



Società Italiana di Radiobiologia

RAO



SIB IMRT, premesse e risultati

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RAO

A I Kadioterapia e Oncologia citnica



XXXII CONGRESSO NAZIONALE AIRO XXXIII CONGRESSO NAZIONALE AIRB XII CONGRESSO NAZIONALE AIRO GIOV/

Radioterapia di precisione per un'oncologia innovativa e sostenibile

DICHIARAZIONE

Relatore: Anna M

Come da nuova regolamentazione della Commissione Nazionale per trasparenza delle fonti di finanziamento e dei rapporti con

- Posizione di dipendente in aziende con interest
- Consulenza ad aziende con interessi com
- Fondi per la ricerca da aziende con inter
- Partecipazione ad Advisory Board ()
- Titolarità di brevetti in comparte
- Partecipazioni azionarie in azience
- Altro

ntinua del Ministero della Salute, è richiesta la rinteressi commerciali in campo sanitario.

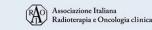
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ende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)

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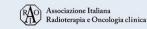


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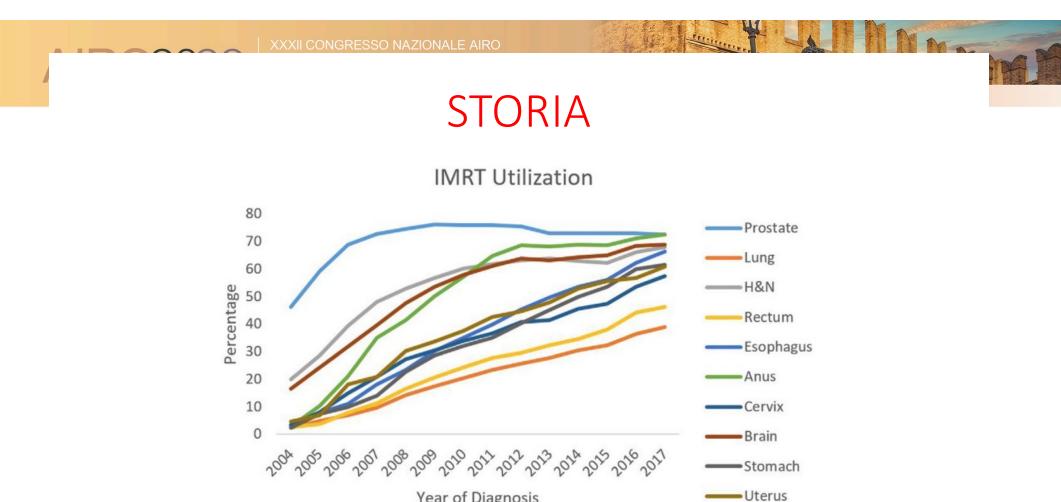


Storia Narrazione Fatti: confronto seq-SIB



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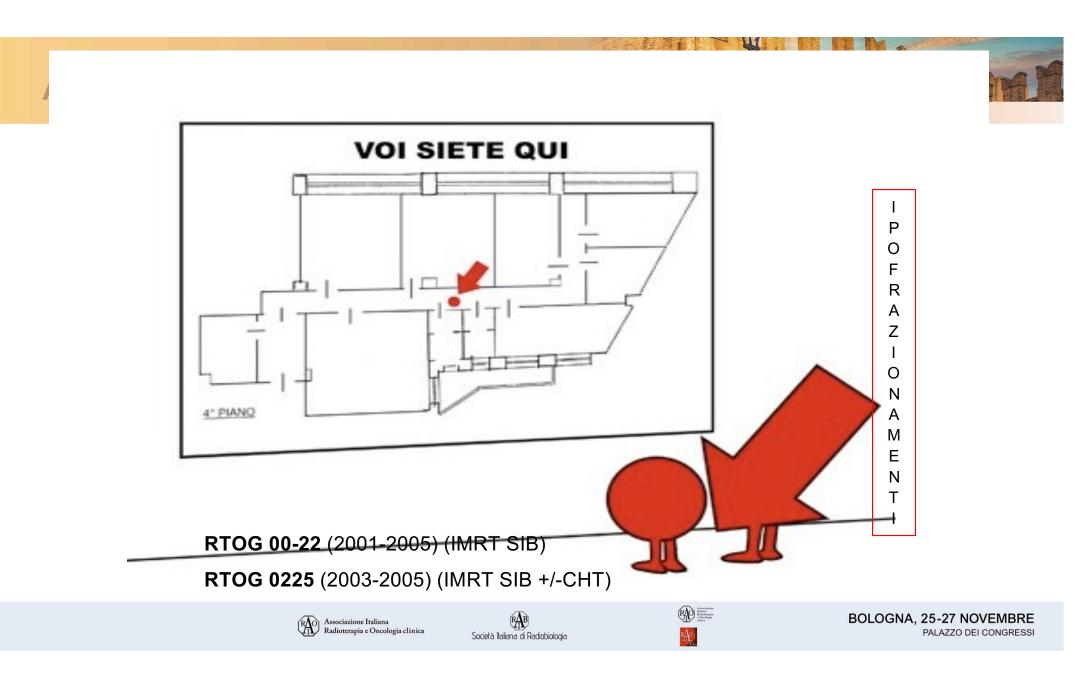




Year of Diagnosis

Fig. 2 Rates of IMRT utilization between 2004 and 2017. Abbreviations: H&N = head and neck; IMRT = intensity modulated radiation therapy.





