pelvic RT 48.6Gy in 27 daily fractions of 1.8 Gy) with concomitant weekly cisplatin 40 mg/m^2 and a sequential RT boost of 10,6 Gy in 6 fractions. The radiation treatment ended in April 2019. We reported G2 genitourinary and G3 hematologic Common Terminology Criteria for Adverse Events (CTCAE v.5) acute toxicity.

Results: After 3 months from the end of CCRT the MRI scan showed a partial response of disease. However, the woman was in good clinical condition until February 2020 when she developed peritoneal carcinosis and so, in March 2020, she died of disease.

Conclusion: The prognosis of MDA is known as

extremely poor, probably due to clinical understaging, misdiagnosis and undertreatment. Early diagnosis is essential in the management of MDA and clinicians should consider MDA among the differential diagnosis in patient with vaginal discharge also with negative PAP test.

PO188

MIR-200C-3P CONTRASTS PD-L1 INDUCTION BY COMBINATORIAL THERAPIES AND SLOWS PROLIFERATION OF EPITHELIAL OVARIAN CANCER THROUGH DOWNREGULATION OF -CATENIN AND C-MYC

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Aims: Conventional/targeted chemotherapies and ionizing radiation (IR) are being used both as monotherapies and in combination for the treatment of epithelial ovarian cancer (EOC). Several studies show that these therapies might favor oncogenic signaling and impede anti-tumor responses. MiR-200c is considered a master regulator of EOC-related oncogenes.

Methods: In this study, we sought to investigate if chemotherapy and IR could influence the expression of miR-200c-3p and its target genes, like the immune checkpoint PD-L1 and other oncogenes in a cohort of EOC patients' biopsies. Indeed, PD-L1 expression was induced, while miR-200c-3p was significantly reduced in these biopsies post-therapy. The effect of miR-200c-3p target genes was assessed in miR-200c transfected SKOV3 cells untreated and treated with olaparib and IR alone.

Results: Under all experimental conditions, miR-200c-3p concomitantly reduced PD-L1, c-Myc and β-catenin expression and sensitized ovarian cancer cells to olaparib and irradiation. In silico analyses further confirmed the anti-correlation between miR-200c-3p with c-Myc and β-catenin in 46 OC cell lines and showed that a higher miR-200c-3p expression associates with a less tumorigenic microenvironment.

Conclusions: These findings provide new insights into how miR-200c-3p could be used to hold in check the adverse effects of conventional chemotherapy, targeted therapy and radiation therapy, and offer a novel therapeutic strategy for EOC.

PO189

OTX015 EPI-DRUG EXERTS ANTITUMOR EFFECTS IN OVARIAN CANCER CELLS BY BLOCKING GNL3-MEDIATED RADIORESISTANCE MECHANISMS: CELLULAR, MOLECULAR AND COMPUTATIONAL EVIDENCE

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Aims: Ovarian cancer (OC) is the most aggressive gynecological tumor worldwide and, notwithstanding the increment in conventional treatments, many resistance mechanisms arise, this leading to cure failure and patient death. So, the use of novel adjuvant drugs able to counteract these pathways is urgently needed to improve patient overall survival. A growing interest is focused on epigenetic drugs for cancer therapy, such as Bromodomain and Extra-Terminal motif inhibitors (BETi).

Methods: Here, we investigate the antitumor effects of OTX015, a novel BETi, as a single agent or in combination with ionizing radiation (IR) in OC cellular models.

Results: OTX015 treatment significantly reduced tumor cell proliferation by triggering cell cycle arrest and apoptosis that were linked to nucleolar stress and DNA damage. OTX015 impaired migration capacity and potentiated IR effects by reducing the expression of different drivers of cancer resistance mechanisms, including GNL3 gene, whose expression was found to be significantly higher in OC biopsies than in normal ovarian tissues. Gene specific knocking down and computational network analysis confirmed the centrality of GNL3 in OTX015-mediated OC antitumor effects.

Conclusions: Altogether, our findings suggest OTX015 as an effective option to improve therapeutic strategies and overcome the development of resistant cancer cells in patients with OC.

PO190

ADJUVANT RADIOTHERAPY IN ELDERLY VULVAR CANCER PATIENTS: A MONOINSTITUTIONAL EXPERIENCE

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Aims: Vulvar cancer is a rare gynecologic tumor, typical of elderly women. The most common histological type is squamous cell carcinoma. Aim of this retrospective study was to assess the feasibility and patterns of recurrence of adjuvant radiotherapy (RT) for elderly patients with high-risk vulvar squamous cell carcinoma.

Methods: Between January 2012 and November 2018, 58 patients with histological diagnosis of vulvar squamous cell carcinoma were consecutively treated at our institution. All patients were primarily evaluated by a multidisciplinary team in order to choose the best treatment. Data from patients who underwent primary surgery and adjuvant RT were retrospectively collected. Primary end-points of the study were overall survival (OS) and disease free survival (DFS); secondary endpoint was to evaluate the toxicity profile.

Results: 30 patients with vulvar cancer were considered for the study. Median age was 77 (range 65-88). All patients underwent radical (60%) or partial (40%) vulvectomy with bilateral inguinal lymphadenectomy (76.6%), followed by adjuvant concurrent chemoradiotherapy (63.3%) or RT alone (36.7%). Prophylactic dose on lymph nodes was 50.4 Gy in 28 fractions. Median dose to vulva and perineal area was 58.7 Gy (range 50.4-70 Gy), pathologic lymph nodes received a median dose of 66 Gy (range 60-70 Gy). At a median follow-up of 21 months (range 3-83) 11 patients relapsed and the most common site of relapse was loco-regional (30%). Median OS was 25.5 months (range 6-87), median DFS was 19 months (range 3-78). According to the Common Toxicity Criteria Adverse Event (CTCAE) 4.0 score, acute genitourinary and gastrointestinal toxicities were G1-G2 in 73% and 77% respectively. Skin toxicity was G3 in 57% and two patients interrupted RT beacuse of this.

Conclusions: Adjuvant RT for elderly vulvar cancer patients provides high rates of local control with acceptable toxicity profile. Multidiscplinary approach is essential to choose the best treatment for these patients.

PO191

OLDLADY: PRELIMINARY RESULTS OF A LARGE, MULTICENTER, RETROSPECTIVE STUDY ON EFFICACY OF ADJUVANT (CHEMO)RADIOTHERAPY FOR VULVAR CANCER

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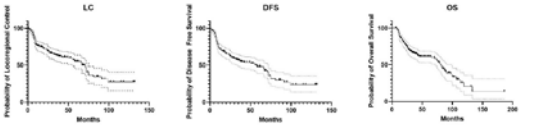
Aims: Vulvar cancer (VC) is an uncommon gynaecologic cancer. The aim of this study was to evaluate in a large, real-world dataset of patients affected by VC efficacy and safety of adjuvant (chemo)radiotherapy (aRT) with special attention on treatment prescription among participant centers joining the Observational itaLian stuDy on vuLvar cAncer adjuvant raDiotherapY (OLDLADY) project endorsed by the GYN study group of the AIRO (Italian Association of Radiotherapy and Clinical Oncology).

Methods: Nine Italian radiotherapy centers retrospectively collected clinical data of patients treated by aRT from January 2010 to December 2018, analysing tumour staging, treatment prescription, clinical outcomes and toxicities.

Figure 1. Kaplan meier curves for LC, DFS and OS.



Results: A total amount of 181 patients were collected. The median age was 71.5 (range 17-90) years. A large heterogeneity in therapeutic approaches to VC patients was reported in terms of prescribed volumes, radiotherapy doses and chemotherapy schedules. The main acute toxicity registered was cutaneous (22.1%), and a low rate of severe chronic lymphoedema (1.1%) was registered. The 24-month actuarial local control (LC) rate, disease free (DFS) and overall survival (OS) were 57.2%, 49.4%, and 55.1%, respectively, with a median follow-up of 30 months (range 1-185 months). Kaplan-Meier curves were reported in Figure 1.

Conclusions: A broad spectrum of therapeutic options in adjuvant VC setting was reported. To allows an higher treatment standardisation regarding prescription doses and volumes and to improve outcomes, cooperative prospective studies are needed.

PO192

OLDLADY: PRELIMINARY RESULTS OF A LARGE, MULTICENTER, RETROSPECTIVE STUDY ON EFFICACY OF EXCLUSIVE (CHEMO)RADIOTHERAPY FOR VULVAR CANCER

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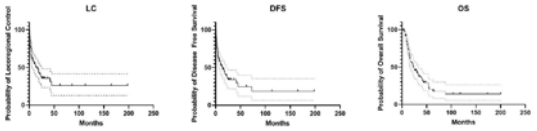
Aims: Vulvar cancer (VC) is an uncommon gynaecologic cancer. The aim of this study was to evaluate in a large, real-world dataset of patients affected by VC efficacy and safety of exclusive (chemo)radiotherapy (eRT) with special attention on treatment prescription among participant centers joining the Observational itaLian stuDy on vuLvar cAncer radical raDiotherapY (OLDLADY) project endorsed by the GYN study group of the AIRO (Italian Association of Radiotherapy and Clinical Oncology).

Methods: Seven Italian radiotherapy centers retrospectively collected clinical data of patients treated by eRT from January 2010 to December 2018, analysing tumour staging, treatment prescription, clinical outcomes and toxicities.

Results: A total amount of 90 patients were collected. The median age was 76 (range 32-92) years. A large heterogeneity in therapeutic approaches to VC patients was reported in terms of prescribed volumes, radiotherapy doses and chemotherapy schedules. The main acute toxicity registered was cutaneous (26%), and a low rate of severe skin fibrosis (4.4%) was registered. The 24-month actuarial local control (LC) rate, disease free (DFS) and overall survival (OS) were 42.2%, 40%, and 36.7%, respectively, with a median follow-up of 10 months (range 1-199 months). Kaplan-Meier curves were reported in Figure 1.

Figure 1. Kaplan Meier curves for LC, DFS and OS.



Conclusions: A broad spectrum of therapeutic options in exclusive VC setting was reported. Unfortunately, clinical outcomes still remaining poor. The needs of a better treatment standardisation regarding prescription doses and volumes have to be further investigated in a prospective study.

PO193

AN ITALIAN "MAP" ON ENDOMETRIAL CANCER: A FIRST STEP OF THE "LA.D.I.E.S PROJECT" (LARGE DATABASE IN ENDOMETRIAL CANCERS)

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Objective: This questionnaire aimed at documenting the current practice patterns of postoperative radiotherapy, including vaginal vault brachytherapy and external beam radiotherapy (EBRT), in patients with endometrial cancer. It was conducted to assess the feasibility of an italian multicentric study which would like to define pre-

dictive models of toxicity and survival.

Materials and Methods: In January 2020, an anonymous 5 questions-online questionnaires on general management of endometrial cancer and planning techniques was distributed electronically to differents Italian radiotherapy departments.

Results: Thirty-five questionnaires were completed. 50% of respondents practiced in the centre of Italy. A median of 39 patients/year (range 10-130) were treated in each Radiotherapy Departments. EBRT with or without a vaginal brachytherapy boost and adjuvant brachytherapy alone was performed in a median of 20 patients (range 2-38) and 14 patients (range 0-95) for centre, respectively. Clinical cases were discussed in a multidisciplinary tumor board in 78% of cases.

Conclusions: This was a questionnaire to assess the Italian experience in the management of endometrial cancer in radiotherapy departments to exploit italian center interesting to participate to a future large database project on endometrial cancer. We want to create an italian large database on endometrial cancer to develop and validate a multi-factorial prediction models for different treatment outcomes.

PO194

WEEKLY HYPOFRACTIONATED RADIATION THERAPY FOR BASAL CELL SKIN CANCER FOR ELDERLY PATIENTS

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Aims: Basal cell carcinoma (BCC) of the skin is a very frequent malignancy that develops prevalently in people over 40 yrs. Currently, surgical resection is the first choice for definitive treatment of localized BCC and just in selected cases (tumor location, patient comorbidities, patient refusal of surgery) definitive radiotherapy (RT) is considered. Moreover, hypofractionation scheme could ameliorate the adherence of elderly patients to RT. We reviewed cases of weekly hypofractionated RT in late elderly.

Methods: Patients (pts) with BCC were treated with definitive electron beam radiation with total dose of 24 Gy delivered in 3 weekly fractions. For all pts, photos were taken before RT starting and at 1-2 weeks, and-2-3 months after treatment's end, in order to independently assess clinical response. Response rate was assessed clinically and independently evaluated by two physicians. Acute toxicity was evaluated using the RTOG grading system. Cosmesis was defined as "good", "fair" or "poor".

Results: During the last year, 14 late elderly pts with high-risk localized BCC, were treated at our institution, with median age of 85 (range: 73-97 years old). Site of BCC were: face (10 pts), scalp (1 patient), retrorbital region (1 patient), trunk (2 pts). 10 BCC were < 3cm, the other 4 were between 3-5 cm. All patients completed the planned treatment. At the end of RT treatment 8 pts (57,1%) presented complete disease response and 6 pts (42,9%) presented partial response; 4 pts (28,6%) had not toxicity, 9 pts (64,3%) had G1 toxicity and just 1 patient (7,1%) had G2 toxicity. Nine pts had already their follow up control after at least 8 weeks from the end of the treatment (median follow up: 17 weeks). The other six pts finished treatment less than two months ago so the last available control was on the day of the end of RT. About the 9 pts that had follow up control, 5 (55,6%) had complete response at the last visit and 4 (44,4%) presented partial tumor control rate. Cosmesis at the last control resulted "good" for 11 pts (78,6%) and "fair" for 3 pts (21,4%).

Discussion: Weekly hypofractionated RT can be used for the treatment of localized BCC in late elderly pts with acceptable tumor control and good cosmetic outcomes. A longer follow-up and more pts are need to evaluate local recurrence rate and late toxicity.

PO195

PALLIATIVE SHORT-COURSE SURFACE-IMAGE GUIDED RADIOTHERAPY COMBINED WITH CHECKPOINT INHIBITORS IN METASTATIC MERKEL CELL CARCINOMA

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Aims: Immunotherapy with Avelumab has shown objective response rates of 56% as first line therapy for unresectable or metastatic Merkel Cell Carcinoma (MCC), however a progressive disease have few additional treatment options and chemotherapy demonstrated median progression-free survival suboptimal. Local radiotherapy (RT) can enhance the systemic effect of immunotherapy and trigger the regression of non-irradiated metastatic lesions. This work aims to explore the feasibility, acute toxicity and response of a short-course palliative RT in the management of a patient with metastatic MCC of the scalp.

Methods: A 73 year patient underwent resection of a non-metastatic MCC of the frontal-parietal scalp. After 3 weeks, the patient developed in-transit cutaneous recurrences which were surgically excised; staging was pT4 pN2 cM0 G3 R0. The patient quickly progressed on the left parotid gland, left neck nodes and liver metastasis, so left parotidectomy and neck dissection were performed. Avelumab 10 mg/kg every 2 weeks was started, then local relapse on the scalp occurred. A palliative RT was proposed, in combination with Avelumab. The patient was

simulated supine, with an open mask as the scalp lesions were quite large and easily bleeding. He received a single fraction of 8Gy to the whole scalp with intensity-modulated RT with 2 coplanar arcs. Being a long-duration treatment, 1557.75 Monitor Unit, 3D Surface Image Guided Radiation Therapy (SIGRT) was used to monitor real-time intra-fraction motion.

Results: The site setup was well tolerated; the patient received the full planned treatment. A good haemostatic effect was obtained after few days; two weeks later, a consistent shrinkage of the scalp lesions was observed. A month later, the patient performed a second irradiation of 8Gy to the scalp, developing a complete clinical response after 2 week without any acute radiation effects and stable disease in the liver. The patient is still on immunotherapy.

Conclusions: A short-course palliative RT of the scalp can be easily performed using an open mask with SIGRT with short-term response on bleeding MCC; the combination with immunotherapy is safe and could allow delaying the beginning of chemotherapy for metastatic lesions. Long-term evaluation is required to analyse possible synergic effect between immunotherapy and short-course palliative RT.

PO196

HYPOFRACTIONATED OR ACCELERATED RADIOTHERAPY IN ULTRA-ELDERLY PATIENTS WITH NON-MELANOMATOUS SKIN CANCER OF THE HEAD AND NECK AREA (HN-NMSC): A PRELIMINARY EXPERIENCE

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Background: Non-melanomatous skin cancer frequently occurs in the elderly population, often in a locally advanced stage when surgery is not feasible. Radiotherapy can achieve high response rates but it is limited by acute side effects, expecially in very elderly patients with involvement of the head and neck area. Furthermore, very elderly patients are not compliant with long radiotherapy schedules for logistical reasons. A preliminary evaluation of efficacy, tolerability and compliance of hypofractionated or accelerated schedules in elderly patients with HN-NMSC was performed.

Patients and Methods: From June 2019 to April 2021, 9 very elderly patients > 80 years with non operable HN-NMSC and without lymph nodal or distant metastases were treated. Only one patient was also treated with immunotherapy. The gross tumor volume (GTV) with margin was irradiated with Volumetric Modulated Arc Therapy (VMAT) technique and bolus. Hypofractionated or accelerated schedules were chosen.

Results: Mean age was 89 years (median 85, range 83-98). The most common hystology was squamous cell carcinoma (1 case of leiomyosarcoma of the scalp). Mean tumor diameter was 4 cm (range 2-6 cm). In 8 cases, a hypofractionated schedule was chosen. The mean number of fractions was 12 (range 4-20), and the mean total dose was 36 Gy (15-55). Dose/fraction ranged between 2.75 Gy and 4 Gy. In 1 case a hyperfractionated schedule was preferred (1.4 Gy x 2 fractions/die x 2 consecutive days). All patients completed the treatment, without unplanned interruptions. Five patients (55%) experienced G1-G2 oral mucositis with no impact on normal diet and in 5 cases we observed G1-G2 skin toxicity. No cases of ≥G3 toxicities were observed. Median follow-up was 9 months (range 1-12). Eight patients presented a clinical response: complete and durable response in 2 cases (22%), ≥50% response in 4 cases (44%), a slight response 25-50% in 2 patients (22%) and no response in 1 patient (11%). All patients experienced an improvement of symptoms as a reduction of pain and bleeding. Among responders, 2 patients had disease recurrence 4-6 months after RT. No late toxicities were observed.

Conclusions: This preliminary experience confirms that hypofractionated or accelerated radiotherapy are effective options of treatment in ultra elderly frail patients with HN-NMSC, with low toxicity profiles, rapid resolution of symptoms, optimal results (clinical response in almost 90% of cases) and good compliance.

PO197

ABSTRACT WITHDRAWN

PO198

TOTAL BODY IRRADIATION (TBI) IN HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT). ANALYSIS AFTER 16 YEARS MEDIAN FOLLOW-UP. FOCUS ON SURVIVORS

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Aims: Total Body Irradiation represents one important component of pre-hematopoietic stem cell transplant in patients (pts) with Acute Lymphoblastic Leukemia(ALL), Myeloblastic Leukemia and others hematological diseases. The increased overall survival pays more attention to the evaluation of side effects and quality of life. We investigated chronic lung and cardiac toxicities (according to CTCAE 5.0 scale), chronic Graft Versus Host Diseases (cGVHD, stratified from grade 1 to

4) and second cancers of pts treated with TBI in our Center, after 16 years (ys) median follow-up.

Methods: Since 1994 to 2020, 276 TBI treatments were performed in our Center in pts aged 16-66 ys (median age 37y). 110 pts were affected by ALL, 105 pts by Acute or Chronic Myeloblastic Leukemia. The others were affected by refractory Non-Hodgkin Lymphoma(26) and Myelodysplastic Syndromes(35). The hematological indications for HSCT have not changed over time, as well as chemo-conditioning regimes. 187 HSCT were conditioned by myeloablative regimes (TBI prescribed dose=12Gy in double daily administration of 2Gy). 89 HSCT by nonmyeloablative regimes (<12Gy). Since 1994 to 2015 the standard procedure for TBI was in a sitting position with antero-posterior irradiation. Since 2016 to 2020 the set-up was modified in a more comfortable supine position with lateral-lateral irradiation 6MeV Xrays. In vivo dosimetry was maintained. All pts from the date of transplantation were examined annually.

