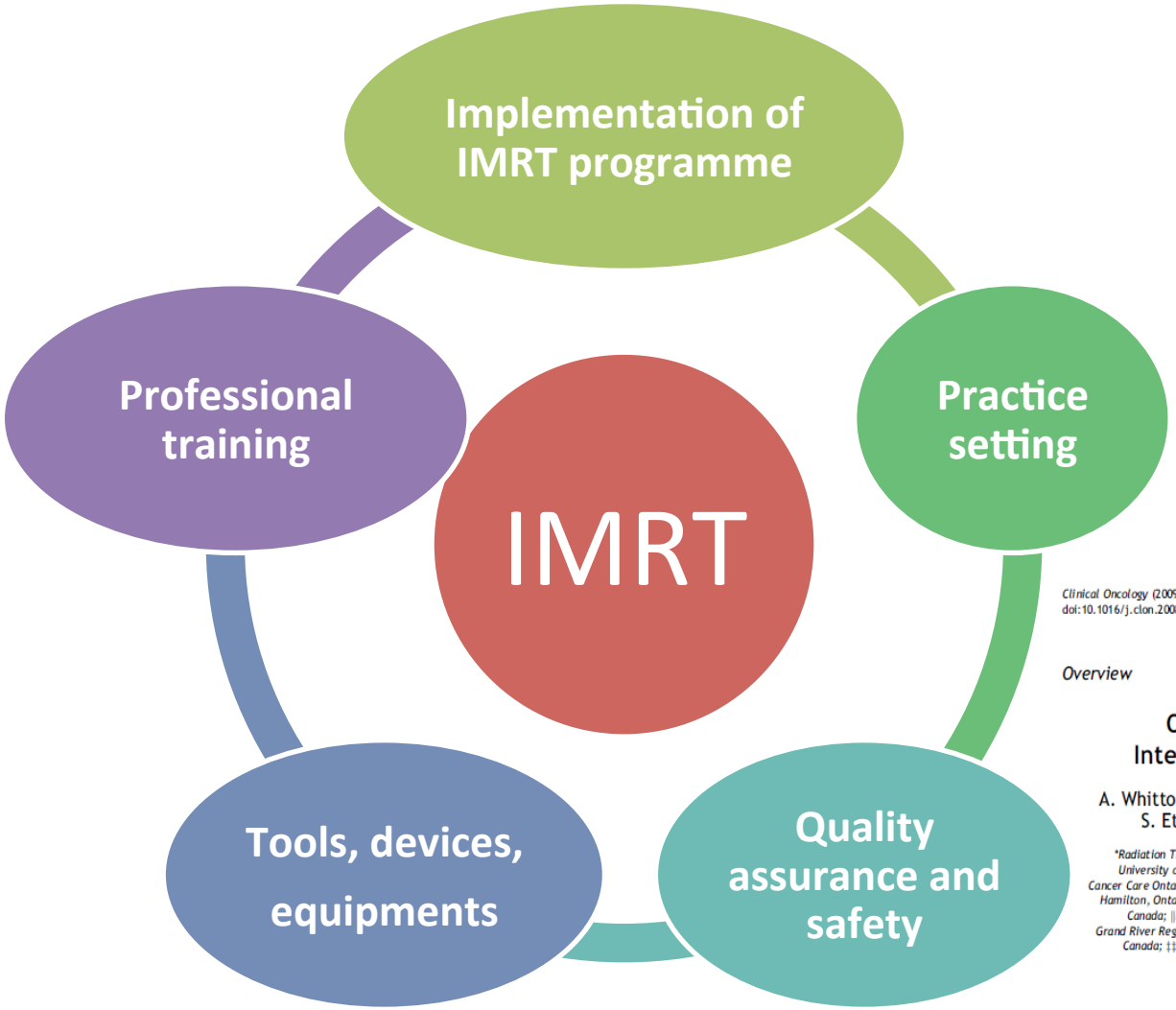
Radiation Therapy for breast with Tomotherapy: When?

Quarto incontro italo-francese sul carcinoma mammario: Problematiche attuali
Assisi 22/23 novembre 2013

Roberto Orecchia
Chair of Radiation Therapy at the University of Milan, IEO & CNAO

IEO
Arc Advanced Radiotherapy Center

IMRT demands a level of higher complexity and infrastructure



Clinical Oncology (2009) 21: 192–203
doi:10.1016/j.clon.2008.10.005

Overview

Organisational Standards for the Delivery of Intensity-modulated Radiation Therapy in Ontario

A. Whitton*, P. Warde†, M. Sharpe†, T. K. Oliver‡§, K. Bak*, K. Leszczynski‖, S. Etheridge¶, K. Fleming**, E. Gutierrez*, L. Favell††, E. Green‡‡