RTOG 00-22



- to investigate whether the early successes of IMRT reported by few institutions could be reproduced in a multi-institutional setting
- (T1-2, N0-1, M0) Oropharynx -IMRT- no cht
- Multiple fraction was initially desired for this study- not feasable



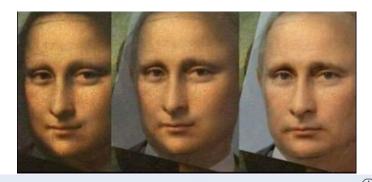
2.2 Gy	30 fx	66 Gy (PTVHD)
2 Gy	30 fx	60 Gy (PTV HR)
I.8 Gy	30 fx	54 Gy (PTV LR)



Eisbruch A. Int. J. Radiat Oncol Biol Phys, Vol. 76, No. 5, pp. 1333–1338, 2010

Ripopolamento cellulare H&N

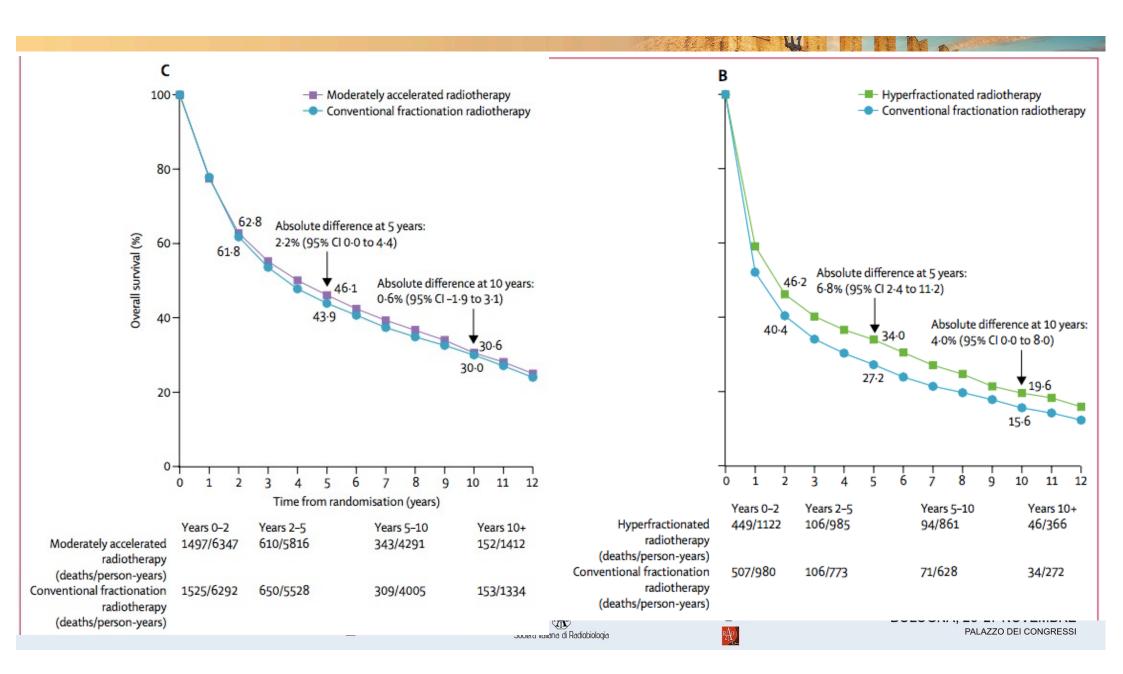
- Inizia dopo 3-4 settimane per carcinomi squamosi
- Fino a 0.6 Gy vanno a "compensare" l'aumento di cellule tumorali dovuto al ripopolamento.
- Per ogni giorno di prolungamento del tempo totale di trattamento si perde 1% di controllo tumorale



Withers HR et al. Acta Oncol 1988;27:131-46.

Nei pazienti H&N: MARCH

- 33 trials, 11 423 patients. Follow-up 7.9-10 y. Per lo più orofaringe e laringe; 5221 (74%) pazienti di stadio III-IV della malattia.
- significant benefit on overall survival for hyperfractionated group: absolute differences at 5 years of 8.1% (3.4 to 12.8) and at 10 years of 3.9% (-0.6 to 8.4).
- Altered fractionation radiotherapy absolute difference at 5 years of 3.1% (95% Cl 1.3-4.9) and at 10 years of 1.2% (-0.8 to 3.2).
- Overall survival was significantly worse with altered fractionation radiotherapy compared with concomitant chemoradiotherapy: absolute differences at 5 years of -5.8% (-11.9 to 0.3) and at 10 years of -5.1% (-13.0 to 2.8).





