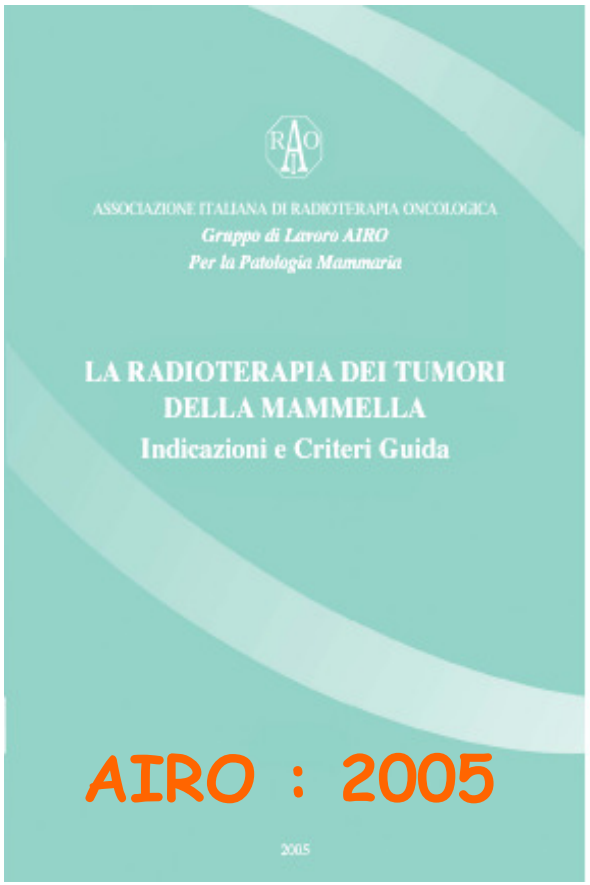
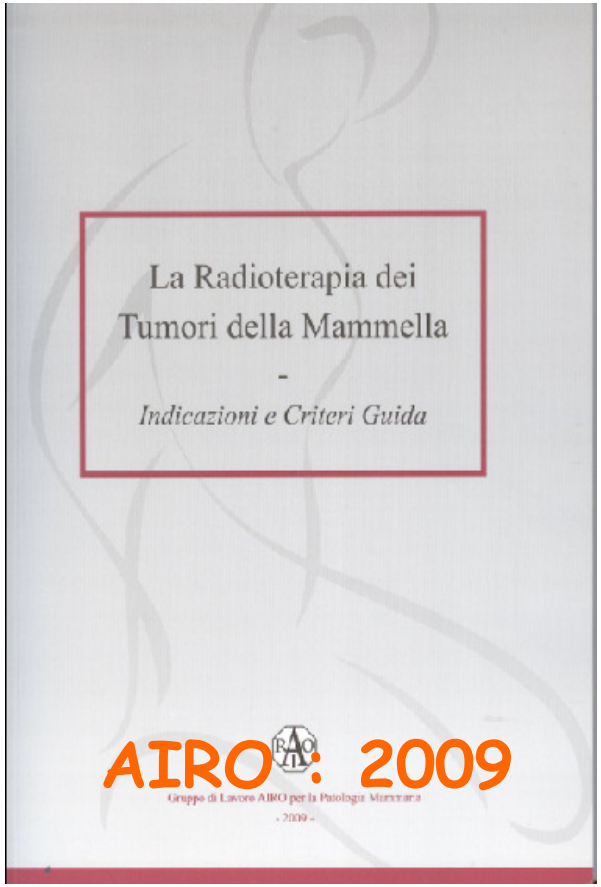
Hi-tech treatments: results, perspectives, suggestions for future comparative effectiveness studies: BREAST CANCER

Dr. A.Bruni, Dr. F. Bertoni
- AOU Policlinico di Modena -

Brescia – October 5th 2012





….Several irradiation modalities are well defined in many different *"AIRO documents"* from 1997 until now….

Radiotherapy and Oncology 51 (1999) 79–85

Patterns of radiotherapy for early breast cancer in Northern Italy compared with European and

Riccardo Valdagni[a,*], Maurizi
[a]Department of Radiation Oncology, Cusa & Cur
[b]Department of Radiation Oncology, Ospedale S.Chi
Received 13 August 1998; received in revised form

Table 2 - Treatment position and immobilization systems in 66 Italian radiation oncology centers

	Number (percentage)
Position	
supine	66 (100)
prone*	1 (1.5)
Arm position	
perpendicular to the trunk	4 (6)
above the head	25 (38)
both arms above the head	24 (36)
not specified	13 (20)
Use of breast board°	
regularly	22 (33)
occasionally	14 (21)
Use of immobilization device	
never	33 (50)
always or occasionally†	33 (50)
Recording of immobilization system and patient position	
photography	37 (56)
description	35 (53)
drawing	20 (30)
not documented	9 (14)

* To treat women with large, pendulous breasts.
° The breast board was used to 1) level the patient in the craniocaudal direction, 2) shift the breast downwards or 3) avoid collimator rotation and, consequently, junction problems between breast and supraclavicular fields, when the latter needed to be irradiated.
† Depending on treatment complexity.

Tumori, 94: 333-341, 2008

Radiotherapy in Italy after conservative treatment of early breast cancer. A survey by the Italian Society of Radiation Oncology (AIRO)

Cynthia Aristei[1], Maurizio Amichetti[2], Mario Ciocca[3], Luigia Nardone[4], Filippo Bertoni[5], and Cristiana Vidali[6]

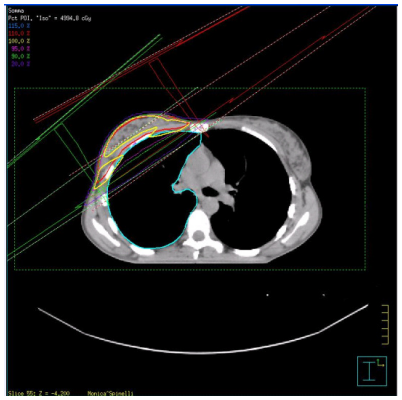


Table 4 - Irradiation technique in 66 Italian radiation oncology centers

	Number (percentage)
Two tangential opposing fields	66 (100)
Technique	
isocentric	49 (74)
fixed source-skin distance	11 (17)
not specified	6 (9)
Treatment units	
linear accelerator	62 (94)
^{60}Co unit	13 (20)
X-ray energy	
4-6 MV	60 (91)
7-10 MV	6 (9)
>10 MV*	2 (3)
Wedge filters	
routine†	65 (98)
not routine	1 (1.5)
Bolus°	10 (15)
Posterior field borders were matched with lung profile by	
rotating collimators	51 (77)
using a breast board	28 (42)
Beam divergence removal methods	
hemifield technique using	24 (36)
independent jaw	6/24
half-beam blocks	18/24
beam central axis disalignment	10 (15)
not specified	32 (48)
Accepted maximum central lung distance[14]	
2 cm	43 (65)
3 cm	9 (13.5)
from 1.5 to 2.5 cm	11 (17)
no limitation to lung irradiation	1 (1.5)
not specified	2 (3)
Adjacent field junction optimization by	
couch isocentric rotation	23 (35)
asymmetric collimator	6 (9)
not specified	37 (56)

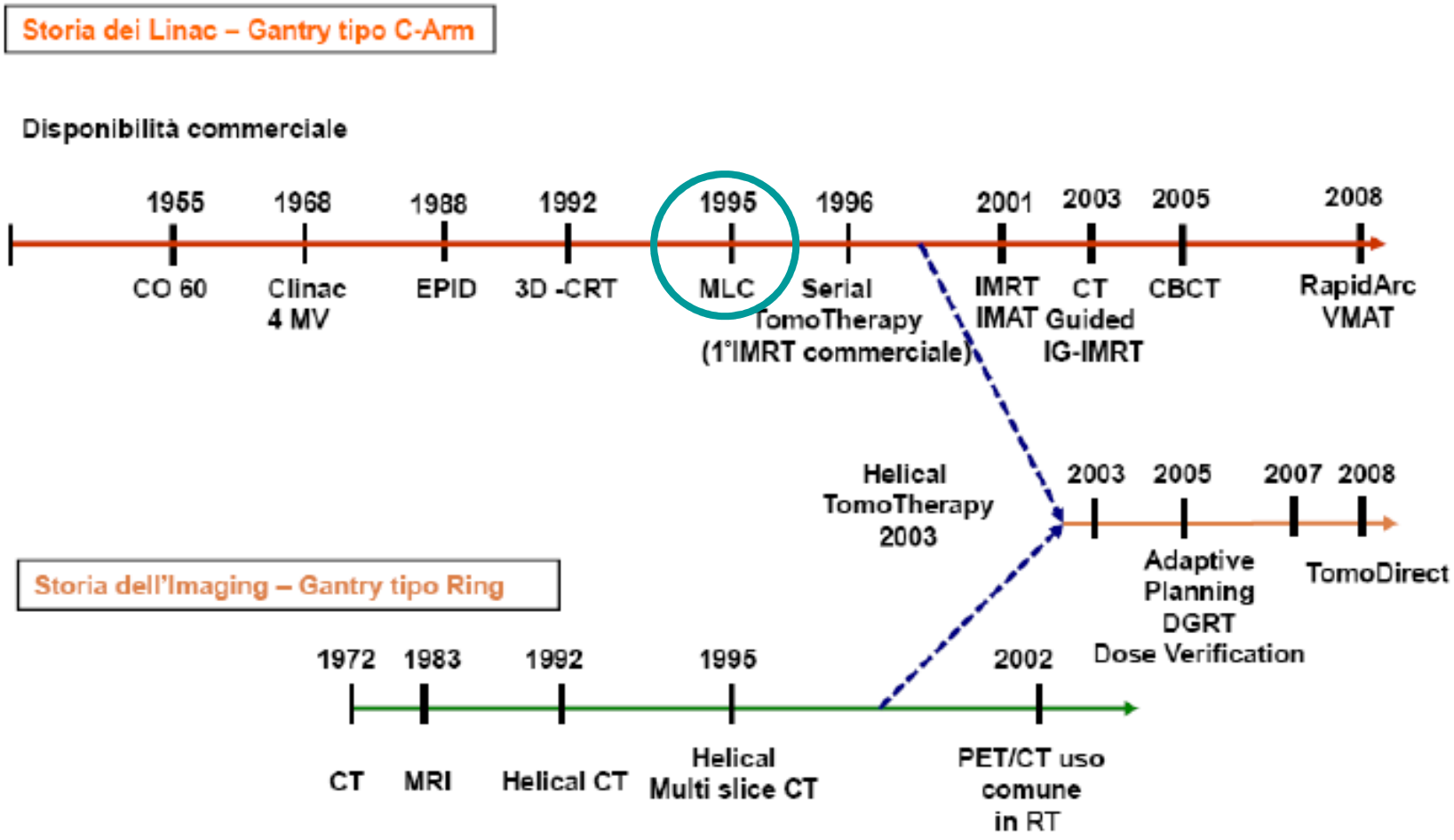
* To treat large breasts.
† Mostly wedge filters (94%), rarely 3-D Ellis compensators.
° To shift the maximum dose to the breast surface when over 4-6 MV were used or to treat the skin at any energy level.

Usually :

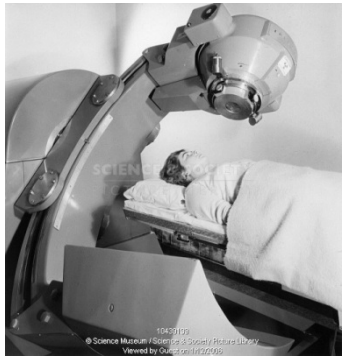
- Supine set up
- High energy X Ray photons and/or electrons
- Static techniques using tangential opposite beams and w/f
- Multiportal techniques to deliver RT to nodal stations

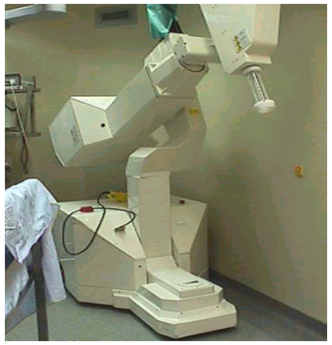
C. Aristei, et al. : Tumori 2009

Radiotherapy Evolution



...and so on....





