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ACCREDITAMENTO ECM/CFD Regione Lombardia per:
Radioterapisti, Fisici Sanitari, TSRM di Radioterapia
Pec assegnati nr 5,25 crediti ECM/CFD

**Congresso Inter-regionale
AIRO Lombardia e AIRO Piemonte-Liguria-Valle d'Aosta**



**L'INNOVAZIONE TECNOLOGICA
IN RADIOTERAPIA:
NUOVI STANDARD CLINICI
E PROBLEMATICHE GESTIONALI**

Centro Congressi VILLA CAGNOLA
Via Cagnola, 19 - Gazzada Schianno (VA)

Sabato 29 novembre 2014

IMRT: in quali patologie e con quali tecnologie?

Salvina Barra



*IRCCS Azienda Ospedaliera Universitaria San Martino - IST
Istituto Nazionale per la Ricerca sul Cancro-Genova*

Since 2007

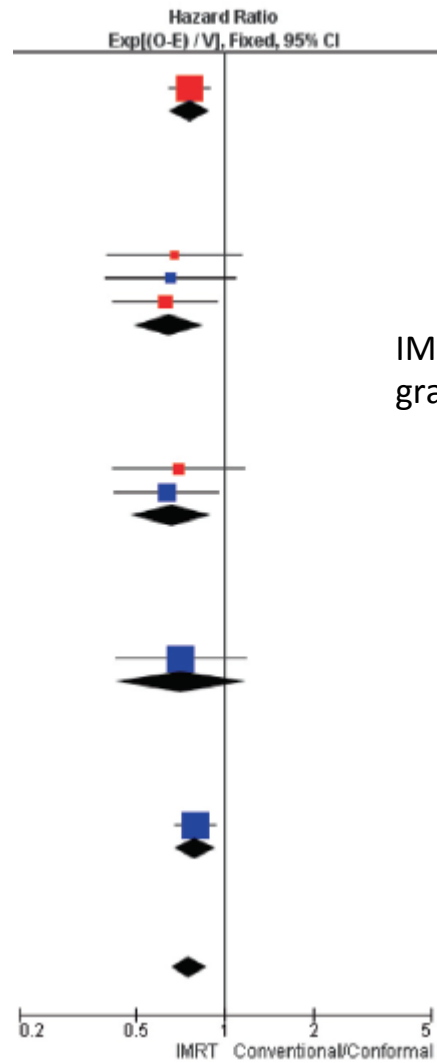
Rational Use of Intensity-Modulated Radiation Therapy: The Importance of Clinical Outcome

Study Tumor Site	Number of Patients		Endpoint	IMRT Group	Non-IMRT Group	P Value
	IMRT	Non-IMRT				
Nutting, 2011 ¹⁰ Oro- and hypopharynx	47	47	2-year overall survival, %	78	76	NA
			2-year locoregional progression-free survival, %	78	80	.34
			Xerostomia G \geq 2 (12 months/24 months), %	38/29	74/83	.0027/<.0001
			Acute fatigue G \geq 2, %	74	41	.0015
Parsport			Patients with unstimulated saliva flow from the contralateral parotid (12 months/24 months), %	47/44	0/0	<.0001/.0068
			Patients with stimulated saliva flow from the contralateral parotid (12 months), %	NA	NA	<.0001
Kam, 2007 ¹¹ Nasopharynx	28	28	Xerostomia G \geq 2 (6 weeks/6 months/12 months), %	46.4/75/39.3	85.7/92.9/82.1	.002/.069/.001
			Fractional SWSFR (6 weeks/6 months/12 months)	.32/.30/.41	.28/.20/.20	0.43/.06/.001
			Fractional SPFR (6 weeks/6 months/12 months)	.39/0.70/.90	.09/.04/.05	<.0001/<.0001/<.0001
			Patient-reported xerostomia (6 weeks/6 months/12 months)†	-38.4/-30.7/-24.3	-37.2/-31.8/-33.1	0.99/0.86/0.32
			Difficulty in speaking without need for drinking (12 months)	-30.7	-5.0	.05
Tejpal Gupta 2014	32	28	acute salivary gland toxicity	19/32	25/28	0.009
			3-years Overall survival	68	70.6	
			3-years loco-regional control.	80.5	88	



Systematic review

Intensity-modulated radiation therapy for head and neck cancer:
Systematic review and meta-analysis



IMRT versus conventional/conformal RT and xerostomia
grade 2–4



Seminars in
**RADIATION
ONCOLOGY**

Rational Use of Intensity-Modulated Radiation Therapy: The Importance of Clinical Outcome

Study Tumor Site	Number of Patients		Endpoint	IMRT Group		Non-IMRT Group		P Value
	IMRT	Non-IMRT		IMRT Group	Non-IMRT Group			

VOLUME 31 · NUMBER 36 · DECEMBER 20 2013

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Randomized Controlled Trial of Intensity-Modulated Radiotherapy for Early Breast Cancer: 5-Year Results Confirm Superior Overall Cosmesis

Conclusion

Improved dose homogeneity with simple IMRT translates into superior overall cosmesis and reduces the risk of skin telangiectasia. These results are practice changing and should encourage centers still using two-dimensional RT to implement simple breast IMRT.

Mukesh B. Mukesh 2013	228	233	overall cosmesis	good	43%	37%	0.27
				moderate	45%	41%	
				poor	12%	22%	

Clinical Investigation: Breast Cancer

Five-year Results of Whole Breast Intensity Modulated Radiation Therapy for the Treatment of Early Stage Breast Cancer: The Fox Chase Cancer Center Experience

Table 3 Frequency of treatment related effects observed in follow-up after whole-breast IMRT

Follow-up interval	Edema	Erythema	Infection	Fibrosis	Telangiectasia
≤3 mo (<i>n</i> = 377)	4.2%	5.0%	1.1%	0.00%	0.00%
3-6 mo (<i>n</i> = 402)	26.4%	14.2%	1.2%	2.2%	0.00%
6-12 mo (<i>n</i> = 592)	17.9%	8.1%	0.34%	3.7%	0.84%
12-18 mo (<i>n</i> = 426)	14.8%	6.3%	0.00%	4.2%	0.23%
18-24 mo (<i>n</i> = 394)	9.9%	5.1%	0.01%	0.05%	0.02%
24-30 mo (<i>n</i> = 308)	7.8%	0.03%	0.00%	0.04%	0.02%
30-36 mo (<i>n</i> = 299)	0.03%	0.03%	0.00%	0.08%	0.04%
≥36 mo (<i>n</i> = 427)	3.7%	3.3%	0.00%	6.8%	8.2%

Conclusions: Whole-breast IMRT is associated with very low rates of local recurrence at 5years, 83%-98% “good/excellent” cosmetic outcomes, and minimal chronic toxicity, including late fibrosis



Practical Radiation Oncology (2014) 4, 349-355



Guidelines



Refer

Retro Special Article

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Choosing Wisely: The American Society for Radiation Oncology's Top 5 list

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Prospect

[18]

Randomised controlled trial

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5. Don't routinely use intensity modulated radiation therapy (IMRT) to deliver whole-breast radiation therapy as part of breast conservation therapy.