Radioterapia di precisione per un'oncologia innovativa e sostenibile

Narrazione

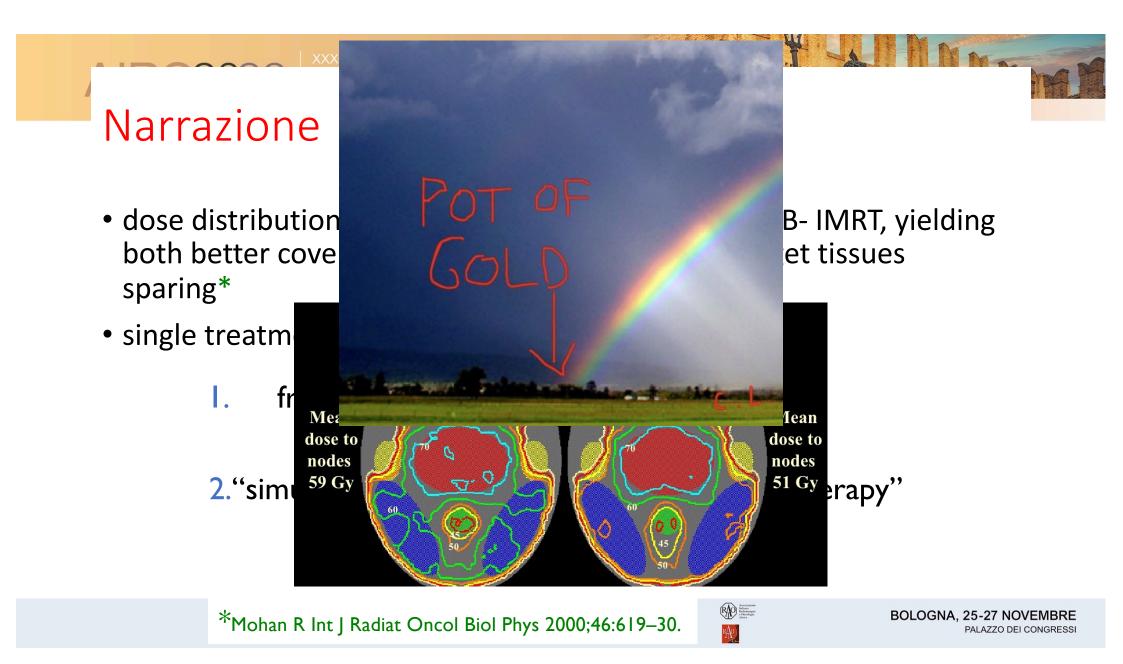
«MA CI SONO ALTRI VANTAGGI»

- Pianificazione ed esecuzione più semplice, efficiente
- Possibilità di associare cht
- Stesso piano dall'inizio alla fine del trattamento
- Vantaggio dosimetrico

Associazione Italiana





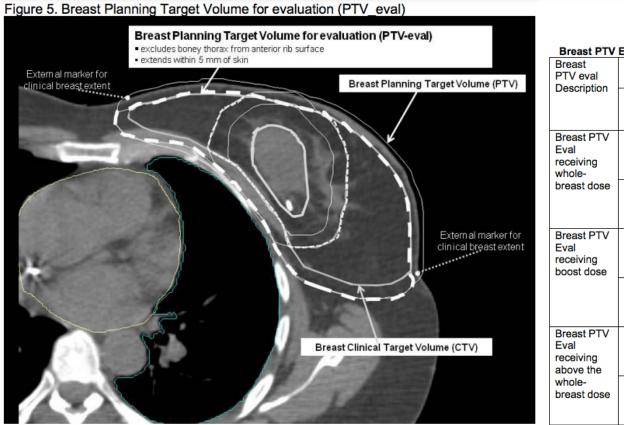


RADIATION THERAPY ONCOLOGY GROUP

RTOG 1005

A PHASE III TRIAL OF ACCELERATED WHOLE BREAST IRRADIATION WITH HYPOFRACTIONATION PLUS CONCURRENT BOOST VERSUS STANDARD WHOLE BREAST IRRADIATION PLUS SEQUENTIAL BOOST FOR EARLY-STAGE BREAST CANCER





APPENDIX VII

DOSE VOLUME HISTOGRAM CONSTRAINTS

Breast PTV	Eval					
Breast PTV eval Description	Goal	Constrain	t Dose	ARM I 50 Gy in 25 sequential 12-14 Gy boost total 62-64 Gy	ARM I 42.7 in 16 sequential 12- 14 Gy boost total 54.7-56.7 Gy	ARM II 40 Gy in 15 concurrent boost to 48 Gy
Breast PTV Eval receiving whole-	Ideal	≥ 95% of the breast PTV Eval receives	≥ 95% of whole breast dose	≥ 47.5 Gy	≥ 40.6 Gy	≥ 38 Gy
breast dose	Acceptable	≥ 90% of the breast PTV Eval receives	≥ 90% of whole breast dose	≥ 45 Gy	≥ 38.4 Gy	≥ 36 Gy
Breast PTV Eval receiving boost dose	Ideal	≤ 30% of the breast PTV Eval receives	≥ 100% of boost dose	≥ 62-64 Gy	≥ 54.7-56.7 Gy	≥ 48 Gy
	Acceptable	≤ 35% of the breast PTV Eval receives	≥ 100% of boost dose	≥ 62-64 Gy	≥ 54.7-56.7 Gy	≥ 48 Gy
Breast PTV Eval receiving above the	Ideal	≤ 50% of the breast PTV Eval receives	≥ 108% of whole breast dose	≥ 54 Gy	≥ 46.1 Gy	≥ 43.2 Gy
whole- breast dose	Acceptable	≤ 50% of the breast PTV Eval receives	≥ 112% of whole breast dose	≥ 56 Gy	≥ 47.8 Gy	≥ 44.8 Gy

Table 5

Ν

Ideal dose-volume criteria for heart and corresponding achieved values (averages and standard deviations). Averages and standard deviations were calculated separately for left and right breasts for all plan options with data from applicable cases. V_{16 Gy} and V_{8 Gy} of heart for right breast, which were trivial for all plan options, are not listed