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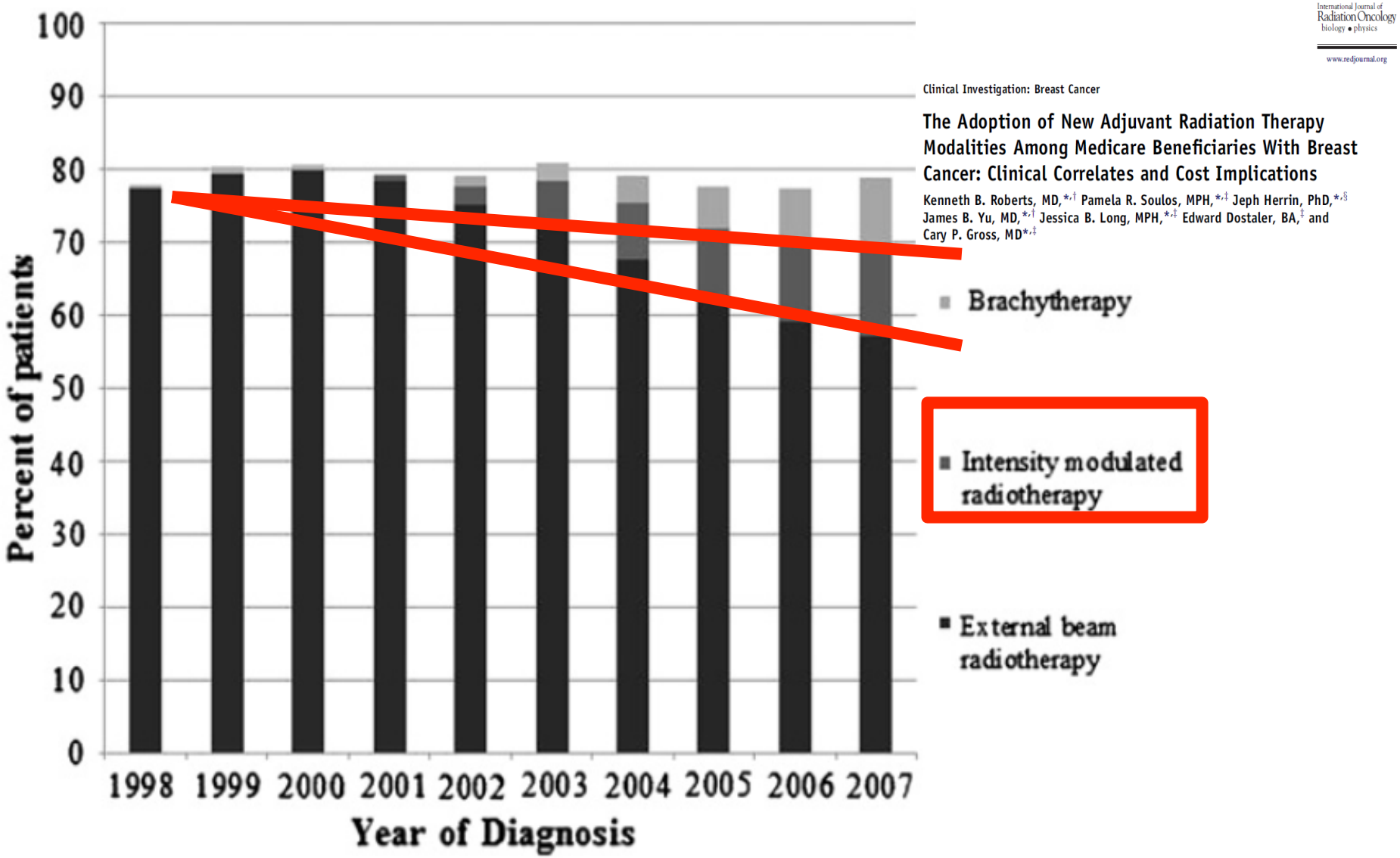

International Journal of Radiation Oncology biology • physics
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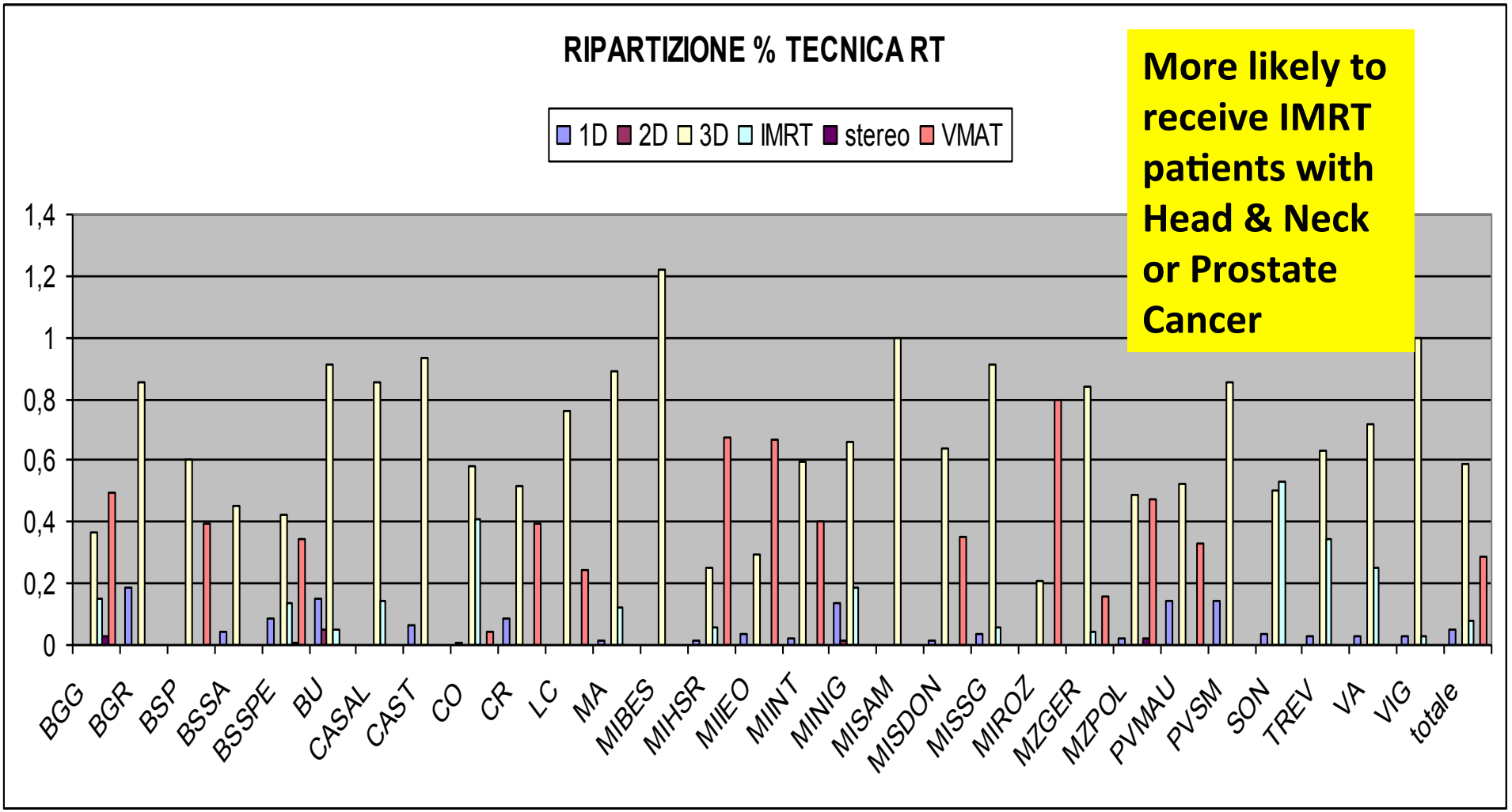
Clinical Investigation: Breast Cancer