Radiation Therapy Units

Radiotherapy : impact of recent technical advances

3DCRT	3D-conformal radiation therapy: treatment technique using the standard three-dimensional CT information to shape treatment fields to the contour of the tumor and to minimize the dose to normal tissues
4DCT-scan	Four-dimensional computed tomography scan: respiration-correlated CT scan used to visualize and account for tumor motion. The fourth dimension is time
4DRT	Four-dimensional radiation therapy is the explicit inclusion of the temporal changes in anatomy during the imaging, planning, and delivery of radiotherapy [56]
CBCT	Cone-beam CT refers to the use of a cone shaped kilovoltage X-ray beam and a flat panel imaging device integrated into a linear accelerator to generate CT images. CBCT permits visualization of the tumor position during treatment
Coaching	Audio-coaching is used to optimize breathing regularity during RGRT. Visual-coaching provides visual feedback of the breathing pattern to the patient in order to optimize breathing depth during RGRT
DVH	Dose volume histograms graphically display doses to the tumor and all separate normal organs. A DVH is used to optimize treatment plans, and to compare different treatment plans
IGRT	Image-guided radiation therapy: modern linear accelerators have integrated X-ray imaging devices and cone-beam CT scanners, making it possible to verify tumor position before and during treatment. The ability to check the tumor position during treatment allows for smaller safety margins and better sparing of normal tissues
IMRT	Intensity modulated radiation therapy techniques use treatment fields with varying dose intensity within each field, thereby improving target coverage and (mostly) sparing normal tissue
Hypofractionation	Treatment delivery in a reduced amount of treatment fractions, using high doses per fraction. Extreme hypofractionation is used in stereotactic radiation therapy
MVCT	See cone-beam CT: megavoltage CT is a cone-beam CT scanner integrated in a linear accelerator using the megavoltage treatment beam instead of a separate kilovoltage source
RGRT	Respiration-gated radiation therapy, also known as Gating. Advanced treatment technique that switches the radiation beams on and off according to respiration. Irradiating only during end-inspiration or only during end-expiration allows for smaller radiation fields in moving tumors, sparing normal tissues. The availability of 4DCT scanning and IGRT is mandatory for this treatment technique
SRT	Stereotactic radiation therapy is a high-precision technique used to deliver high-dose fractions of radiation in only 3–8 sessions

BIGART???

C.J.A. Haasbeek et al, 2009

WHAT'S NEW in 2012 ?????

Translational Research

…. Breast cancer α/β ratio is estimated to be around four. It suggests that hypofractionated regimens should be more effective than conventional fractionation. Moreover, to enforce the radiobiological rationale of hypofractionation in breast cancer is the shorter treatment time from 6 weeks to 3 weeks: the shorter the total treatment time, the lower the potential of repopulation of cancer cells, thus improving local control.

Qi XS et al., Radiother Oncol 2011

RMH/GOC trial **(2006)**

START-A trial **(2008)**

START-B trial **(2008)**

ONTARIO trial **(2010)**

Past Experience

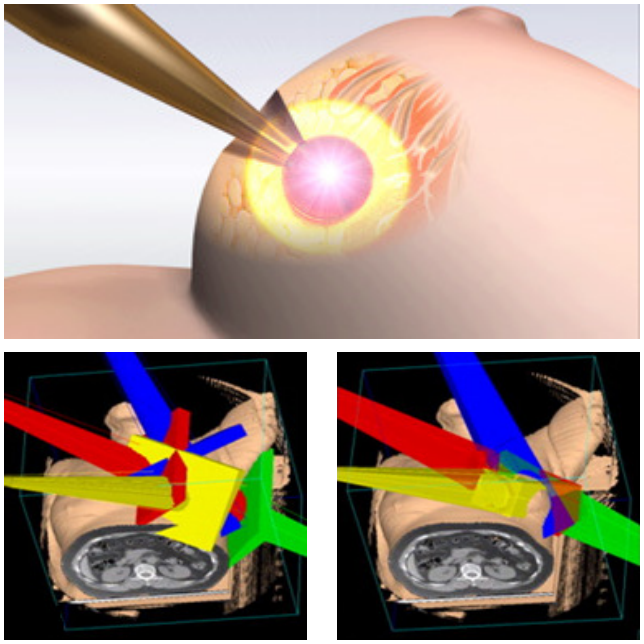
Reference (N)	Whole-Breast Dose Fractionation Schedule	Boost Sequence Dose Fractionation Schedule	Total Dose to Lumpectomy Site/ Treatment Time	Grade 0/1	Grade ≥ 2
Fisher et al[26] N = 171	2 Gy in 23 fractions	Sequential 2 Gy × 7 fractions	60 Gy/6 weeks	62%	38%
van der Laan et al[27] N = 90	1.81 Gy in 28 fractions	Simultaneous 0.49 Gy × 28 fractions	64.4 Gy/5.5 weeks	68%	32%
Freedman et al[28] N = 73	2 Gy in 23-25 fractions	Sequential 2 Gy × 7 fractions	60-66 Gy/6.5 weeks	79%	21%
Freedman et al[20] N = 74	2.25 Gy in 20 fractions	Simultaneous 0.55 Gy × 20 fractions	56 Gy/4 weeks	77%	23%
Vicini et al[29] N = 262	1.8 Gy in 25 fractions	Sequential 2 Gy × 8 fractions	61 Gy/6.5 weeks	56%	44%
Chadha[a] N = 74	1.8 Gy in 23 fractions	Sequential 2 Gy × 7 fractions	60.8 Gy/6.5 weeks	76%	24%
Chadha[a] n = 50	2.7 Gy in 15 fractions	Simultaneous 0.3 Gy × 15 fractions	45 Gy 3 weeks	96%	04%

[a] Current study.

PBI

....Several large, prospective, randomized trials are nearing target accrual or have been completed.... .

- **IRMA Trial**
- **Florence Trial**
- **IORT (ELIOT/TARGIT)**
- **NSABP RTOG 0413**
- **RAPID (Canadian trial)**
- .....



The American Society for Radiation Oncology has also published a *consensus statement* to guide the use of PBI until some of the phase III trials are more mature

McCormick, J Natl Comp C Netw 2012

Accelerated Hypo-RT

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ELSEVIER FULL-TEXT ARTICLE

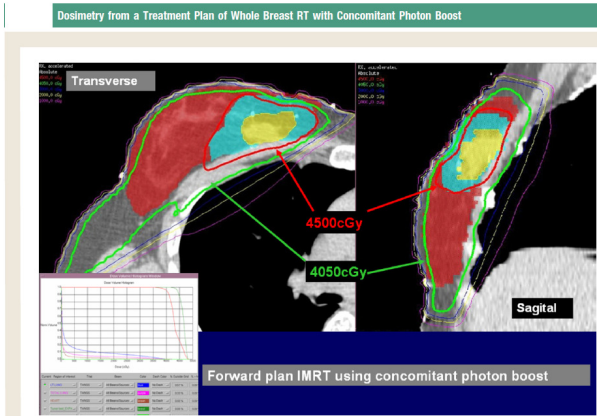
2012

Clin Breast Cancer. 2012 Feb;12(1):57-62. doi: 10.1016/j.clbc.2011.09.002. Epub 2011 Nov 6.

Comparative acute toxicity from whole breast irradiation using 3-week accelerated schedule with concomitant boost and the 6.5-week conventional schedule with sequential boost for early-stage breast cancer.

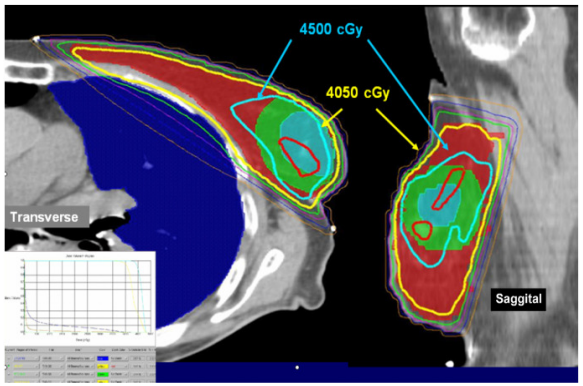
Chadha M, Vongtama D, Friedmann P, Parris C, Boolbol SK, Woode R, Harrison LB.
Department of Radiation Oncology, Beth Israel Medical Center, New York, NY 10003, USA. mchadha@chpnet.org

The 3d-CRTusing 2 tangent fields with dynamic wedge
+
1-3 conformal fields for the boost dose



40.5 Gy/15Fx of 2.7Gy each to WB
45 Gy/15Fx of 3Gy each to surgical bed
with concomitant boost

4- to 7-segment field-in-field forward plan
+
1 to 3 conformal fields with Photons or e- for boost dose

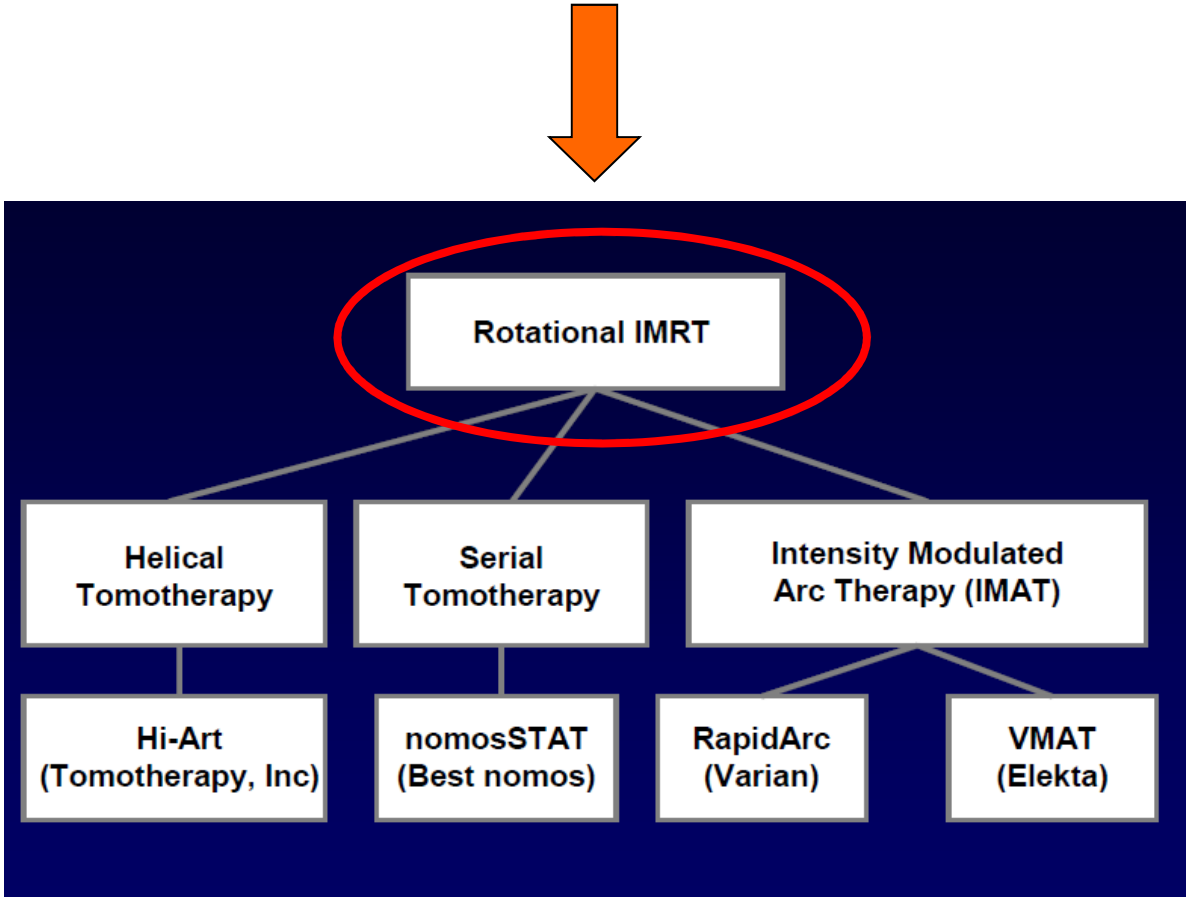


Toxicity profile of
accelerated schedule is acceptable

Novel Technologies and IMRT

.....From Static IMRT

(“Step and Shoot” or “Sliding indows”)...