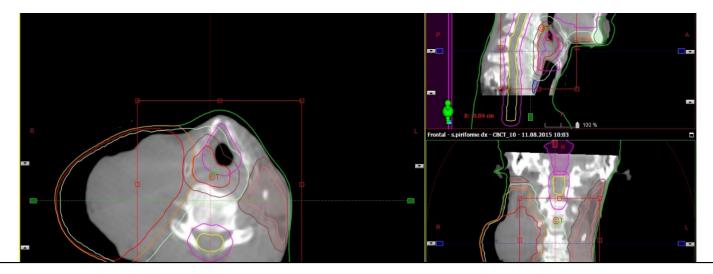
		Right		
V ₁	′ _{16 Gy} ≤ 5%	V _{8 Gy} ≤ 30%	$D_{mean/40 Gy} \le 8\%$	$D_{mean/40 Gy} \le 8\%$
3D + e 1.8 3D + IMRT 2.0 IMRT + 3D 1.9	$.8 \pm 1.8$ $.0 \pm 1.8$ $.9 \pm 1.6$ $.7 \pm 1.7$	3.5 ± 2.5 3.9 ± 2.4 4.3 ± 3.5	4.9 ± 2.1 4.4 ± 2.1 5.0 ± 2.1 4.6 ± 1.7 4.4 ± 1.7 4.6 ± 1.7	2.0 ± 1.5 2.3 ± 2.0 1.8 ± 1.6 2.1 ± 1.8 1.9 ± 1.2 1.6 ± 1.1

MA

EMBRE ONGRESSI



Quando è meglio Seq-IMRT o SIB



SIB-IMRT when OARs were not adjacent to the boost volume (PTV2) that received a high dose per fraction (2.2 Gy/fraction).





Radiation Oncology

BioMed Central

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Research Radiation Oncolo

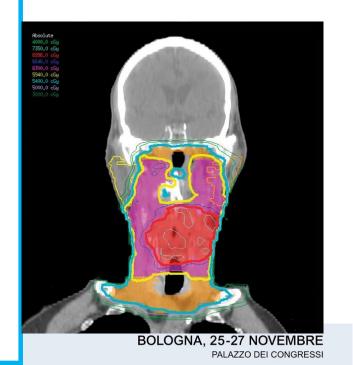
Radiation Oncology 2006, 1:7 doi:10.1186/1748-717X-1-7

IMRT using simultaneously integrated boost (SIB) in head and neck cancer patients

G Studer*1, PU Huguenin1, JB Davis2, G Kunz2, UM Lütolf1 and C Glanzmann1

La dose/frazione che possiamo somministrare senza aumentare troppo le sequele è organo dipendente:

 dosi/frazione superiori a 2.2 Gy non sono raccomandate per la laringe



Original Research Article

Stereotactic body radiotherapy for TI glottic cancer: dosimetric data in 27 consecutive patients

Giuseppe Sanguineti¹, Raul Pellini², Antonello Vidiri³, Simona Marzi⁴, Pasqualina D'Urso¹, Irene Terrenato⁵, Alessia Farneti¹, Valentina Fuga¹, Sara Ungania⁴ and Valeria Landoni⁴

- Piccoli volumi!
- Alta precisione!

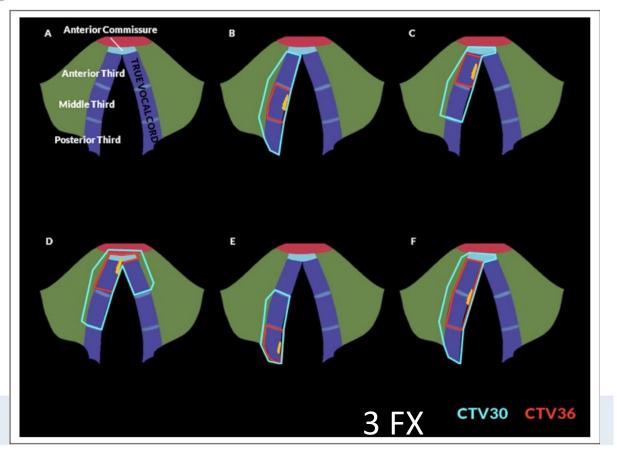


Tumori Journal



osteni

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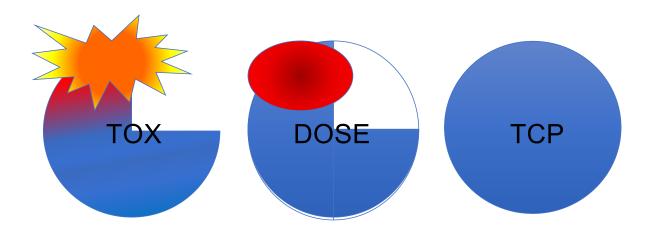














"farmacocinetica" e "farmacodinamica" della Radioterapia

FARMACOCINETICA: assorbimento, distribuzione, (metabolismo, eliminazione)

• Numerosissimi studi di comparazione dosimetrica

FARMACODINAMICA: effetti sull'organismo e meccanismo d'azione.