The Adoption of New Adjuvant Radiation Therapy Modalities Among Medicare Beneficiaries With Breast Cancer: Clinical Correlates and Cost Implications

Kenneth B. Roberts, MD,*,† Pamela R. Soulos, MPH,*,‡ Jeph Herrin, PhD,*,§ James B. Yu, MD,*,† Jessica B. Long, MPH,*,‡ Edward Dostaler, BA,‡ and Cary P. Gross, MD*,‡

While the overall proportion of patients receiving RT remained relatively constant (80%),

the use of IMRT increased from 0.0% to 12.6% from 1998 to 2007



More likely to receive IMRT patients with Head & Neck or Prostate Cancer

Regione Lombardia: 1D 5%; 3D 59%; IMRT 8%; VMAT 28%

Clinical Oncology 22 (2010) 643–657

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.elsevier.com/locate/clon

Overview

A Review of the Clinical Evidence for Intensity-modulated Radiotherapy

J. Staffurth on behalf of the Radiotherapy Development Board[1]

Cardiff University, Velindre Hospital, Whitchurch, Cardiff, UK

REVIEW ARTICLE

American College of Radiology (ACR) and American Society for Radiation Oncology (ASTRO) Practice Guideline for Intensity-modulated Radiation Therapy (IMRT)

*Alan (Am J Clin Oncol 2012;35:612–617) † David C. Beyer, MD,‡ Thomas J. Eichler, MD,§ Geoffrey S. Ibbott, PhD,‖ Brian Kavanagh, MD,¶ Christopher J. Schultz, MD,# and Seth A. Rosenthal, MD***

Clinical consensus for breast cancer IMRT has not been achieved yet

Clinical situations where benefit is clear:

- **Bilateral breast irradiation**
- **Unilateral irradiation of a patients with bilateral breast implants**
- **Pectus excavatum**

Critical aspects for breast IMRT

- Potential for increased geographical miss
- More time is demanded due to contouring, planning, checking and delivery times
- Daily IGRT
- Bath dose (larger volume of normal tissues receiving low doses of radiation)
- Complex treatment which requires additional resources for education, outlining, planning and process quality assurance

IMRT advantages

Improved dose distribution

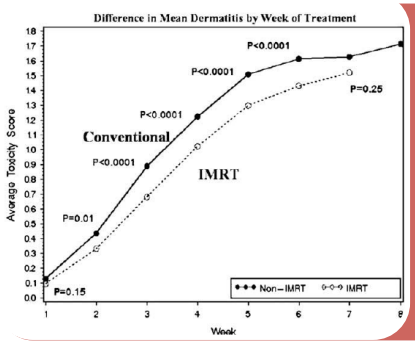
Steep dose gradient

Concave distribution

Sparing normal tissues

Reduced Toxicity Skin

(comparative studies with historical 3D groups)



Reduced the rate of G 2/3 dermatitis

- IMRT pts spent 18% of treatment period with Grade 2/3 dermatitis compared to 71 % of CR pts

ELSEVIER
doi:10.1016/j.ijrobp.2008.08.071

Toxicity	IMRT (%)	Wedges (%)	*p*
Acute grade ≥2			
Dermatitis	41	85	<0.001
Breast edema	1	28	<0.001
Pain	8	8	0.78
Hyperpigmentation	5	50	<0.001
Chronic grade ≥2			
Hyperpigmentation	7	17	0.06
Breast edema	1	25	<0.001
Fat necrosis	0	1	0.46
Induration/fibrosis	0	6	0.11
Good/excellent cosmesis	99	97	0.60

Reduced rate of acute G2 toxicity

- reduced rate of late grade oedema, equivalent cosmesis
- larger benefit for larger breasts

CLINICAL INVESTIGATION Breast

BREAST INTENSITY-MODULATED RADIATION THERAPY REDUCES TIME SPENT WITH ACUTE DERMATITIS FOR WOMEN OF ALL BREAST SIZES DURING RADIATION

Gary M. Freedman, M.D.,* Tianyu Li, M.S.,† Nicos Nicolaou, M.D.,* Yan Chen, Ph.D.,* Charlie C.-M. Ma, Ph.D.,* and Penny R. Anderson, M.D.*

ELSEVIER
doi:10.1016/j.ijrobp.2007.02.044

CLINICAL INVESTIGATION Breast

INTENSITY-MODULATED RADIOTHERAPY RESULTS IN SIGNIFICANT DECREASE IN CLINICAL TOXICITIES COMPARED WITH CONVENTIONAL WEDGE-BASED BREAST RADIOTHERAPY

Asif Harsolia, M.D.,* Larry Kestin, M.D.,* Inga Grills, M.D.,* Michelle Wallace, R.N.,* Shruti Jolly, M.D.,* Cortney Jones, M.D.,* Moinaktar Lala, M.D.,* Alvaro Martinez, M.D., F.A.C.R.,* Scott Schell, M.D., Ph.D.,† and Frank A. Vicini, M.D., F.A.C.R.*