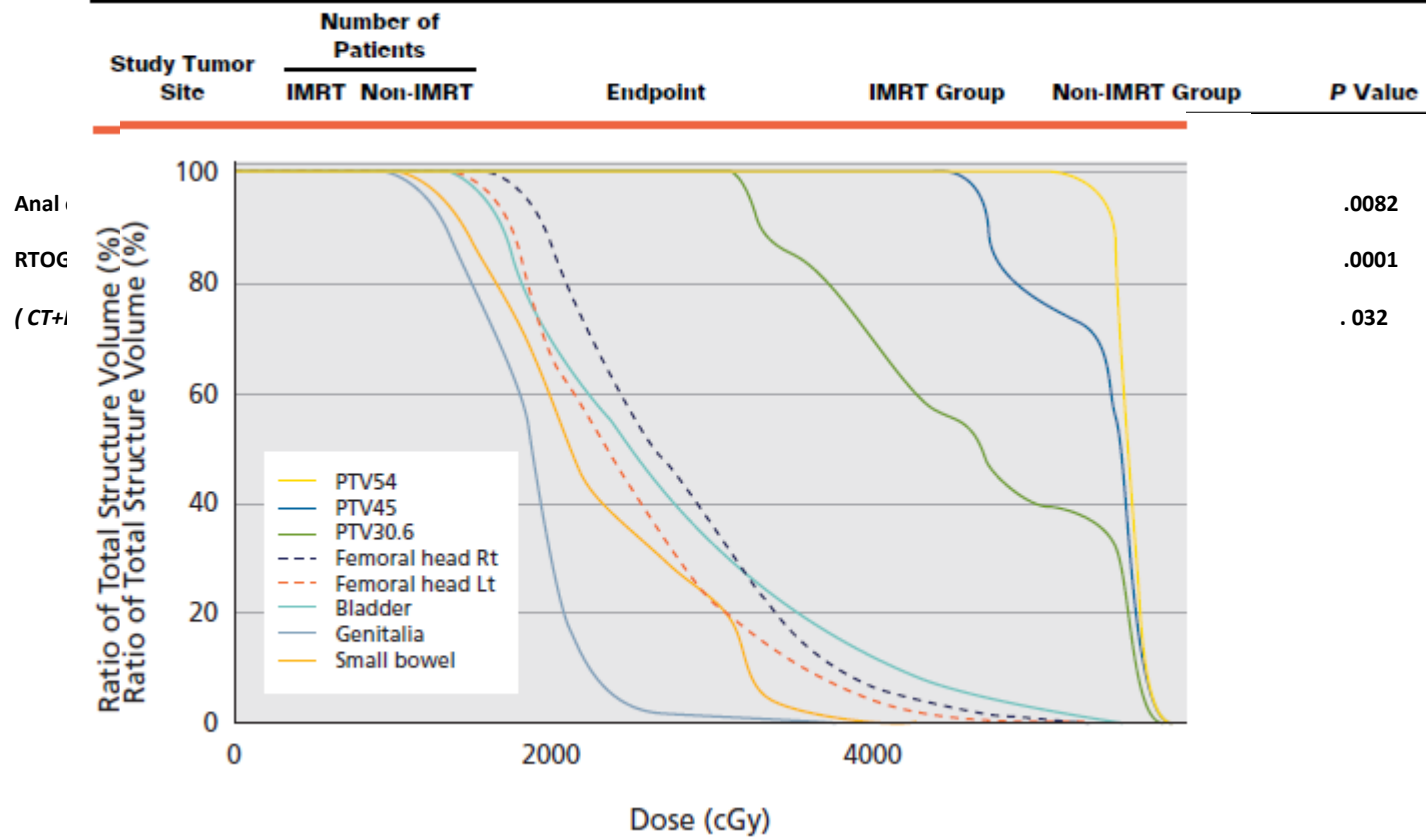
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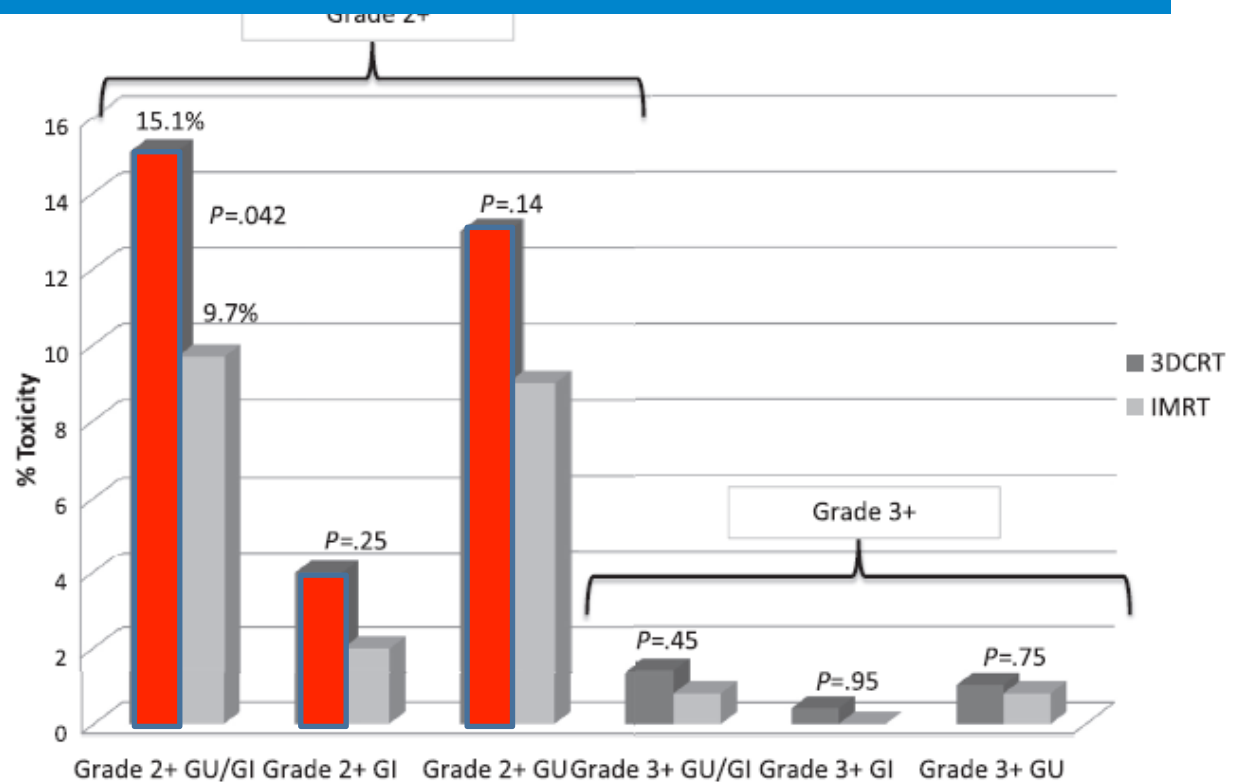
46

d focus on
recurrence



Conclusions: Intensity modulated RT is associated with a significant reduction in acute G2+ GI/GU toxicity. There is a trend for a clinically meaningful reduction in late G2+ GI toxicity with IMRT. The occurrence of acute GI toxicity and large (>15%) volumes of rectum >70 Gy are associated with late rectal toxicity.