 Pochissimi studi di analisi delle tossicità in relazione alle aree che hanno ricevuto dosi frazione > 2 Gy



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Obiettivi per ottimizzazione del pdt

Per ridurre tox

- no more than 20 % of any PTV will receive >110 % of it's prescribed dose.
- no more than 1 % or 1 cc of the tissue outside the PTV will receive > 110 % of the dose prescribed to the primary PTV

Per mantenere TCP

- no more than 1 % of PTV1 will receive < 93 % of its prescribed dose
- The prescription dose is the isodose which encompasses at least 95 % of the PTV







XXXII CONGRESSO NAZIONALE AIRO

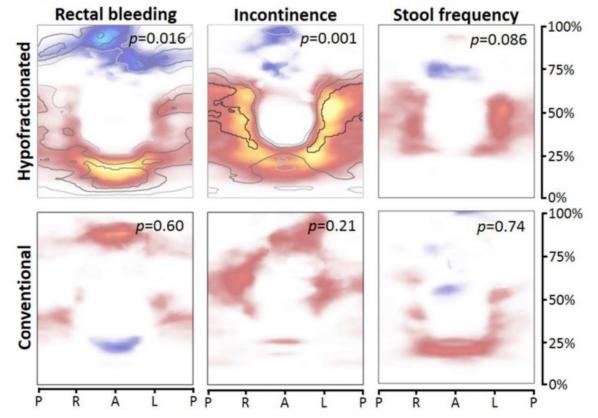
Handling hypofx doses to OARS: HYPRO trial

- HF (64.6 Gy in 19 fractions) or CF (78.0 Gy in 39 fractions). EQD2 was 90.4 Gy for HF versus 78.0 Gy for CF NEGATIVE STUDY
- function and radiosensitivity may vary within an organ, and that dose-shapes might be relevant.
- voxel-based dose mapping procedures have been introduced to take into account the spatial dose distribution by co-registering dose distributions to a region of interest. For hollow organs such as the rectum, a spatial 2D dose distribution of the rectal wall (i.e., virtual unfolding of the rectum to a 2D structure).
- just by calculating EQD2 for a HF schedule, this might not completely capture the biological effect of a HF treatment.

WD Heemsbergen et al. Front Oncol. 2020 Apr 3;10:469

XXXII CONGRESSO NAZIONALE AIRO

 for the endpoint fecal leakage (age and diabetes) and for the endpoints rectal bleeding and mucus (T stage) predictive clinical covariates were identified.



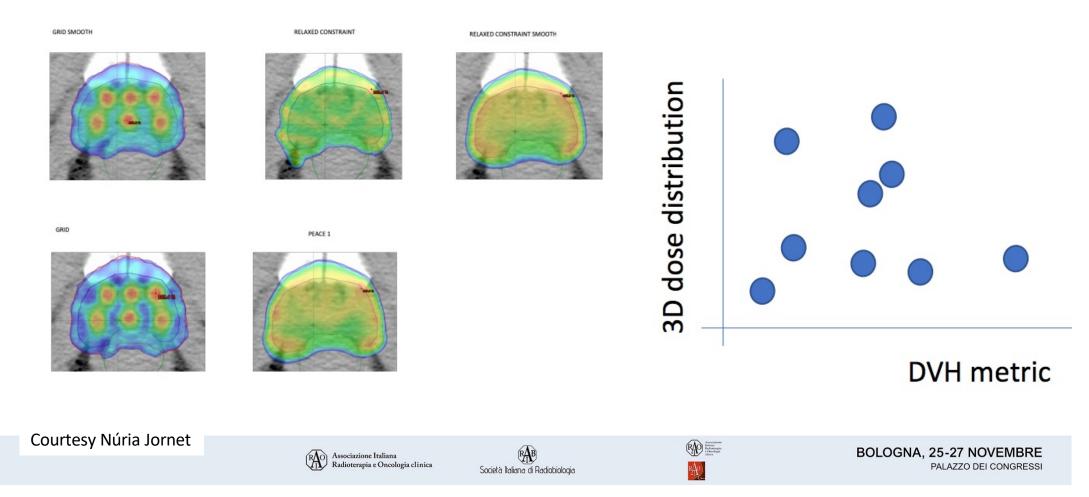
Dose difference maps (1EQD2) based on total rectum dose mapping, for the toxicity endpoints (moderate to severe), for the hypofractionated and conventional group separately.

IBRE GRESSI



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• The same two histograms can hide completely 3D dose distributions





MDPI



Article

A Multicentre Evaluation of Dosiomics Features Reproducibility, Stability and Sensitivity

Lorenzo Placidi ^{1,*,†}⁽¹⁾, Eliana Gioscio ^{2,†}, Cristina Garibaldi ³, Tiziana Rancati ²⁽¹⁾, Annarita Fanizzi ⁴⁽⁰⁾, Davide Maestri ⁵, Raffaella Massafra ⁴, Enrico Menghi ⁶⁽¹⁾, Alfredo Mirandola ⁵, Giacomo Reggiori ⁷, Roberto Sghedoni ⁸, Pasquale Tamborra ⁴, Stefania Comi ⁹, Jacopo Lenkowicz ¹, Luca Boldrini ¹⁽¹⁾ and Michele Avanzo ¹⁰⁽¹⁾

- Patients' 3D dose distributions can be considered as an image with spatial and statistical distributions of dose levels that can be investigated using texture analysis
- Dosomics can be considered as an effective method to parameterize dose distribution in specific region of interest (ROIs) by intensity, textural and shapebased dose features, able to describe the dose distribution at a higher complexity level than those obtain using DVHs. The integration of these parameters with the DVH could potentially improve the predictive performance of NTCP models







COMPLEX CORRELATION!