	IMRT	Conventional	*p*
Acute (%)			
Dermatitis RTOG Grade 0–1	61	48	0.047
Dermatitis RTOG Grade 2–3	39	52	0.047
Breast cellulitis	2	4	0.45
Late (%)			
Radiation pneumonitis	1	2	1.0
Lymphedema	0	4	0.06
Fat necrosis	0	2	0.5
Second malignancy	3	4	0.84

Reduced rate of RTOG G 2/3 dermatitis

(39% vs. 52% p=0.047)

- equivalent LC and survival
- at more than 6 years median FU

ELSEVIER
doi:10.1016/j.ijrobp.2008.02.053

CLINICAL INVESTIGATION Breast

LONG-TERM OUTCOMES OF IMRT FOR BREAST CANCER: A SINGLE-INSTITUTION COHORT ANALYSIS

Mark W. McDonald, M.D.,* Karen D. Godette, M.D.,* Elizabeth K. Butker, M.S.,* Lawrence W. Davis, M.D., M.B.A., F.A.C.R.,* and Peter A. S. Johnstone, M.D., F.A.C.R.†

VOLUME 26 · NUMBER 13 · MAY 1 2008
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

A Multicenter Randomized Trial of Breast Intensity-Modulated Radiation Therapy to Reduce Acute Radiation Dermatitis

Jean-Philippe Pignol, Ivo Olivotto, Eileen Rakovitch, Sandra Gardner, Katharina Sixel, Wayne Beckham, Thi Trinh Thuc Vu, Pauline Truong, Ida Ackerman, and Lawrence Paszat

Results

A total of 358 patients were randomly assigned between July 2003 and March 2005 in two Canadian centers, and 331 were included in the analysis. Breast IMRT significantly improved the dose distribution compared with standard radiation. This translated into a lower proportion of patients experiencing moist desquamation during or up to 6 weeks after their radiation treatment; 31.2% with IMRT compared with 47.8% with standard treatment ($P = .002$). A multivariate analysis found the use of breast IMRT ($P = .003$) and smaller breast size ($P < .001$) were significantly associated with a decreased risk of moist desquamation. The use of IMRT did not correlate with pain and quality of life, but the presence of moist desquamation did significantly correlate with pain ($P = .002$) and a reduced quality of life ($P = .003$).

End Point	BIMRT (%) (n = 170)	Standard RT* (%) (n = 161)	*P*
Skin toxicity grade 3-4 (NCI CTC 2.0)	27.1	36.7	.06
Moist desquamation, all breast	31.2	47.8	.002
Moist desquamation, inframammary crease	26.5	43.5	.001
Pain grade 2-4 (NCI CTC 2.0)	23.5	25.5	.68

Late toxicity

Radiotherapy and Oncology 82 (2007) 254–264
www.thegreenjournal.com

Phase III randomised trial

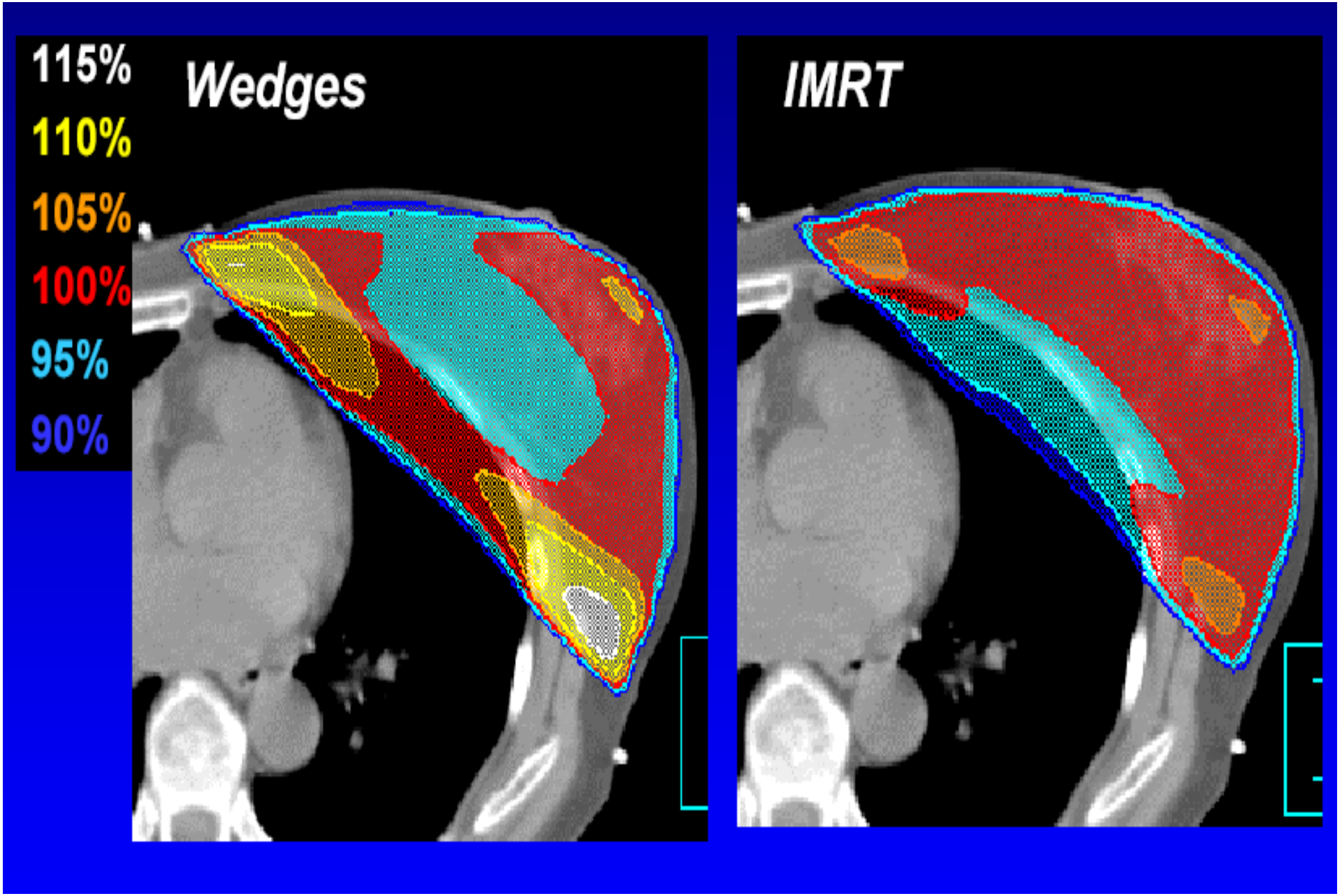
Randomised trial of standard 2D radiotherapy (RT) versus intensity modulated radiotherapy (IMRT) in patients prescribed breast radiotherapy