Results: After a median follow-up of 16 ys (range 0.5-26 ys), we found only 3 cases of chronic severe (grade 3) lung toxicity and 2 of cardiac toxicity, documented by spirometry and echocardium annually performed. We found 19 cases (16%) of severe cGVHD (grade 3) requiring first-line steroid therapy and/or photoapheresis or drugs (rituximab, imatinib); in 12 cases it affects skin, in 3 lungs, in 2 eyes, in 2 mouth and gut. We found 15 cases (12%) of moderate cGVHD (grade 2). 18 pts/119 alive (15%) have had a diagnosis of second cancer, respectively 11 basal cells carcinoma, 3 squamous carcinoma (1 of esophagus and 2 oral cavity), 2 thyroid carcinoma, 1 meningioma and 1 neurinoma. These have been diagnosed after an average of 206 months (17.1 years); 16 are related with myeloablative regime and all with antero-posterior irradiation.

Conclusions: In the examination population as regard late side effects, we observe the maintenance of a good quality of life. The second cancers were treatable (surgical excision or chemoradiation) as well as most of the cGVHD.

PO199

COMBINED APPROACH IMMUNOCHEMOTHERAPY PLUS INVOLVED FIELD RADIOTHERAPY IN PRIMARY MEDIASTINAL B-CELL LYMPHOMA: PRELIMINARY REPORT

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Introduction: Primary mediastinal B-cell lymphoma (PMBCL) is a rare but aggressive lymphoma, representing less than 3% of non Hodgkin lymphomas. It mainly affects the young adult population (peak incidence between 30 and 40 years old). Diagnosis of primary mediastinal lymphoma is based on integration of clinical, morphological, immunophenotypic, genetic and molecular data. A combined approach with rituximab-doxorubicin based chemotherapy and adjuvant involved site radiotherapy is considered the standard of care.

Methods: We retrospectively evaluated a consecutive series of patients with PMBCL, treated from August 2016 to May 2021 with combined approach with rituximab-chemotherapy plus adjuvant involved site radiotherapy ISRT. All patients were staged and restaged by PET-CT scan. Cardiac toxicity was monitored by echocardiography and ECG every six months for the first year and annually for subsequent years.

Results: Patient's characteristic are reported in tab. 1. 15/17 patients were PET negative after chemo-immunotherapy and before RT. 3/17 patients did not undergo radiotherapy, one of these die for lung infection, the second go to surgical debulking and another one refused radiotherapy. With a mean follow up time of 29 months, no recurrence has been recorded. No acute pulmonary or gastric toxicity (esophagitis) >G2, evaluated by CTC-AE vers. 5.0 scale, was observed.

Conclusions: We observed that the combined chemo-radiotherapy treatment was effective. Our aim is to continue patient follow-up to assess local recurrence and late toxicity.

PO200

HELICAL TOMOTHERAPY IN NON-HODGKIN LYMPHOMA RADIOTHERAPY OF THE SCALP: ARTIFICES FOR A BEST OUTCOME. A CASE REPORT

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Aims: Helical Tomotherapy (HT) has been shown effective for total scalp radiotherapy (TSCRT). Herein we show the outcome of TSCRT in a patient with extensive cutaneous B cell Non-Hodgkin lymphoma (NHBL) of the scalp using HT with some artifices to obtain the best dosimetry and clinical outcome.

Methods: A 70 years old woman suffering of cutaneous NHBL of the scalp with 4 nodular masses, after 4 R-CHOP cycles, needed a consolidative RT on the remaining disease. RT on the whole scalp was planned in HT and IMRT-SIB modality in 20 fractions. CTV1 consisted of the entire scalp from the skull base to the frontal skin up to the orbits roof. The prescribed dose (PD) to PTV1 was 36 Gy/1.8 Gy. CTVs2 consisted of the residual lesions spread in the scalp as GTV1-4 plus margins. The PD to each PTVs2 was 40 Gy/2 Gy. To irradiate the scalp surface, a bolus 3 mm thick with neoprene suit cap was worn on the bald head under a customized thermoplastic

mask. In vivo dosimetry with Mosfet (MTDs) was assessed. Further, a directional blocking dictates were given to spare the underlying OARs. A field width of 2.5 cm, a pitch of 0.315, and a modulation factor of 2.3 were used. RT was delivered by Tomotherapy Radixact (Madison, USA). Acute toxicity was checked every 5 days while the chronic toxicity at 3 and 6 months in the early follow-up time. The response to treatment was assessed at 3 and 6 months after the completion of radiotherapy on CT scan imaging.

Results: The delivered plan showed for PTV1 a mean dose of 36.7 Gy with D98= 96.5%, D2= 102%, HI and CI=1.05. For PTV2, D98=95.5%, D2=103% Dmean 40.5 Gy; HI and CI were 1.05 and 1.04 respectively. The Dmax to the brain was 11Gy while for the eyes Dmax was 3Gy. The mean surface dose for the 4 remnants by MTDs was 192cGy/fr (> 95%) of the PD 200cGy7fr. In the setup, the lateral mean shift was -0.7 mm, longitudinal -0.5 mm, vertical 1 mm. The patient completed the entire treatment without acute symptoms except a diffuse mild erythema and desquamation of the scalp surface. The CT scan after 6 months showed a complete resolution of the disease. No chronic sides effects were reported.

Conclusions: HT is ideally suited for brain-sparing holo-cranial RT in IMRT-SIB modality for TSCRT in NHL of the scalp. Successfully is the use of two artifices: the directional blocking dictates to spare OAR's and a Neoprene cup as bolus to assure the dose coverage of the scalp surface and minimal set-up errors.

PO201

RADIATION THERAPY FOR MULTIPLE MYELOMA: A SINGLE INSTITUTION EXPERIENCE ON 41 PATIENTS

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Aims: To review the outcome of patients with multiple myeloma (MM) treated at our institution in the last years, and to evaluate the Radiation Therapy (RT) role in 18-FDG PET/TC defined oligoprogressive patients (1-3 sites only in progression).

Methods: The patients with a MM diagnosis who have undergone a radiation treatment from January 2015 to February 2021 in our Institute have been enrolled. The data on the clinical history of patients, from diagnosis to radiotherapy consultancy, radiation treatment and follow-up (FUP), treatment response (TR), symptoms-free interval (SFI), progression-free survival (PFS) and overall survival (OS) were collected.

Results: Forty-one patients have been included in this study, 22 males and 19 females. Median age at the time of RT was 68 years (51-90). Seventy-seven sites have been treated, 69% (n=53) with three-dimensional conformal RT (3D-CRT) technique, and 31% (n=24) with Volumetric Modulated Arc Therapy (VMAT). Total dose ranged from 8 to 30 Gy, energy from 6 to 18 MV. The median FUP time is 18 months. TR has been observed for 88% (n=68) sites. Pain recurrence has been observed in 36% (n=28) sites with a median SFI of 8.5 (1-39) months. Only 2 sites (3%) underwent a re-treatment. Thirteen patients, (32%) have been identified as oligoprogressive (Table 1). Median age at the time of RT was 69 (51-83), 15 sites treated, 47% (n=7) with VMAT, 6MV/MV FFF energy. For them, the median FUP time is 27 months. To date, the median PFS interval time is 9.5 (1-48) months for the oligoprogressive subgroup, 8 (1-48) for the others. Six-, 12-, 18- and 24-month OS is, respectively, 100%, 100%, 100% and 89% for the oligoprogressive, 96%, 65%, 50% and 38% for the others.

Conclusions: Although MM substantially remains an incurable disease, our data confirms that RT on MM sites plays an essential role for a rapid and lasting palliation. In the oligoprogressive setting, in which a longer survival seems to be expected, RT could play a role in the global control of the disease, allowing the maintenance of an off-therapy condition, or delaying the need to transition to a subsequent line of chemotherapy (this occurs either by biochemical, clinical, or instrumental progression). However, to better define this last role, further studies are needed.

Table 1.

Table 1. Overview of the oligoprogressive patient and treatment characteristics

Pt	Age	Sex	Site	PET ia (SUV max)	Target volume (PTV, cm^3)	Dose	Technique - energy (photons)
#1	58	F	Shinbone dx Sternum	3.3 5.61	296.45 172.008	20 Gy in 5 fx 20 Gy in 5 fx	3DCRT - 6 MV 3DCRT - 6 MV
#2	73	M	Humeral head dx Humeral head sn	48.6 58.9	229.8 223.37	8 Gy in 1fx 8 Gy in 1fx	3DCRT - 6 MV 3DCRT - 6 MV
#3	51	M	Hemibacin sn	8	1713.58	30 Gy 10 fx	3DCRT - 6 MV
#4	54	F	IV dx rib	6.8	134.868	30 Gy 10 fx	VMAT - 6 MV
#5	51	F	Sacrum	20.5	591.068	30 Gy 10 fx	3DCRT - 6 MV
#6	46	F	II metatarsus sn	5.1	15.315	10 Gy in 1 fx	VMAT - 6 MV
#7	51	F	Sacrum	3.9	33.5706	12 Gy 1 fx	VMAT - 6 MV FFF
#8	51	F	VII sn rib	8.2	63.1249	20 Gy in 5 fx	3DCRT - 6 MV
#9	67	M	LS	8.6	57.7555	10 Gy in 1 fx	VMAT - 6 MV FFF
#10	65	M	Shoulder blade sn	12.6	323.202	20 Gy in 5 fx	3DCRT - 6 MV
#11	68	M	D11 solid paravertebral tissue	10.3 9.6	494.904	30 Gy in 10 fx	VMAT - 6 MV
#12	83	F	Left iliac mass	5.2	543.75	30 Gy in 10 fx	VMAT - 6 MV
#13	83	F	Sacrum	3.8	339.001	25 Gy in 5 fx	VMAT - 6 MV FFF

PO202

CAVEOLIN-1 PROMOTES RADIORESISTANCE IN RHABDOMYOSARCOMA THROUGH INCREASED OXIDATIVE STRESS PROTECTION AND DNA REPAIR

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Aims: The aim of this work was to investigate whether Caveolin-1 (Cav-1), a membrane scaffolding protein widely implicated in cancer, may play a role in radiation response in rhabdomyosarcoma (RMS), a pediatric soft tissue tumor.

Methods: For this purpose, we employed human RD cells in which Cav-1 expression was stably increased via gene transfection.

Results: After radiation treatment, we observed that Cav-1 limited cell cycle arrest in the G2/M phase and enhanced resistance to cell senescence and apoptosis via reduction of p21Cip1/Waf1, p16INK4a and Caspase-3 cleavage. After radiotherapy, Cav-1-mediated cell radioresistance was characterized by low accumulation of H2AX foci, as confirmed by Comet assay, marked neutralization of reactive oxygen species (ROS) and enhanced DNA repair via activation of ATM, Ku70/80 complex and DNA-PK. We found that Cav-1-overexpressing RD cells, already under basal conditions, had higher glutathione (GSH) content and greater catalase expression, which conferred protection against acute treatment with hydrogen peroxide. Furthermore, pretreatment of Cav-1-overexpressing cells with PP2 or LY294002 compounds restored the sensitivity to radiation treatment, indicating a role for Src-kinases and Akt pathways in Cav-1-mediated radioresistance. These findings were confirmed using radioresistant RD and RH30 lines generated by hypofractionated radiotherapy protocol, which showed marked increase of Cav-1, catalase and Akt, and sensitivity to PP2 and LY294002 treatment.

Conclusions: In conclusion, these data suggest that concerted activity of Cav-1 and catalase, in cooperation with activation of Src-kinase and Akt pathways, may represent a network of vital mechanisms that allow irradiated RMS cells to evade cell death induced by oxidative stress and DNA damage.

PO203

THE ROLE OF PREOPERATIVE RADIOTHERAPY IN EWING SARCOMA

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Aims: Ewing sarcoma (EWS) is an heterogeneous group of malignancy with an high incidence in children. Most frequently, the main EWS treatment is surgery. About preoperative chemotherapy, a good pathological response correlates with better outcome in terms of disease control and quality of surgical resection. The role of radiotherapy (RT) in the neoadjuvant setting is still unclear. Our aim is to find a correlation between pathological response and preoperative radiotherapy.

Methods: Data from consecutive EWS patients treated with neoadjuvant chemotherapy and RT from july 2002 to january 2020 were collected. Picci score was used to define the pathological response and Local Control (LC) was calculated as the time from diagnosis to local relapse. Statistical analysis was performed to assess correlation between clinical and pathological features and outcome.

Results: Data of 39 patients were analyzed. All of them received preoperative chemotherapy, with 90% of R0 resection rate at the surgical specimen. Radiotherapy was administered in 21 patients, 10 in the preoperative setting (26%) and 11 postoperatively (28%) respectively. The median dose was 54 Gy (range 42-54), with a median of 36 fractions (range 28-36) twice a day. The primary tumor has a skeletal and extra-skeletal origin in 33 patients (84%) and (16%) respectively, with 46% of lesions localized on the trunk (n=18) and 54% on limbs (n=21). Fifteen patients had metastatic disease at diagnosis (38%). Pathological response according to the Picci score was graded as 1 (n=30, 77%), 2 (n=2, 5%) and 3 (n=7, 18%). We observed 6 local recurrences after a median follow up of 22 months (range 8-72 months). LC was 92% at 1 year and 85% at 2 years. At univariate analysis, only trunk location was correlated with impaired LC (median not reached, p=0.018). The use of preoperative RT was correlated to none of the pathological downstaging, neither with grade 3 complete tumor response (24% versus 20% p=0.79); also positive margin status has no correlation with the use of RT (8% versus 20%, p=0.24).

Conclusions: We found that the only prognostic factor affecting local disease control is the primary location of the tumor; in particular trunk sites have a worse outcome when compared to limbs sites. No correlation emerged between preoperative RT and LC, nor surgical resection or complete response. Further studies should be performed to assess the role of preoperative RT in case of high risk features, like trunk EWS.

P0204

RADIATION-INDUCED BREAST ANGIOSARCOMA: A MONOCENTRIC ANALYSIS

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Aims: Radiation-induced breast angiosarcoma is defined as a malignancy arising in a previously irradiated area with a latency of 3 years, associated with poor prognosis. In patients treated with breast surgery and adjuvant radiotherapy (RT) the incidence of secondary breast angiosarcoma (SBA) may range between 0.05 and 0.3%. SBA develops within a median interval of 6 years from previous RT. Our aim was to retrospectively analyse a population diagnosed with SBA at our center Ospedale Bellaria between 2002 and 2020.

Methods: We analysed retrospectively patients with a diagnosis of angiosarcoma made at our institution between 2002 and 2020. Following Cahan's criteria, SBA was defined as angiosarcoma originating on a formerly irradiated area, after 3 years from previously RT, with histological evidence of different malignancy from primary tumor.

Table 1. SBA patients.

patient no.	sex	age	treatment	margins	grading	stage	∅ (mm)	recurrence
1	F	70	mastectomy	negative	3	T2NxMx	25	yes
2	F	83	mastectomy	negative	3	T2NxMx	35	no
3	F	69	mastectomy	negative	3	T2NxMx	50	yes
4	F	85	mastectomy	positive	3	T1NxMx	10	NR
5	F	62	mastectomy	close	2	T1NxMx	15	yes
6	F	63	mastectomy	positive	2	T1NxMx	20	yes
7	F	73	mastectomy	NR	3	T2NxMx	45	yes

NR, not reported

Results: In our hospital, from 2002 to 2020 a total of 6710 patients were treated for breast cancer with surgery and adjuvant RT. Seven of these patients developed SBA due to previously irradiation, representing 0.1% of the total. RT for primary breast cancer was delivered with photons. Whole breast irradiation represented the most preferred technique (45 Gy in 18 fractions), although one patient was submitted to partial breast irradiation (38.5 Gy in 10 fractions). SBA patients are presented in Table 1. All patients were female and mean age at diagnosis was 72 years (range 62-85 years). Focusing on tumor characteristics, they were classified as T1 or T2 (42,9% and 57.1% respectively); 2 patients had intermediate histological grade G2 and 5 high grade G3 (28.6% and 71.4% respectively). All patients were treated with radical mastectomy and none of them was submitted to adjuvant chemotherapy. Surgical margins were negative in 5 patients, positive in 2 patients and close in 1 patient. Data about surgical margins is missing for 1 patient. Recurrence after surgery affected 5 patients with a mean period of 13.4 months (range 3-25 months). The mean latency defined as the time between last exposure to irradiation and angiosarcoma diagnosis was 7.7 years (range 3-13 years).

Conclusions: Radiation-induced breast angiosarcoma remains a rare and aggressive malignancy, with high rates of recurrence. Incidence of SBA and latency from previous RT was compatible with literature.

P0205

INTEGRATED THERAPIES FOR SOFT TISSUE SARCOMAS: A SINGLE INSTITUTION EXPERIENCE USING HYPERTHERMIA IN ASSOCIATION WITH RADIOTHERAPY AND CHEMOTHERAPY

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Aims: The purpose of the study is to analyze the response rate and the side effects of the combined treatment including hyperthermia, radiotherapy and chemotherapy for patients with soft tissue sarcomas (STS).

Methods: We retrospectively reviewed patients affected by STS treated at our institution with hyperthermia combined with radiotherapy and/or chemotherapy. Two radiative hyperthermia (HT) devices were used: BSD-500 system for superficial HT and BSD-2000 for deep regional HT for target sited >4 cm from the skin. Duration of each HT session was of 60 minutes with target temperature >40°. The dose for neoadjuvant or adjuvant treatments was 45-50 Gy and 60-66 (conventional fractionation) in case of radical intent. Chemotherapy consisted of gemcitabine 300 mg/mq administered weekly during radiotherapy or HD-ifosfamide i.c. The response rate was evaluated by CT scan and MRI scan. The assessment of adverse events was reported according to NCI CTCAE v4.0.

Results: Eighteen patients were treated for STS from November 2019 to May 2021 with the combination. Fifteen patients had localized disease and 3 had metastastic disease. The most frequent sites of treatment were the lower limb and the abdominal-pelvic region. The mean target size was 7.1 cm (range 1-20 cm). Thirteen patients were treated with radiotherapy alone, four with concomitant radiochemotherapy (ifosfamide or gemcitabine) and

one with chemotherapy alone. The intent of treatment was neoadjuvant in 11 patients (61.1%), adjuvant in 2 (11.1%), radical in 2 patients (11.1%) and palliative in 3 cases (16.6%). Twelve patients (66.6%) were treated with superficial HT and 6 (33.3%) with deep HT. Overall radiological Response Rate was 44.4% (8/18 pts). Nine patients underwent surgery after neoadjuvant therapy. In all cases R0 resection was obtained and in 2 cases a complete pathological response was reported. The integrated treatment of radiotherapy and chemotherapy in association with HT was well tolerated: no hyperthermia session was interrupted due to side effects. No skin toxicity > grade 2 was detected and only one patient had haematological toxicity ≥ grade 3.

Conclusions: In our experience the addition of HT in the therapeutic protocol of patients with STS did not increase the toxicity of the treatment. The trimodal combination of HT, radiotherapy and chemotherapy should be investigated on a larger number of patients in order to confirm its feasibility and efficacy.

PO206

NEUROFIBROMATOSIS TYPE 1-ASSOCIATED MALIGNANT SCHWANNOMA: A CASE REPORT

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Aims: Malignant peripheral nerve sheath tumor schwannoma (MPNST), also know as malignant schwannoma, is a very rare tumor representing only 2% of all sarcomas. The risk of developing a MPNST is higher in individuals suffering from neurofibromatosis type 1 (NF 1), in which the clinical outcome is even worse. The treatment options for NF-1 associated MPNSTs include surgery , chemotherapy and radiotherapy but their role is still unclear.