Radiation Therapy Oncology Group protocol 0126 is a phase 3 trial that compares conventional-dose (70.2 Gy) radiation therapy with dose-escalated (79.2 Gy) conformal radiation therapy for the management of early-stage, intermediate-risk prostate cancer. The primary objective of the trial is to determine whether an improvement in overall survival can be achieved with dose escalation. In September 2003 the trial was amended to allow IMRT

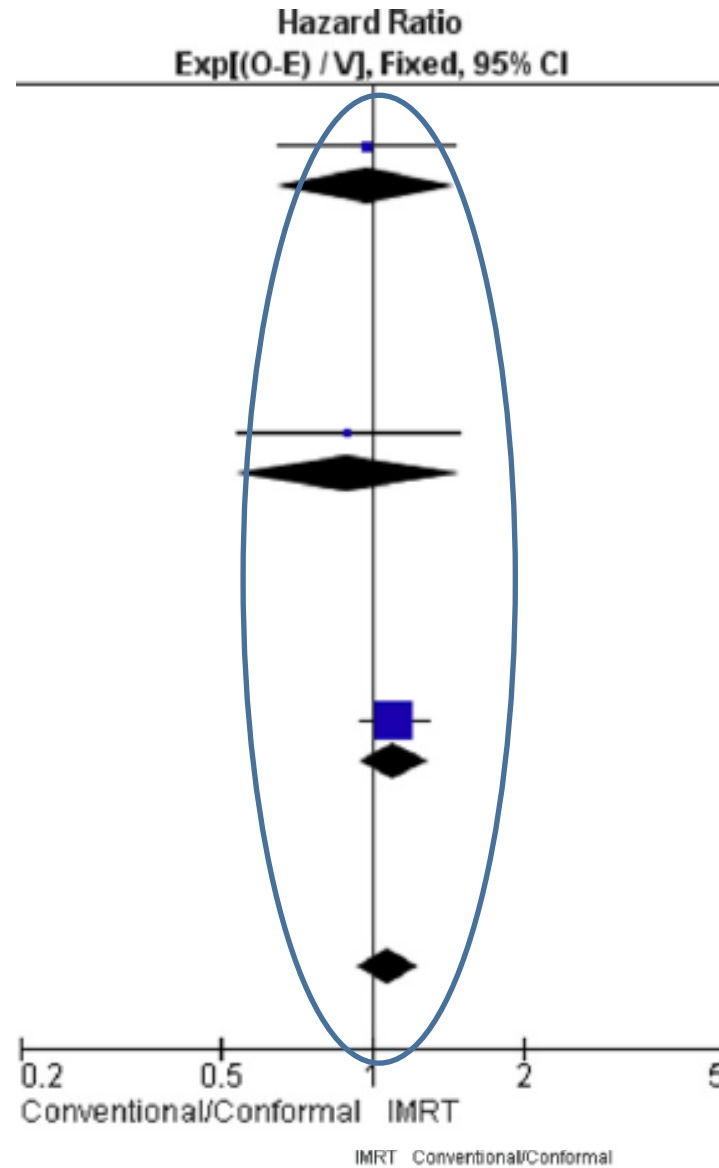


Study Tumor Site	Number of Patients		Endpoint	IMRT Group	Non-IMRT Group	P Value
	IMRT	Non-IMRT				
Chen, 2011 ¹⁵ Head and neck CUP	27	24	2-year overall survival, %	87	86	0.43
			2-year locoregional control, %	92	87	0.44
Clavel, 2011 ¹⁶ Oropharynx	100	149	3-year overall survival, %	92.1	75.2	<.001
			3-year disease-free survival, %	85.3	69.3	.001
			3-year locoregional control, %	95.1	84.4	.005
Givens, 2009 ¹⁹ All head-and-neck subsites	89	15	5-year overall survival, %	NA	53.3	0.45
Madani, 2008 ²¹ Head and neck CUP	23	18	2-year overall survival, %	74.8	61.1	0.97
			2-year freedom from distant metastases, %	76.3	68.4	0.99
Fang, 2008 ²² Nasopharynx	110	93	3-year overall survival, %	85.4	81.7	0.58
			3-year distant metastasis-free survival, %	82.6	76.7	0.37
Tejpal Gupta 2014	32	28	3-years Overall survival	68	70.6	
			3-years loco-regional control.	80.5	88	
McDonald, 2008 ²⁸ Breast	121	124	7-year overall survival,* %	91	91	0.86
			7-year disease-specific survival,* %	97	95	0.42
			7-year freedom from ipsilateral breast tumor recurrence,* %	95	90	0.36
Al-Mamgani, 2009 ³² Prostate	41	37	5-year freedom from failure, %	70	61	0.3
			5-year freedom from clinical failure, %	90	72	.07
Bazan, 2011 ³⁹ Anal canal	29	17	Distant metastasis-free survival	HR, 1.05; 95% CI, .72-1.53		0.81
			3-year overall survival, %	88	52	<.01
			3-year locoregional control, %	92	57	<.01
			3-year progression-free survival, %	84	57	<.01
			3-year colostomy-free survival, %	91	NA	NA



Systematic review

Conventional/conformal RT versus IMRT and loco-regional control
 meta-analysis



Conventional/conformal RT versus
 IMRT and loco-regional control



Available online at www.sciencedirect.com
SciVerse ScienceDirect

journal homepage: <http://www.elsevier.com/locate/rpor>



Review

The role of intensity modulated radiotherapy in gynecological radiotherapy: Present and future



Author/year	n	Patients	Technique	Field							
Mundt 2002 ¹²	40	Cervix/Endo ^a	EBRT 4F ^b vs IMRT ^c	Pelvic	<p>$p = 0.002$</p> <p>$p = 0.22$</p> <p>Reduced Tox^gG2 for IMRT vs EBRT 4F</p> <p>$p = 0.001$</p>						
Mundt 2003 ²³											
		<table border="1"> <thead> <tr> <th>Local failure</th> <th>Distant failure</th> </tr> </thead> <tbody> <tr> <td>EBRT: 4F 6%</td> <td></td> </tr> <tr> <td>IMRT: 7%</td> <td></td> </tr> </tbody> </table>		Local failure	Distant failure	EBRT: 4F 6%		IMRT: 7%			
Local failure	Distant failure										
EBRT: 4F 6%											
IMRT: 7%											
Beriwal 2007 ²¹					<p>$p < 0.05$, but Late Tox GU</p> <p>$p = 0.231$</p> <p>$p = 0.0017$</p>						
		p value ns	p value ns								
		13.8% 3 years	22%								
		14% @ 3 years	17% @ 3 years								
Kidd 2010 ²⁵											
Chen 2011 ²⁰											
			3.4%	27%							
Hasselle 2011 ²²											
Zhang 2012 ²⁴	58	Radical and Adjuvant Cervix I-II Adjuvant	IMRT + QT	Pelvic + Para							

Conclusions: Consistency in approach and reporting are vital in order to acquire the data to justify the considerable increased expense of IMRT.