Ellen Donovan[a], Natalie Bleakley[a], Erica Denholm[b], Phil Evans[a], Lone Gothard[c], Jane Hanson[c], Clare Peckitt[b], Stephanie Reise[a], Gill Ross[d], Grace Sharp[c], Richard Symonds-Tayler[a], Diana Tait[c], John Yarnold[c,*], on behalf of the Breast Technology Group

Breast IMRT using a static field in field method resulted in fewer changes in breast appearance at 5 years compared to 2D technique

Proportion of patients with any clinician-assessed breast induration (a little, quite a bit or very much) within number of assessments performed according to randomisation arm, standard 2D dosimetry or 3D intensity modulated radiotherapy (IMRT)

	Year 2 assessment		Year 5 assessment		*P*-value (from GEE)
	Standard 2D	IMRT 3D	Standard 2D	IMRT 3D	
Centre of the breast	33/122 (27%)	19/117 (16%)	37/117 (32%)	25/118 (21%)	0.02
Pectoral fold	32/119 (27%)	13/113 (12%)	34/118 (29%)	26/119 (22%)	0.006
Inframammary fold	35/121 (29%)	18/113 (16%)	28/116 (24%)	20/117 (17%)	0.009
Boost site	65/120 (54%)	44/118 (37%)	70/114 (61%)	43/115 (37%)	<0.001


115%
110%
105%
100%
95%
90%
Wedges
IMRT

Randomized controlled trial of Intensity-Modulated Radiotherapy for early breast cancer: 5-year results confirm superior overall cosmesis

Mukesh BM et al, MRC & RCR, UK. JCO, September 2013

- 1,145 patientswith standard tangential plans
- 815 had inhomogeneius plans (<2cm3 receiveing 107% of the dose: 40 Gy in 15 frs over 3 weeks)
- Randomly assigned to standard or IMRT

- No skin telangiectasie: 76% versus 85% (p .02)
- Overall good cosmesis: 78% versus 88% (p .03)

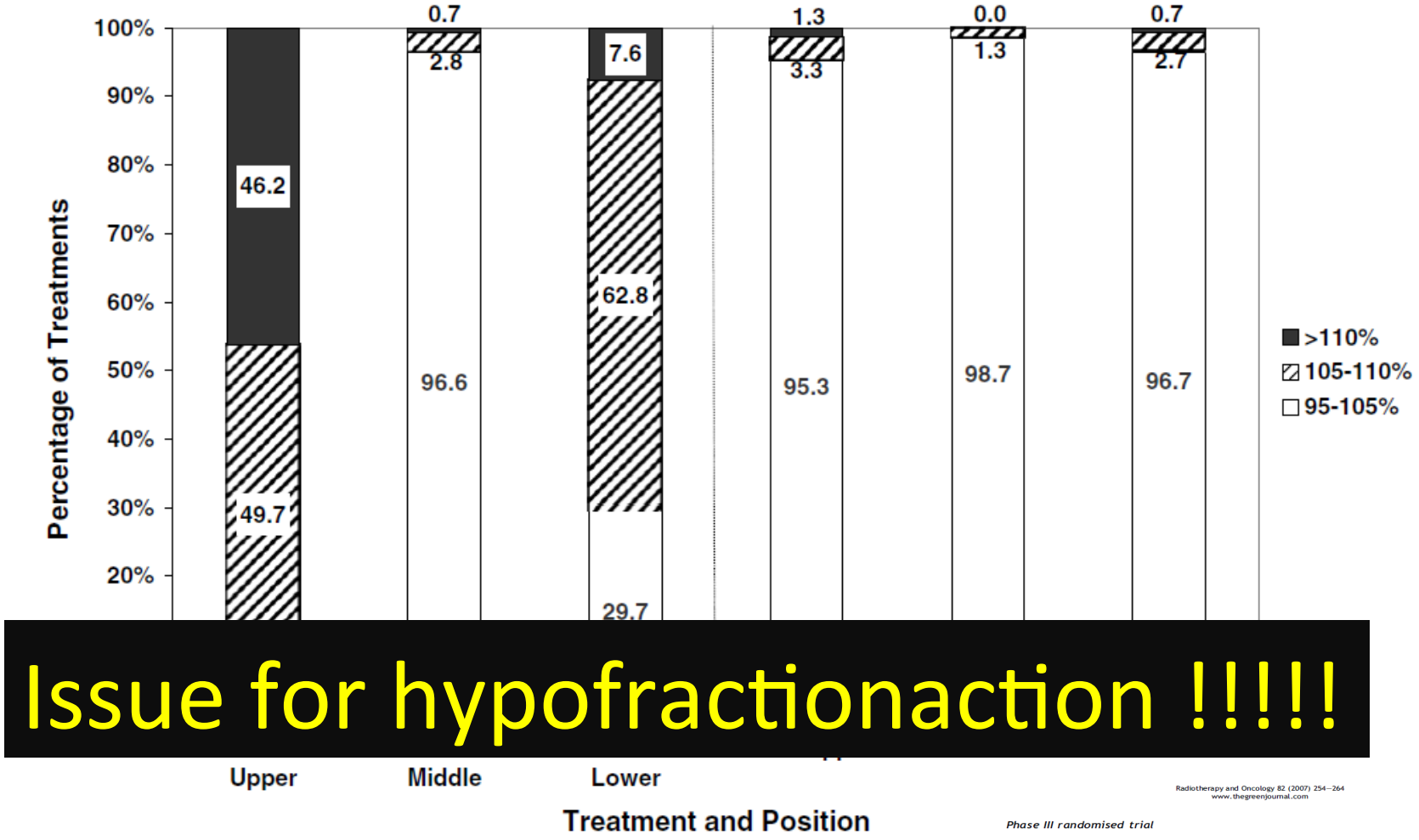
Hypofractionation

Evidence supports the equivalence of hypofractionated WBI with conventionally fractionated WBI for patients who satisfy all these criteria