Methods: The research reports the case of a 53-year-old woman suffering from Von Recklinghausen syndrome . In 2018 a computed tomography revealed a large (63 x 34 mm) inhomogeneus lesion of the left chest wall (Figure 1) originating from the third intercostal nerve with pleural adhesion wich was subsequently diagnosed as a MPNST via biopsy. A preoperative positron emission tomography (PET-CT) scan showed no abnormal fluorodeoxyglucose uptake out of the chest wall. The patient underwent videothoracoscopy surgery, the histology confirmed MPNST with high cellularity (17/10 HPFs) and there was no radical resection (R2). The postoperative course was good and the patient had no neurological deficit. Adjuvant external fractionated radiotherapy was administered to the tumor bed area with a total dose of 6000 cGy, 200 cGy daily, 5 days/week. Radiotherapy treatment was performed with LINAC 6-10 MV x-Rays with three-dimensional conformal technique (Figure 2). RT was well tolerated and only a moderate acute cutaneous toxicity (grade 1 according to NCIC criteria) has been reported. Chemotherapy wasn't administered.

Results: The patient was clinically evaluated every three months and she underwent a CT scan every six months. The latest CT scan, (Figure 3) performed 26 months after the diagnosis of MPNSt, showed no tumor tissue; the patient had no local recurrence or distant metastasis and she is in good health conditions.

Conclusions: The treatment options for malignant schwannoma are surgical excision, systemic chemotherapy or radiotherapy. Complete surgical excision with a safety margin is the mainstay treatment in patients with localized diseases. The role of radiotherapy and chemotherapy remains controversial; however, radiotherapy has been indicated in cases in which the tumor cannot be completely resected and high doses are chosen because of potential radioresistance.

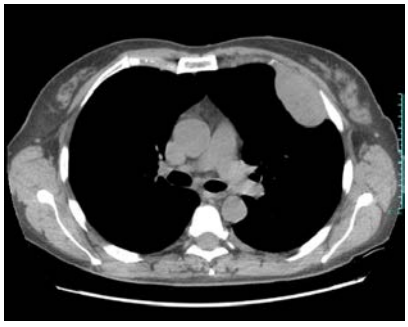

Fig.1 (October 2018)

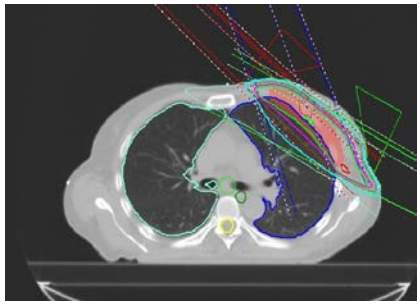

Fig.2

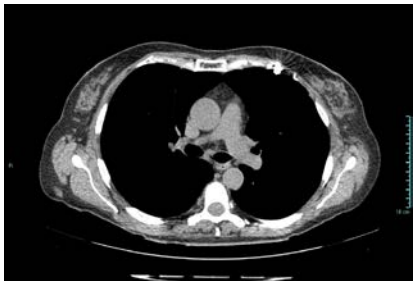

Fig.3 (January 2021)

Figures 1, 2, 3.

PO207

ADJUVANT RADIOTHERAPY IN A SPORADIC INTRAVENTRICULAR MALIGNANT PERIPHERAL NERVE SHEATH TUMOR: A CASE REPORT

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Aims: Malignant peripheral nerve sheath tumors (MPNSTs) are rare tumors, representing 5-10% of soft tissue sarcomas and affecting only 0.001% of population. Intracranial MPNSTs are even more uncommon, with no more than 25 cases in literature. We report a case of intracranial MPNST and we describe the therapeutic process, with regard to radiotherapy (RT) contouring and planning.

Methods: A 35 years old man, due to perduring visual changes, headache and cognitive-motor slowing, underwent a cranial magnetic resonance imaging (MRI) that showed an intraventricular lesion of 57 mm. Management consisted on radical neurosurgery, followed by adjuvant radiotherapy. A total dose of 60 Gy (2 Gy/fraction) using a Volumetric Modulated Arc Therapy technique on the tumor cavity with exclusion of edema and anatomic barriers.

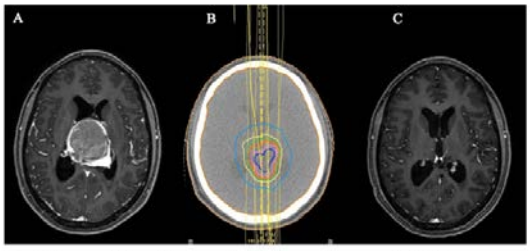

Figure 1. Pre-operative Magnetic Resonance T1-weighted contrast images on axial plan (A), treatment planning (B) and post-treatment Magnetic Resonance T1-weighted contrast images on axial plan (C).

Figure 1.

Results: RT treatment was performed without neither interruption or toxicities. After a month from the end of RT he presented confusion and movement disorders, so he was conducted to the medical ward, where dexamethasone was prescribed with good relief of symptoms. At the last follow-up visit the physical examination revealed an enlarged supraclavicular lymph node, but no suspicious ultrasound appearance were detected. Neurological examination did not showed deficit any nervous system abnormalities, the lung computed tomography and ultrasound of the abdomen did not showed any signs of distant metastases. Currently, the patient presents a good performance status without neurological deficits at 9 months after diagnosis, and first control MRI (Figure 1) after the end of RT confirmed the absence of microscopical residual disease.

Conclusions: Intracranial MPNSTs are extremely rare tumors, with a very poor prognosis. The optimal therapeutic strategy is unknown and the role of adjuvant radiotherapy is debated. In the present case, considered unfavorable risk factors as tumor site, natural history, young age, we believed reasonable to intensify therapies, integrating surgery with adjuvant radiotherapy. Till now, considered the short observation time, our experience suggested a good tolerance profile and good response to adjuvant RT, but we are waiting to observe long term outcomes.

PO208

FRACTIONATED STEREOTACTIC RADIOTHERAPY IN THE TREATMENT OF RECURRENT TYMPANOJUGULAR PARAGANGLIOMA: A CASE REPORT

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Aims: Tympanojugular paragangliomas (TJP) are rare, slow-growing and highly vascular tumors arising from the paraganglionic tissue of the IX-X cranial nerves. TJP are generally benign lesions but locally aggressive and patients can present with CN deficits, typically 7 through 12. The long-term aim of treatment is to preserve function while controlling tumor growth. Both surgery and radiotherapy provide a high local control, but associated morbidity is usually significantly less for RT. Due to the critical anatomic location surgery is often suboptimal. Post-operative RT in case of persistence/recurrence is an useful and safe option, as we propose to confirm with the following clinical case.

Methods: We herein present the case of a 72-years old woman, good PS, affected by residual growing TJP, following 2 partial surgery of the endotympanic component, with pre-operative embolization (2014 – 2019). After surgery there was a grade V facial nerve paralysis; partial hearing loss pre-existing remained unchanged. At the MRI performed 1 year later, the lesion presented growing towards the middle cranial fossa, with the presence of a more caudal jugular fossa component, in the absence of symptomatic progression. We performed a fractionated stereotactic radiotherapy on progressing lesion. For a target definition, our simulation CT was associated with brain MRI (Figure 1): our CTV included all the detectable desease (intracranial extention, endotympanic component and parajugular tissue); a further margin of 3 mm was added to obtain the PTV (volume measure was 5,5 cm3). VMAT was used in order to better spare the surrounding normal tissues, especially the inner ear. The patient received 45 Gy in 25 fractions. Mean PTV dose was 45 Gy (D2% 101,9%, D98% 97,6%, D95% 98,3%), with a

mean dose to the cochlea of 43,3 Gy (recommended QUANTEC mean dose: ≤ 45 Gy). Daily CBCT was performed.

Results: At the end of RT no acute toxicity was registreted. In the follow-up, the patient had MRI at 6 and 12 months that showed a stability of the lesion, no further tumor progression was observed. Subsequent to RT, facial nerve paralysis and partial hearing loss remained stable. No late toxicity was observed.

Conclusions: In our experience, RT for patients with recurrent TJP proved to be safe and effective modality approach in order to stop further growth and promote possible tumor shrinkage over time, without significant neurological toxicity.

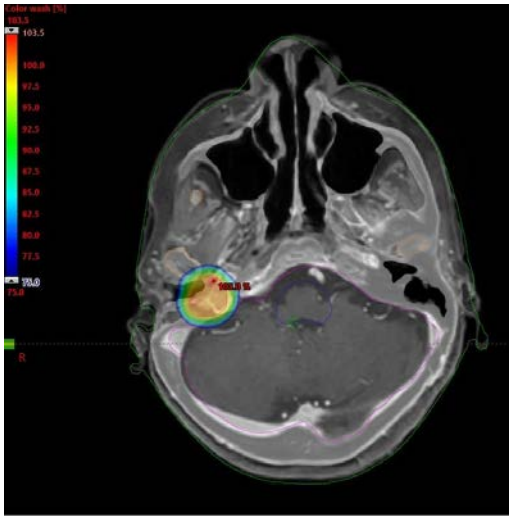

Figure 1.

PO209

RADIOTHERAPY IN NON VESTIBULAR NEUROMA: A CASE REPORT

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Aim: This report aims to describe the safety and efficacy of fractional stereotaxic radiotherapy (FSRT) for the treatment of non-vestibular neuroma (NVN). The lack of data due to the rare occurrence and high variability of the NVN leads to the absence of a common consensus for the management of this pathology. Major therapeutic strategies include radiological monitoring, microsurgical resection, or radiotherapy. Available data suggest that FSRT for patients with NVN is effective and with low toxicity.

Method: We report the case of an 80-year-old male patient who underwent amputation of his left leg, presenting a painful lesion in the space between the left gluteal muscles. This lesion, 30x15 mm, was stable over time without affecting the adjacent structures and insensitive to the use of contrast medium. The radiological diagnosis is, therefore, ischial neuroma caused by nerve trauma. Over time, the injury became painful. The anesthetist developed pain relief therapy which proved to be ineffective, so he decided to implant an electro-stimulator resulting in pain relief for 5 years. Subsequently, the neuropathic pain increased in frequency and intensity. During the follow-up for prostate adenocarcinoma, the patient reports his problem that has compromised his quality of life. FSRT was proposed to the patient, who accepted after being briefed on the benefits and risks. Simulation CT (2 mm slices) was registered with MRI available. The GTV representing the entire neurinoma was delineated and the PTV was given by the 5 mm isotropic expansion of the GTV. The patient underwent a 21 Gy FSRT in 3 fractions with a volumetric modulated arc therapy (VMAT). The iterative CBCT-based IGRT was performed daily. The treatment was delivered using Auto Beam Hold, an option available on the TrueBeam, which automatically searches for implanted fiducials in planned positions within the activated images. Auto Beam Hold automatically pauses the treatment beam whenever implanted markers are not detected where they should be.

Result: During treatment, the patient reported no toxicity. After 30 days, the patient reported a reduction in pain frequency and intensity. He also showed increased sensitivity to gabapentin. He will now continue with the clinical and radiological follow-up.

Conclusion: Fractional stereotaxic radiotherapy is an effective treatment for non-vestibular neuroma. A decrease in the presence and intensity of pain was achieved without acute toxicity to adjacent normal tissues.

PO210

A RARE CASE OF SEBACEOUS CARCINOMA OF THE EYELID TREATED WITH ADJUVANT VMAT RADIOTHERAPY

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Aims: Squamous cell carcinoma (SCC) of the eyelid is a rare malignancy with metastatic potential. We report the case of SCC of the eyelid metastasized to the left parotid gland that was treated using orbital exenteration (OE) and adjuvant radiotherapy (aRT) to improve local control.

Methods: A 58-year-old man, being treated for chronic blefaroconjunctivitis, underwent Orbital MRI detecting

the presence of tissue in the left orbital cavity. Metastatic involvement was confirmed at total body CT. Surgery consisted of radical OE and ipsilateral parotidectomy for SCC of the left eyelid infiltrating the tarsal plane and the peri, retro-orbital soft tissues with metastasis to the left parotid gland, perineural lymphovascular invasion and multiple positive surgical margins (pT4aNxM1 AJCC 7th). No residual mass was detected on postoperative orbital MRI and the patient was referred for aRT due to the high risk of further progression. CT simulation was acquired from the vertex to the tracheal carina with the patient in supine position, immobilized with a head and shoulder thermoplastic mask. RT treatment consisted of a sequential VMAT technique delivering 66 Gy, 56 Gy and 50 Gy to the high (HR), intermediate (IR) and low risk (LR) targets, respectively, in 33 fractions. CTVHR included the orbital and parotid surgical bed, CTVIR included the preauricolar nodes and left neck level Ib-II, while CTVLR included the left neck level III-Va. Planning Target volumes (PTVHR, PTVIR, PTVLR) were created using a 5-mm expansion around the respective CTVs, except in the skin direction. The treatment was delivered with an Elekta Versa HD linac. Daily CBCT was performed before each treatment fraction to correct for translations and rotations of patient positioning.

Results: Dosimetric results for the PTVLR were D95%=98.8%, V95%=98.7%, D2%=101.1%, D98%=96.4%, while for PTVIR D95%=96.4%, V95%=98.9%, D2%=101.9%, D98%=96.6%. Regarding PTVHR D95%=97.7%, V95%=99.6%, D2%=103.9%, D98%=96.2% (ICRU 83). Maximum doses to the contralateral lens, optical nerve, chiasm and brain stem were 4, 18, 25 and 24 Gy, respectively. The contralateral parotid gland was spared as much as possible receiving a mean and maximum dose of 8 and 12 Gy, respectively. During RT, the patient was seen at least once weekly and evaluated for side effects. Grade 2 pruritus, Grade 1 dermatitis of the periocular skin and Grade 1 mucositis were observed during the course of treatment but well controlled using topical agents.

Conclusions: This was a rare case of SCC of the eyelid treated with a VMAT sequential treatment after OE and ipsilateral parotidectomy. The results demonstrate that the treatment is feasible, effective and well tolerated.

PO211

INTRADURAL EXTRAMIDULLARY DORSAL MELANOCYTOMA: A CASE REPORT

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Aims: Meningeal Melanocytoma is a benign lesion arising from leptomeningeal melanocytes, which could mimic malignant counterpart melanoma. It's a rare tumor of the peripheric nervous system, and the intradural location is absolute rare.

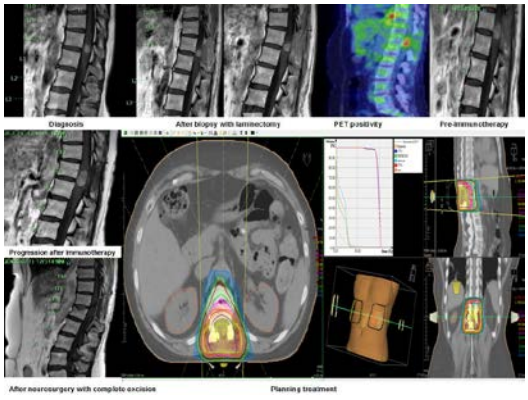

Figure 1.

Methods: We report the case of a 59 years' old woman with a progressive difficult in walking from June 2020 who underwent neurosurgical intervention to remove an expansive intradural endocanalicolar lesion at D12-L1 level and subsequent adiuvant radiation therapy. (Figure 1). After a first neurosurgery laminectomy with incomplete removal of the lesion and a histological examination which demonstrate the presence of a neoplasm with spindle cells classifiable as melanocytoma, the multidisciplinary group agree to submit the patient to immunotherapy with Ipilimumab+Nivolumab. The MRI after 3 cycle of Immunotherapy demonstrate the progression of the lesion, so the patient underwent to a new neurosurgical intervention. (Figure 1). The histological examination reveals the presence of a "neoplasm fragments composed of oval and fused cellular elements, with some nucleole evident and eosinophil cytoplasm, sometimes charged with pigmented material referable to melanin, presence of 2-3 mitosis x 10 HPF, focal infiltration of nervous tissue: the histologic picture lays for an intermediate grade melanocytic neoplasia (WHO 2016)". After surgery, the MRI revealed the complete removal of the lesion with residual of neurological symptoms of incomplete spinal cord injury. After a collegial discussion with Neurosurgery, Oncologist, Pathologist and Radiotherapist we decided to submit the patient to a adjuvant radiotherapy due to the uncertain malignancy potential.

Results: From 07.04.2021 to 11.05.2021 the patient underwent 3DCRT with daily IGRT for a total dose of 4560 cGy (24 fractions/190 cGy) without worsening of neurological symptoms, with a great attention to the spinal cord and the kidneys (Figure 1).

Conclusions: This is a rare neoplasm, with a uncertain evolution and in literature a few number of cases is reported. The patient will be evaluated after 2 month of the end of Radiotherapy with MRI, so data will be shown at the Congress.

PO212

ASTROBLASTOMA OF TEMPORAL LOBE IN A ELDERLY PATIENT

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Aims: We report a case of a 71-year-old patient with Astroblastoma treated with chemo-radiotherapy.

Materials and Methods: The onset of the disease started with an episode of confusion in September of 2019. A brain MRI showed an infiltrating lesion of temporal lobe In November 2019 he underwent brain surgery, with the macroscopically complete removal of mass which was found to be an Astroblastoma at microscopic examination. The immunophenotipic profile was consistent with this diagnosis (IDH1-, GFAP+, OLIG2+, CD34, MIB1 5%). After surgery, the patient received 4 cycles of chemotherapy with Temozolomide (TMZ) 150 mg/mq days 1-5 q28. In May 2020 he experienced clinical progression with the appearance of motor disorder. MRI confirmed signs of progression of the disease and the patient underwent a second surgery in June 2020 with removal of neoplastic mass which resulted to an Astroblastoma relapse at microscopic examination. From July 2020 to august 2020 the patient was treated with volumetric modulated arc therapy on the surgical bed (60Gy,2 Gy for fraction) concomitant with TMZ 75mg/mq die. Three weeks after the end of the treatment a quick deterioration of general conditions occurred and the patient died one month later.

Results: Despite the aggressive treatment a fast clinical-radiological progression took place leading the death of the patient in just few months.

Conclusion: Astroblastoma is a rare disease generally affected children and young adult. This case shows an inauspicious form developed in a 71 years old men.

PO213

DERMATOFIBROSARCOMA PROTUBERANS: WHY NOT ONLY RADIOTHERAPY? A CASE REPORT

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Aims: Dermatofibrosarcoma protuberans (DFSP) is a rare tumor of soft tissue with a high propensity for local invasion and recurrence. Clinically, DFSP is characterized by a rapid and exophytic growth with frequent ulceration of the epidermis of trunk, head and neck, and proximal extremities. Local recurrence after surgery is high, ranging from 10% to 60%. We present a case report of a woman with DFSP multi- surgical treated.

Methods: In January 2020, a 82-years-old female patient (PS ECOG 1) affected by recurrence of DFSP in the trunk , was referred to our Radiation Oncology Department. The patient was also affected by some comorbidities with a Charlson Comorbidity Index of 8. The patient's medical history start in 2013 when she underwent to a wide local excision of tumor-bearing area with a surgical margins of 3 cm in all directions. No adjuvant radiotherapy was proposed but only close monitoring. After 7 months, she relapsed locally and, also this time, only a wide re-excision was made. During dermatological follow-up 2014-2020, she had annully local recurrences, all treated surgicall, to avoid a speculated high grade transformation due to the use of radiation therapy. Finally, in January 2020 she presented a pink dermal painless plaque of 4 cm, with the same histology. This time, a MR revelead a solid mass with irregular deep extension. In multidisciplinary cutaneous board, this medical history was discussed and was proposed a radical radiotherapy. A treatment using photons with energy of 6 MV was delivered using a bolus skin surface a total dose of 55Gy in 22 fractions (2.5 Gy daily) with IG-IMRT.

Results: The treatment was well tollerated. The patient presented a moderate G2 erythema (according to RTOG toxicity scale). After a follow-up of 18 month, we observed a flattening of treated lesion without signs of disease progression. Actually, we are studing the microenvironment of patient.