IMRT - Beam Delivery

Pencil Beam



Cyberknife

Fan Beam



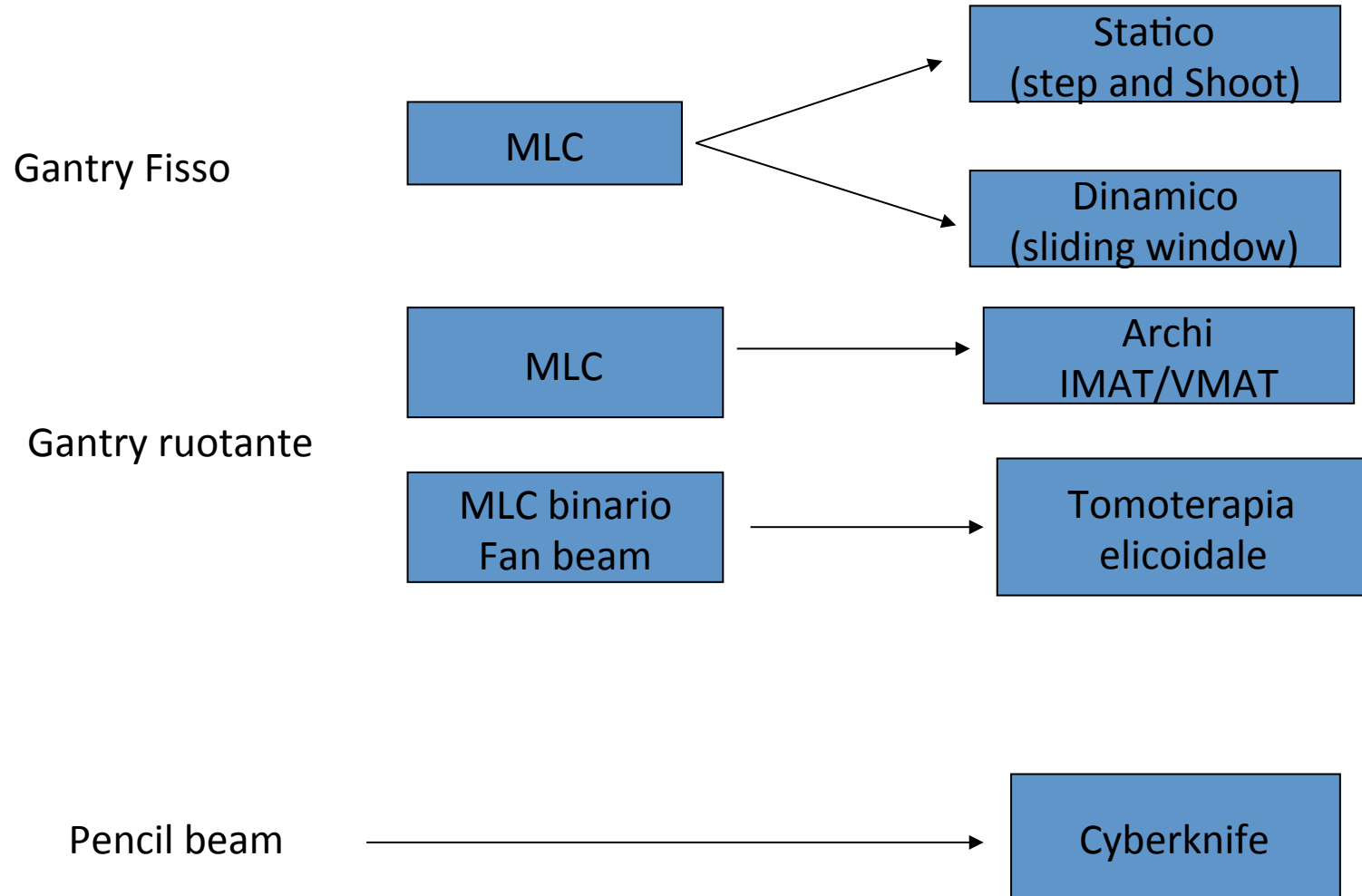
Tomotherapy

Cone Beam

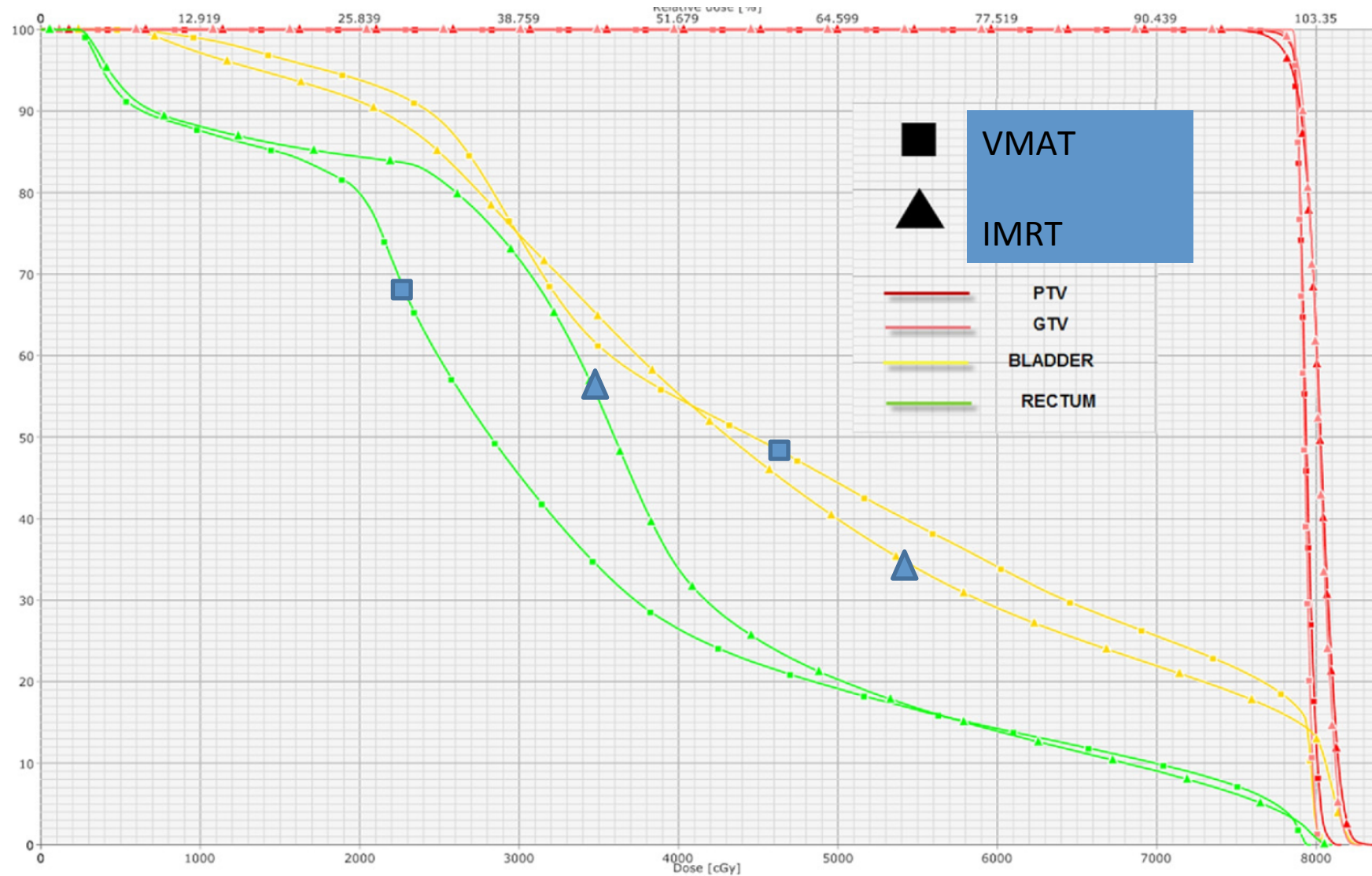


LINAC

Produzione Intensity Modulated Radioterapy (IMRT)