ASTRO evidence-based guidelines, IJROBP, 81: 59-68, 2011

- 50 years or older at diagnosis
- T1-2 N0 pathological stage and BCS
- No systemic chemotherapy
- Within the breast along the central axis, the minimum dose is no less than 93% and the maximum dose is no greater than 107% of the prescription dose (2D calculation)

The minimisation of unwanted dose inhomogeneity in the breast reduces late adverse effects



Issue for hypofractionaction !!!!!

Radiotherapy and Oncology 82 (2007) 254–264
www.thegreenjournal.com

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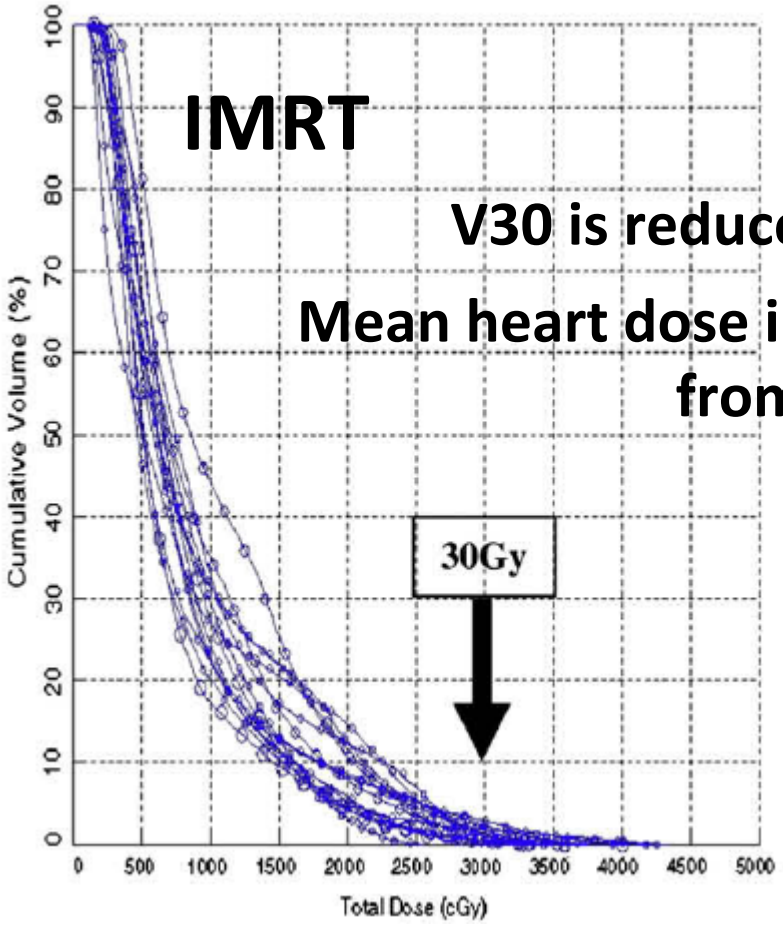
Pushing the limits of hypofractionation for adjuvant whole breast radiotherapy

Yarnold J & Haviland J, Breast, June 2011

- ….. Based on current evidence, testing the effectiveness of a 5-fraction schedule of hypofractionated whole breast radiotherapy appears to be realisable research objective

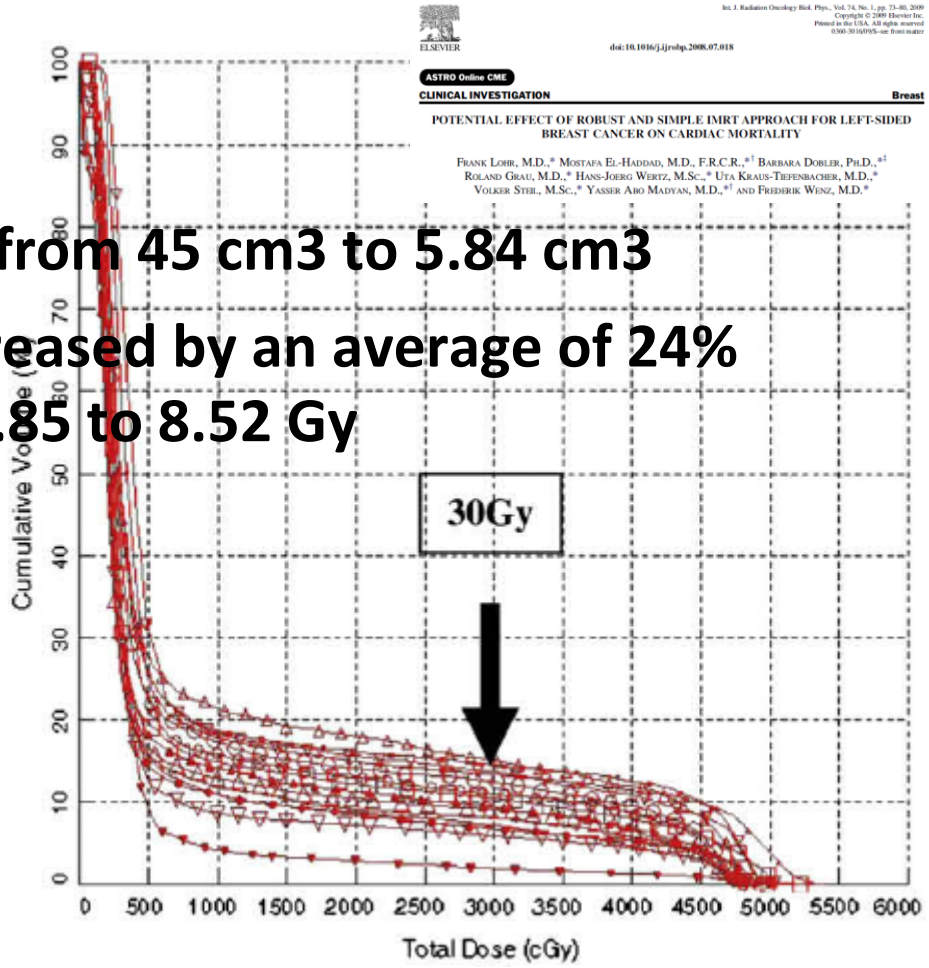
…..