IMRT-1

Review, 2012

NCBI Resources How To

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National Institutes of Health

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ELSEVIER FULL-TEXT ARTICLE

Clin Oncol (R Coll Radiol). 2012 Sep;24(7):488-98. Epub 2012 Jun 28.

Intensity-modulated Radiotherapy in the Treatment of Breast Cancer.

Dayes I, Rumble RB, Bowen J, Dixon P, Warde P; Members of the IMRT Indications Expert Panel.
McMaster University, Hamilton, ON, Canada.

MedLine → 125 Articles
Embase → 173 Articles
NIH → 1 Guideline
Astro Conference → 2 Conference
ASTRO Congress → 13 Abstract

For Fully Review

13 articles

2 Conference
5 Abstract

Reference	Comparison	Dose	Total *N*	Disease stage	Median follow-up (months)	Outcomes reported
Retrospective cohort study						
[20]	IMRT	46–50 Gy/2 fractions + 14–20 Gy	399	T0–2	NR	AE
	TanRT	46–50 Gy + 10–18 Gy	405			
[16]	IMRT	45 Gy/1.8 fractions + 16 Gy/2 fractions	93	T0–2B	56.4	AE
	TanRT	45 Gy/1.8 fractions + 16 Gy/2 fractions	79			
[17]	IMRT	50 Gy [37–68 Gy]	121	T0–3	75.6	TRO
	TanRT	50 Gy [44–50.4 Gy]	124		90	AE
Historically controlled trial						
[15]	IMRT	60 Gy/2 fractions [60–66]	73	T0–2	NR	AE
	TanRT	64 Gy/2 fractions [50–64]	60			
Prospective cohort study						
[18]	MARA1-IMRT	40 Gy/2.5 fractions + 4 Gy/0.25 fractions	99	pT1–3	24	TRO
	MARA2-IMRT	50 Gy/2 fractions + 10 Gy/0.40/fractions	102	pT1–4	24	AE
	TanRT	50.4 Gy/1.8 fractions + 10 Gy/2.5 fractions	131		42	
Randomised controlled trial						
[19]	IMRT	50 Gy/2 fractions	170	Early stage breast cancer	NR	AE
	TanRT (WC)	50 Gy/2 fractions	161			

IMRT, intensity-modulated radiotherapy; TanRT, tangential radiotherapy; NR, not reported; AE, adverse effects; TRO, treatment-related outcomes.

Only 2 of 8 articles were about **TRO**

IMRT-1

Reference	Adverse effects	IMRT (%)	TanRT (%)	*P* value
MARA2 vs. TanRT: OR=1.47, p=0.16				
Randomis				
[19]				
				P value
				0.06
				0.002
				0.001
	Pain (grade 2–4, NCI CTC 2.0)	23.5	25.5	0.68

MACDONALD MW, IJROBP, 2008
MORGANTI AG, Radiother Oncol, 2009

Reference	Adverse effects	IMRT (%)	TanRT (%)	*P* value
Retrospective cohort study				
[20]	Acute dermatitis			
	Grade 0/1	48	25	<0.0001
	Grade 2/3	52	75	
	Time with acute dermatitis			
	Grade 0/1	82	29	<0.0
	Grade 2/3	18	71	
	Subgroup analysis detected significant improvements in grade 2/3 toxicity in favour of treatment with IMRT for patients with small ($P = 0.0015$), medium ($P < 0.0001$) and large ($P < 0.0001$) breast sizes.			
[16]	Acute toxicity (Grade ≥2)			
	Dermatitis	41	85	<0.001
	Breast oedema	1	28	<0.001
	Pain	8	8	0.78
	Hyperpigmentation	5	50	<0.001
	Late toxicity (grade ≥2)			
	Hyperpigmentation	7	17	0.06
	Breast oedema	1	25	<0.001
	Fat necrosis	0	1	0.46
	Induration/fibrosis	0	6	0.11
	Good/excellent cosmesis	99	97	0.60
[17]	Acute toxicity (RTOG scale)			
	Grade 2–3 dermatitis	39	52	0.047
	Breast cellulitis	2	4	0.45
	Late toxicity			
	Radiation pneumonitis	1	2	1.0
	Lymphedema	0	4	0.06
	Fat necrosis	0	2	0.5
	Second malignancy	3	4	0.84

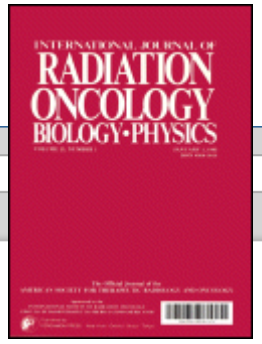
Only 2 papers reported on breast cancer outcomes, perhaps due to the short FUP times in some studies.

- No evidence for differences in local recurrence rates.
- Less Acute Toxicity

Whether this potential advantage is true of locoregional IMRT treatments remains unknown

Dayes I. et al,Clin. Onc., 2012

IMRT-2



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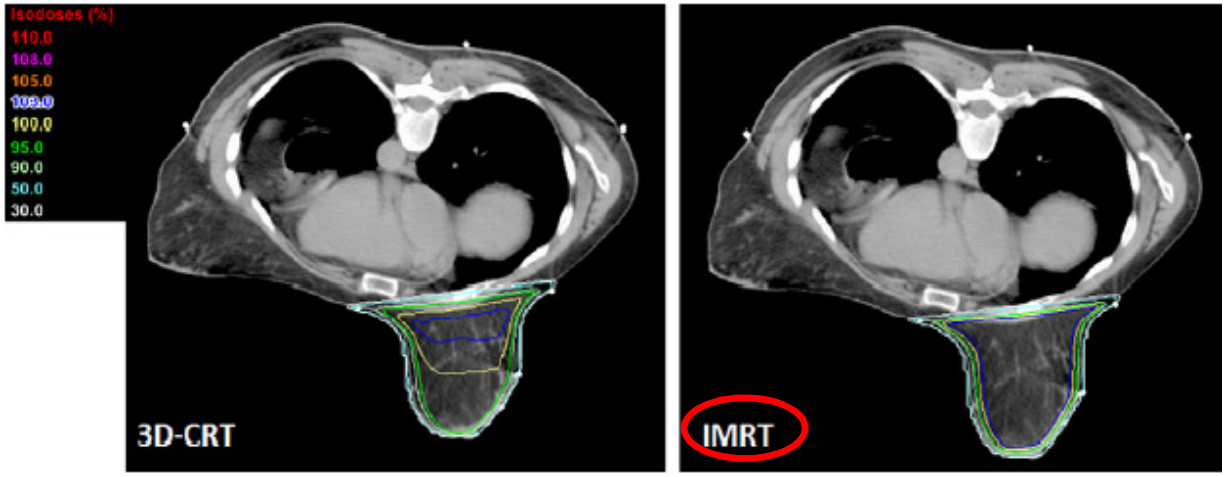
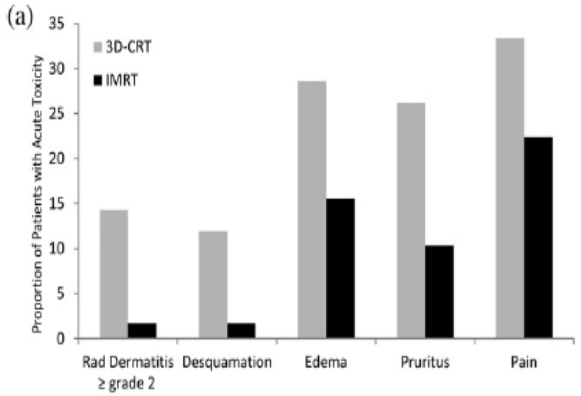
Int J Radiat Oncol Biol Phys. 2012 Mar 1;82(3):e415-23. Epub 2011 Oct 20.

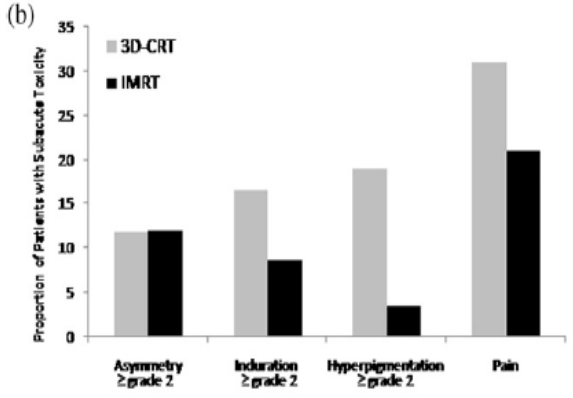
Prone hypofractionated whole-breast radiotherapy without a boost to the tumor bed: comparable toxicity of IMRT versus a 3D conformal technique.

Hardee ME, Raza S, Becker SJ, Jozsef G, Lymberis SC, Hochman T, Goldberg JD, DeWyngaert KJ, Formenti SC.
Department of Radiation Oncology, New York University School of Medicine, New York, NY 10016, USA.

From 2007 to 2010 → 97 pts





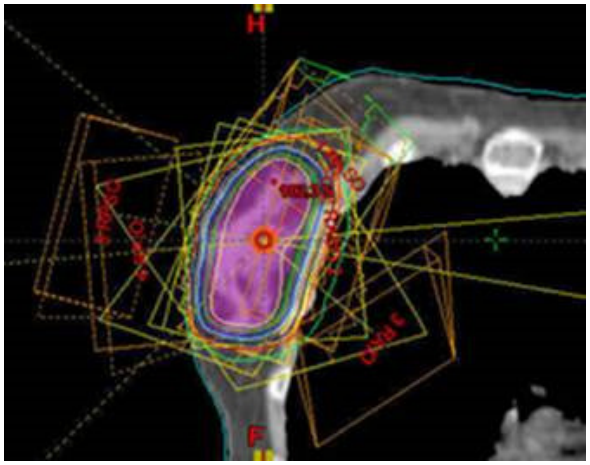


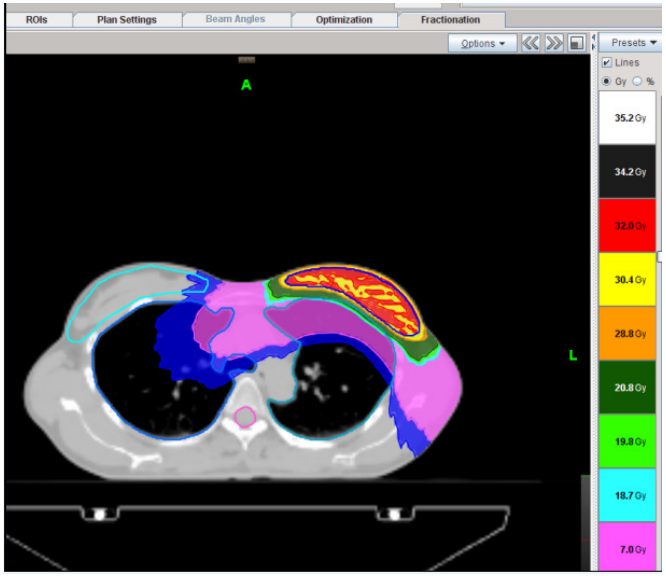
- Median mean dose p< 0,0001
- Median Dmax p<0,0001
- Dose Homogeneity p<0.0001

IMRT better

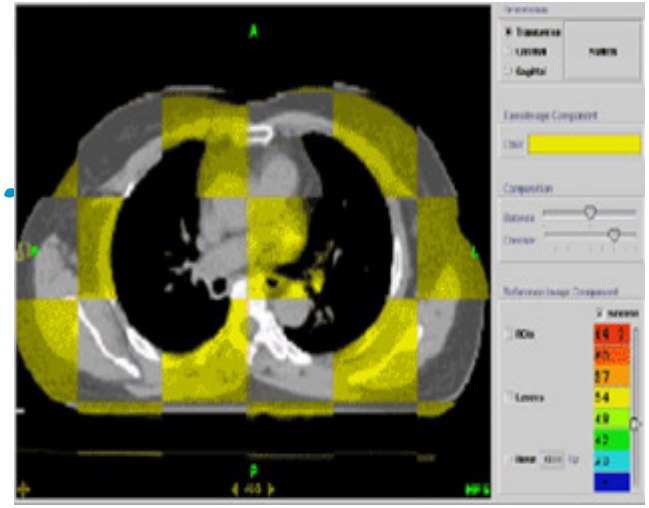
Less G2 hyperpigmentation during subacute FUP

.. From IMRT….