Conclusions: In this case report, the patient succeeded in obtaing a clinical control time major than surgery with radiotherapy. It is very intruiguing to speculate that an immunity response driven by RT could be responsable of this phenomen. It would be interesting to collect other DFSP treated with only RT.

PO214

RADIO-CHEMOTHERAPY INDUCED MIELODISPLASTIC SYNDROME: CASE REPORT

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Aims: Treatment related myelodysplastic syndrome has been reported in various solid and hematological tumors and to our knowledge this is the first case of MDS induced by radio-chemotherapy in the context of mesothelioma. Myelodysplastic syndromes (MDS) are clonal haematopoietic stem cell (HSC) disorders predominating in the elderly, characterized by ineffective haematopoiesis leading to blood cytopaenias and by progression to acute myeloid leukaemia (AML). In one third of cases, MDS has been identified to be associated with previous cancer treatment by using chemotherapy (CT) or radiotherapy (RT).

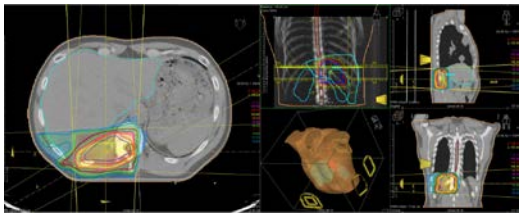

Figure 1.

Methods: Hereby we describe the case of a 49 year-old patient with a mesothelioma diagnosed in 2015 treated by chemotherapy and localized radiotherapy ; I-line chemotherapy treatment with carboplatin-pemetrexed was performed for six cycles. Following progression of the disease to PET, the patient was enrolled in an experimental protocol with Tremelimumab and MEDI4736 of which he performed twelve cycles. At the control CT TB of November 2016 disease progression at the level of the paravertebral lesion with involvement of the canal at the level of D11-12. Not neurosurgical indication. He performed radiotherapy treatment for palliative purposes: total dose 20 Gy in 5 daily fractions. July 2017, ongoing maintenance immunotherapy, bone progression of the disease with radiotherapy treatment on the right and left costal arch, total dose. 27 Gy daily fraction dose 3 Gy. September 2017 radiotherapy treatment on L5 / S1, single dose of 8 Gy. November 2017 8 Gy radiotherapy flash treatment on right femur head and left humeral and beginning of therapy with bisphosphonates. February 2018 retreatment on L5-S1 total dose 12 Gy in two fractions . June 2018 retreatment of the left humeral region and L2-L4 metamers, total dose 20 Gy in 5 fractions Decembr2 2018 retreatment L2, total dose 16 Gy in 4 fractions.

Results: January 2019 following pancytopenia, he performed osteomedullary biopsy diagnosed with myelodysplasia Start therapy with Vidaza. June 2019 the patient dies from disease progression

Conclusions: Treatment related myelodysplastic syndrome should be suspected in patients with signs and symptoms related to the blood cytopenias and who were exposed to cytotoxic agents and/or radiotherapy.

PO215

THE ROLE OF RADIOTHERAPY IN THE MANAGEMENT OF A RECURRENT SYMPTOMATIC THORACIC VERTEBRAL HEMANGIOMA: A CASE REPORT

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Aims: Vertebral hemangioma (VH) is the most common benign spinal tumor. It is usually asymptomatic but in 0.9-1.2% of cases it can be aggressive (symptomatic) with expansion, pain and diffusion into the spinal canal with possible spinal cord compression. The management of symptomatic VH require surgery and/or radiotherapy. There are several clinical reports of the effectiveness of RT in symptomatic VH, but the optimal dose, fractionation schemes, and possible long-term effects are controversial. A large retrospective German study compared results in terms of pain relief after RT for patients treated with EQD2 of about 40 Gy *vs* approximately 30 Gy. We present a case report to describe the role of radiotherapy (RT) in reducing tumor volume and neurological disfunctions in a thoracic spine recurrent hemangioma.

Methods: A 32 years-old man presented with asthenia and walking disorders. Brain and spinal MR performed in January 2020 showed D6 structural subversion with spinal stenosis and hypointense tissue in extra-dural space. In February, D6 laminectomy and decompression surgery was performed. After 11 months, MR showed a new volumetric increase of the lesion with initial spinal cord compression and reappear of neurological deficits. A new surgery was excluded, so RT was indicated for this case.

Results: No relevant differences in toxicity between the two groups was observed but a better pain control was reported in the first group of German study. Therefore we decided to administrate RT with a total dose of 40 Gy (2 Gy/fraction) with conformational 3D technique. Our

CTV was represented by vertebra D6 with tumoral extensions to the upper and lower vertebra, including spinal cord that was compressed. After 3 months, clinical outcome of our patient and new MR imaging demonstrated improvement of neurological symptoms and initial decreasing in tumor size. No acute or late toxicities were observed.

Conclusions: Our case report, as well as other cases reported in literature, RT is a safe and effective treatment choice for recurrent and symptomatic VH. In order to prevent a relapse of malignancy and symptoms, postsurgical irradiation of the more complicated cases could be recommended.

PO216

AN INVASIVE DUCTAL CARCINOMA IN ACCESSORY BREAST TISSUE IN AXILLARY: A CASE REPORT

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Aims: To report a rare entity of invasive breast cancer grown in accessory axillary breast tissue

Methods: A 51 years old female arrived at our Breast Unit complaining of a mass in the left axilla. A mammography and a MR were performed and both excluded a primary left breast cancer. The ultrasound of the left axilla revealed a hypervascular and hypoechoic nodule measuring 37 x 27 x 25mm and the presence of enlarged lymph nodes, which the major had a 20 mm diameter. The axillary nodule's biopsy demonstrated an invasive grade 3 carcinoma with positive estrogen receptors (80%) and positive progesterone receptors (5%), HER-2 negative (score 0), Ki 67: 52%, staged as cT2cN1. Furthermore, the major lymph node resulted positive for a secondary localization. Her past medical history was unremarkable and the family history revealed breast cancer in her sister at age 47. The patient was discussed in our multidisciplinary team's meeting and we proposed a neo adjuvant chemotherapy approach with 4 cycles of Epirubicin-Cyclophosphamide followed by 12 cycles of Taxane. After, a wide local excision of the entire accessory breast and axillary dissection was then performed. The histology of the specimen revealed an 18mm invasive G3 carcinoma and a lymph node with ITC over 6 examined, instead the other five lymph nodes presented signs of tumor regression: the patient was staged as ypT1c ypN0(1+). To the patient was administered hormonal suppressive treatment. A dose of 50 Gy in 25 daily fractions was administered to the whole breast and to the locoregional nodes.

Results: This case history illustrates a rare entity of invasive carcinoma grown from an ectopic breast tissue in the axilla. The patient was treated with neoadjuvant chemotherapy, wide local excision, axillary dissection, hormonal suppression therapy and adjuvant radiotherapy.

Discussion: Due to its rarity management guidelines for invasive carcinoma of ectopic axillary breast are lacking and controversial. Limited published data suggest that radiotherapy should be limited to the tumor cavity and ipsilateral nodal sites. We decided to irradiate the whole breast because the pathological evaluation was unable to distinguish between a primary on ectopic breast tissue or a lymph node containing methas.

PO217

MANAGEMENT AND OUTCOMES IN RADIOINDUCED ANGIOSARCOMA OF THE BREAST: A CASE REPORT

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Aims: Angiosarcoma of the breast (AB) is a rare malignancy (<1% of all soft tissue tumors). Primary AB is rare but radioinduced angiosarcoma of the breast (RASB) is more common, specially in women who had previous breast radiotherapy (RT). In order to define a radioinduced angiosarcoma it is necessary that RT has been performed at least 3 years before, that it arises in the context of previously irradiated tissues and that has different histology compared to the previously irradiated tumor. Clinical presentation of RASB is purple, teleangectasia-like formations that may appear as nodules, plaques or patches. Radical surgery of the tumor is the most common treatment. In contrast to the well-established role of surgery, the value of re-irradiation and chemotherapy (CT) is less clear.

Methods: A 66 year old woman presented with purple skin nodule of 3 cm and satellite lesions of the inner-lower quadrant of previously irradiated right breast (RB). She performed breast-conserving surgery 6 years before for a RB cancer.It was a lobular carcinoma staged pT1cpN1aM0, estrogen and progesterone receptor positive and HER2 negative. Adjuvant RT to the RB(50 Gy/25 fractions, 15MV photons) and boost (10Gy, 18 MeV electrons) on the tumoral bed was performed, followed by anastrozole. RASB was diagnosed by biopsy and mastectomy with negative resection margins was performed in May 2020 after 4 cycles of Gemcitabine-Taxole.Adjuvant CT with 3 cycles of Epirubicine-Ifosfamide was performed until October 2020. In April 2021 new dark purple nodule was noted in the context of a paramedian cutaneous area of the left equatorial inner. Histological diagnosis was AB. PET scan showed cutaneus node.

Results: Dosimetric analysis showed a maximum dose of 1.5 Gy in this new localisation of AB. New radical surgery is planned. Considering the recurrent presentation of RASB, a study of microsatellite instability

(MSI) in our patient is ongoing to evaluate the presence of genomic instability (GI) that is considered to contribute to RABS development.

Conclusions: We reported a rare case of repeated local recurrences of RASB also in areas which received very low RT doses. We believe that patients with GI need careful attention in the RT technique choice, in order to reduce the spread of low doses to normal tissues and controlateral breast.

PO218

QUALIFIER: A PROSPECTIVE MULTIPROFESSIONALITY QUALITY ASSURANCE (QA) PROGRAM FOR FRACTIONATED ENDOVAGINAL INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY)

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Aims: Aim of this study is to propose the QUALIFIER (QUALIty assurance For IntervEntional Radiotherapy) project for fractionated endovaginal interventional radiotherapy (IRT, brachytherapy) as a system for guarantee a high-quality and resource-saving patient workflow.

Methods: A monoinstitutional multidisciplinary discussion was undertaken to evaluate, discuss and optimise all current processes and documents in managing, treatment planning and delivery of endovaginal interventional radiotherapy. For this purpose, three radiation oncologists with IRT experience, one medical physics expert in IRT, one radiotherapy technologist with IRT experience were interviewed to identify critical points and propose documents improvement followed by a literature research on this topic. Results of the interviews and of the literature research, were shared in the multidisciplinary interventional oncology tumor board (IOC-GYN MDTB), were each member reviewed the proposal of a new shared documentation that, after a discussion of critical points and adequate integrations, were validated. Finally, a multidisciplinary committee approved the proposed documentations and forms.

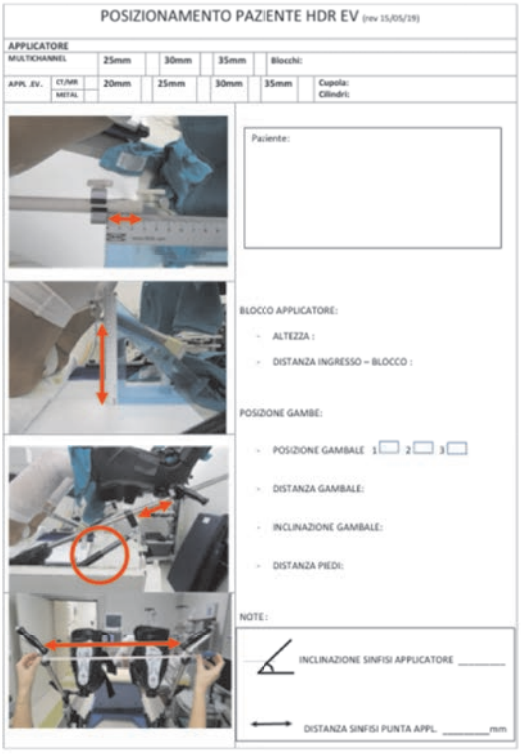

Figure 1. Example of quality assurance documentation.

Results: The complete patient pathway within the Interventional Oncology Center (IOC) was summarised in a dedicated document and critical points were defined. Practical recommendations were introduced to standardise the treatment documentation and establish an internal quality assurance protocol. For endovaginal interventional radiotherapy, the identified critical points were: i) the first clinical evaluation, including indication and prescription; ii) the interventional board, which independently checked the clinical appropriateness of indication and prescription; iii) outpatient procedure, target definition, and planning; iv) follow-up indication. Documents were integrated with an information brochure for patients, a dedicated prescription module with an obligatory procedural checklist, a medical physicist checklist for treatment planning and delivery, a quality check to confirm the summary information of the approved plan, as well as the follow-up indication with the standard supportive therapy. IOC-GYN MDTB members and the multidisciplinary committee approved the shared documentation. An example of the form produced for quality assurance is shown in Figure 1.

Conclusions: We introduced a quality assurance protocol for fractionated endovaginal interventional radio-

therapy, with a dedicated quality assurance documentation.

PO219

DEMOGRAPHIC, CLINICAL AND TECHNICAL CHARACTERISTICS OF INTRAOPERATIVE RADIOTHERAPY FOR RECTAL CANCER: AN ANALYSIS OF THE ISIORT DATABASE

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Background: Intraoperative radiotherapy (IORT) has been considered as an alternative or complementary treatment to external beam radiation treatment (EBRT) for rectal cancer over the last decades. The International Society of Intraoperative Radiation Therapy (ISIORT) has collected the demographic, clinical and technical data of all the IORT procedure which took place in its member institutions.

Materials and Methods: Since 2007, the members of ISIORT have been invited to record demographic, clinical and technical data about the IORT procedures performed in their centers, using a standardized model of collection. Centers have been yearly invited to upload data in a joint online database. The entry of retrospective data and the modification or update of previous uploaded data was possible. The collected data were analyzed by IBM SPSS statistical software.

Results: The database included 46 centers, 9 of which outside Europe. Rectal cancer represents the second most frequent tumor (955 cases, 7.2%) in the ISIORT database. The mean age was 62,6 years (range 21 – 94), the 63,1% of the patients were male. The main histology of the tumor was adenocarcinoma (98,5%), T3 was the most common stage at the time of surgery (66,6%), followed by T4 (20,1%), T1 (2,3%) and T2 (1,1%). The intent was curative for the 96% of patients and the 24% of the delivered treatment was for recurrent tumors. Main energy used was 12 MeV (33%), followed by 15 MeV (29%), 10 MeV (20%), 50 kV (2,7%). The bewel angle was 45° for the 84% of the cases. The diameter of the applicator was 6 cm for the 33% of the cases, followed by 5 cm (28%), 7 cm (26%) and 8 cm (6%). The administered dose was 12,5 Gy for the 60% of patients, followed by 10 Gy (27%), 15 Gy (6%) and 8 Gy (2%).

Conclusions: This analysis represented the first report on a large cohort of rectal IORT procedures performed in last decades, highlighting the consensus beneath the patient selection and treatment modalities.

PO220

RADIOSURGERY WITH CYBERKNIFE® FOR BRAIN ARTERIOVENOUS MALFORMATIONS: TECHNICAL AND DOSIMETRICAL ANALYSIS

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Aims: Radiosurgery (SRS) obtain a successful obliteration of arteriovenous malformations (AVMs). Radiation injury to the vascular endothelium induced the proliferation of smooth-muscle cells and the elaboration of extracellular collagen, which leads to progressive stenosis and obliteration of the AVM nidus thereby eliminating the risk of hemorrhage. SRS, compared to microsurgical and endovascular treatments, is a noninvasive and outpatient procedure, with minimal risk of acute complications, but results are not immediate. Thrombosis of the lesion is achieved in most cases, but it does not occur until 2-3 years after treatment. SRS has been shown to be less effective for lesions over 10 cc in volume. Aim of the study is to describe a monoinstitutional series of AVMs patients (pts) treated with CyberKnife® system (CK) in collaboration with dedicated neuroradiologist.

Methods: All pts performed angiography, CT-angio and MR-angio and were evaluated by an expert neuroradiologist after possible embolization and before CK treatment. All imaging data were accurately co-registered in the CK-TPS and used for target contouring delineation. The AVM target was the nidus, without embolization areas in pts with prior embolization, and was delineated by an experienced radiation oncologist and neuroradiologist. All pts received a single fraction of radiation. The PTV was equal to GTV. Follow-up was performed with MR-angio after 2-3 months and angiography 1 year after the treatment.

Results: From Dec 2017 to May 2021, 9 pts (4m, 5f), mean age 42 (18-56) with AVMs were treated with CK. AVMs were located within cerebellum (3), temporal lobe (3), parietal lobe (2) and frontal lobe (1). 6 pts had previously undergone endovascular embolization. Median GTV was 1,67 cc (0,09-11,99) and median marginal dose was 18 Gy (18-21) with median isodose prescription of 80% (74-85). The PTV median coverage was 99,88%

(97,54-100), the median PTV CI of 1,6 (1,16-2,14), the median treatment duration is 31 minutes (29-63). 7 pts completed the RT course, 1 pt had asymptomatic brain radionecrosis 19 months after the RT, 5 pts had > 1-year angiographic follow-up: 4 had stable disease and 1 AVM obliteration.

Conclusions: A specialized team approach is necessary for CK treatment of AVMs, including an SRS expert radiation oncologist and medical physicist, and an interventional neuroradiologist or neurosurgeon. CK is safe and effective for AVMs treatment, but long-term data are needed

Fig 1. Example of a CK contouring and planning of a 35-years old patient with left frontal lobe AVM, baseline and 1-year fup angiography

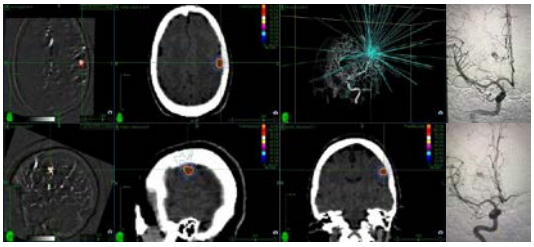

Figure 1.

PO221

COMBINED SURGERY-BRACHYTHERAPY TREATMENT FOR RELAPSING KELOID IN PEDIATRIC PATIENTS

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Aim: Keloids are abnormal scar lesions that occur on the skin following trauma and burns. In this case report we present an integrated treatment of Surgery and Brachytherapy (BRT) performed for eradication and prophylactic purposes on the production of a new keloid in a 13 year old patient.

Methods: A 13-year-old patient reported multiple scars with the development of keloids of various sizes in the abdominal, thoracic, neck following burns to the whole body at the age of nine. In particular, a right retroauricular exophytic formation of about 7 x 5 cm was identified on the patient's skin. This lesion was painful throughout the day or in case of impact, and had been subjected to surgical removal in July 2019. However, in a span of 6 months this lesion had grown back and increased in size. The patient was referred to our attention from the Large-Burn-Centre to evaluate possible radiotherapy immediately after the surgery to limit the further growth of this keloid formation. When he visited our clinic he reported pain only at the level of the keloid with associated hearing loss due to the traction of the auricle. On 25th-26th and 27th of June, after packaging a personalized Freiburg-Flap applicator and a centering CT scan, we carried out a prevention BRT program with the aim of preventing the production of further keloid.The first of the three sessions of Brachytherapy took place 7 hours after the surgery to remove the keloid and was performed in a regimen of deep sedation. With Flexitron HDR, which uses a source of 192 IRIDIUM, we delivered 1500 cGy to the keloid removal site in the behind-the-ear region in three sessions of 500 cGy per session.

Results: The subsequent FU at 3, 6 and 10 months did not show acute side effects on the irradiated region except for G1 erythema in the first 15 days post BRT. To date, no documented keloid regrowth on the irradiated area is noted and in accordance with the Large-Burn-Centre a new treatment was planned at the level of a further Keloid formation at the level of the right auricle.

Conclusion: The integrated Surgery-BRT in accordance with the data in the literature proved to be feasible and devoid of significant side effects in acute and subacute. Furthermore no re-growth of the keloid on the treated site is noted at 12 months follow up. Longer follow up is however necessary to evaluate any long-term side effects and better define the timing of a possible regrowth of the keloid.