IMRT reduced the risk of therapy-associated cardiac death from 6.03% for the 3D plans to 0.25%



V30 is reduced from 45 cm3 to 5.84 cm3

Mean heart dose increased by an average of 24% from 6.85 to 8.52 Gy



IMRT reduced heart volume in the high dose region at the expense of a greater cardiac volume receiving low dose

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Int. J. Radiation Oncology Biol. Phys., Vol. 78, No. 1, pp. 104–110, 2010

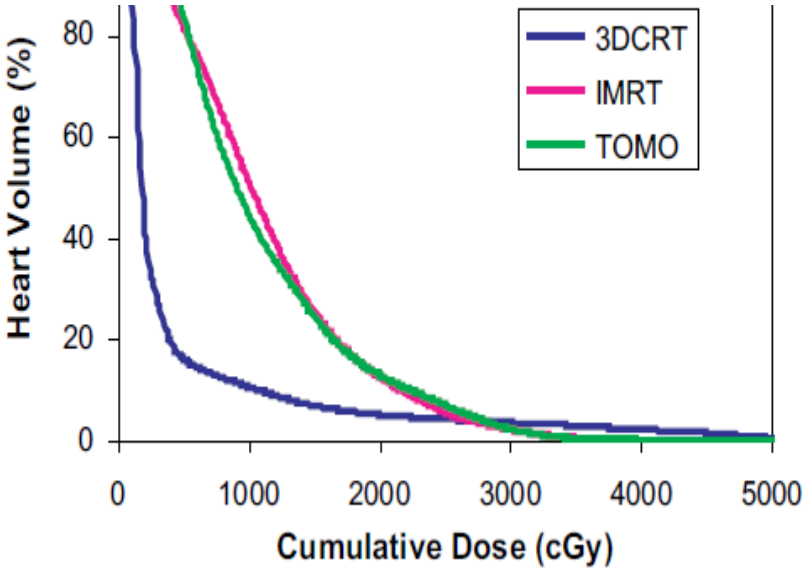
0360-3016/$–see front matter

doi:10.1016/j.ijrobp.2009.07.1705

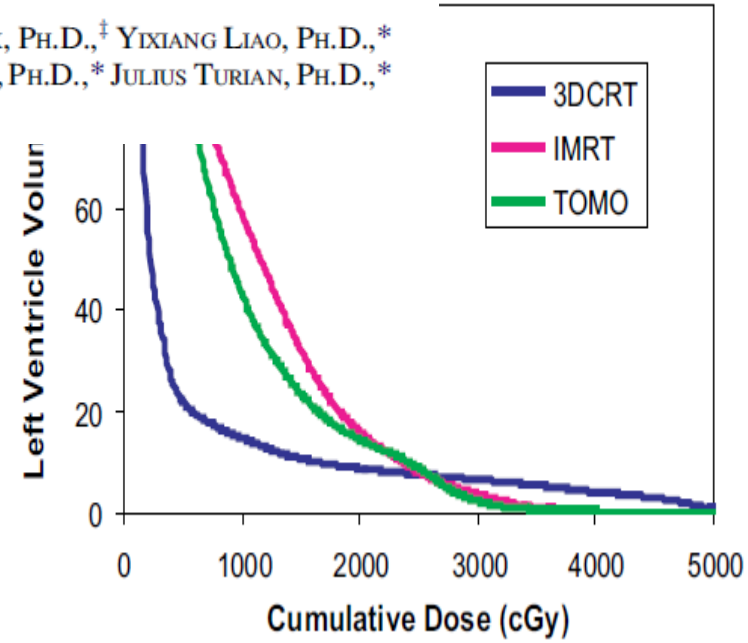
CLINICAL INVESTIGATION **Breast**

TOMOTHERAPY AND MULTIFIELD INTENSITY-MODULATED RADIOTHERAPY PLANNING REDUCE CARDIAC DOSES IN LEFT-SIDED BREAST CANCER PATIENTS WITH UNFAVORABLE CARDIAC ANATOMY

ALAN B. COON, M.D., PH.D.,* ADAM DICKLER, M.D.,† MICHAEL C. KIRK, PH.D.,‡ YIXIANG LIAO, PH.D.,* ANAND P. SHAH, M.D.,* JONATHAN B. STRAUSS, M.D.,* SEA CHEN, M.D., PH.D.,* JULIUS TURIAN, PH.D.,* AND KATHERINE L. GRIEM, M.D.*



Mean DVH for the heart



Mean DVH for left ventricle

V35 for IMRT (0.7%) and TOMO (0.5%) were lower than for 3DCRT (3.6%)