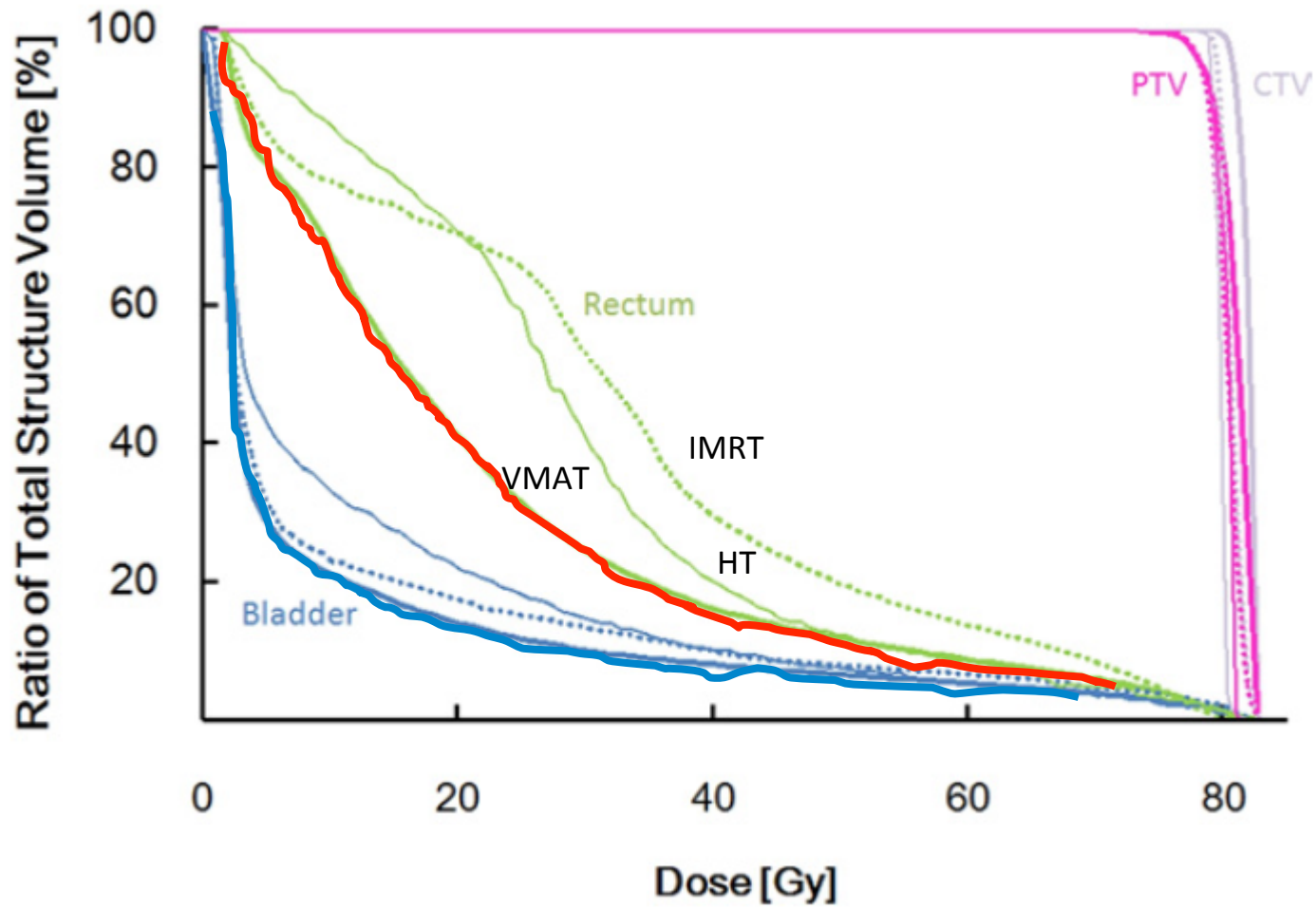


VMAT VS. 7-FIELD-IMRT: ASSESSING THE DOSIMETRIC PARAMETERS OF PROSTATE CANCER TREATMENT WITH A 292-PATIENT SAMPLE





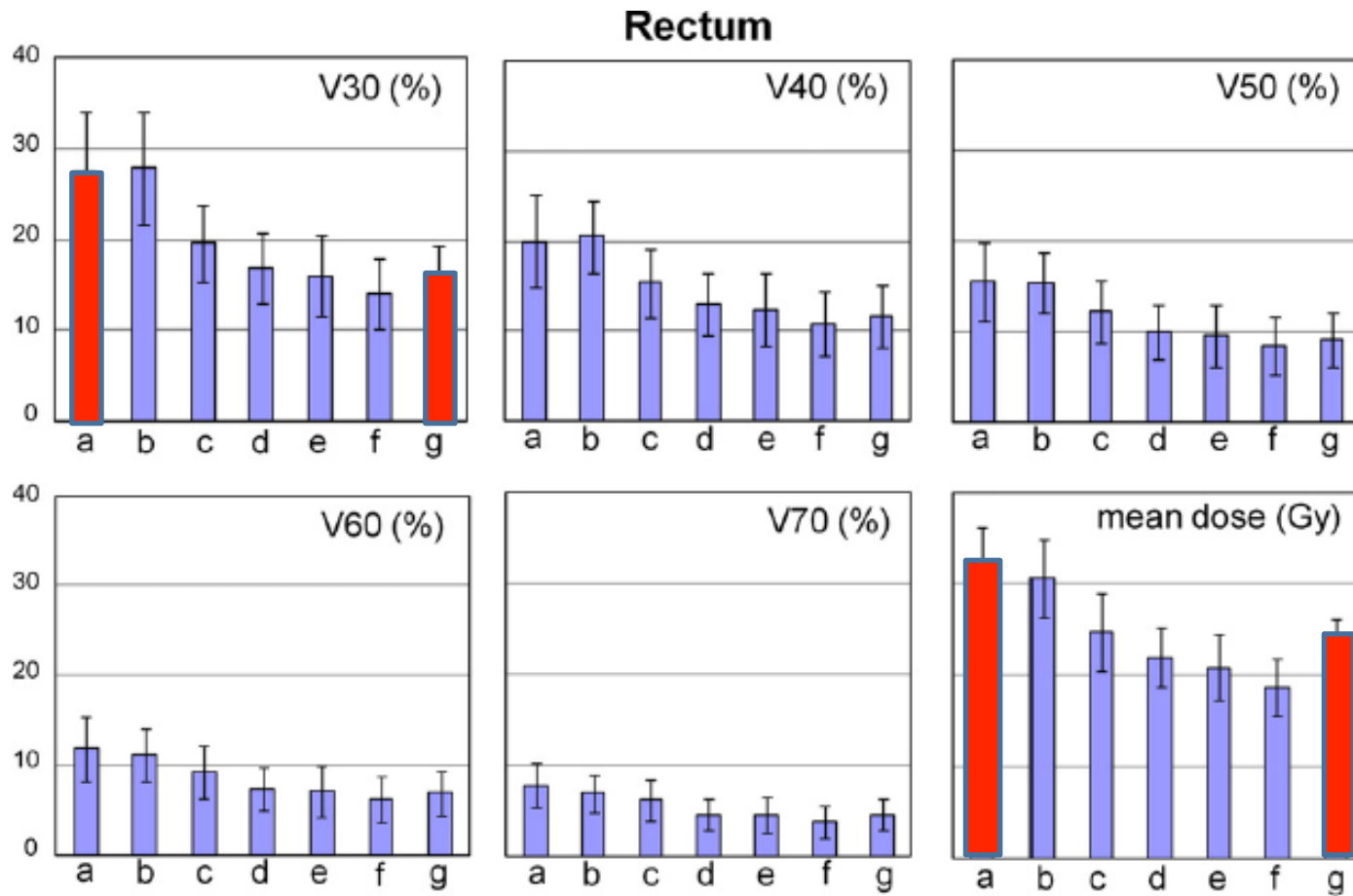
TREATMENT AND DOSIMETRIC ADVANTAGES BETWEEN VMAT, IMRT, AND HELICAL TOMOTHERAPY IN PROSTATE CANCER



Clinical Investigation: Genitourinary Cancer

A Comprehensive Comparison of IMRT and VMAT Plan Quality for Prostate Cancer Treatment

IMRT 8 beam \longrightarrow 24 \longrightarrow VMAT



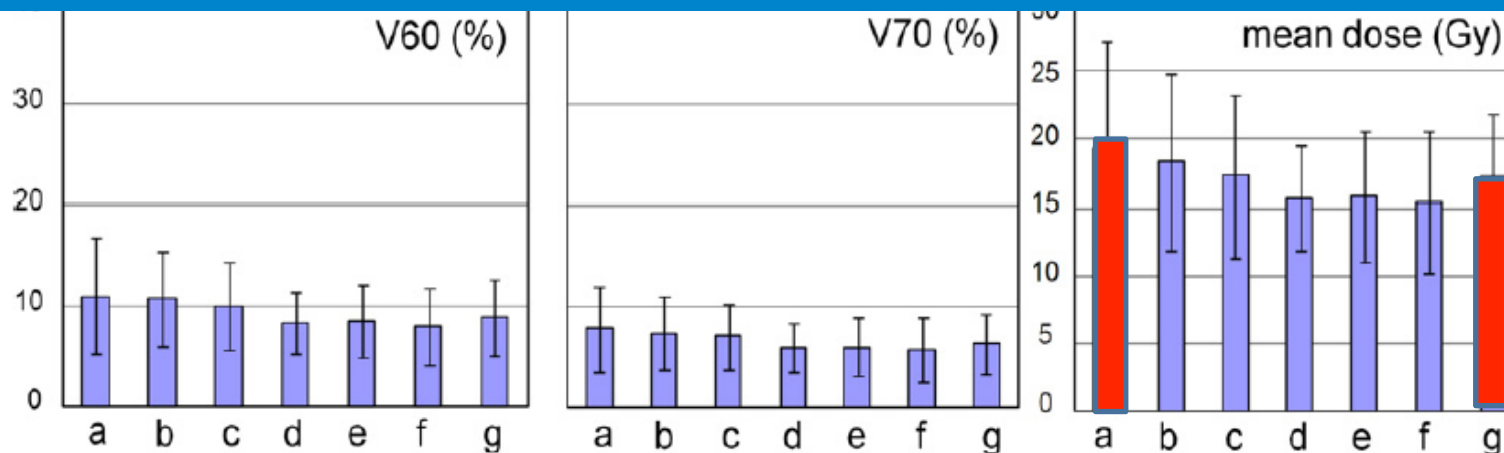
Clinical Investigation: Genitourinary Cancer

A Comprehensive Comparison of IMRT and VMAT Plan Quality for Prostate Cancer Treatment

Bladder



For IMRT plan quality to be improved such that it is comparable to that of an optimized VMAT plan, a sufficiently large number of beams has to be used. However, this would come at the expense of even longer dose delivery, increased treatment times (leading to increased intra-fractional motion) and higher economic cost





Head and neck cancer radiotherapy