PO222

HIGH-DOSE-RATE BRACHYTHERAPY USING LEIPZIG APPLICATORS FOR BREAST CANCER CUTANEOUS METASTASIS: A CASE REPORT

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Aims: We report our experience in treating a patient with breast cancer cutaneous metastasis with a palliative intent, using Leipzig applicators and high-dose-rate brachytherapy.

Methods: An 84 years old female with metastatic breast cancer, presented 2 nodular cutaneous metastasis: on the left nasal pyramid and on the right chest wall. She had a previous history of breast cancer treated first with radical left mastectomy and later, after a local recurrence (2002), re-treated with re-excision surgery and adjuvant local radiotherapy (50Gy). In 2021 two suspicious cutaneous lesions were reported; a biopsy confirmed skin

metastasis from breast cancer. Because of previous treatments and disease sites, we decided to treat these cutaneous metastasis by HDR brachytherapy (HDR-BT) hypofractionated regimen using Leipzig applicators with palliative intent. The Nucletron Leipzig applicator is designed for HDR-192Ir surface brachytherapy. The left nasal pyramid lesion was 19x11 mm without ethmoid invasion and the right chest wall lesion was 22x16mm; we used Leipzig applicator H3 (30mm) for both lesions. The precision machined source channel in this applicator guarantees a reproducible prescribed target dose. The treated area was defined as the visible lesion plus a safety margin of 5 mm around the lesion. Treatment doses were prescribed at 3mm in depth from skin surface. The total prescription dose was 12Gy in 4 fractions (3Gy/fr) for each nodular lesion, twice a week. Only for left nasal pyramid lesion, a dose verification to the target and eyeball was performed with termoluminescent dosimeters (TLD 100 liF). Left eyeball received 18.36cGy (standard deviation 0.006Gy). After treatment the patient was followed-up with monthly clinical checks for the first 3 months.

Figure 1.

Results: Surface HDR-BT treatment was well tolerated without acute side effects. At the first follow-up a partial response (PR) of the left nasal pyramid lesion and stability (SD) of the left thoracic lesion were found. After 3 months the nasal lesion completely disappeared leaving only a small superficial teleangectasia Figure 1; the thoracic lesion showed a slight reduction in size.

Conclusions: Our experience supports surface HDR-BT as an effective treatment option for cutaneous metastasis, especially in critical sites. It offers a convenient treatment schedule for patients and satisfactory local control associated with a highly focal dose distribution, greater organs at risk sparing with excellent clinical outcome.

PO223

STEREOTACTIC BODY RADIOTHERAPY FOR PROSTATE CANCER LYMPH NODE METASTASES: A SYSTEMATIC REVIEW

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Aims: Androgen deprivation therapy is still considered the standard treatment for oligometastatic prostate cancer (PC). However, increasing evidence suggests that a more targeted management (metastases-directed therapies) could play a "curative" role. In fact, it allows satisfactory local control (LC) and could delay the start of systemic treatments. Lymph nodes (LN) isolated oligorecurrences identify a favorable subset of patients (pts) in terms of disease progression. Therefore, we performed a systematic review on stereotactic body radiotherapy (SBRT) as metastases directed therapy in this setting. Primary objectives of the study were LC and progression-free survival (PFS).

Methods: A systematic literature search for relevant studies was conducted in PubMed, Scopus, and Cochrane library up to July 1st, 2020. Papers reporting LC and/or PFS in pts with LN oligorecurrent PC treated with SBRT alone or in combination with systemic treatments were selected. Data on toxicity were also collected from the selected studies.

Results: Fifteen studies were eligible (414 pts). All but three studies were retrospective analyses. LC and PFS results were reported in 15 and 12 papers, respectively. The median number of pts per study was 25 (range 7-94), with only one study reporting results on more than 50 pts and six studies reporting results on less than 20 pts. A high heterogeneity was observed in terms of pts selection (i.e., number of treated lesions, systemic therapies, evaluation modalities). In one study SBRT was delivered as a single 20 Gy fraction, while in the others the median total dose ranged between 24 and 40 Gy (median: 30 Gy) in 3-6 fractions (median: 3 fractions) (Table 1). LC was reported as a crude percentage in 13 studies with 100% rate in 7/13 and ranging from 63.2% to 98.0% in 6/13.

Overall, only 2/13 studies reported a crude LC lower than 90.0%. Five studies reported actuarial LC with 2-year rates ranging from 70.0% to 100% (median: 84.0%). PFS was reported as crude rate in 11 studies, with a median of 42.9% (range: 27.3-68.8%). Two-year PFS was reported in four studies, ranging from 30.0% to 50.0% (median: 38.6%). SBRT tolerability was excellent, with only one pt presenting grade 3 acute toxicity and two pts presenting grade 3 late toxicity.

Conclusions: SBRT for LN oligorecurrence from PC provides optimal LC and high tolerability. However, its effect on disease progression is still unclear as well as which pts are more suitable for this approach.

Table 1.

Table 1. Radiation treatment characteristics

Author, year	Dose, fractionations	GTV to PTV expansion	RT delivery technique	SBRT associated to ENI	ADT associated to SBRT, median duration
Jereczek-Fossa et al, 2009	20-45 Gy in 2-3 fr	5-9 mm (anisotropic margins)	VMAT	NO	57.1%, mean 15 mo
Casamassima et al, 2011	30 Gy in 3 fr	5 mm	VMAT	28.0%*	NR
Jereczek-Fossa et al, 2012	33 Gy in 3 fr	1-2 mm	CK	NO	75%, 17.5 mo
Decaestecker et al, 2014	30-50 Gy in 3-10 fr	3 mm	IMRT/VMAT	NO	NO§
Detti et al, 2015	24-36 Gy in 1-5 fr	2 mm	CK	NO	33.3%
Napieralska et al, 2016	24-45 Gy in 1-3 fr	4-5 mm	CK	11.1%	100%
Pasqualetti et al, 2016	24-27 Gy in 1-3 fr	3mm	VMAT	NO	NR
Bouman-Wammes et al, 2017	30-45 Gy in 3-5 fr	3-5 mm	VMAT	NO	NO
Franzese et al, 2017	25-45 Gy in 4-6 fr	5 mm	VMAT	NO	57.7%
Ingrosso et al, 2017	12-50 Gy in 1-5 fr	5-8 mm	NR	NO	47.5%
Jereczek-Fossa et al, 2017	15-36 Gy in 3-6 fr	2-3 mm	10.6% CK 89.4%VMAT	NO	36.2%, 14.5 mo*
Kneebone et al, 2018	PTV HD: 30-50 Gy in 3-5 fr PTV LD: 24-30 Gy in 3-5 fr	PTV HD: GTV+5 mm PTV LD: CTV LD+10 mm	VMAT	NO	NO
Siva et al, 2018	20 Gy in 1 fr	5 mm	NR	NO	NR
Oehler et al, 2019	30-45 Gy in 3 fr	2-4 mm	CK	NO	NO
Ong et al, 2019	35-40 Gy in 5 fr	5 mm	VMAT	NO	NO

ADT: androgen deprivation therapy; CK: cyberknife; CTV: clinical target volume; ENI: elective nodal irradiation; GTV: gross tumor volume; HD: high dose; IMRT: intensity modulated radiotherapy; LD: low dose; LN: lymph nodes; mo: months; NR: not reported; PTV: planning target volume; RT: radiotherapy; SBRT: stereotactic body radiation therapy; VMAT: volumetric modulated arc therapy. * 50 Gy in 25 fr to whole pelvis/boost on positive LN (4 Gy in 3 fr); § until 05/2012 patients were treated with single injection of short acting LHRH analogue concomitant with SBRT. ° 1.1% (1 pt) treated with heavy-based chemotherapy

PO224

STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR SOFT-TISSUE SARCOMAS (STS) LUNG OLIGOMETASTASIS

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Aims: Sarcomas are malignant tumors of the connective tissue classified into numerous different subtypes. Lung is one of the most common site of metastatic disease; the first choice treatment is surgical resection and few data are available regarding radiation therapy. Aim of the present study is to evaluate safety and efficacy of Linac-based SBRT of lung oligometastasis from STS in terms of local control (LC) and toxicity. Progression-free survival (PFS) and overall survival (OS) are evaluated as secondary endpoints.

Methods: Patients with lung oligometastasis (considered as a maximum of 4 lesions at the same time) from STS treated between 2015 and 2021 were included in the present evaluation. All patients were treated with Linac-based SBRT with different schedule of treatment according to site and sizes of lesions. Patients outcome and toxicities were assessed using RECIST criteria and CTACE scale.

Results: 38 patients were enrolled, for 48 lung treatments. 79% were peripheral lesions and 21% central. Median follow-up was 41 months (range 4-125). Local recurrence occurred in 2 cases. The median PFS was 14 months (95%CI 7-18). The median OS was 55 months (95%CI 30-92). Prognostic factors significantly impacting outcome were: age of patients at diagnosis (p=0,0246) and primitive site (limbs, trunk, pelvis or H&N; p=0,0008) according to PFS; grading of the primitive (≤ or > than G2; p=0,0082) and number of lung lesions (1-4, p=0,0057) in relation to OS. No severe acute or late toxicities was recorded.

Conclusions: SBRT seems to be a valid treatment option for the management of lung oligometastasis from soft-tissue sarcomas, with a satisfactory local control and negligible toxicity.

PO225

A POST HOC ANALYSIS FROM TWO PHASE I TRIALS ON STEREOBODY RADIOTHERAPY FOR NODAL LESIONS IN OLIGO-PROGRESSIVE PROSTATE CANCER PATIENTS

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Purpose: To evaluate the rate of biochemical responses (BR) and the time to next systemic therapy (NEST), in oligoprogressive prostate cancer (PC) patients treated with stereobody radiotherapy (SBRT) for nodal metastases.

Material/Methods: We retrospectively collected the clinical data of PC patients enrolled in two institutional phase I prospective studies (DESTROY-1; DESTROY-2) and treated with SBRT on nodal lesions. The first trial was a multi-arm study on SBRT delivered with fixed non-

coplanar conformal fields or Volumetric Modulated Arc Therapy in patients with primary or metastatic tumours in various extra-cranial body sites. In the second one radiosurgery (SRS) was delivered by VMAT technique in patients with primary or metastatic tumours in various extra-cranial body sites. Four-months after treatment BR was evaluated: a reduction of PSA value >10% (complete if >50%) with respect to pre-SBRT PSA value was considered a response; stable disease was defined as a PSA<10% of the pre-SBRT value, while a PSA increase >10% was classified as biochemical progression. Moreover, the NEST (hormonal or chemotherapy) start/change were analysed.

Table 1.

All lesions	61	
	Median	*(Range)*
Age, years	73.5	(62.0 – 85.0)
Weight, Kg	77.0	(60.0 – 98.0)
BMI	28.0	(21.8 – 38.0)
	n°	*(%)*
Eastern Cooperative Oncology Group performance status		
0	48	(78.6)
1	11	(18.0)
2	1	(1.7)
3	1	(1.7)
4	0	(0)
Comorbidities[a]		
Hypertension	18	(54.5)
Heart disease	4	(12.1)
Diabetes	5	(15.1)
Liver disease	1	(3.2)
Chronic pulmonary disease	5	(15.1)

[a] calculated on the number of comorbidities (N=33)

Results: 36 PC oligoprogressive patients harbouring 61 nodal lesions were treated with SBRT at our institution between the 2005 and 2020. The clinical characteristics are reported in the Table 1. Thirty-two lesions (52.5%) were treated by SBRT (multiple fractions), and 29 (47.5%) lesions were treated by single fraction radiotherapy. The median dose delivered by SBRT was 45Gy (20-50) with a median BEDα/β10 of 85.5Gy (28-100). The most frequent schedule for SBRT was 9Gyx5 fractions (37.9%). The median dose delivered by SRS was 20Gy (12-24), with a median BEDα/β10 of 60Gy (26.4-125.4). The most frequently adopted schedule for SRS was 20 Gy x1 fraction (44.8%), In terms of BR, the median PSA before the SBRT/SRS treatment was 5.3 ng/ml (0.03-382 ng/ml), while the median PSA at the first evaluation after treatment (4 months) was 2.41 ng/ml (0.001-346ng/ml). In particular, we recorded 20 (33.0%) complete, and 12 (19.0%) partial reponses, 5 (8.0%) stable PSA values and 19 (32.0%) progressions; the PSA dosage was not available in five cases (8.0%). The actuarial1-, 3- and 5- years NEST were 79.9%, 67.7% and 56.4% respectively.

Conclusion: In this scenario SBRT can be considered an efficacious treatment in patients harbouring isolated PC nodal metastases, especially in order to slow down the start or change of a new systemic therapy.

PO226

NEUTROPHIL-TO-LYMPHOCYTE RATIO PREDICTS RESPONSE IN PATIENTS WITH BRAIN METASTASES TREATED WITH FRACTIONATED STEREOTACTIC RADIOTHERAPY

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Aims: Metastatic brain tumors standard of care is constantly evolving along with technological development in radiation therapy (RT) and with the identification of new prognostic and predictive factors. In the last few years, inflammatory blood markers have emerged as predictive and prognostic factors, particularly the neutrophil to lymphocyte ratio (NLR). This reflects the squilibrium between immune surveillance and tumor progression. In this scenario we aimed to assess the predictive role of NLR on early response in-field control, intracranial control and overall survival after fractionated stereotactic radiotherapy (FSRT) for brain metastases.

Methods: We retrospectively evaluated 34 patients with initial presentation of metastatic brain disease, treated with FSRT in our center. Laboratoristic parameters were obtained from blood count performed within one week before the start of RT. NLR, Hemoglobin and Platelets count to lymphocyte ratio were examined to establish their prognostic role respect to overall survival, disease progression and treatment response. Treatment response was evaluated with brain MRI at 3 months from the end of FSRT and then on a quarterly basis for the first two years, according to RECIST criteria. We analyzed time-to-event distributions using Kaplan-Meier's method. Kaplan-Meier curves illustrate the probability of progression in response time for patients with NLR ≥ or < MEDIAN.

Results: With a median follow-up of 14 months (3-58), a single brain metastasis (range 1-3) was treated in 74% of patients. Treatment schedules adopted ranged from 20 Gy (5 Gy/fx) to 27 Gy (9 Gy/fx). The median age was 59 years (41-81): female=20, male=14. A good Karnofsky Performance Status was detected in 88% of our sample. At the time of treatment 59% of patients was not on steroid therapy. The median NLR value was 2.72 (IQR: 1.69 - 4.54). Patients with a NLR ≥ 2,72 showed a probability of progression 1.2 times higher than the patient with a lower value (HR 1.20; 95% CI 0.49–2.95, p=0.700) (Figure 1). A statistically significant mean difference (p=0.012) was found for NLR between patients who had a complete response and those who did not.

Conclusions: Pre-treatment immune markers of systemic inflammation have been reported as independent prognostic factors for outcomes in different neoplasms. In our study, higher values of NLR were associated with a lower response to FSRT and higher probability of disease progression.

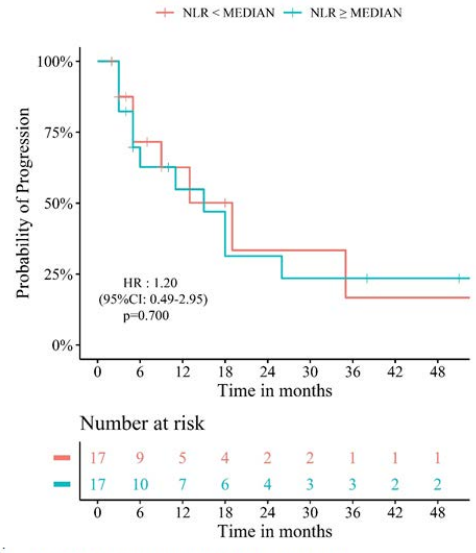

Figure 1.

PO227

STEREOTACTIC BODY RADIATION THERAPY (SBRT) AS ABLATIVE TREATMENT FOR ADRENAL METASTASES IN OLIGOMETASTATIC OR OLIGO-PROGRESSIVE TUMOR PATIENTS

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Aims: To evaluate survival outcomes in oligometastatic/oligoprogressive patients treated with stereotactic body radiation therapy (SBRT) for adrenal metastases.

Methods: We retrospectively analyzed 25 metastatic adrenal lesions in 24 oligometastatic/oligoprogressive patients treated with ablative SBRT between February 2010 and November 2019 at our institution. SBRT was delivered by volumetric-modulated arc therapy (V-MAT). All patients underwent image-guided radiotherapy (IGRT) using cone-beam computed tomography (CBCT) system as daily pre-treatment imaging. The following follow-up was performed with a CT scan with contrast medium or FDG/PET-CT every three months for the first two years after SBRT and every six months afterwards The primary endpoint was overall survival (OS). Secondary endpoints were local overall response rate (ORR), acute and late toxicities.

Results: Median age was 73 years (range, 45– 91 years). Most common primary tumor was non-small cell lung cancer (54%). Twenty-one patients received chemo or immuno-therapy. The median planning target volume (PTV) was 41.7 cm3. Median SBRT dose was 36 Gy. Median dose per fraction was 15 Gy. The median survival was 35 months and the actuarial 6-months, 1-year and 2-year OS was 100%, 87.5% and 66.7% respectively. Clinical response after SBRT evaluated using RECIST criteria revealed local overall response rate (ORR) of 66.5% (CR=50%, PR=12.5%), stable disease in 6 patients (25%) patients and progressive disease in 3 patients (12.5%). Patients with metachronous adrenal metastases (*i.e.,* diagnosed within six months from original diagnosis) had better outcomes regarding overall survival compared with the whole cohort including patients with synchronous and adrenal metastases. The 1-year and 2-year OS for metachronous group 94% and 70% compared to 71% and 57% for those with synchronous metastases (CI 95%: 45.15-100.20 p=0.76). 12 patients experienced acute toxicities, mostly grade 1-2 (8 patients, 32%).

Conclusions: SBRT for oligometastatic/oligoprogressive patients with adrenal metastases showed acceptable survival outcomes and a safe toxicity profile. Although adrenal metastases resection remains the standard of care in this setting of patients, SBRT may represent a feasible alternative, especially for patients are not candidates for surgical resection.

PO228

A POST HOC ANALYSIS FROM A PHASE I CLINICAL TRIAL ON STEREOBODY RADIOSURGERY IN ISOLATED BONE LESIONS IN OLIGO-PROGRESSIVE PROSTATE CANCER PATIENTS

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Purpose: To evaluate the rate of biochemical responses and the time to next systemic therapy (NEST), in oligoprogressive prostate cancer (PC) patients treated with stereobody radiosurgery (SRS) for bone metastases.

All lesions	50	
	Median	*(Range)*
Age, years	73.5	(57.0 – 90.0)
Weight, Kg	75.0	(55.0 – 108.0
BMI	26.3	(21.1 – 39.7)
	n°	*(%)*
Eastern Cooperative Oncology Group performance status		
0	44	(88.0)
1	4	(8.0)
2	2	(4.0)
3	0	(0)
4	0	(0)
Comorbidities[a]		
Hypertension	17	(63.0)
Second Tumor	3	(11.1)
Diabetes	2	(7.4)
Renal failure	1	(3.7)
Chronic pulmonary disease	1	(3.7)
Other	3	(11.1)

[a] calculated on the number of comorbidities (N=33)

Figure 1.

Material/Methods: DESTROY-2 was a prospective SRS trial delivered by volumetric arc therapy (VMAT) technique in patients with primary or metastatic tumours in various extra-cranial body sites. We retrospectively selected the clinical data of PC patients enrolled in DESTROY-2 and treated with SRS-VMAT on oligometastatic/oligorecurrent bone metastases. Four-months after treatment we evaluated the biochemical response: a reduction of PSA value > 10% (complete if > 50%) with respect to pre-SBRT PSA value was considered a response; stable disease was defined as a PSA < 10% of the pre-SBRT value, while a PSA increase > 10% was classified as biochemical progression. Moreover the ITT (hormonal or chemotherapy) start/change were analysed.