….to IGRT……



…to obtain more accurate treatment planning and delivering with a more accurate set up control…

Novel Technologies and IGRT

RapidArc-Varian

Imaging 2-D: Kilovoltaggio

Megavoltaggio

Imaging 3-D: CT-on rails

CBCT

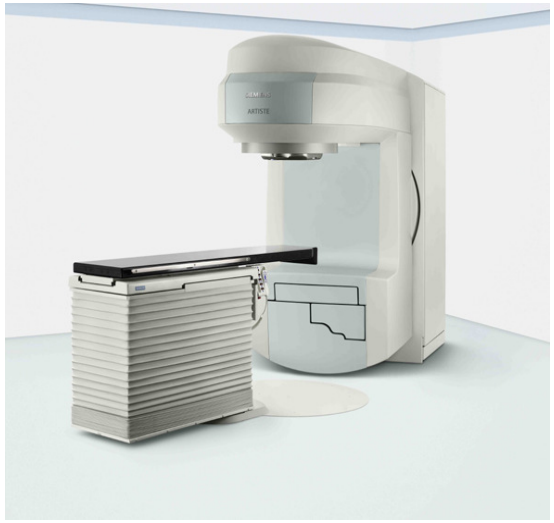
MVCBCT

MVCT

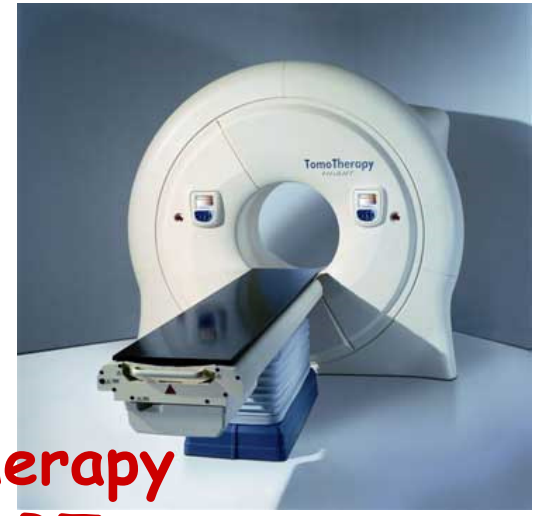
RMN

Imaging 4D : ????

VMAT - Elekta



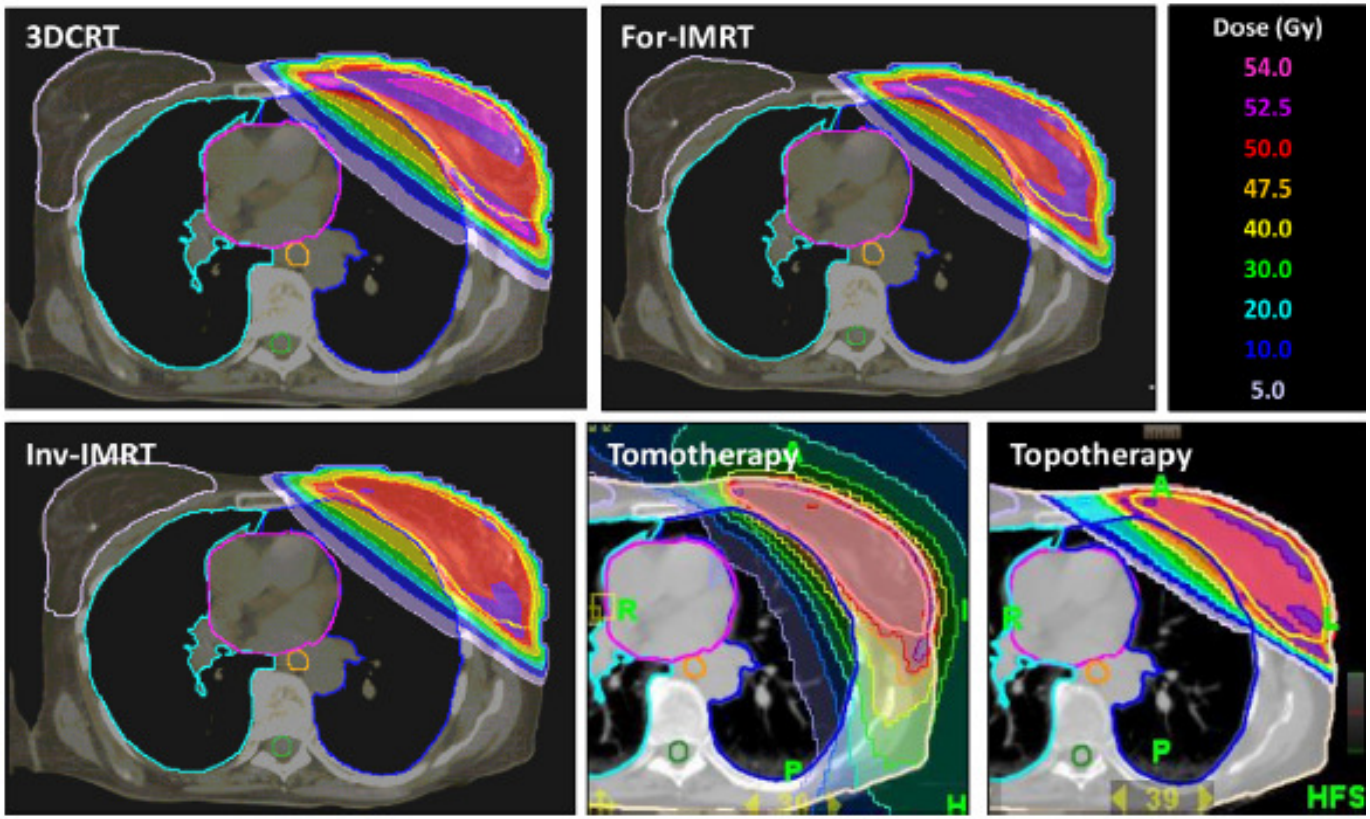
Artiste- Siemens



Tomotherapy
Hi-aRT

IGRT/IMRT

Datas about dosimetric comparison and variations between different treatments are (probably!) well known



Schubert L et al , Radiot Oncol, 2011

IGRT/VMAT - 1

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RADIATION ONCOLOGY

2012

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Radiat Oncol. 2012 Aug 28;7(1):145. [Epub ahead of print]

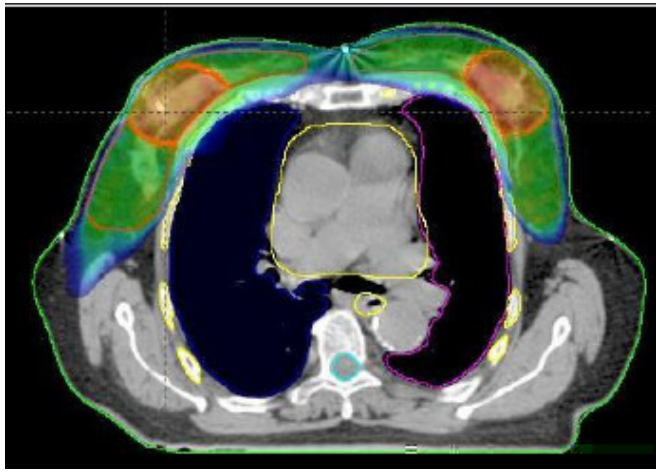
Phase i-ii study of hypofractionated simultaneous integrated boost using volumetric modulated arc therapy for adjuvant radiation therapy in breast cancer patients: a report of feasibility and early toxicity results in the first 50 treatments.

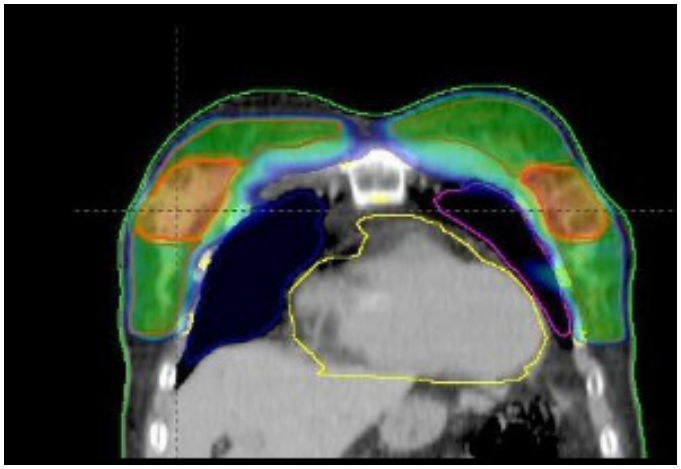
Scorsetti M, Alongi F, Fogliata A, Pentimalli S, Navarria P, Lobefalo F, Garcia-Etienne CA, Clivio A, Cozzi L, Mancosu P, Nicolini G, Vanetti E, Eboli M, Rossetti C, Rubino A, Sagona A, Arcangeli S, Gatzemeier W, Masci G, Torrisi R, Testori A, Alloisio M, Santoro A, Tinterri C.

50 patients → **40.5Gy/15fx to PTV-WB**

50 patients → **48.0Gy/15Fx to PTVboost**

} SIB-IMRT



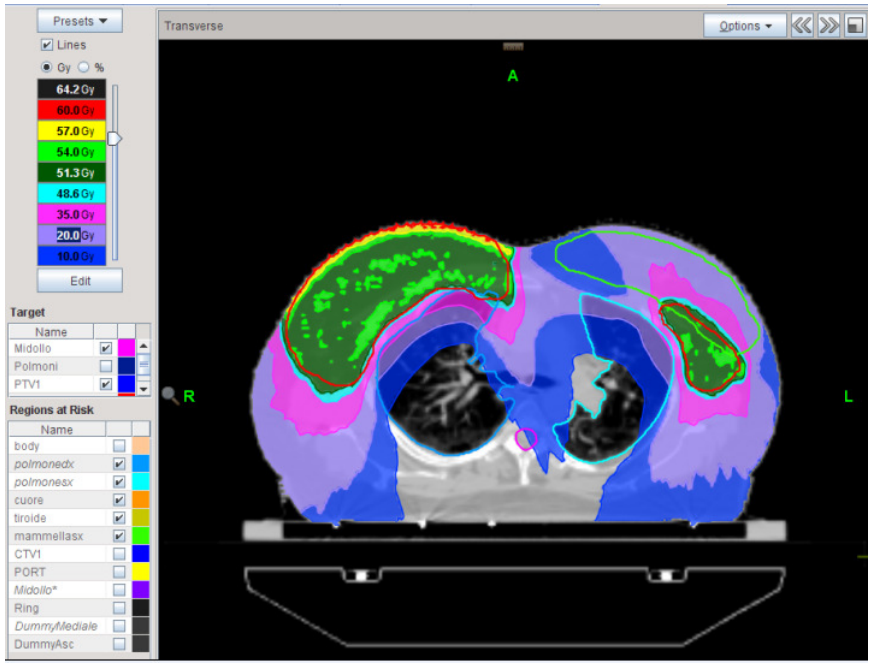


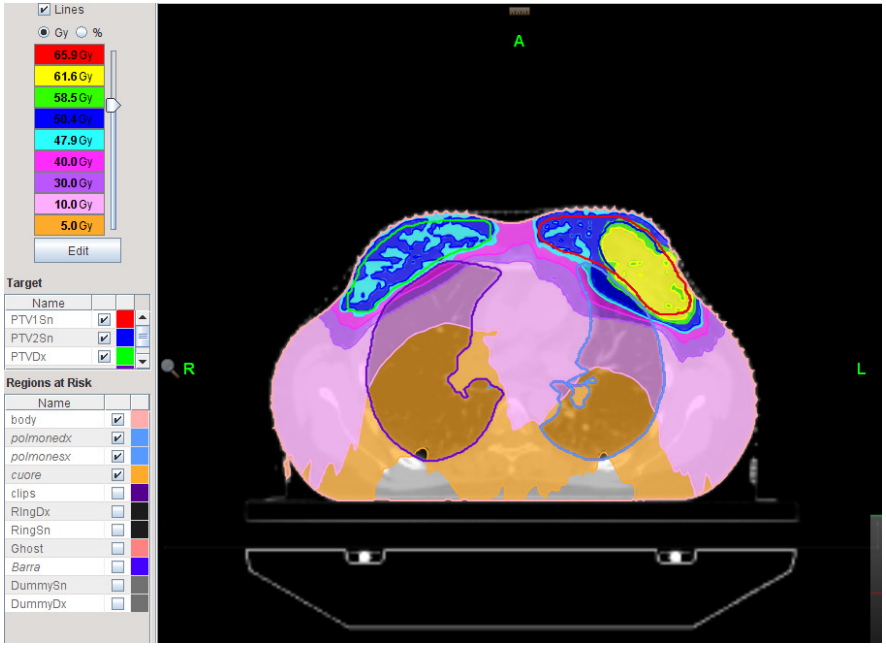
In conclusion, the presented experience of a 3-week course of postop RT using **VMAT** with SIB is feasible and it was associated with acceptable acute skin toxicity