A comparison of several modulated radiotherapy techniques for head and neck cancer and dosimetric validation of VMAT

	MIMiC (Corvus)	IMRT 7F (Hyperion)	IMRT 9F (Hyperion)	VMAT (Monaco)
D_{meanPTV1}	59.9 ± 0.1	60 ± 0.4	60.1 ± 0.5	60.6 ± 0.3
$D_{99\%PTV1}$	56.0 ± 0.4	51.7 ± 1.5	52.0 ± 1.6	53.3 ± 0.6
D_{maxPTV1}	67.2 ± 1.3	72.2 ± 3.7	72.4 ± 4.0	67.4 ± 1.4
D_{meanPTV2}	55.7 ± 0.7	56.4 ± 0.4	56.5 ± 0.4	56.7 ± 0.7
$D_{99\%PTV2}$	53.0 ± 0.7	50.3 ± 0.8	50.6 ± 0.8	51.6 ± 1.7
D_{maxPTV2}	62.3 ± 1.0	64.5 ± 1.4	63.4 ± 1.2	62.0 ± 0.8
$D_{\text{meanParotid}}$	19.5 ± 0.9	14.1 ± 1.1	13.9 ± 1.5	14.9 ± 0.6
$D_{\text{maxSpinalCord}}$	43.6 ± 2.4	40.8 ± 1.9	41.6 ± 1.7	42.6 ± 1.4
$D_{\text{maxBrainStem}}$	44.2 ± 7.0	45.8 ± 9.7	43.9 ± 10.3	47.8 ± 5.3
CI	1.98 ± 0.13	2.23 ± 0.13	2.23 ± 0.12	1.82 ± 0.12
HI_{PTV1}	1.12 ± 0.02	1.20 ± 0.06	1.20 ± 0.07	1.11 ± 0.01
HI_{PTV2}	1.11 ± 0.02	1.15 ± 0.02	1.13 ± 0.02	1.12 ± 0.02
MU	2551 ± 349	945.2 ± 201	925 ± 234	521.5 ± 53
Treatment tin	12.8 ± 1.7	7.6 ± 0.3	8.5 ± 0.4	6.2 ± 1.0^a
				4.3 ± 0.6^b