Results: Data on 37 PC patients harbouring 50 bone metastases treated with SRS-VMAT at our institution between the 2010 and 2020 were collected. The clinical characteristics of patients are reported in the Table 1. The median dose delivered by SRS was 24 Gy (range 12-24Gy), with a median BED α/β10 of 81.6 Gy (range 26.4-81.6). The most frequently adopted schedule for SRS-VMAT was 24 Gy x1 fraction (60.0%), In terms of biochemical response, the median PSA before the SRS-VMAT treatment was 1.83 ng/ml (0.02-85 ng/ml), while the median PSA at the first evaluation after treatment (4 months) was 1.33 ng/ml (0.001-129.2ng/ml). In particular, we recorded 20 (40.0%) complete, and 7 (14.0%) partial biochemical responses, 5 (10.0%) stable PSA values and 17 (34.0%) biochemical progressions; the PSA dosage was not available in one case (2.0%). The actuarial ITT at 1, 3 and 5 years were 74.0%, 45.0% and 30.0% respectively.

Conclusion: SRS can be considered an efficacious treatment in patients harbouring isolated PC bone metastases, especially in order to slow down the start or change of a new systemic therapy.

PO229

TRIMODAL APPROACH FOR DIAGNOSIS AND RE-IRRADIATION OF LOCAL RECURRENT PROSTATE CANCER

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Aims: Computed Tomography (CT) is the imaging used for target volumes and organs at risk delineation for radiotherapy (RT) treatment planning. Biparametric Magnetic Resonance Imaging (bMRI) with specific sequences (*i.e.*, T2-weighted imaging - T2WI and diffusion-weighted imaging - DWI), is used in pts with recurrence from prostate cancer (PCa). Positron emission tomography (PET) with specific tracers (*e.g.*, choline or PSMA) provides excellent functional but poorly defined images. We report our experience on the use of a trimodal approach (*i.e.*, CT, bMRI and choline- PET/CT) for diagnosis and re-irradiation of pts with local recurrent PCa after prior RT.

Methods: From May 2018 to February 2021, 17 pts with recurrent PCa were re-irradiated. Diagnosis of recurrence was done using choline -PET/CT and bMRI. bMRI criteria for a recurrent tumor was as a focal area with:1) low signal intensity on T2WI; 2) restricting diffusion on apparent diffusion coefficient maps and high signal intensity at a b value 1400 s/mm^2 on DWI. PET/CT scan was

obtained with a hybrid PET/CT and all pts received an iv injection of 3.3 MBq/kg of fluoro-choline. Before re-RT all pts underwent CT-based stereotactic body planning with a 2 mm slice thickness in supine position. The gross tumor volume (GTV) was identified with a co-registration with choline-uptake and DWI. The clinical target volume (CTV) was considered as prostate gland delineated using T2WI. We adopted a rigid fusion between CT and T2WI and the planning target volume was generated from the CTV plus a 6 mm isotropic and 4 mm posterior margin, respectively. All pts were submitted to a stereotactic VMAT-IGRT technique and received a total dose of 30 Gy in 5 daily fractions.

Results: After a median follow-up of 9.5 months, 14 of 17 pts accrued were evaluable for toxicity. A complete concordance on the identification of the GTV using DWI and PET/CT images was observed in all cases. The acquired T2WI and the fusion with CT planning images permitted to well delineate the CTV and to reduce the PTV dimensions. Treatment was well tolerated and we not observed acute (CTCAE v. 4.03) g. ≤2 neither genitourinary nor gastrointestinal toxicities.

Conclusions: Trimodal approach appears to be an appropriate technique not only for diagnosis but also for treatment planning of recurrent PCa re-irradiation. It provides anatomical and functional information of high spatial resolution and allows to improve the definition of target volumes in RT.

PO230

LIVER OLIGOMETASTASES TREATED BY STEREOTACTIC BODY RADIATION THERAPY: A RETROSPECTIVE SINGLE CENTER ANALYSIS

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Aims: Liver is one of the most common site for metastatic spread. Approximately 30–40% of all patients with solid tumors develop liver metastases during the natural course of the disease. Surgical resection represents the standard of care with a 5-year survival rate of up to 30−60% when unique syn- or meta-chronous site of tumor disease. However, only 10–20% of these patients are amenable to resection due to comorbidities, unfavorable liver involvement, uncontrolled primary tumor or extrahepatic progression. Different techniques of minimally invasive therapies for liver metastases have been used in patients ineligible for surgery, including radiofrequency ablation (RFA), microwave ablation, transarterial chemo embolization (TACE) and cryotherapy. The role of stereotactic body radiation therapy (SBRT) in the management of liver metastases is increasing, using ablative doses with the goal of local control (LC) and survival improvement. The aim of this study is to evaluate our preliminary results regarding LC, progression free survival (PFS), overall survival (OS) and toxicities in patients with liver metastases treated with this technique.

Methods: We conducted a retrospective analysis of 19 patients with a total of 27 lesions treated with Varian TrueBeam Novalis STx linear accelerator using a 10 MV Flattening Filter Free beam at our Institute from April 2017 to April 2020. Tumor response was evalueted according to RECIST and/or PERCIST criteria. LC, PFS and OS were estimated using the Kaplan-Meier method. Median follow-up period was 8 months (range, 1-25 months).

Results: Median age at the time of SBRT was 70 years (range, 51-82 years), 9 patients were male and 10 female. Three patients only had multiple lesions. The median tumour volume pre-SBRT was 19.51 cm3 (range, 5.32-149.95 cm^3). The mean prescription dose was 48 Gy (range, 36-60 Gy) in 3-5 fractions. Two patients (10.5%) developed a local recurrence, 8 (42.1%) showed stable disease, 5 (26.3%) partial response and 4 (21.1%) complete response. Median OS following SBRT was 10 months (range 1–27 months). The 1-, and 2-years actuarial survival rates following SBRT were 62 and 39% respectively. The 1- and 2-years actuarial PFS rates were 47 and 23% respectively. No acute or late grade 3 or 4 toxicity was observed.

Conclusions: Our data suggest that SBRT is a safe and effective treatment option for patients with liver metastases. Further randomized trials are required to compare with other local therapies.

PO231

HIGH-DOSE SALVAGE ROBOTIC SBRT FOR PROSTATE/PROSTATE-BED RELAPSE AFTER PREVIOUS RT

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Objective: To evaluate short term outcomes of salvage robotic re-irradiation of patients with intraprostatic/prostatic bed recurrences of prostate cancer.

Material and Methods: Between November 2018 and August 2020, 12 patients (pts) were treated with a salvage robotic SBRT re-irradiation. All patients were staged with choline / PSMA PET-CT and / or MRI (n=10) and / or biopsy (n=2) proving intraprostatic / or prostate bed recurrence of prostate cancer after radiotherapy (RT). Eight pts were previously treated with radical RT and four

pts with adjuvant/salvage RT between 2006 and 2017. Median previous RT dose was 73.4 (50.4-78) Gy and the median interval to SBRT salvage therapy was 90 (45-181) months. Median PSA before robotic SBRT was 2.665 (1.14-17) ng/ml. Fiducial markers were implanted into the target in 11 of 12 patients. Median SBRT total dose was 35 (30-40) Gy in 5 fractions (EQD2=85 Gy, for α/β 1.5). Median prescription isodose was 70% (59-81%). In five patients, a "urethral sparing technique" was used prescribing to the median isodose of 70% (59-81%), to escalate the dose inside the target up to and EQD2 of 160 Gy. In 7 cases a precautionary therapy with steroids and alpha-lytics was used during the salvage treatment. Five patients received neoadjuvant or concomitant/adjuvant androgen suppressive therapy during their SBRT course. Toxicity was scored in accordance with CTCAE v 5.0.

Results: Median follow-up was 15 months (3-26). Acute genitourinary (GU) toxicity (minimal stranguria, urgency and occasional urinary incontinence) was observed in 5 of 12 pts and was limited to grade 1(n=4) and 2 (n=1). Two pts reported early late GU grade 3 toxicity (urinary retention requiring catheterization and subsequent transurethral resection). No acute and early late gastrointestinal toxicity were observed. At the last follow up 1 pt died due to a non cancer-related cause, 2 pts had biochemical failure (one with radiologic progression) and 10 pts had local control with a median post-salvage PSA level of 0.35 (<0.006-37.9) ng/ml.

Conclusions: Prostate robotic SBRT high dose re-irradiation is feasible with acceptable short term and early late toxicity. Longer follow-up is necessary to assess late toxicity and long-term biochemical control.

PO232

BIOCHEMICAL FAILURE (BF) WITH METASTASIS DIRECTED THERAPY (MDT) IN METACHRONOUS OLIGORECURRENT PROSTATE CANCER (MOR-PC): A MONOCENTRIC RETROSPECTIVE ANALYSIS

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Aims: MOR-PC is an increasingly common disease state. Investigations about outcomes and factors that influence survival in these patients are still ongoing. We aimed to provided prognostic factors for BF post-MDT in patients with MORPC previously treated with radical prostatectomy.

Methods: In this monocentric analysis we retrospectively collected data of patients who underwent radical prostatectomy for PC (± salvage RT) and with MOR-PC treated with MDT detected by 68Ga-PSMA or Choline PET/CT. We analyzed any treatment and clinical features potentially correlated with BF and BFFS (Biochemical Failure Free Survival) by the end of MDT. Main inclusion criteria were: 1) a maximum of 5 metastases, 2) time to metastases of ≥6 months from surgery and 3) MDT administered with radical intent. Logistic regression and Kaplan-Meier method were utilized to determine variables associated with BF and BFFS.

Results: Between 2016 and 2021, thirty-eight (41%) bone mets and fifty-five (59%) node mets were treated in fifty-three patients, with a median of two site of oligorecurrence for each patient. Median follow-up was 20 months (range 2-63). Median age was 63 years (range 47-74), median treatment EQD2 (alfa/beta 1.5 Gy) was 85 Gy (range 47.6-138.9). At initial diagnosis all patients were classified as at high risk group (75%) and intermediate risk group (25%), respectively. After radical prostatectomy, positive margins and N1 stage were found in 26% and 38% of the patients, respectively. Twenty-two patients (41%) received ART (Adjuvant Radiotherapy) due to high risk features or R1 and twenty-seven (51%) patients receveid SRT (Salvage Radiotherapy). Concomitant ADT was administered in thirty-one (58%) patients and eighteen (34%) patients had CRPC at the time of first MDT. Metastases detection was obtained by either 68Ga-PSMA (40%) or Choline (60%) PET/CT. Median time to BF was 7 months and 1-2y BFFS were 51% and 40%, respectively. At statistical analysis, MTD with EQD2 ≥ 78 Gy (BED 182 Gy, alfa/beta 1.5 Gy) was associated with a lower risk of BF (OR: 3.70; p=0.036). No correlation was found between BFFS and any analyzed variables.

Conclusions: MTD with EQD2 ≥ 78 Gy (BED 182 Gy, alfa/beta 1.5 Gy) in patients with MOR-PC is associated with lower risk of BF, although without a BFFS benefit. This study highlights the need to deliver a radical dose to each site of metastasis, both nodal and bone. Prospective data are needed to confirm these findings.

PO233

HYPOFRACTIONATED RADIOTHERAPY FOR BREAST CANCER ORBITAL LESION: A RETROSPECTIVE MONOCENTRIC EXPERIENCE

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Aims: Orbital metastases in breast cancer (OM-BC) patients are a rare occurrence, usually symptomatic, with a huge impact on quality of life. Local control (LC) might be difficult to obtain due to the proximity of critical structures. Hypofractionated radiotherapy (HFRT) could constitute a viable treatment option for OM-BC. Here a monocentric retrospective experience about patients with OM-BC treated with HFRT is presented.

Materials: Clinical data records of 10 patients consecutively treated for OM-BC with Cyberknife^{R} (CK) system were collected. LC, objective response rate (ORR), symptoms control, treatment-related toxicity according to CTCAE v5.0 and survival outcomes (PFS-OM and OS) were analyzed. Dosimetric data are reported as well.

Table 1.

Patient characteristics		
Age at BC diagnosis (mean)		51.5 years [41 - 66]
ECOG PS at BC diagnosis (median)		0
Histological subtype BC		
	Invasive ductal carcinoma	4 (40%)
	Invasive lobular carcinoma	6 (60%)
Molecular subtype BC		
	Luminal A	1 (10%)
	Luminal B	9 (90%)
Metastatic BC ab initio		
	Yes	1 (10%)
	Not	9 (90%)
Burden of metastatic BC		
	1-4 lesions	2 (20%)
	≥5 lesions	8 (80%)
Age at OM-BC diagnosis (mean)		60.0 years [44 - 76]
ECOG PS at OM-BC diagnosis (median)		
	0	5 (50%)
	1	5 (50%)
Eye OM-BC		
	Right	6 (60%)
	Left	4 (40%)
Anatomical involvement OM-BC		
	Ocular involvement	0
	Extraocular involvement	10 (100%)
	Ocular-extraocular involvement	0
Burden of OM-BC		
	1-2 sites	5 (50%)
	≥3 sites	5 (50%)
Previous surgery		
	Not executed	0
Previous radiotherapy		
	Not executed	0
Status		
	Live with metastatic disease	3 (30%)
	Died of extra OM-BC disease	7 (70%)
Patients		
	Total	10 (100%)

Table 1: baseline features of study population

Results: From July 2013 to January 2020 10 treatments were performed. Patients' baseline characteristics are summarized in Table 1. The prescribed dose was 2500.0 cGy in 5 fractions with a median maximum dose of 3125.0 cGy (95% CI 3112.9 - 3179.3) at a median isodose line (IDL) of 80% (95% CI 78.6 - 80.3). At mean follow-up of 12.7 months (range 1-30) the overall response rate was 50.0%, with 4 and 1 patients presenting a partial and complete response, respectively. The mean time to best-measured response was 6.8 months (range 1-15). Three patients were still alive at the time of analysis, with a local control rate of 100%. We did not report local progression after HFRT treatment. Fifty percent of patients had symptomatic OM-BC at diagnosis: 1, 1 and 3 patients had amaurosis, ptosis with lagophthalmos and diplopia, respectively. Ocular motility at OM-BC diagnosis was compromised in 9 patients. Overall, 1 patient reported improvement of symptoms after treatment. Ten percent of patients presented acute toxicity (<3 months) after HFRT (xerophthalmia G1). Mean PFS was 12.7 months (range 1-30) and mean OS was 739.7 months (range 557-924). In our series, the mean planned target volume (PTV) dose coverage was 96.4% (range 92.9 - 99.0). The mean eye globe maximum dose (EG-Dmax) was 1952.9 cGy (range 467.0 - 2500.0). The mean optic nerve, optic chiasm and lens maximum dose (ON-Dmax, OC-Dmax, L-Dmax) were 2297.0 cGy (945.0 - 2500.0), 1183.4 cGy (226.0 - 2382.0) and 262.1 cGy (48.0 - 702.0), respectively.

Conclusions: HFRT for OM-BC is a feasible and tolerable approach with a significant impact on oncological and quality of life outcomes.

PO234

ABSTRACT WITHDRAWN

PO235

STEREOTACTIC RADIOTHERAPY (SRT) FOR THYROID CANCER METASTASES: AN AIRO (ITALIAN ASSOCIATION OF RADIOTHERAPY AND CLINICAL ONCOLOGY) SYSTEMATIC REVIEW

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Purpose: The aim of this systematic review was to examine efficacy of stereotactic radiotherapy (SRT) in patients with oligometastatic thyroid cancer.

Materials and Methods: A systematic search was conducted by means of PubMed, Scopus, and Cochrane library. ClinicalTrials.gov was searched for ongoing or recently completed trials, and PROSPERO was searched for ongoing or recently completed systematic reviews. We analyzed only clinical studies as full text carried out on patients with oligometastatic thyroid cancer treated with SRT. Conference papers, surveys, letters, editorials,

book chapters, and reviews were excluded. Time of publication was restricted to the years 1990-2018.

Results: The number of evaluated patients was 85 (168 lesions) and the median age was 69 years. The median 1-year local control (LC) was 92% (range 67.0%-97.1%); the median disease-free survival (DFS) was 14.6 months (range 4-53); the median 1-year overall survival was 72% (range 66.6%-85.0%); the 3-year cancer specific survival was 75.0% and the 4-year cancer specific survival was 37.5%. One study found that the single strongest factor associated with LC was prior radiotherapy (β-coefficient -27.72, p=0.01). No grade 3-5 acute toxicity was reported. No late effects were recorded.

Conclusions: SRT for metastases from thyroid cancer as salvage therapy is well tolerated and yields high rates of LC and prolonged DFS.

PO236

OLIGOMETASTATIC BREAST CANCER DISEASE AND STEREOTACTIVE RADIOTHERAPY: THE NATIONAL CANCER INSTITUTE OF MILAN EXPERIENCE

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Aims: To evaluate the impact of stereotactic radiotherapy in breast cancer patients (pts) with oligometastatic disease

Methods: We retrospectively collected pts with oligometastatic breast cancer with ≤5 metastatic sites and/or maximum 2 systems involved. Inclusive criteria were: FDG-PET/CT or MRI staging, no brain metastases, primary tumor controlled. Radiotherapy (RT) was delivered using volumetric modulated arc therapy (VMAT). Various dose-fractionation schedules were used depending on metastasis sites. Objective response rate (ORR), disease control rate (DCR), progression free survival (PFS) and the overall survival (OS) were calculated from the end of RT to the last follow up.

Results: 15 patients with 19 metastatic lesions were enrolled. Median age was 62 years (range 39-81 y). Thirteen pts (86%) received a form of systemic therapy concomitantly to RT. Sites of metastatic disease were the following: bones 5 lesions, lymph nodes 10 lesions, lung 2 lesions and parasternal 2 lesions. All lesions were treated with VMAT. Depending on site of metastasis was delivered a dose between 21-50 Gy in 3-7 fractions. RT was well tolerated, and no Grade ≥3 toxicity was documented. After a median follow-up of 15 months (range, 3-73 months) 13 pts are alive with stable disease with the same systemic therapy. 2 pts died for progression of disease. ORR and the DCR were 66,67% and 86,67% of pts, respectively. The median PFS was 47.9 months (Figure 1) while the median OS was 68.9 months.

Conclusions: Stereotactic RT in pts with oligometastatic breast cancer was safe and well tolerated. Pts had obtained a significant benefit in terms of local control without necessity of switch of systemic therapy. The limit of this study is the dimension of sample but the good results encourage further studies on oligometastatic pts.

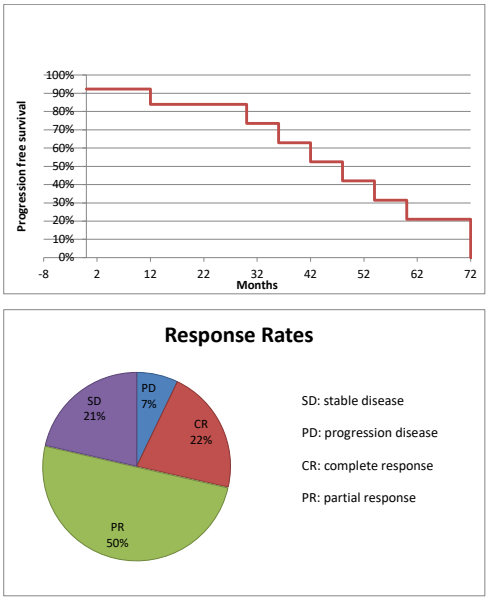

Figure 1.

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THE STEREOTACTIC APPROACH IN THE RADIOTHERAPY TREATMENT OF OLIGOPROGRESSIVE CANCER OF THE IODINE-REFRACTORY THYROID AS A STRATEGY FOR DELAYING THE NEED FOR SYSTEMIC TREATMENT

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Aims: Differentiated thyroid carcinoma (DTC) is generally associated with high cure rates and good long-term prognosis. Many cases however show a metastatic Radioactive Iodine (RAI)-refractory disease, possibly requiring the use of Tyrosine-Kinase Inhibitor (TKI). In case of oligometastatic disease (OMD), a locoregional ablative approach could effectively control tumor progression, and possibly defer the need of systemic therapies. In this setting stereotactic body radiotherapy (SBRT) has shown great results in other types of cancer Our aim was to verify the efficacy of SBRT in OMD RAI-refractory DTC patients.