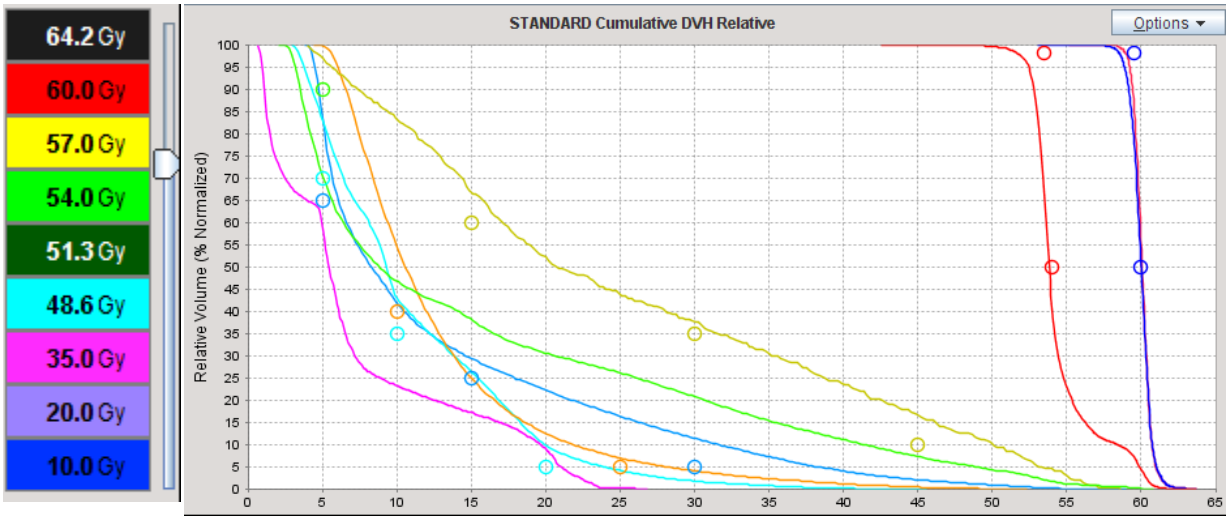
With Courtesy of Dr.Scorsetti

IGRT/TOMO - 3

Modena Experience

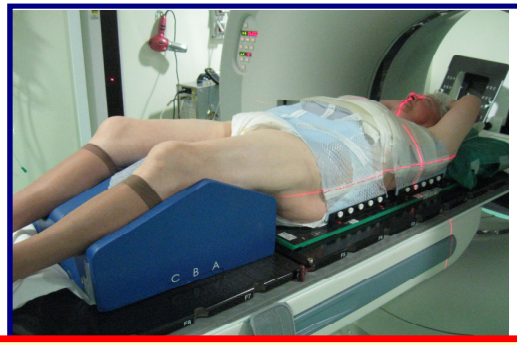






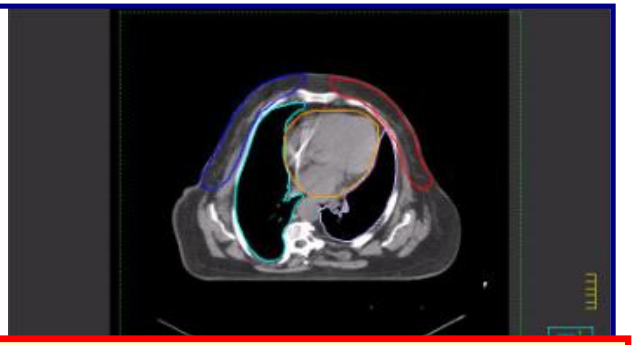
IGRT/TOMO - 3
Modena Experience

Pt with "pectum excavatum" submitted to bilateral mastectomy → indication for RT sulla on Right and Left anterior chest wall and bilateral suvraclavear nodes



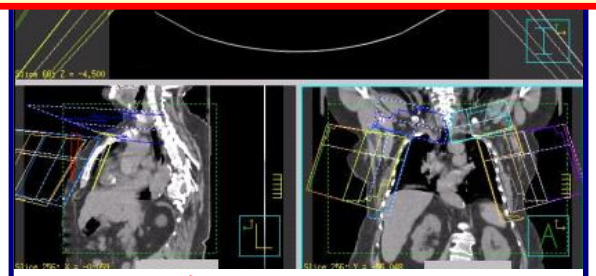
Set up for IGRT

T P S



TOMO showed

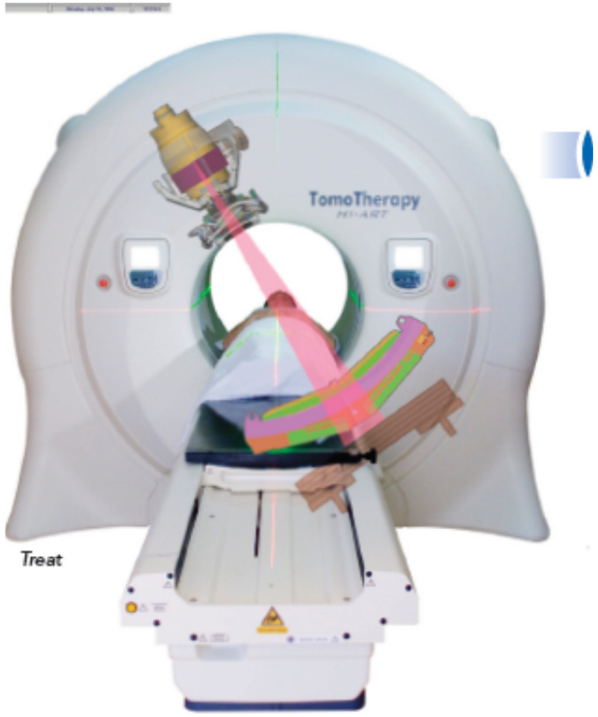
- Better Coverage
- Shorter Set Up and Treatment time
- Adequate Normal Tissue Sparing

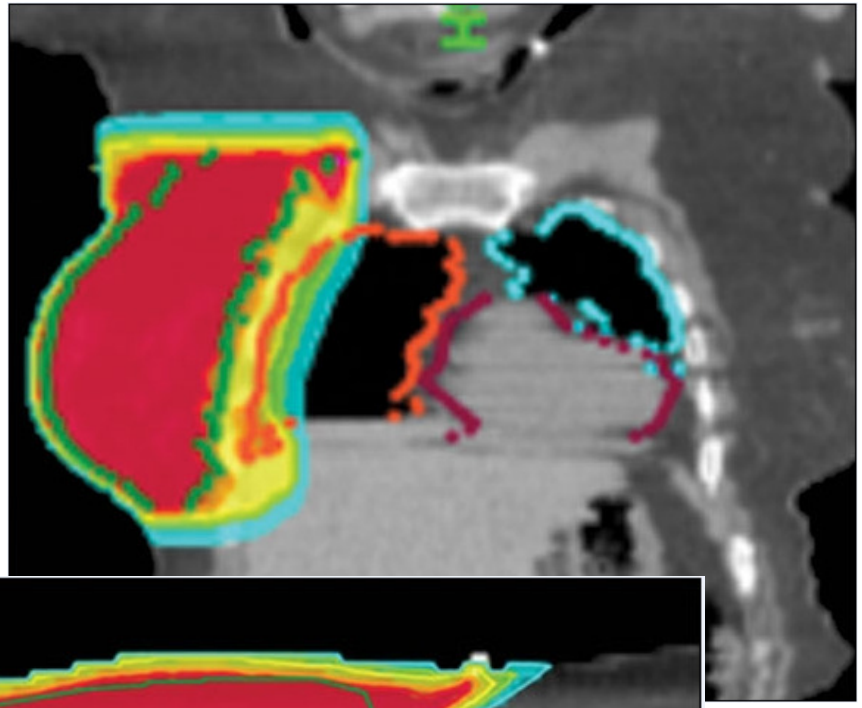


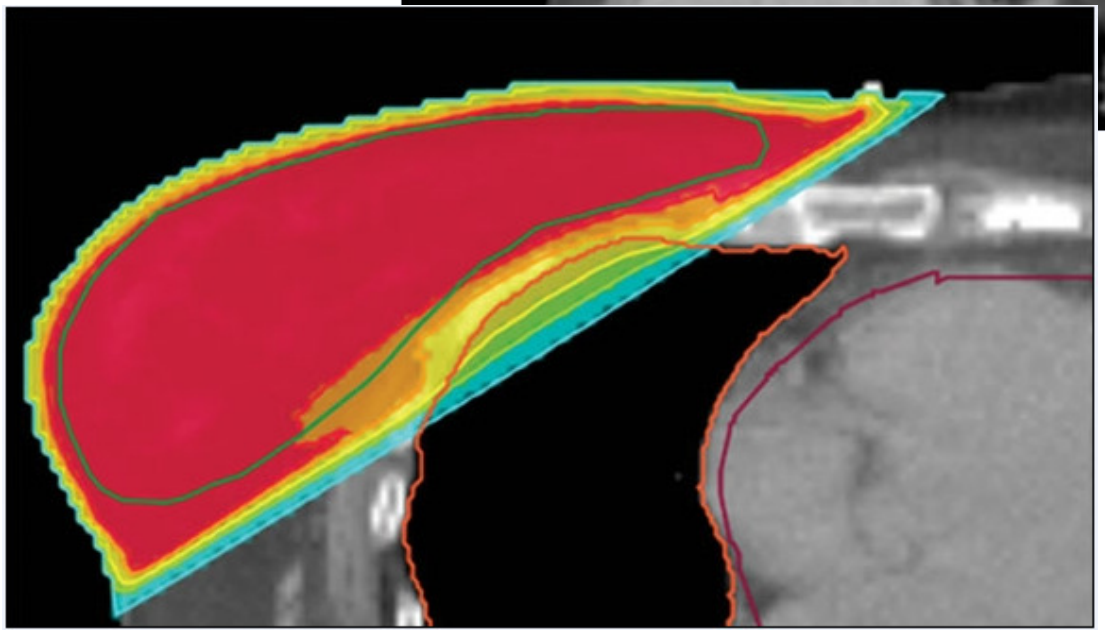
3D-cRT

TOMO

TOMODIRECT RT







Modena
Radioterapy Unit
Experience

IGRT/TOMO - 1

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

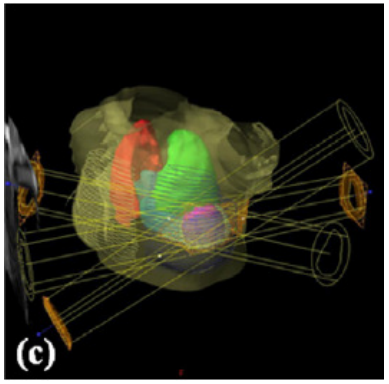
2009

Partial breast irradiation

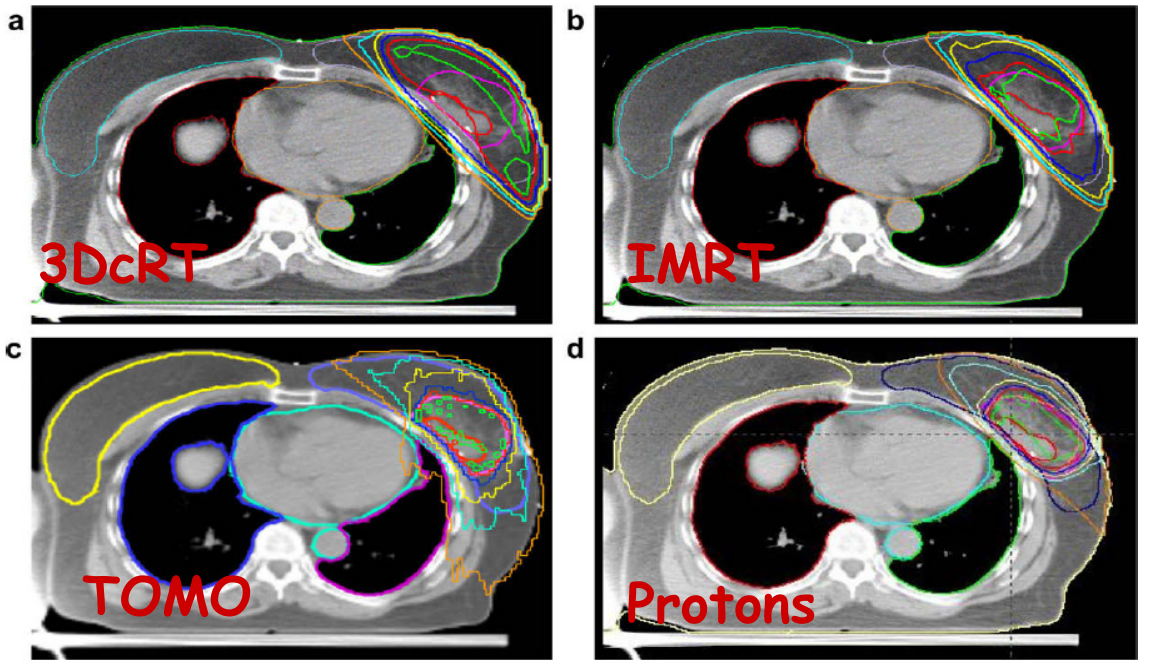
Dosimetric comparison of four different external beam partial breast irradiation techniques: Three-dimensional conformal radiotherapy, intensity-modulated radiotherapy, helical tomotherapy, and proton beam therapy