STILL LIMITED LONG TERM OUTCOME DATA

Radiobiological basis and clinical results of the simultaneous integrated boost (SIB) in intensity modulated radiotherapy (IMRT) for head and neck cancer: A review

> Ester Orlandi^{a,*}, Mauro Palazzi^a, Emanuele Pignoli^b, Carlo Fallai^a, Antonella Giostra^b, Patrizia Olmi^a

Author	FS/NF/TD	Tur	nor	Acute responding	Late reacting tissues
		BED	NTD2Gy	tissues BED	BED
Conventional	2/35/70	71.5	70	56.3	116.9
Butler et al.	2.4/25/60	68.2	66.8	56.4	108
Schwartz et al.	2.4/25/60	68.2	66.8	56.4	108
Studer et al.	2.11/33/69	72.5	71	58	119.6
	2.2/30/66	71.1	69.6	57.6	115.4

41-K_

Critical Reviews in Oncology/Hematology 73 (2010) 111–125

Radiobiological basis and clinical results of the simultaneous integrated boost (SIB) in intensity modulated radiotherapy (IMRT) for head and neck cancer: A review



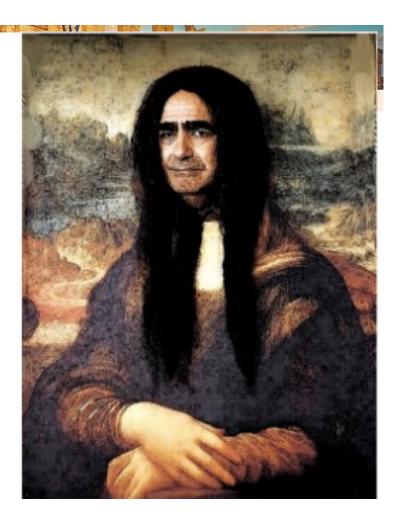
Ester Orlandi^{a,*}, Mauro Palazzi^a, Emanuele Pignoli^b, Carlo Fallai^a, Antonella Giostra^b, Patrizia Olmi^a

	Worst acı	ite tox %	Worst late	tox %
Butler	Mucosite G3	80%	-	-
	Faringite G3	50%	-	-
Shwartz	Mucosite G3	55%		
	Disfagia G3	20%	Disfagia G3	4
Studer	Mucosite G3	15%	Mucosite G3-4	10.4
	Disfagia G3	20%	Disfagia G3	1.7

Tossicità accettabili ?

- 20 patients with primary head and neck carcinomas were treated with SMART boost technique.
- 2.4/2 Gy 5 weeks 60/50 Gy tot
- worsen the acute toxicity

Tox RTOG	
Mucosite G3	80%
Faringite G3	50%
Calo peso > 10%	15%
EN/FT	50%
Xerostomia G2	45% (< 6 mesi)



• Better tumor response (95% CR mean F-up 15.2 months)

Acceptable toxicity

Butler EB Int J Radiat Oncol Biol Phys. 1999 Aug 1;45(1):21-32

Moderately accelerated intensity-modulated radiation therapy using simultaneous integrated boost: Practical reasons or evidence-based choice? A critical appraisal

of literature

Head Neck. 2020 Nov;42(11):3405-3414

Francesca De Felice MD1|Pierluigi Bonomo MD200|Giuseppe Sanguineti MD300|Ester Orlandi MD400

 moderately accelerated IMRT using SIB has been largely adopted in clinical practice, but no high- quality evidence is available on its safety and efficacy compared to recommended standard cisplatin-based CRT using CF. SIB-IMRT remains an exquisite technical solution mainly dictated by logistic issues, such as machine slots and patient convenience.

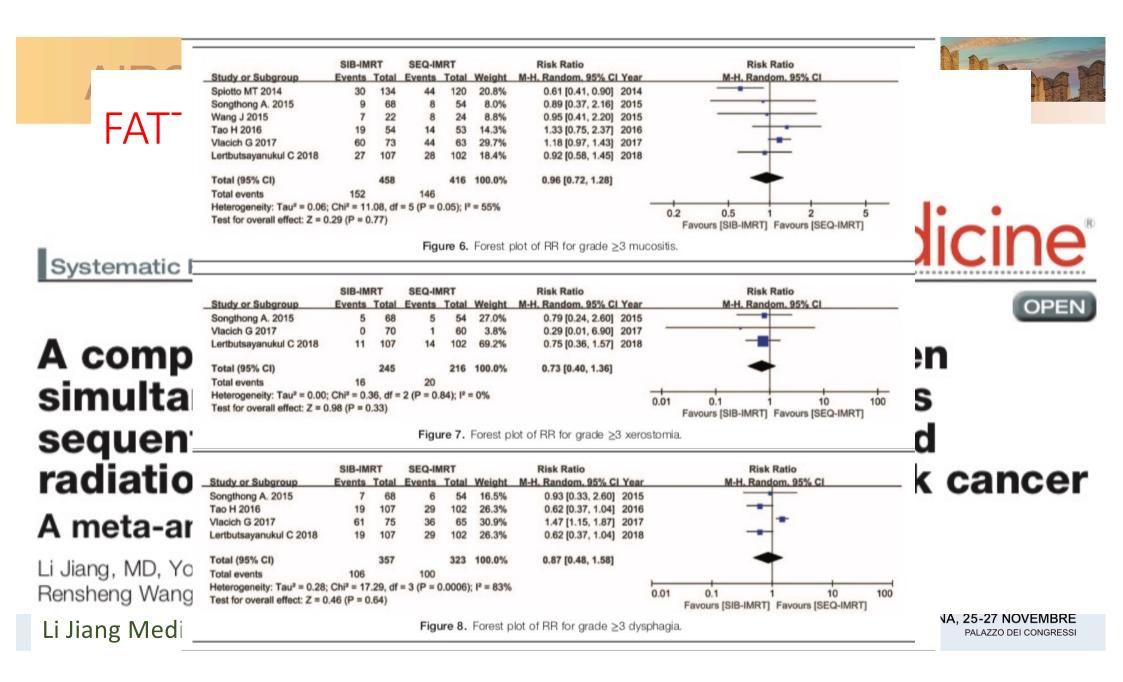




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FATTI: BREAST

3-year adverse effects in the IMPORT HIGH trial (CRUK/06/003) CE Coles et al.