Methods: We retrospectively analyzed patients with oligometastatic DTC treated with SBRT from April 2011 to May 2019. Patients with anaplastic histology or incomplete follow-up (FU) informations were excluded. For each patient we collected clinical and treatment-related features, including adverse-events (AE). We calculated rates of local control (LC) and progression free survival (PFS).

Results: A total number of 15 patients were eligible for a total of 42 lesions treated by SBRT. All patients underwent total thyroidectomy and at least one RAI treatment. The mean age at the time of the first SBRT was 63.3 years, the median FU after SBRT was 47,7 months (range 14,4–105). 19 lesions were located in bone (45%) and 11 in lymph nodes (26%). The treatment was delivered with single or multifractional schedules (1-8 fractions), with a median dose of 30 Gy (range 24-60 Gy). After SBRT we observed complete response for 21 lesions (50%), partial response for 13 lesions (31%), stable disease for 7 lesions (16,7%), and disease progression in one case (2,4%), with a median Thyroglobulin reduction of 63.5% (range 1.3% to 97.7%). No patients experienced AE of grade 3. PFS at 6 months, 1- and 2-years was 79%, 46% and 33%, respectively. At univariate analysis only a Biological Equivalent Dose>50Gy was related to an improved LC (p=0,05), while male sex was associated to a higher risk of relapse (p =0,0263). After SBRT 10 patients (66,7%) underwent TKI treatment for progressive disease: median time to TKI treatment from the SBRT for these 10 patients was 17,7 months (range 1-47,7 months). 5 patients (33.3%) were still without systemic therapy after a median FU of 50,6 months (range 35.3-57).

Conclusions: In our experience, SBRT represents a safe and effective approach, yielding satisfying local control in OMD refractory iodine thyroid cancer patients.

PO238

STEREOTACTIC BODY IMAGE-GUIDED VOLUMETRIC MODULATED ARC THERAPY (IG-VMAT) FOR OLIGOMETASTATIC/OLIGOPROGRESSIVE MEDIASTINAL AND HILAR LYMPHADENOPATHY: PRELIMINARY CLINICAL EVIDENCE

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*Aim: U*ultra-hypofractionated radiation therapy to metastatic hilar and mediastinal lymphadenopathy is a challenge for the radiotherapist due to the potential toxicity of centrally located organs-at-risk. A limited body of clinical evidence exists on the toxicity and efficacy of stereotactic body radiation therapy (SBRT) for hilar and mediastinal lymphadenopathy. Here we provide preliminary clinical findings concerning the toxicity and the oncological outcome.

Methods: Oligometastatic (<5 total metastases) and/or oligoprogressive (<5 progressive metastases in the context of otherwise stable metastatic disease) patients were included in this retrospective analysis. The rate of acute and late toxicity was the primary clinical endpoint as defined to the RTOG toxicity scale. The rate of local control, progression-free survival (PFS) and overall survival (OS) were the other study endpoint. All plans were optimized for dose coverage of the target volumes using Image-Guided Volumetric Modulated Arc Therapy (IG-VMAT). The prescribed dose of 40 Gy was delivered in 8 consecutive fractions. Contoured OARs included Lungs, esophagus, bronchi and trachea, spine, great vessels, heart and pericardium. The GTV was defined using the peak inspiratory and expiratory phases image sets. CTV expansions were not used and GTV contours were combined to form an internal target volume (ITV). An isotropic expansion of 5 mm was applied to create the final PTV. VMAT plans were optimized to have a point D0,1cc < 105% to 107%.

Results: Seventeen patients (62 metastases) with primary tumors of lung (5 cases), breast (4 cases), kidney (4 cases), thyroid (1 cases) and head and neck (3 cases) were retrospectively studied. The majority of subjects (10 cases) received SBRT to more than 2 lymphadenopathies. BED3Gy and BED10Gy was 106,67 Gy and 60Gy respectively. The majority of patients (82,3%; 14/17 patients) reported no toxicity. The only reported toxicity was esophageal G1 acute toxicity in 3 patients. One patient also experienced late G1 toxicity consisting of mild dysphagia 18 months after treatment. The in-filed

LC rate at one year was 94,1%. The one year PFS and OS rate was 70,5% and 85,7%, respectively.

Conclusions: SBRT for metastatic hilar and mediastinal lymphadenopathy is an effective low toxic treatment for oligometastatic/oligoprogressive diesease. Further studies should identify subjects who benefit most from SBRT, as well as the correct timing and dosage of SBRT in the integrated treatment strategies.

PO239

RE-IRRADIATION IN RECURRENT GLIOBLASTOMA: OUTCOMES AND TOXICITY

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Aims: The aim of this paper was evaluate the efficacy of re-irradiation in patients with recurrent glioblastoma and to assess outcomes: Progression Free Survival (PFS), Overall Survival (OS) and toxicity.

Methods: Between January 2018 and December 2020, 8 patients received re-irradiation for recurrent glioblastoma (GBM) at the Department of Radiation Oncology in our institution. All had initially received adjuvant radiation treatment with doses of 60 Gy, concomitant and adjuvant Temozolamide according to the Stupp protocol. Re-irradiation was offered to patients with recurrent GBM, good Performance Status and at least 6 months after initial RT. The total doses were 35 Gy in 10 fractions or 36 Gy in 18 fractions, according to volume, site of recurrence and dose to organs at risk. The technique was VMAT with daily-Conebeam-CT. Baseline evaluations included gadolinium-enhanced brain MRI, physical examination, and neurologic assesment before re-irradiation. Treatment outcomes and toxicities according to CTCAE version 4 were evaluated at each follow-up visit, by brain MRI and neurological status after re-irradiation. To compensate for varying dose-fractionation schedules, radiation doses were expressed as biological equivalent dose (BED) values (α/β= 2 Gy for normal brain tissue).

Results: The median time interval between initial RT and re-irradiation was 13 months (range 7–41 months). Median cumulative doses was 96 Gy (range, 95-96 Gy) for the two irradiations and 192 Gy (range, 192-216 Gy) for median cumulative BED (α/β=2 Gy). Salvage surgery at recurrence before re-irradiation was performed in 3 patients. Concurrent or sequential chemotherapy with Temozolamide was administered to 4 patients. Median follow-up for surviving patients was 14.5 months (range 6–19 months), with 5 patients died of the disease at 8–19 months after re-irradiation, 2 alive with disease at 6 months after re-irradiation and 1 alive without disease at 7 months after re-irradiation. Median OS was 15 months (95% CI, range 14-NA months) and median PFS was 10 months (95% CI, range 6-NA months). We reported no severe acute or late toxicities. The most common side effect was grade 1-2 headaches in 50% of patients.

Conclusions: Despite a few number of patients, our study showed that re-irradiation of recurrent GBM was a feasible and safe treatment in selected patients. Radiotherapy with surgery and/or chemotherapy or new drugs could be a salvage treatment for recurrent GBM.

PO240

REIRRADIATION OF RECURRENT MENINGIOMA: ANALYSIS OF CLINICAL OUTCOMES AND TOXICITIES IN A RETROSPECTIVE MONOISTITUTIONAL STUDY

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Aims: Meningiomas are the most common non-malignant tumors of the brain, representing up to 30% of primary brain tumors. The majority of meningioma patients enjoy high rates of control after conventional therapies: complete surgical excision remains the standard treatment. Radiation therapy is currently uses in atypical, malignant or recurrent meningioma. The aim of this study was to define the outcome of patients with recurrent meningiomas who underwent a second course of radiation therapy.

Methods: We retrospectively identified 11 patients with recurrent meningiomas treated with radiation therapy between 2007 and 2018. All patients received prior radiation therapy (RT) to a median dose of 54.9 Gy (range 59.4-18). Median time to retreatment after prior RT was 44 months (range 92-4). Tumor volumes ranged from 1.4 cm3 to 273.8 cm3. The majority of patients was treated with a radiation dose of 25 Gy in five fractions (range 16-50).

Results: The median follow-up was 26 months (range 4-54). The overall survival and the progression-free survival rates for 5 years were 36.3%, and 44.4% respectively. In 91% the symptoms had were stable. Clinically significant acute toxicity (grade II) was seen in only 1 case (9%). Only one patient developed late toxicity: radionecrosis. No other neurological deficits occurred during follow-up. At last follow up 36% of patients were alive.

Conclusion: Re-irradiation was well tolerated in patients with recurrent meningiomas and appeared effective.

PO241

RE-TREATMENT SALVAGE FOR LOCAL RECURRENCE OF PROSTATIC CARCINOMA AFTER PRIOR IRRADIATION: A SINGLE CENTER CLINICAL EXPERIENCE

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Aims: We evaluated the efficacy and safety of stereotactic body radiation therapy (SBRT) retreatment for patients (pts) with biochemical failure and evidence of local recurrence in prostate cancer (PC) after an initial treatment course of radiotherapy (RT).

Methods: From May 2019 to April 2021, 12 pts with evidence of clinical/radiological local relapse in the prostate or prostatic bed and no distant metastasis,were retreated with a SBRT. Local relapses were assessed with pelvic multiparametric MRI or PSMA/choline PET in 42% and in 58% of pts, respectively. The precedent radiotherapy was delivered in 9 pts as adjuvant / salvage RT and in 3 pts as radical treatment RT. At recurrence, median prostate-specific antigen (PSA) was 1.2 ng/mL (range, 0.16-1.8) in the 9 patients treated with postoperative RT and 3.5 ng/ml (range, 2.3-5.4) in patients treated radically. An androgen deprivation therapy was administered in 7 pts at the time of SBRT. The median time interval between the 2 treatments was 5 years (range 1-8). The median SBRT dose was 36 Gy (range, 25-36) in 5 consecutive fractions (range 5-6). Salvage SBRT was delivered using volumetric arc therapy (VMAT) and image-guided radiotherapy (IGRT) (Elekta Versa HD™).

Results: After a mean follow-up of 11.2 months (range, 1-22 mo) no patients had gastrointestinal and genitourinary toxicity early and/or late ≥ G3. Median age at salvage SBRT was 78 years (range, 71-86), median post-salvage SBRT PSA was 0.1 ng/mL (range, 0.0-1.1) in the adjuvant/salvage RT group and 2.75 ng ml (range, 1.8-4.2) in the radical treatment RT group. Five pts had a clinical relapse: 3 lymph nodes and 2 bone metastases, all outside the radiotherapy target. These patients underwent a second course of SBRT and actually there is no radiological evidence of disease.

Conclusions: Despite the small sample examined, our experience shows that salvage SBRT is an effective and safe treatment option, allowing a good control of disease without excessive toxicity.

PO242

MRI-GUIDED STEREOTACTIC RADIOTHERAPY IN THE RE-TREATMENT OF PROSTATE CANCER: PRELIMINARY EXPERIENCE FROM A SINGLE CENTER

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Aims: Early diagnosis and advancement of treatment strategies have played an important role in the management of prostate cancer (PC), but relapse rates still remain substantial and the treatment approach in these cases is not standardized. Efficacy and safety of PC re-irradiation have recently been investigated and the biggest concern still remains the potential toxicity to the adjacent organs at risk (OARs). The adoption of stereotactic body radiation therapy (SBRT) allows the delivery of an effective Biological Equivalent Dose (BED) while sparing of surrounding OARs. Magnetic resonance guided radiation therapy (MRgRT) has shown promising results in delivering SBRT effectively and safely. We report our case series of patients underwent re-irradiation with MRgRT technique.

Methods: In this retrospective analysis, we evaluated patients affected by relapsed PC treated at our Institution from June 2019 to February 2020. MRgRT was delivered with a total dose ranging from 25 to 30 Gy in 5 fractions every other day. Patients were instructed to use an evacuation enema 2 hours before each treatment and to drink 500ml of water 30 minutes before the procedure. In selected cases, the OAR spacer use was evaluated. Planning was carried out with step-and-shoot intensity modulated radiation therapy (IMRT) with urethral sparing approach (Figure 1). Intrafraction motion was managed using the prostate as a tracking structure with an isotropic boundary margin of 3 mm. Toxicity and treatment response were assessed at follow-up. Acute and late toxicities were registered and scored according to the CTCAE scale version 5.0. Response to treatment was assessed in terms of biochemical, local and distant control.

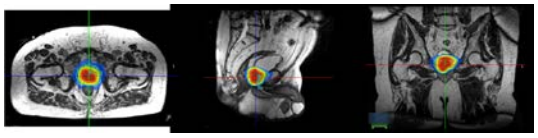

Figure 1.

Results: Six patients affected by relapsed PC who had previously received a dose of external beams radiation therapy (EBRT) between 66 and 73.8 Gy were observed. The median BED was 138,3 Gy (108,3- 150) considering an α/β of 1.5. The OAR spacer was positioned in 2 (33.3%) patients. At a median follow-up of 11.4 months (range 4,3-15,8), all patients were alive and only one patient (16,7%) experienced distant failure, otherwise no biochemical or instrumental recurrences occurred. Only two patients (33.3%) experienced acute genito-urinary G1 toxicity.

Conclusion: The MRgRT technique could represent a valid therapeutic approach to relapsed PC, by ensuring the precise delivery of the prescribed dose and a good saving of OARs thanks to an accurate visualization and tracking of the target during the entire treatment session.

PO243

VMAT INTRACRANIAL STEREOTACTIC RADIOSURGERY: COMPARISON OF A MICRO-MULTILEAF COLLIMATOR WITH A 5 AND 10 MM-LEAF-WIDTH COLLIMATOR

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Aims: To compare the results of VMAT Radiosurgery (SRS) planning using radiotherapy equipment (Elekta Platform and Elekta Synergy equipped with a 160-Agility MLC) versus an add-on micro MLC (Apex).

Methods: A new Italian SRS service was implemented at the Radiotherapy Unit of Arezzo-Valdarno. To investigate the difference achieved with 10 mm *vs* 5 and *vs.* 2.5 mm MLC, six SRS plans (with six targets of brain metastases) were outlined, calculated and compared. Radiotherapy plans for VMAT SRS were calculated using a Monte-Carlo algorithm with the Monaco v5.11.03 treatment planning system for our Elekta PLATFORM linac with 10 mm MLC, for the same Elekta PLATFORM linac equipped with Apex and for our Elekta Synergy equipped with Agility (5 mm leaves width at isocenter). The selected energy was 6MV for PLATFORM linac and both 6MV FF and FFF for the Agility-Linac. A standard technique was adopted with the isocenter placed in the center of lesions, with one full arc. All plans were single isocenter and irradiated 1 target per plan. The VMAT plans obtained were compared according the following dosimetric parameters: coverage ratio (VPTV100%/PTVvol), selectivity index (VPTV100%/VBody100%), Paddick conformity index (PCI=(VPTV100%) 2/(PTVvol VBody100%)), Gradient index (GI=VBody50%/VBody100%), R100% conformity index (VBody100%/PTVVol), R50% conformity index (VBody50%/PTVVol), Monitor units (MU), Total V12 Gy (brain exclusive GTVs) and mean brain dose, mean doses for brain stem, optic chiasm, lens and optic nerves. Student's t-test was performed on the paired plan parameters.

Results: No statistically significant difference in the quality indices and doses to organs at risk (OARs) between the Elekta Agility (FF and FFF), the Elekta Platform and Apex plans were observed. Ten and 5 mm MLC plans required less MUs on average, with reduced delivery time, than the 2.5 mm MLC plans.

Conclusions: Clinically adequate plans for VMAT based SRS treatments of brain metastases can be produced with 5 and 10 mm MLC linac, with comparable dose conformity and similar OARs sparing. An add-on micro MLC required prolonged delivery time, and there are concerns also over the practicalities of this device.

PO244

ABSTRACT WITHDRAWN

PO245

A SINGLE CASE OF SIMULTANEOUS VMAT TREATMENT OF BOTH BRAIN AND CHOROIDAL METASTASIS

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Aims: Choroidal metastasis is the most frequent intraocular secondary tumor from breast cancer often associated with limited life expectancy. We describe the case of a 38 years old patient (pt) with a past medical history of advanced breast cancer and bone metastasis who developed diffused brain metastasis and a single right orbital metastasis after a chemo-immunotherapy treatment lasting 7 years.

Methods: In 2013 and at the 29th week of pregnancy, our pt found at self-examination a left breast nodule. She underwent radical left breast mastectomy with axillary lymphnodes dissection. The histopathology revealed a ductal invasive carcinoma, pT2pN1 (1/12) M0, negative for receptors, Ki-67 20% and HER2 positive. Chemotherapy followed surgery, however, after 3 years, our pt developed multiple bone metastases and she started chemoimmunotherapy (CHI). During CHI, she complained of headaches and progressive loss of visual acuity. Fundoscopy of the right eye revealed a choroidal mass. MRI suggested a thickening of the right eye choroid and of the ipsilateral vestibular nerve and the

presence of numerous subcentimetric secondary brain lesions. The pt was candidate to Radiation Therapy and we decided to simultaneously treat both the brain and the choroidal metastasis with a VMAT technique delivering a palliative dose of 30 Gy in 10 fractions. The pt underwent a simulation CT (CTp) of 3mm slice thickness, immobilized with a thermoplastic mask. The CTV of the brain was contoured on the CTp and isotropically expanded of 5 mm (PTV). A CTp/MRI fusion was then performed and the CTV of the choroidal metastasis (CTVc) consisted of the posterior uvea-choroid of the eye, as seen on MRI. CTVc was expanded by 3 mm in all directions (PTVc). The VMAT plan consisted of four single arcs with the isocenter at the center of mass of both targets. The arcs were arranged so that the contralateral eye, lens and optical nerve were spared as much as possible. Daily CBCT was performed in order to check for translations or rotations of the pt positioning before each fraction. Treatment was delivered with a Versa HD linear accelerator.

Results: Regarding the whole brain, D95%, V95%, D2% and D98% of PTV were 95.7%, 96.4%, 103.8% and 93%, respectively, while D95%, V95%, D2% and D98% of PTVc were 96%, 96.4%, 106.7% and 93.3%. Maximum doses to the contralateral lens and optical nerve were 3.8 and 14 Gy, respectively. Three months after treatment the patient reported a partial improvement in visual symptoms and a complete regression of the choroidal mass was noted with both magnetic resonance imaging and fundoscopy.

Conclusions: Radiation therapy with the VMAT technique is an efficient and safe palliative treatment for choroidal and brain metastases secondary to breast cancer allowing good local control, and improved visual acuity.

PO246

TREATMENT OF HYPOFRACTIONATED RADIOTHERAPY, ABIRATERONE AND PREDNISONE IN THE TREATMENT OF BONE METASTASES IN PATIENTS WITH HORMONE REFRACTORY PROSTATE CANCER

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Aims: The hypofractionated radiotherapy plays a fundamental role in the treatment of bone metastases. At our center, we evaluated the feasibility and effectiveness of two schemes hypofractionation: 8 Gy single dose and 8 Gy in two fractions to be made within a week of each other. The two irradiation techniques have been associated with the new molecules used in medical therapy.

Methods: From July 2014 to March 2021 they were treated 75 patients with bone metastases from hormone refractory prostate cancer. The median age of patients studied was 71 years with bone metastasis respectively localized in the dorsal and lumbar spine in 50% of cases, 30% at the level of bilateral lower limbs and the remaining 20% at the level of the pelvis. Radiation therapy was by hand in a single dose in 60% of cases in patients with worse P.S. while in the remaining 40% it was backed bifractionation treatment. All patients were administered simultaneously, the abiraterone acetate 1 g / day, prednisone 10 mg/day in combination with LHRH analogue every three months.

Results: All patients were reassessed after 30-40 days of therapy. In no case were registered signs of toxicity. In 80% of cases there has been a reduction in their analgesic therapy administered dose.