Sung Ho Moon [a], Kyung Hwan Shin [a,b,*], Tae Hyun Kim [a], Myonggeun Yoon [a], Soah Park [a], Doo-Hyun Lee [a], Jong Won Kim [a], Dae Woong Kim [a], Sung Yong Park [a], Kwan Ho Cho [a]

APBI with four different techniques → **30Gy in 5 fractions**



Lumpectomy cavity (red), PTV (pink) isodose lines of 103% (green), 100% (red), 90% (blue), 70% (yellow), 50% (cyan), and 30% (orange)



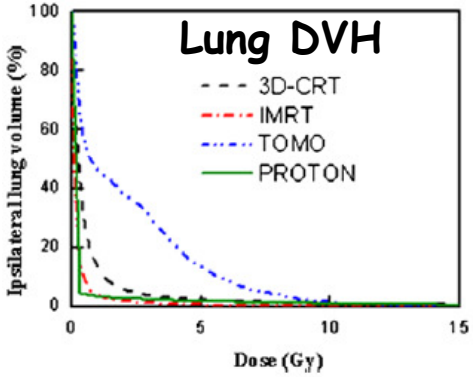
IGRT/TOMO - 1

Dosimetry Evaluation [HI,CI,CovI,PTV, Breast Dosimetry]

	Range (mean)				p^a
	3D-CRT	IMRT	TOMO	PBT	
HI	4.7–13.1 (8.10)	1.80–13.50 (5.48)	6.81–10.9 (8.34)	5.0–12.1 (7.37)	TOMO vs. 3D-CRT (1.000), 3D-CRT vs. PBT (1.000), PBT vs. IMRT (0.005)
CI	1.9–8.9 (3.04)	1.42–2.85 (1.99)	1.10–1.44 (1.21)	1.66–2.20 (1.95)	3D-CRT vs. IMRT (<0.001), IMRT vs. PBT (1.000), PBT vs. TOMO (<0.001)
CovI	0.87–0.99 (0.95)	0.94–1.00 (0.97)	0.95–0.96 (0.95)	0.95–0.98 (0.96)	3D-CRT vs. TOMO (1.000), TOMO vs. PBT (0.331), PBT vs. IMRT (0.165)

[a] By Bonferroni post hoc analysis with statistical significance defined as $p < 0.008$.

	Range (mean)				p^a
	3D-CRT	IMRT	TOMO	PBT	
PTV coverage (%)					
V_{100_PTV}	87.3–98.8 (94.8)	94.4–99.9 (97.1)	94.5–95.8 (95.2)	95.0–97.9 (96.1)	3D-CRT vs. TOMO (1.000), TOMO vs. PBT (0.331), PBT vs. IMRT (0.165)
V_{95_PTV}	99.3–100 (99.9)	97.3–100 (99.4)	98.8–99.9 (99.2)	98.6–100 (99.8)	TOMO vs. IMRT (0.731), IMRT vs. PBT(0.003), PBT vs. 3D-CRT (1.000)
V_{90_PTV}	100 (100)	98.7–100 (99.8)	99.7–99.9 (99.8)	99.5–100 (100)	IMRT vs. TOMO (1.000), TOMO vs. PBT (0.010), PBT vs. 3D-CRT (1.000)
Ipsilateral breast (%)					
V_{100_IB}	18.1–55.9 (32.8)	15.1–44.9 (27.2)	10.0–31.8 (18.7)	9.9–29.0 (18.2)	3D-CRT vs. IMRT (0.016), IMRT vs. TOMO (<0.001), TOMO vs. PBT (1.000)
V_{75_IB}	33.2–69.8 (48.9)	27.3–56.4 (41.4)	17.8–42.9 (27.4)	16.2–41.5 (26.8)	3D-CRT vs. IMRT (0.002), IMRT vs. TOMO (<0.001), TOMO vs. PBT (1.000)
V_{50_IB}	42.2–82.2 (57.6)	35.5–66.3 (50.3)	23.1–62.2 (39.8)	21.0–50.1 (33.0)	3D-CRT vs. IMRT (0.009), IMRT vs. TOMO (<0.001), TOMO vs. PBT (0.018)
V_{25_IB}	54.6–92.4 (67.3)	47.8–85.1 (60.5)	34.9–81.3 (62.9)	25.4–55.2 (38.0)	3D-CRT vs. TOMO (0.503), TOMO vs. IMRT (1.000), IMRT vs. PBT (<0.001)
Non-PTV breast (%)					
$V_{50\_IB-NPTV}$	25.0–64.7 (40.9)	22.1–48.7 (33.3)	10.6–32.4 (22.8)	10.3–23.2 (16.5)	3D-CRT vs. IMRT (<0.001), IMRT vs. TOMO (<0.001), TOMO vs. PBT (0.002)



All techniques have acceptable PTV coverage.

- **PBT** had the greatest capacity to spare normal breast tissue without increasing the dose delivered to the lung and heart.
- **TOMO** achieves high conformity to PTV and effective breast tissue sparing but showed higher dose exposure to the lung and heart.

Moon HS et al, Rad Onc, 2009

IGRT/TOMO - 2

RADIATION ONCOLOGY

2012

Display Settings: Abstract

Radiat Oncol. 2012 Jun 1;7:80.

Short course radiotherapy with simultaneous integrated boost for stage I-II breast cancer, early toxicities of a randomized clinical trial.

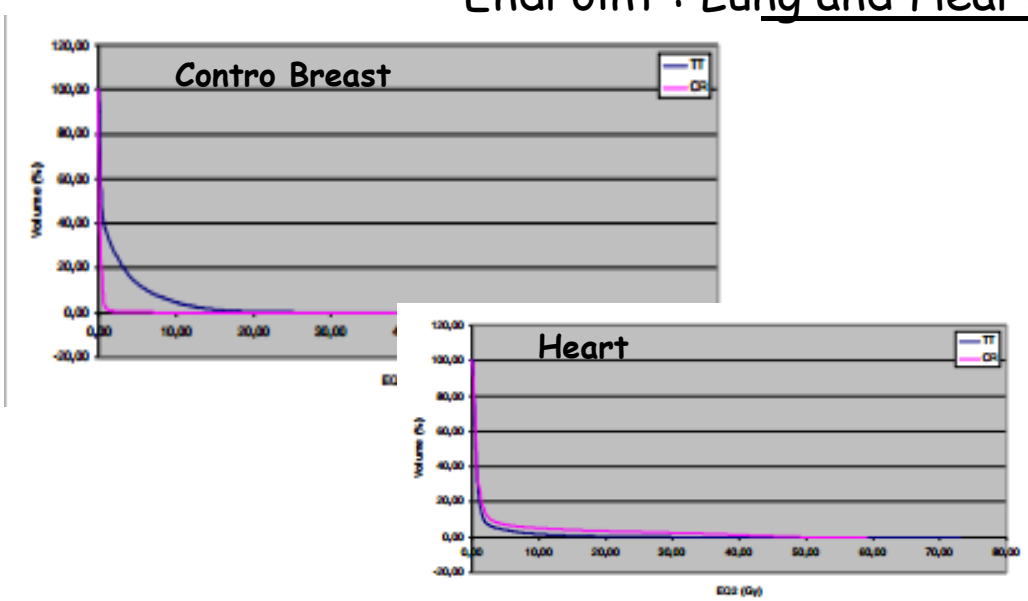
Van Parijs H, Miedema G, Vinh-Hung V, Verbanck S, Adriaenssens N, Kerkhove D, Reynders T, Schuermans D, Leysen K, Hanon S, Van Camp G, Vincken W, Storme G, Verellen D, De Ridder M.

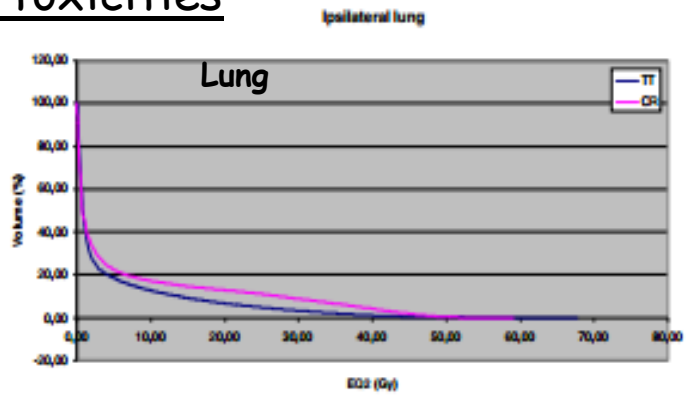
Department of Radiotherapy, UZ Brussel, Laarbeeklaan 101, 1090, Brussels, Belgium. hilde.vanparijs@uzbrussel.be.

Analisys of 70 pts in a *non-blind RCT*

25x2 Gy/5 weeks on WB + sequential boost 8x2 Gy/2 weeks using 3DcRT	**VS**	**15x2.8 Gy/3 weeks + SIB 0.6/die Gy using Tomotherapy**

EndPoint : Lung and Heart toxicities

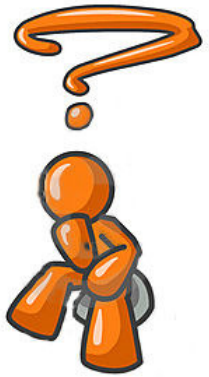




Only a trend of reduced lung toxicity in the hypofractionated arm

Concerns

....Are still present many concern bout :



- Daily Set
- Orc

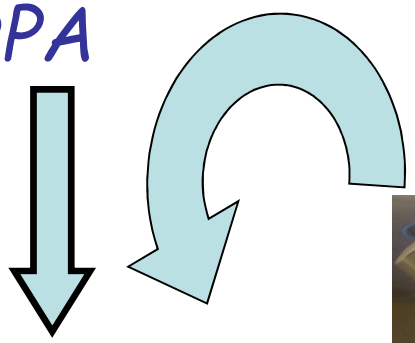
...YES.....

... he right Tools??????