- San Antonio Breast Cancer Symposium 2019
- 840 pts f-up 3Y
- Randomisation was 1:1:1 between 40Gy/15F to whole breast (WB) + 16Gy/8F sequential photon boost to tumour bed (40+16Gy), 36Gy/15F to WB, 40Gy to partial breast + 48Gy (48Gy) or + 53Gy (53Gy) in 15F SIB to tumour bed.
- rates of moderate/marked AEs were similar between SIB IMRT and WB + sequential boost IMRT delivered over 3 and 4.5 weeks respectively. Slightly increased risk for breast induration in 53Gy compared with control (borderline significance)

UCIELO ILOIIOLIO UL MOULUUUUU



Long-term results of hypofractionation with concomitant boost in patients with early breast cancer: A prospective study Plos ONE October 7, 2021 K Saksornchai et al.

- 50 Gy in 25 fractions followed by a sequential 10–16 Gy boost to the tumor bed or 43.2 Gy in 16 fractions with a concurrent boost of 0.6 Gy for each fraction.
- 73 pts, f-up mediano 10 y
- DFS and OS were comparable
- no statistical difference in late toxicity between the 2 groups (p = 0.072).

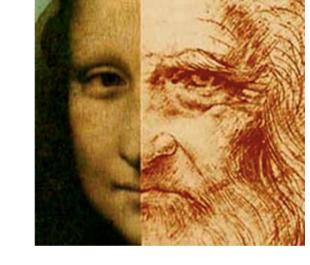


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Intensity Modulated Radiation Therapy (IMRT) With Simultaneously Integrated Boost Shortens Treatment Time and Is Noninferior to Conventional Radiation Therapy Followed by Sequential Boost in Adjuvant Breast Cancer Treatment: Results of a Large Randomized Phase III Trial (IMRT-MC2 Trial) J Hörner-Rieber et al. Int J Radiat Oncol Biol Phys. 2021 Apr 1;109(5):1311-1324

- 502 pts, median follow-up time of 5.1 years
- SIB IMRT:
 - whole-breast IMRT 50.4 Gy in 1.8-Gy d/fx
 - tumor bed SIB 64.4 Gy in 2.3 Gy d/f
- In the control arm, 3-D-CRT
 - whole breast 50.4 Gy in 1.8-Gy d/f
 - seqBoost 66.4 Gy 2 Gy d/f



• No differences 2yLC, cosmesis (primary end-points) and OS



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FATTI: GE

2021



Article

A Pattern of Care Report on the Management of Patients with Squamous Cell Carcinoma of the Anus—A Study by the Italian Association of Radiotherapy and Clinical Oncology (AIRO) Gastrointestinal Tumors Study Group

Pierfrancesco Franco ^{1,2,*}, Giuditta Chiloiro ³, Giampaolo Montesi ⁴, Sabrina Montrone ⁵, Alessandra Arcelli ^{6,7}, Tiziana Comito ⁸, Francesca Arcadipane ⁹, Luciana Caravatta ¹⁰, Gabriella Macchia ¹¹, Marco Lupattelli ¹², Marina Rita Niespolo ¹³, Fernando Munoz ¹⁴, Elisa Palazzari ¹⁵, Marco Krengli ^{1,2}, Francesca Valvo ¹⁶, Maria Antonietta Gambacorta ³, Domenico Genovesi ^{10,17} and Giovanna Mantello ¹⁸

Franco *et al. Radiation Oncology* (2018) 13:172 https://doi.org/10.1186/s13014-018-1124-9

2018 Radiation Oncology

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RESEARCH

Comparing simultaneous integrated boost vs sequential boost in anal cancer patients: results of a retrospective observational study

Pierfrancesco Franco^{1*}, Berardino De Bari², Francesca Arcadipane¹, Alexis Lepinoy³, Manuela Ceccarelli⁴, Gabriella Furfaro¹, Massimiliano Mistrangelo⁵, Paola Cassoni⁶, Martina Valgiusti⁷, Alessandro Passardi⁷, Andrea Casadei Gardini⁷, Elisabetta Trino¹, Stefania Martini¹, Giuseppe Carlo Iorio¹, Andrea Evangelista⁴, Umberto Ricardi¹ and Gilles Créhange⁸

 Most participants use volumetric intensity modulated radiotherapy (89.7%) and a simultaneous integrated boost (84.5%)

Median follow up was similar for the 2 groups (34 vs 31 months for SIB and SeqB). Higher proportion of patients with high risk features in the SeqB group. No significant outcome differences were observed





Article

cancers

Radiotherapy with Intensity-Modulated (IMRT) Techniques in the Treatment of Anal Carcinoma (RAINSTORM): A Multicenter Study on Behalf of AIRO (Italian Association of Radiotherapy and Clinical Oncology) Gastrointestinal Study Group

Luciana Caravatta ^{1,*}, Giovanna Mantello ², Francesca Valvo ³, Pierfrancesco Franco ⁴, Lucrezia Gasparini ¹, Consuelo Rosa ¹, Najla Slim ⁵, Stefania Manfrida ⁶, Francesca De Felice ⁷, Marianna A. Gerardi ⁸,

 Table 6. Univariate analysis treatment characteristics and clinical outcomes.