Conclusions: In our experience, the radiotherapy hypofractionated 8 Gy in a single session or, alternatively, 8 Gy in two weekly sessions in conjunction with the abiraterone acetate was well tolerated and had a good impact both as regards the control of the pain is the improvement of quality of life.

PO247

IMPACT OF PALLIATIVE RADIOTHERAPY ON QUALITY OF LIFE OF PATIENTS WITH SYMPTOMATIC BONE METASTASIS. A MONOINSTITUTIONAL EXPERIENCE

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Aims: Bone metastasis (BM) is one of the most common complications of many solid tumors that leads to serious sequelae of pain, fractures, spinal cord compression. Radiotherapy (RT) has an important role in relieving pain caused by BM. Worldwide different RT schedules are being used for BM. Aim of this study is to evaluate the quality of life (QoL) and pain resolution after RT treatment in this setting of patients.

Methods: We performed a retrospective analysis of the Qol of patients treated at our centre for painful uncomplicated BM from October 2020 to February 2021. Patients were treated with three different fractionation schedules (3 Gy x 10, 4 Gy x 5, 8 Gy in single fraction) using the 3DCRT technique. Factors influencing choice of RT fractionation scheme were: age, Performance Status (PS), life expectancy and primitive tumor. Response to treatment at one and three months was assessed by analyzing the pre and post treatment symptomatology according to visual analog pain scale (VAS).

Results: 124 patients (53 women and 71 men) with symptomatic uncomplicated BM were consecutiveley treated at our centre. Median age was 65 (range 37-92). 37% (n=46) had lung cancer, 28% (n= 34) had genitourinary (GU) cancer (kidney, bladder, prostate, penis), 24% (n=30) had breast cancer; 8% (n=10) had gastrointestinal

(GI) cancer (stomach, colon, rectum, anus, liver) and 3% (n=4) had gynecological cancer (cervix, endometrium, ovary). The treated seats were: spine (33%), pelvic bones (25%), ribs (9%), skull (6%), extremity (27%). At one month from the end of RT treatment we observed an improvement of the algic symptomatology in 87% of patients (n=108); in 10% (n=13) of them VAS remained stable and only in 3% (n=3) we recorded an increase of pain. At three months from the end of the treatment, 95% (n=118) of patients had a significant improvement in Qol and only 5% (n= 6) of them still presented the same VAS. Fractionation schedule didn't impact on response to RT. All patients completed the treatment without interruptions.

Conclusions: Our analysis shows that palliative RT is well tolerated by patients with uncomplicated symptomatic BM and provides good palliation of pain regardless age, primitive tumor or RT scheme. It significantly improves the Qol of these patients and reduces analgesic use. Fractionation schedule doesn't influence response to treatment and a single fraction scheme can be preferred in patients with a low life expectancy.

PO248

LATTICE RADIOTHERAPY IN LARGE TUMORAL MASSES

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Background and purpose: Lattice Radiotherapy (LRT) is an intriguing therapy for palliation in bulky tumors. Most of the cases in the literature are of lung cancer. it is also considered to be immunogenic stimulation due to the release of substances that inhibit tumor growth.

Materials and methods: Six patients (pts) were treated between 2017 and 2020. The median age was 76. All pts was in stage IV with distant metastasis. The treatment regions were heterogeneous (iliac common node, right armpit, left psoas muscle, lung left, right emithorax and sacro-iliac region). All pts had tumors maximal measure ranging from 8 cm to 15 cm. Follow-up median was 12.5 months. All pts were treated with one initial fraction of LRT on small spheres of 1cm in diameter with separation of about 2 cm created inside the tumor with dose of 15 Gy with volumetric modulated arc therapy and the treatment was continued with moderate hypofractionated external beam radiotherapy using 10 daily fractions of 3 Gy with tridimensional conformal radiotherapy (3D) started 2 weeks after the first.

Results: Three months after the end of radiotherapy 5 out 6 pts obtained a tumor mass reduction between 30% and 60%. The most common symptom was pain which was mitigated or disappered.

Conclusion: LRT can be a safe and effective treatment for bulky tumors in every part of the body. It is effective in the palliation of symptoms. It can be performed also during systemic therapies. The response could be mediated by the release of immunogenic substances.

PO249

ABSTRACT WITHDRAWN

PO250

PALLIATIVE TREATMENT OF METASTATIC LYMPHONODES: STEREOTACTIC BODY RADIOTHERAPY (SBRT) TO POSITIVE CHOLINE PET / CT LYMPH NODES FOR OLIGOMETASTASIZED PROSTATE CANCER (PCA) PATIENTS

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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 2020, 30 oligometastasized PCa patients with a total of twenty 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.

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.

PO251

UNIVERSAL SCREENING FOR SARS-COV-2 IN PATIENTS UNDERGOING ANTICANCER TREATMENT DURING THE SECOND OUTBREAK IN XXX

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Aim: COVID-19 had a remarkable impact on cancer patients, due to higher risk of severe pneumonia and possible treatment discontinuation. Therefore, during the second COVID-19 outbreak we implemented a universal screening for the patients scheduled for antineoplastic treatment.

Methods: All the patients with planned anti-neoplastic therapy at XXX University Radiation Oncology Department were tested for SARS-Cov-2 RNA with naso-pharyngeal swabs from October 31, 2020. If infection was detected, start or prosecution of treatment was defined according to clinical presentation.

Results: In the analyzed period (October 31,2020 - February 06, 2021), 636 patients were enrolled and 1243 NPS were performed. Infection rate was 2.52% and the large majority of the patients with a positive NPS (81.3%) was asymptomatic; only one patien had severe disease, that resulted into death. For the patients with infection detected before treatment start mean delay was 16.5 days, while all the patients with mild or asymptomatic COVID-19 diagnosed while on treatment completed it with no or minimal delay.

Conclusions: Detected incidence of COVID-19 was lower during the second compared with first outbreak in our patients (2.52% *vs* 3.23%); a sharp reduction of mortality (6.3% *vs* 38.5%) was as well reported. The high rate of mild or asymptomatic infections could be due to the universal screening, that allowed an early identification, resulting in a timely management that could improve clinical outcomes and prevent the spread of the infection.

PO252

ADJUVANT ACCELERATED PARTIAL BREAST IRRADIATION FOR EARLY STAGE OF BREAST CANCER DURING THE COVID-19 PANDEMIC

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Aims: The outbreak of Covid-19 pandemic has drastically reduced the possibility for non-covid patients to access proper treatments. However, hospitals have made efforts in order to ensure cancer treatments, albeit with some delay due to redeployment of funds and staff to covid care areas. The International Guidelines on radiation therapy for breast cancer during the covid-19 pandemic (published on Clinical Oncology in 2020) indicated that adjuvant radiotherapy in over 65- year old patients with low-risk breast cancer can be omitted in order to protect patients and health care professionals from potential exposure to COVID-19 as well as reducing the workload for health care providers. In our institution we decided to treat low-risk breast cancer patients with adjuvant accelerated partial breast irradiation (APBI) technique instead of omitting radiotherapy as guidelines have suggested. APBI can be delivered in 5 sessions in order to reduce the numbers of access to the hospital.

Methods: From April 2020 to April 2021, 18 women with low-risk breast cancer were treated in our institute with APBI for a cumulative dose of 30 Gy in 5 fractions (6 Gy/fraction). To minimize the risk of Covid-19 infection all patients were checked with nasopharyngeal swab before the start of radiotherapy and measurement of body temperature before each access into the Hospital. Common areas were systematically sanitized and the waiting rooms reorganized in compliance with the social distancing rules.

Results: The median ages of the patients treated was 71.6 years (49.9-82.3). All cases treated with APBI were pathological N0 and pTis (1), pT1 (16) or pT2 (1). Among the 17 infiltrating carcinoma,13 tumors were Luminal A, 4 were Luminal B Her 2 negative. No acute toxicities over G1, evaluated with RTOG scale, were reported. None of these patients contracted Covid-19 infection during Radiotherapy. With a median follow-up of 5 (0-13) months, only a G1 tumor bed fibrosis was registered.

Conclusion: In our opinion, due to the high life expectancy of Italian women, when feasible, it is preferable not to omit radiation adjuvant treatment for any stage of breast cancer even during the pandemic event. The implementation of hypofractionated regimens and the activation of rigid anti-contagion protocols may be the

right key to guarantee satisfactory oncological treatment in a climate of reasonable safety from infection.

P0253

COVID-RELATED EVENTS AMONG RADIOTHERAPY STAFF DURING THE 2020-2021 PANDEMIC: EXPERIENCE AT A REGIONAL HUB FOR COVID PATIENTS

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Aims: COVID 19 epidemic had a variable impact on clinical activity of radiotherapy (RT) departments. In this study we report the data relating to COVID 19 infections among health workers in our RT department, analyzing their impact on clinical activity and trying to identify the possible reasons for such data.

Methods: Our hospital was defined a regional Hub for COVID 19. The COVID 19 contagion prevention procedures adopted at our division starting from 3/2020 included the use of a surgical mask, frequent disinfection of the hands, and a temperature check of all staff entering and leaving the Unit. A nasopharyngeal swab was performed only in case of symptoms possibly related to COVID 19 infection or of a temperature finding above 37.5°. From 9/2020 we started to deliver RT treatment to COVID 19 positive patients. For such treatments further prevention procedures were defined and adopted. Anonymous data relating to COVID 19 infection were collected from 8 doctors, 4 nurses, 14 therapists and 2 healthcare operators employed in the RT ward from 1/3/20 to 1/3/21 (when 100% of the staff had received the second vaccine dose). We calculated the days of absence from work due to COVID infection and any reduction in the workload of the department. We also identified a subgroup of 19 people who had serological tests 2, 10 and 13 months after the spread of the virus in Italy.

Results: Out of 28 staff members, 2 were diagnosed with COVID 19 infection. Since the two infectious events developed 9 months after each other and a direct source of contagion outside the hospital was identified for both, it is reasonable to conclude that no infectious foci have developed within the RT department during the epidemic. The average time off work due to COVID 19 was 24 days. No significant decrease in the number of patients treated compared with 2019 was recorded. All serological tests performed were negative.

Conclusions: Although extraordinary contagion prevention measures were adopted only in case of potential direct contact with proven COVID 19 positive patients, no infections occurred in our RT department and continuity of care for oncological patients requiring RT was assured in the entire epidemic period. Such favorable data may be explained by the isolated location of our department within the hospital, by the relatively large common and visiting rooms (allowing the staff and the patients to respect social distancing) and by the strict respect of rules preventing contagion by all staff.

P0254

THE IMPACT OF COVID-19 PANDEMIC ON THE RADIOTHERAPY PRACTICE: A RETROSPECTIVE SINGLE-INSTITUTION ANALYSIS

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Aims: COVID-19 has rapidly impacted the livelihoods of many millions of people globally following its escalation to pandemic status on March 2020. AORMN is the reference hospital of an area with 360,000 inhabitants that showed an early and high incidence of COVID-19 positive people, especially during the first outbreak. The aim of this study is to determine the impact of the pandemic consequences on the radiotherapy (RT) practice.

Methods: We retrospectively analyzed the activity of the Radiotherapy Unit at AORMN during the first 12 months (GROUP 1) of the COVID-19 outbreak which includes the first three pandemic peaks in Italy. We also compared the performance analysis to the previous 12 months (GROUP 2) to evaluate the possible influence of COVID-19 on the management patients (pts) undergoing RT treatments. Standard descriptive statistics were used for the comparison.

Table 1.

	Group 1 February 2020 - March 2021	Group 2 February 2019 – March 2021	Difference
New pts admitted	871	1044	173
Re-evaluation	216	298	82
pts treated	757	891	134
SRT	54	58	4
VMAT	513	548	35
3D-CRT	190	285	95
SRT for brain metastases	15	13	-2
Palliative RT	141	141	0
Electronic BRT	9	16	7
Breast cancer pts treated	243	342	99
Prostate cancer pts treated	107	121	14
Lung cancer pts treated	30	31	1
H&N cancer pts treated	40	37	-3
Ano-rectal cancer pts treated	45	43	-2
Brain (primary) cancer pts treated	25	25	0
Total RT sessions	10914	13592	2678
FUP consultations	594	786	192

Results: Between March 2020 and February 2021, 871 new cancer pts (median age: 69, range: 19-94) were addressed for RT consultations, 216 pts already treated were re-evaluated for a new treatment, 757 received radiation treatments (54 stereotactic RT, 513 VMAT and 190

3D-CRT) for a total of 10914 RT sessions. Five hundred ninety-four pts received a follow up consultation. Between March 2019 and February 2020, 1044 (median age: 72, range: 17-98) new cancer pts received the first RT consultation (+16.6%) and 298 irradiated pts were evaluated for a new RT course (+27.5%). Eight hundred ninety-one pts received RT (58 stereotactic treatments, 548 VMAT, 285 3D-CRT) for a total of 13592 RT sessions (+19.7%). Seven hundred eighty-six pts received a follow up consultation (+24.4%). No significant differences in the number of irradiated pts with diagnoses of lung, H&N and anorectal cancers. On the contrary, we observed a reduction of 29% and 12% in breast and prostate cancer RT treatments, respectively. We noticed a significant reduction (-44%) in the number of pts undergoing electronic brachytherapy for small skin cancer tumors. The comparison between GROUP 1 and GROUP 2 according to all estimated variables is included in Table 1.

Conclusions: During COVID-19 pandemic, cancer management and radiotherapy practice became more challenging. The biggest reduction has been seen in the number of RT treatments for asymptomatic cancer types, the ones with a more favorable prognosis and/or detected by screening programs, slowed down for some months due to pandemic consequences.

PO255

IMPACT OF COVID-19 PANDEMIC ON RADIATION ONCOLOGY PRACTICE. AN OVERVIEW OF RECENT HIGHER QUALITY REPORTS

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Aims: To report the emerging knowledge on the impact of COVID-19 pandemic in multiple fields of Radiation Oncology (RO), we update a previously presented overview of clinical experiences and practical proposals published since the beginning of the emergency period of COVID-19 pandemic.

Methods: On 26 February 2021 a Pubmed search via PICO was performed using the following terms: P(cancer patients and Covid) and I(radiotherapy). For this overview, only higher quality reports according to study design (Systematic Reviews, Clinical Trials and Practice Guidelines) were selected and analyzed.

Results: Among a total of 290 titles, 19 higher quality reports in RO were evaluated: 6 Systematic Reviews, 3 Clinical Trials and 10 Practice Guidelines. In particular, international expert consensus recommendations and proposals for managing cancer patients during COVID-19 pandemic were published with specific regard to the following tumors: breast and digestive cancers, as well as thoracic, haematological and gynecologic malignancies. Additionally, as an interestingly non-oncological result, whole-lung irradiation in a single fraction of 0.5 Gy was reported to obtain a response rate of 80% in a clinical trial enrolling oxygen-dependent patients with COVID-19 pneumonia.

Conclusions: We confirm an exponential increase in the COVID-19 publications, also including literature in RO fields. The remarked endpoint of published works was the balance between the risk of oncological disease progression and ill from COVID□19. In general, the use of RADS (Remote, Avoid, Defer, Shorten) principles has been manteined, taking into account the necessity of personalized therapeutic approaches and pandemic containment (*e.g.* managing elderly or COVID-19 positive patients). The use of hypofractionated regimens has been generally encouraged according to patient's and disease's specific conditions. For selected cases, defer radiotherapy (RT) could be considered only if clinically appropriate, while avoid RT could be proposed exclusively if marginal advantages are demonstrated and alternative validated approaches are available. The evaluation of patient-specific risk factors and a multidisciplinary management are crucial. As preliminary knowledge, RT seems to be not associated with increased risk of exacerbation and mortality in SARS-CoV-2-infected cancer patients. To reduce risk of infection, separating patients and optimizing the resources (*e.g.* remote visits) are important strategies.

PO256

COVID-19 PNEUMONITIS AND RADIATION PNEUMONIA AFTER VMAT: MAY LOW DOSES HAVE A ROLE?

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Aim: Radiation pneumonitis (RP) shows specific findings that make easy it to distinguish from Covid-19 pneumonia (Co-19 P). Typical CT features due to pulmonary fibrosis are unilateral and share a parenchymal involvement corresponding to the radiotherapy (RT) treatment fields along the different isodoses distribution to the lung. However, unusual situations may occur after VMAT presenting with overlapping clinical and radiological features of Co-19 P. Herein our experience.

Methods: A retrospective study was carried out to know how many cases of RP had been occurred in the Co-19 pandemic. Chest CT scan images and RT treatment plan were acquired and analyzed to assess factors related to RP.

Results: In 2020-21 five patients with symptomatic RP were observed; mean age was 60 years (42-70). All patients had received curative RT with VMAT modality.

In all of them a common finding was the fibrosis outside the radiation fields occurring after a mean time of 6 months (2-18 ms). Pt 1 with head and neck cancer had received RT 18 ms before; he was positive to Co-19. Symptom was only recurrent mild fever. CT scan showed a recall fibrosis with interstitial thickening in the right supraclavicular area which was included in the low dose RT field (15 Gy). Pt 2 with left upper cancer treated with postoperative RT on mediastinum, 6 ms later RT developed Co-19 infection with fever and cough. Chest CT scan showed a dense ground glass opacity with consolidation in the contralateral lung. This area was included in the 10 Gy isodose. Pt 3 with left breast cancer after 4 ms off RT, recorded fever; she was Co-19 positive. CT scan showed a dense opacity in the hilar left lung included in the 3 Gy isodose. Pt 4 with right breast cancer after 3 ms off therapy, complained of mild fever and dyspnea. She was Co-19 negative. The CT scan of the chest showed bilateral and diffuse nodular opacities due to BOOP. Pt 5 with right lung cancer treated with limited field RT after two ms off RT complained of fever and worsening dyspnea to be admitted in intensive care unit. He was Co-19 negative. Ct scan showed massive bilateral alveolar thickening and diffuse ground-glass opacities evolving into a whited-out lung. He died with ARDS. DVH for lung (V5, V10, V20, MLD) was normal in these two cases.

Conclusions: Pneumonitis in the untreated lung shows atypical findings that make difficult diagnosis in Co-19 pandemic. Whether the low dose bath may a role is unknown but uncertain.

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RADIOTHERAPY IN COVID-19 PATIENT AFFECTED BY MULTIPLE MYELOMA: A CASE REPORT

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Aims: In COVID-19 pandemic, cancer patients may be vulnerable for their immunological status and need of immunosuppressive anti-neoplastic treatments. Choosing the best treatment option in COVID-19 positive cancer patients is still a challenging issue.

Methods: We report the case of a 62-year-old woman diagnosed with multiple myeloma and affected by COVID-19. After the onco-hematologic diagnosis in January 2019, the patient underwent first line therapy followed by bone marrow autologous stem cell transplantation, achieving a complete response in September 2019.

Results: In March 2020, the patient showed intrathoracic progression of the disease, resulting in a severe dysphagia and concomitant positivity to SARS-CoV-2 swab test, cough, fever, and dyspnea related to the involvement of the lung parenchyma, as shown by CT-scan. After her admittance to a COVID-19 dedicated inward, she was administered oral hydroxychloroquine and darunavir-cobicistat for 7 days with stabilization of her general clinical conditions. For the worsening of dysphagia, after multidisciplinary discussion, it was decided to deliver radiotherapy to the mediastinal and paravertebral mass with 8 Gy single fraction. After 5 days, her clinical conditions improved, with reduction of dysphagia. The CT confirmed a partial response with reduction of the mass of about 50%. Viral clearance was confirmed by triple negative search for SARS-CoV-2 on nasopharyngeal swabs, one month after first documentation of positivity. Unfortunately, the patient died three months later due to a pulmonary mycotic infection causing respiratory failure. To our knowledge, this case report describes the first experience of mediastinal radiotherapy in a COVID-19 patient affected by myeloma reported in the literature.

Conclusions: In case of clinical indication, even in presence of SARS-CoV-2 infection, radiotherapy can be safely delivered and might be considered a treatment option, as it is showed by our experience in this challenging case of intrathoracic myeloma.