Set Up Control and Organ Motion System

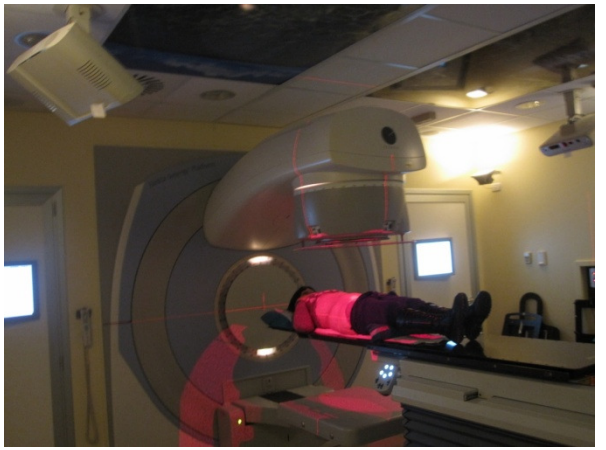
ABC
(Active Breathing Control) System

RPA



4D-CT Planning

Vision RT
(optical tracking) system



ABC SYSTEM

Breast cancer treatment and OARs dosimetry may depend on Organ motion and suffer from inter- and intrafraction variations due to respiratory movements

Lung

Heart

Skin

Soft tissue

ABC system let us to :

- watch over/control patient breathing
- reduce PTV margins due to respiratory movements
- allow and facilitate period of pt breath- hold

VISION RT

New volumetric optical tracking system

Enable to acquire 3D-superficial images in real time calculating variations and movements comparing it with basal optical acquisitions or CT images

Vision RT is composed by:

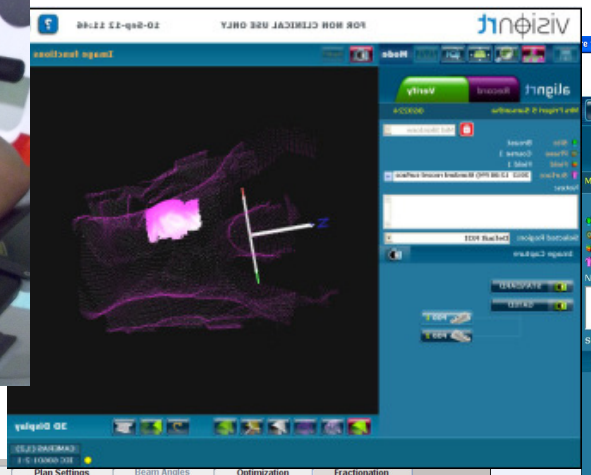
- Three laser systems with cameras
- Advanced software
- Workstation

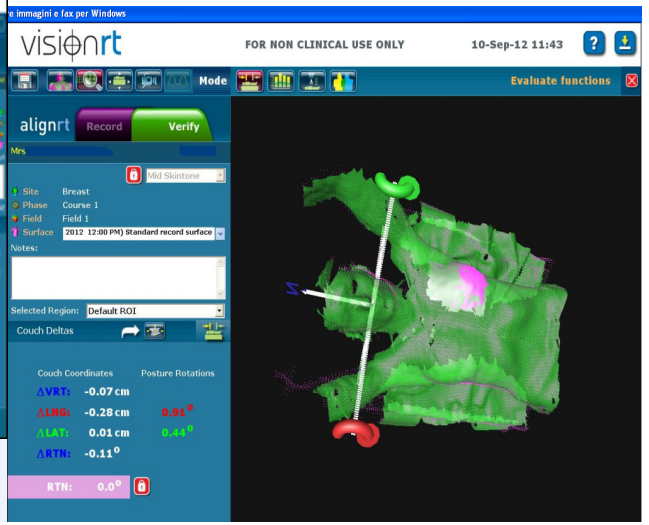
Advantages

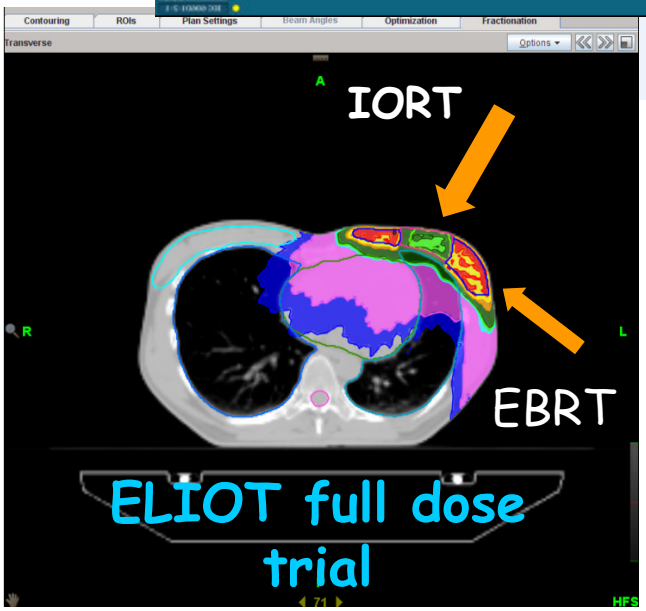
- Fast correction of the daily set-up
- On-line movements monitoring during RT

TOMO/VISION RT

Example of on-line monitoring and set up control







42 Yrs old
Sex Female
Stage pT1c pN0 M0
ER + PGR +
cERb 1+

4D-CT/4D-RT

MEDLine, 2012

Display Settings: Abstract

J Med Imaging Radiat Oncol. 2012 Aug;56(4):464-72. doi: 10.1111/j.1754-9485.2012.02405.x.

Deep inspiration breath hold technique reduces heart dose from radiotherapy for left-sided breast cancer.

Hayden AJ, Rains M, Tiver K.

Department of Radiation Oncology, Nepean Cancer Care Centre, Sydney, New South Wales, Australia.

Display Settings: Abstract

Cancer Radiother. 2012 Feb;16(1):44-51. Epub 2011 Nov 8.

Potential benefits of using cardiac gated images to reduce the dose to the left anterior descending coronary during radiotherapy of left breast and internal mammary nodes.

de Almeida CE, Fournier-Bidoz N, Massabeau C, Mazal A, Canary PC, Kuroki IR, Campana F, Fourquet A, Kirova YM.

Department of Radiation Oncology, Institut Curie, 26, rue d'Ulm, 75005 Paris, France.

Display Settings: Abstract

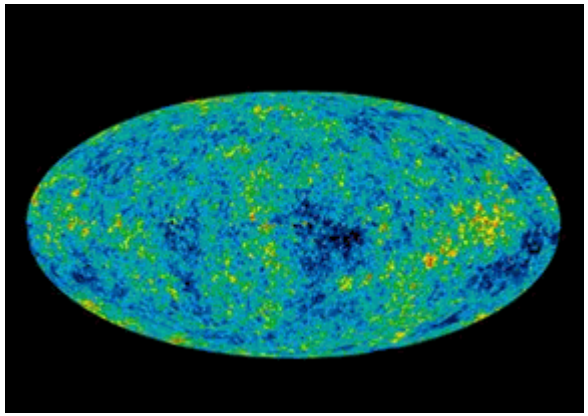
Acta Oncol. 2012 Mar;51(3):333-44. Epub 2011 Dec 16.

Radiation during deep inspiration allows loco-regional treatment of left breast and axillary-, supraclavicular- and internal mammary lymph nodes without compromising target coverage or dose restrictions to organs at risk.

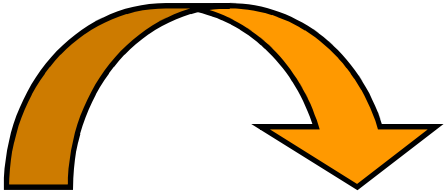
Hjelstuen MH, Mjaaland I, Vikström J, Dybvik KI.

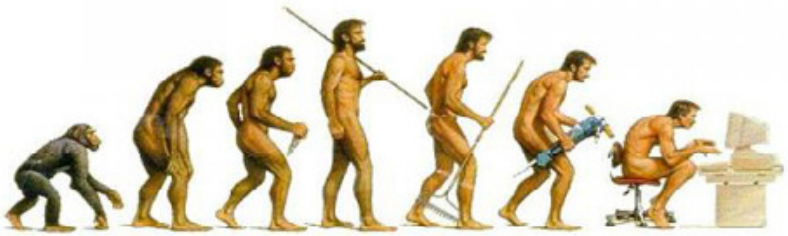
Department of Hematology and Oncology, Stavanger University Hospital, Stavanger, Norway. hjem@sus.no

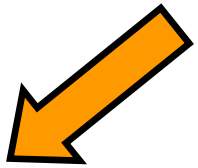
Results, Perspectives Conclusions



...after many years.....







"……improved dose distributions may convince fellow radiation oncologists - but a **real effect on patient-related outcome must be shown to convince the rest of the world**…..".

S.M. Bentzen et al., IJROBF 2004

High Tech RT Vs 3DcRT

…By Doctor's point of view…..

IMRT

Is more sexy...
Is more handsome...
Probably is more envied....
Seems to be better to have a drink with....

Is as comforting as...
Is as reassuring as...
Seems to be more competent....
Inspire more confidence...

Old 3DcRT

High Tech RT Vs 3DcRT

…By technical aspects' point of view…..

IMRT

…fast…

…d course…

… Is more c…

…is a bi…

…is l…

3DcRT

The answer must come from Evidence Based Medicine studies

But……..

….

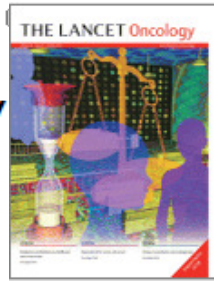
Courtesy of Prof. S.M.Magrini, 2011

EVIDENCE BASED MEDICINE-1

Display Settings: Abstract

THE LANCET Oncology FULL-TEXT ARTICLE

Send to:



Lancet Oncol. 2008 Apr;9(4):367-75.

Evidence behind use of intensity-modulated radiotherapy: a systematic review of comparative clinical studies.

Veldeman L, Madani I, Hulstaert F, De Meerleer G, Mareel M, De Neve W.
Department of Radiotherapy, Ghent University Hospital, Ghent, Belgium

2008

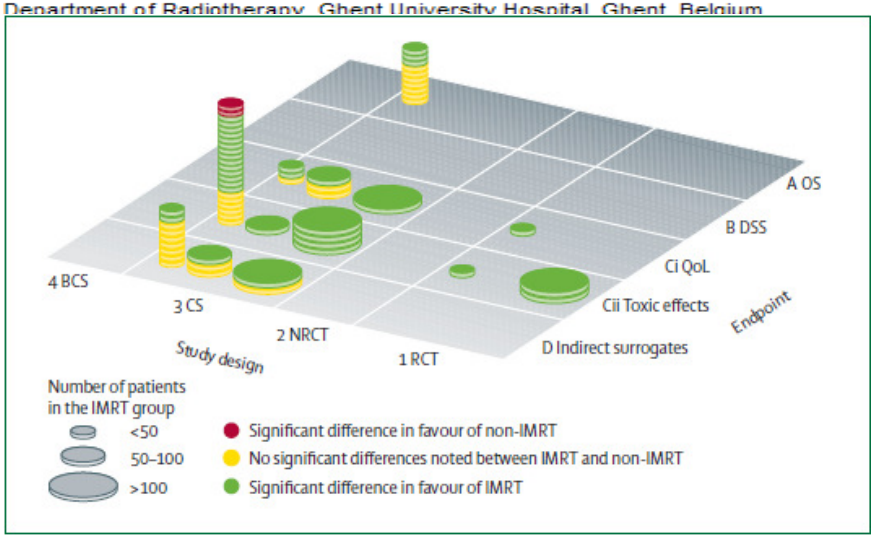


Figure 3: **Evaluation tool for relevance of clinical statements reported in 56 studies of IMRT**
BCS=best case series. CS=case series. NRCT=non-randomised controlled trial. RCT=randomised controlled trial. OS=overall survival. DSS=disease-specific survival. QoL=quality of life.