987 patients, 3y f-up

Variable		LC			CFS			OS			PFS			EFS	
	HR	95% CI	<i>p</i> -Value	HR	95% CI	<i>p</i> -Value	HR	95% CI	p-Value	HR	95% CI	<i>p</i> -Value	HR	95% CI	<i>p</i> -Value
OTT (Ref. <45) ≥45	1 13	(0.80-1.61)	0 478	1 22	(0.93_1.60)	0 140	1 23	(0.86_1.75)	0 243	1 33	(1.00_1.77)	0.050	1 31	(1.03–1.68)	0.030
Total dose 54 Gy (ref. >54 Gy	o sta	atistic	ally	sig	nifica	int a	SSC	ociatio	on w	as	found	d		(0.76–1.26)	0.882
Total dose 55 Gy (ref. >55 Gy be	etwe	en to	otal (dos	se, dc	ose/f	rac	ction a	and/	or	boos	t		(0.79–1.30)	0.904
Dose/Fraction HR F		1:		lini	مما مر	itco	mo								
^{1.8–2 Gy)} M	oda	lity a			Cal Ol	JUU	IIIE	5.						(0.71–1.17)	0.452
1.8–2 Gy) >2 Gy) M Dose/Fraction LR Prov (ref 1.8–2 Gy) <1.8 Gy		(0.67–1.39)	0.835	0.98	(0.74–1.31)	0.908	0.74	(0.52–1.06)	0.102	0.78	(0.58–1.04)	0.090	1.01	(0.71-1.17)	0.452

Lege. 1- OTT = overall areatment time; SIB = simultaneous integrated boost; HR PTV = high-risk planning target volume; LR PTV = low-risk planning target volume. HR = hazard risk; 95% CI = 95% confidence interval. In bold, statistically significant values (*p* < 0.05).

Radiol med (2018) 123:48–62 https://doi.org/10.1007/s11547-017-0806-y

RADIOTHERAPY

FATTI: GBL

Hypofractionated radiotherapy with simultaneous integrated boost (SIB) plus temozolomide in good prognosis patients with glioblastoma: a multicenter phase II study by the Brain Study Group of the Italian Association of Radiation Oncology (AIRO)

Silvia Scoccianti¹^(b) · Marco Krengli² · Livia Marrazzo³ · Stefano Maria Magrini⁴ · Beatrice Detti¹ · Vincenzo Fusco⁵ · Luigi Pirtoli⁶ · Daniela Doino⁷ · Alba Fiorentino⁸ · Laura Masini² · Daniela Greto¹ · Michela Buglione⁴ · Giovanni Rubino⁶ · Federico Lonardi⁹ · Fernanda Migliaccio¹⁰ · Salvino Marzano¹¹ · Riccardo Santoni¹² · Umberto Ricardi¹³ · Lorenzo Livi¹

- 24 pts RPA III-IV, GTV < 4 cm
- Tabella constraints!

Revisione letteratura: Differenti frazionamenti Differenti definizioni volumi Differenti criteri di inclusione Max 40 pts

- 52.5 Gy in 15 fractions of 3.5 Gy and 67.5 in 15 fractions of 4.5 Gy to the SIB volume. + TMZ
- Median OS 15.1 months, median PFS 8.6 months. Actuarial OS at 12 months 65.6% ± 0.09, actuarial PFS at 12 months 41.2% ± 0.10
- Radionecrosis 4.2%

Vantaggio per QoL in shortened course

2017; 21: 3563-3575



Rectal/urinary toxicity after hypofractionated vs. conventional radiotherapy in high risk prostate cancer: systematic review and meta analysis

FATTI: PROSTATA

R. DI FRANCO^{1,2}, V. BORZILLO², V. RAVO², G. AMETRANO^{1,2}, F. CAMMAROTA², S. ROSSETTI¹, F.J. ROMANO¹, C. D'ANIELLO³, C. CAVALIERE⁴, G. IOVANE⁵, M.A. PORRICELLI⁵, M. MUTO⁶, M. BERRETTA⁷, G. FACCHINI^{1,5}, P. MUTO²

- SIB in conventional fractionation treated patients showed a significant reduced risk of acute genitourinary toxicity (OR 0.42 p=0.0001) than standard CV, as well as HypoSIB treated-patients who suffered less from each toxicity than the Hypo counterparts.
- Comparing Hypo-SIB with CV-SIB, a reduction for acute gastrointestinal and late genitourinary toxicity for the Hypo-treated patients was observed.





Confronto conv seq vs hypofx sib pelvi HRPC

Study	n	F-up	> G2 tox acuta	> G2 tox tardiva
Karklelyte 2018	221	nd	Higher with hypo but not statistically significant	nd
Wang 2021	111	38 m	No differences	No differences
Niazi 2018	329	24 m	no significant differences in grade ≥3 GU toxicity or grades ≥2 or ≥3 GI toxicity	





conclusioni

- SIB IMRT= strumento, come ogni tecnica!
- Consapevolezza delle implicazioni favorevoli e non
- Occasione di studio con nuovi metodi e IA della radiobiologia tumorale e dei tessuti sani!