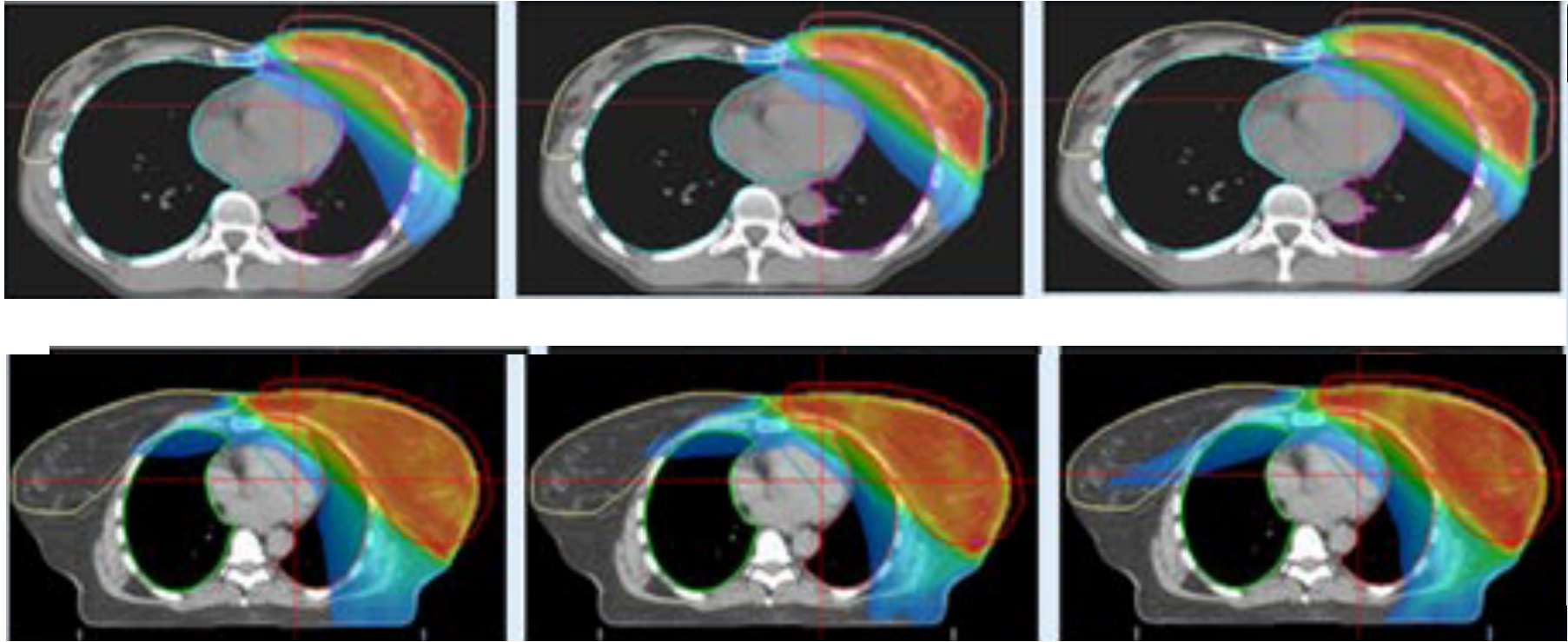
Node-positive left-sided breast cancer: does VMAT improve treatment plan quality with respect to IMRT?

	VMAT			IMRT					
	6 MV	10 MV	15 MV	6 MV	10 MV	15 MV			
	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD			
Lung left									
D _{mean} [Gy]	14.6 ±0.6	0	14.8 ±0.8	0	14.8 ±0.7	0	14.6 ±1.0	14.7 ±1.3	15.0 ±1.5
V _{30 Gy}	16.6 ±1.8	0	17.4 ±1.8	0	16.7 ±2.1	+	16.9 ±3.3	17.8 ±3.3	17.8 ±3.6
Heart									
D _{mean} [Gy]	8.9 ±1.4	0	8.8 ±1.1	0	8.6 ±1.3	0	8.6 ±1.5	8.6 ±1.8	8.4 ±1.5
V _{30 Gy} [%]	2.7 ±1.7	+	3.0 ±2.3	0	2.7 ±2.4	++	4.2 ±3.5	4.4 ±3.6	4.0 ±3.0
Oesophagus									
D _{mean} [Gy]	28.4 ±6.2	0	28.0 ±6.2	+	27.8 ±6.6	+	28.1 ±5.1	28.9 ±5.2	29.3 ±5.9
Myelon									
D _{mean} [Gy]	8.7 ±5.4	0	7.9 ±5.0	+	8.7 ±5.1	+	8.6 ±3.3	9.9 ±4.4	10.1 ±4.1
Lung right									
D _{mean} [Gy]	3.9 ±1.0	0	3.4 ±1.1	0	4.5 ±1.6	0	4.2 ±2.3	4.4 ±2.3	4.5 ±2.5
Breast right									
D _{mean} [Gy]	2.8 ±1.0	-	2.9 ±1.2	0	3.2 ±1.3	0	2.8 ±1.0	3.3 ±1.6	3.3 ±1.5



Obese breast

6 MV
10 MV
15 MV



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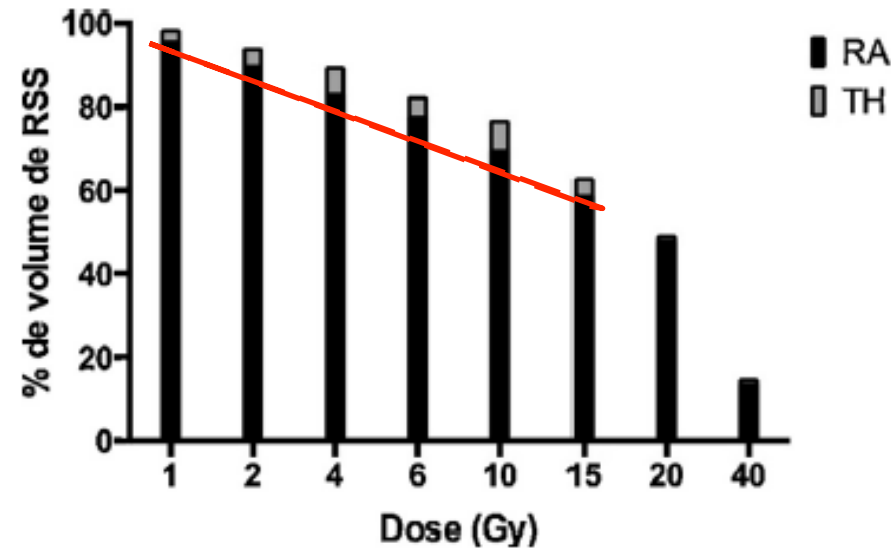
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Article original

Apport de la RCMI rotationnelle et de la tomothérapie hélicoïdale dans les cancers pelviens : étude dosimétrique prospective sur 51 patients



Results. – Although some dosimetric differences were statistically significant, helical tomotherapy and Rapid Arc provided very similar and highly conformal plans. Regarding organs at risk, Rapid Arc® provided better pelvic bone sparing with a lower non-tumoral integral dose.