Only four comparative studies on **IMRT** in ***breast cancer*** were included in this review (two RCTs and two case series)

The ability of IMRT to reduce treatment-induced toxic effects compared with non-IMRT treatment has been shown

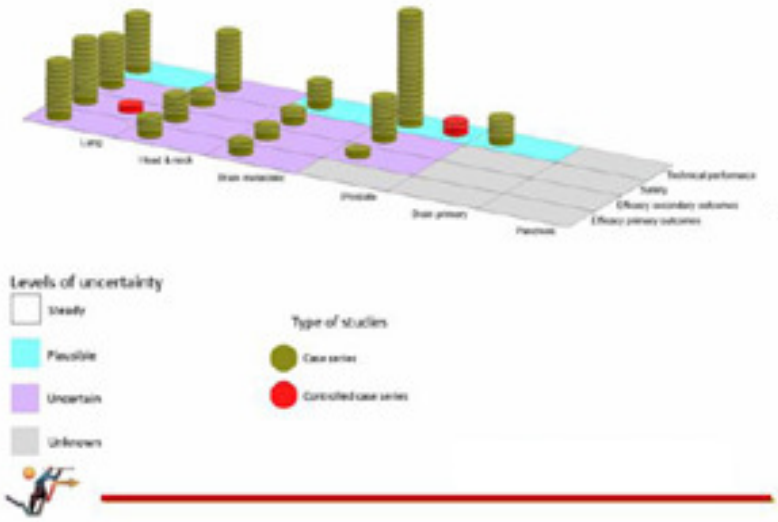
The potential of IMRT to improve locoregional control and survival by total-dose or fraction-dose escalation, as shown in case series

needs to be confirmed

EVIDENCE BASED MEDICINE-2

Literature Analysis about clinical outcomes and role of IGRT/IMRT

Sistematic Review of the Literature : Results



….no clear answer available about toxicities, clinical outcome and efficacy

Dossier RER Emilia Romagna Region, December 2010

Evidence Based Medicine-3

Reference	Adverse effects	IMRT (%)	TanRT (%)	*P* valu
MARA2 vs. TanRT: OR=1.47, p=0.16				
Randomised controlled trial				
[19]	Acute toxicity			
		IMRT (%)	Tan (WC)	*P* value
	Skin toxicity (grade 3–4, NCI CTC 2.0)	27.1		0.06
	Moist desquamation (all breast)	31.2		0.002
	Moist desquamation, inframammary crease	26.5		0.001
	Pain (grade 2–4, NCI CTC 2.0)	23.5		0.68

Reference	Adverse effects	IMRT (%)	TanRT (%)	*P* value
Retrospective cohort study				
[20]	Acute dermatitis			
	Grade 0/1	48	25	
	Grade 2/3	52	75	
	Time with acute dermatitis			
	Grade 0/1	82	29	
	Grade 2/3	18	71	
	Subgroup analysis detected significant improvements in grade 2/3 toxicity in small ($P = 0.0015$), medium ($P < 0.0001$) and large ($P < 0.0001$) breast siz			
[16]	Acute toxicity (Grade ≥2)			
	Dermatitis	41	85	
	Breast oedema	1		
	Pain	8		
	Hyperpigmentation	5		
	Late toxicity (grade ≥2)			
	Hyperpigmentation			
	Breast oedema			
	Fat necrosis			
	Induration/fibrosis			
	Good/excellent cosmesis			0
[17]	Acute toxicity (RTOG scale)			
	Grade 2–3 dermatitis			0.047
	Breast cellulitis			0.45
	Late toxicity			
	Radiation pneu			1.0
	Lymphede			0.06
	Fat ne			0.5
	So gnancy			0.84

....The potential of IMRT and IGRT needs to be confirmed in BC.....

...s reported on ...cancer outcomes, ...due to the short FUP ...mes in some studies.

- No evidence for differences in local recurrence rates.
- Less Acute Toxicity

W... ...ntial advantage is true of locoregional IMRT treatments remains unknown

Dayes I. et al,Clin. Onc., 2012

THOUGHTS

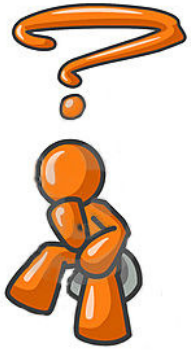
No Data are present about clinical Outcome in terms of Locoregional control and/or Survival advantages with Hi-Tech IMRT, IGRT, 4DRT,....

No data are present about long term Toxicities (skin reaction, soft tissues oedema, arm Lynphoedema, etc..)

.....and.....

.... What about higher percentage of volume exposed to low doses for stocastic damage????

.... ipsilateral/controlateral lung and breast secondary cancer????



"The overall benefit of IMRT in delivering adjuvant breast RT must be balanced against this increased demand on resources"

Dayes I., Clin Onc, 2012

FUTURE ANSWERS

From http://www.cancer.gov/clinicaltrials

IMRT

- **2009-APBI** (NCT01185132) → Leonard CE, USA Multic
- **IMRT-MC2** (NCT01322854) → Debus J, Heidelberg (
- **RTOG-1005** (NCT01349322) → Vicini F, USA Mul
- **ICR-IMPORT-HIGH** (NCT00818051) → Prof. K)
- **ICR-IMPORTLOW** (NCT00814567) → Pro UK)
- **MA-KOSIMA-01** (NCT01403779) → Wen (Germany)
- **S12-01299** (NCT01591811) → Formenti S USA)

IGRT

- **CYBERNEO** (NCT0087263 PY, Nice (France)
- **7326-09-SMC (**NCT0 Ben-David M, (NCI)
- **NKI-AVL-Descart** (NCT01024582) → huizen P,(Netherlands)*

TOMO

- **NCT00459628** (Phase III) → Vinh-Hung V. (B
- **NCT00508352** (Phase I-II) → Ottawa H Canada)

Operative Suggestions

Two different Routes for Hi-Tech in BC

Few Patients
(Particular clinical features)

Most Patients
(Standard clinical features)

High individual risk ofAcute/late toxicity Or comorbidity to perform standard RT

Looking for clinical advantages to guarantee Cost Effectiveness for Health System and pts

Tailored Therapy

Sporadic "Hi-Tech" clinical use (out trial)

General Clinical Governance

Large scale multicenter RCT

Last Suggestions

Agenzia sanitaria e sociale regionale

L'AGENZIA
- Chi siamo
- Programma triennale
- Link

AREE DI PROGRAMMA (in aggiornamento)
- Accreditamento e qualità
- Governo clinico
- Innovazione sociale
- Rischio infettivo
- Sistema Comunicazione Documentazione Formazione

RICERCA & INNOVAZIONE (in aggiornamento)
- Ricerca & Innovazione
- Osservatorio per l'innovazione
- Progetti PRI E-R
- Programma Ricerca Regione-Università
- Governo della ricerca

HOME > PRI E-R II > ONCOLOGIA

INNOVAZIONE IN RADIOTERAPIA ONCOLOGICA

REFERENTE: Susanna Trombetti
e-mail: strombetti@regione.emilia-romagna.it

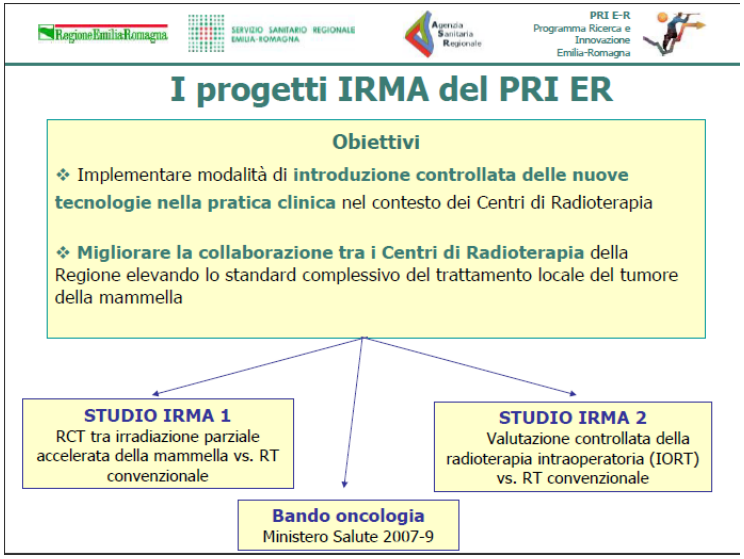
Link al Progetto nell'Area Governo clinico

a cura di: Agenzia sanitaria e sociale regionale
e-mail: asrdirgen@regione.emilia-romagna.it
aggiornamento: 08 settembre 2011

PUBBLICAZIONI, STRUMENTI, ...

Trombetti S.; 2009
INNOVAZIONE NEL TRATTAMENTO CON RADIOTERAPIA DEL TUMORE DELLA MAMMELLA
Il Programma Ricerca e innovazione (PRI E-R) dell'Emilia-Romagna. Report delle attività 2005-2008, Dossier 185, pp. 23-28
Parole chiave: Innovazione
Tipologia: Capitolo di libro
- testo intero PDF, 100 Kb

Area di programma Governo clinico; 2008
PERCORSO OPERATIVO PER PROGETTO "INTRODUZIONE CONTROLLATA IORT" IN REGIONE EMILIA-ROMAGNA
5 p.
Parole chiave: Innovazione
Tipologia: Documento tecnico
- testo intero PDF, 76 Kb

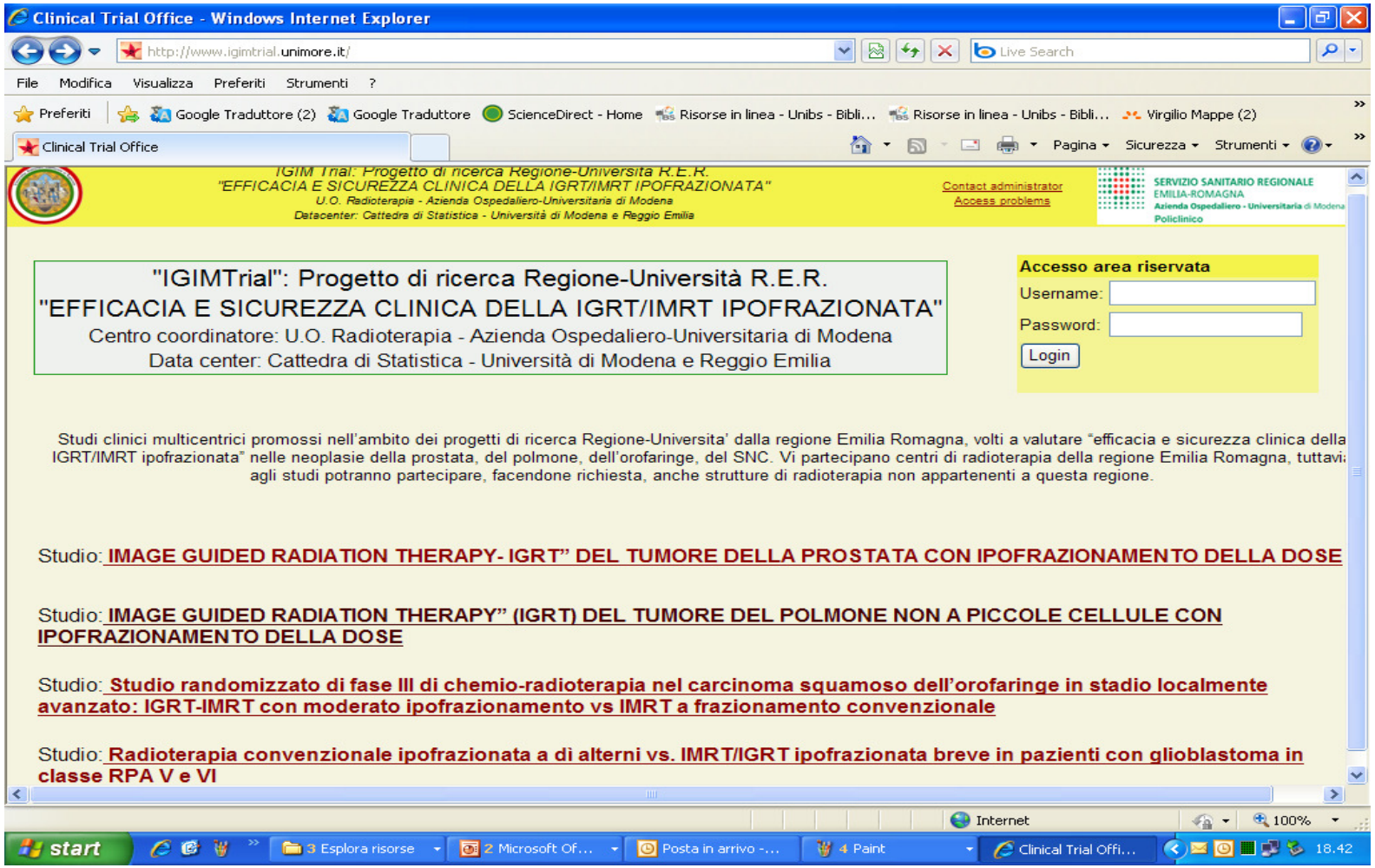


2007-2008

Multicentric clinical trial RER

http://www.igimtrial.unimore.it

.....Coming Soon.....October 2012.....



THANK YOU