COST- EFFECTIVENESS

Clinical Investigation: Head and Neck Cancer

Two-Year and Lifetime Cost-Effectiveness of Intensity Modulated Radiation Therapy Versus 3-Dimensional Conformal Radiation Therapy for Head-and-Neck Cancer

Although HNC patients receiving IMRT will likely experience reduced xerostomia and dysphagia symptoms, the small quality-of-life benefit associated with IMRT is not cost effective in the short term but may be cost-effective over a patient's lifetime, assuming benefits persist over time and patients are healthy and likely to live for a sustained period. Long-term survivors, such as HPV-positive OPSCC patients, may realize the most economic value of IMRT.

Clinical Investigation

Cost-Effectiveness Analysis of Intensity Modulated Radiation Therapy Versus 3-Dimensional Conformal Radiation Therapy for Anal Cancer



In our base model, IMRT was a cost-ineffective strategy despite the reduced acute treatment toxicities and their associated costs of management.

Contents lists available at [ScienceDirect](#)

Radiotherapy and Oncology

ELSEVIER

journal homepage: www.thegreenjournal.com

IMRT was estimated to have a modest long term advantage over 3DCRT in terms of both improved effectiveness and reduced cost

Cost-effectiveness

A decision model to estimate the cost-effectiveness of intensity modulated radiation therapy (IMRT) compared to three dimensional conformal radiation therapy (3DCRT) in patients receiving radiotherapy to the prostate bed



CONCLUSIONI

EVIDENZE - IMRT

NH : minor tossicità

Prostata: r

Mammella:

Ano: minor

T.Ginecolo

POSSIBILITÀ

Tecniche S

Riduzione

Dose escalation

Ipo-frazion



VMAT vs IMRT

VMAT vs IMRT :

VMAT vs TOMO :

VMAT vs TOMO :

VMAT vs IMRT e TOMO :

VMAT vs IMRT e TOMO :

in casi semplici risultati comparabili ,in casi complessi la TOMO può migliorare la copertura del target

riduzione MU quindi minore scatter e leakage

riduzione tempi di trattamento quindi maggiore confort paziente , minori movimenti intra-fraction

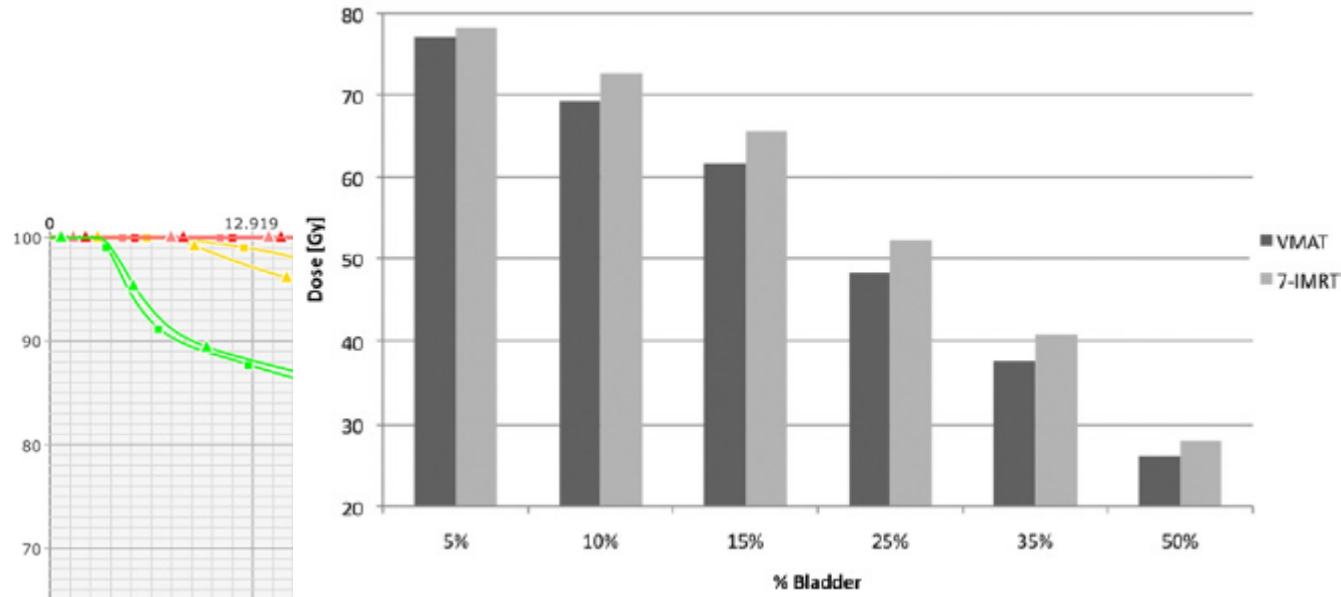
minor dose a OAR)

in casi semplici risultati comparabili ,in casi complessi la TOMO può migliorare la copertura del target

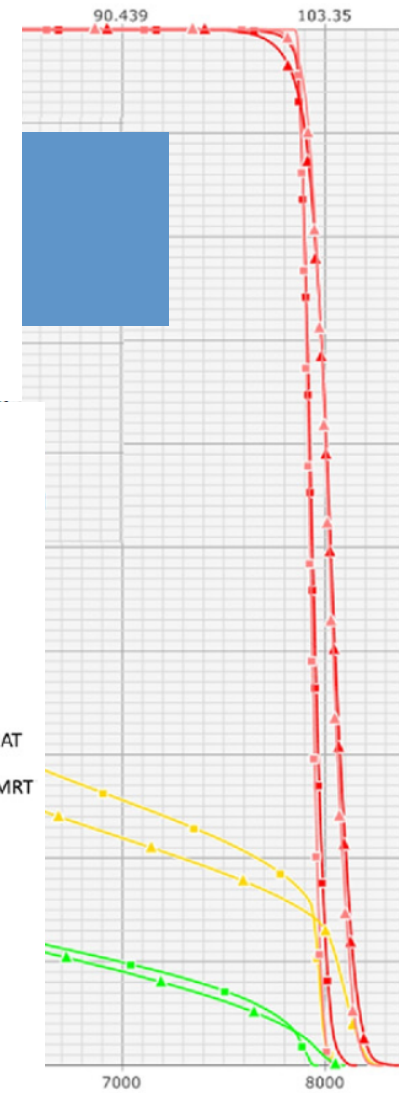
riduzione MU quindi minore scatter e leakage

riduzione tempi di trattamento quindi maggiore confort paziente , minori movimenti intra-fraction

Dose Received as % of Bladder Volume



ETERS
MPLE



Dose Received as % of Rectal Volume