Radiotherapy and Oncology xxx (2011) xxx–xxx

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

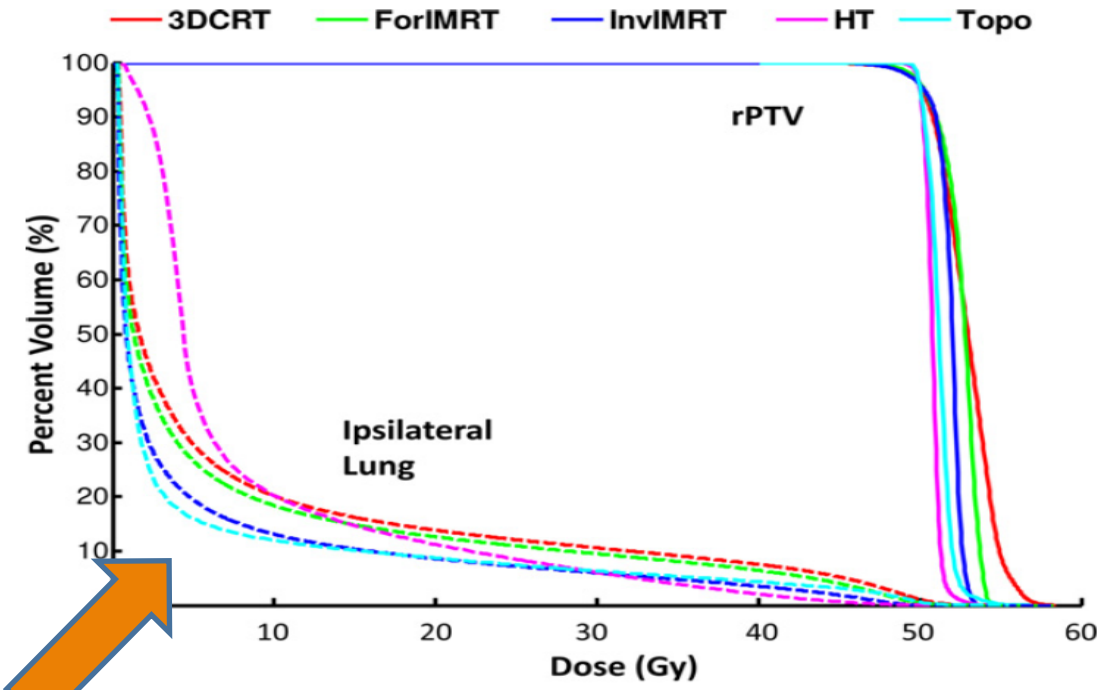
Original article

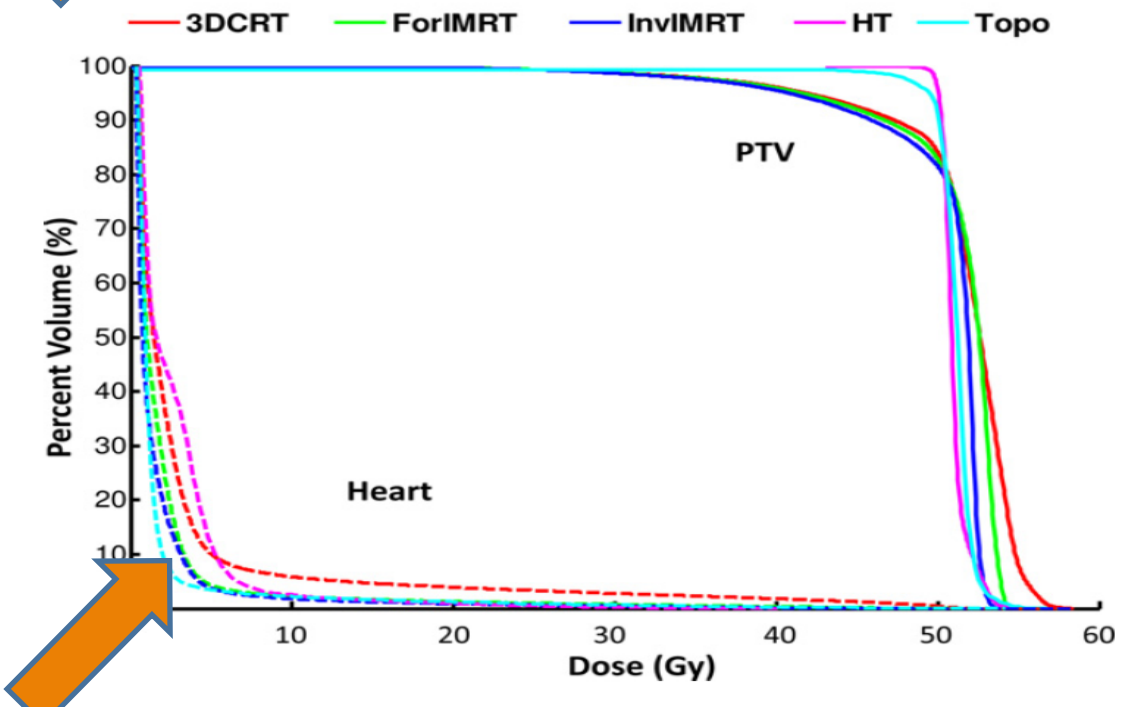
Dosimetric comparison of left-sided whole breast irradiation with 3DCRT, forward-planned IMRT, inverse-planned IMRT, helical tomotherapy, and topotherapy

Leah K. Schubert [a,*], Vinai Gondi [b], Evan Sengbusch [c], David C. Westerly [d], Emilie T. Soisson [e], Bhudatt R. Paliwal [b,c], Thomas Rockwell Mackie [b,c,f], Minesh P. Mehta [b], Rakesh R. Patel [b,g], Wolfgang A. Tomé [b,c], George M. Cannon [b]

Helical tomotherapy (HT) resulted in lowest heart and lung max doses but had higher mean doses

TomoDirect reduced ipsilateral lung mean and max doses compared to for-IMRT and 3D-CRT





Int. J. Radiation Oncology Biol. Phys., Vol. 78, No. 1, pp. 104–110, 2010

0360-3016/$–see front matter
doi:10.1016/j.ijrobp.2009.07.1705

CLINICAL INVESTIGATION Breast

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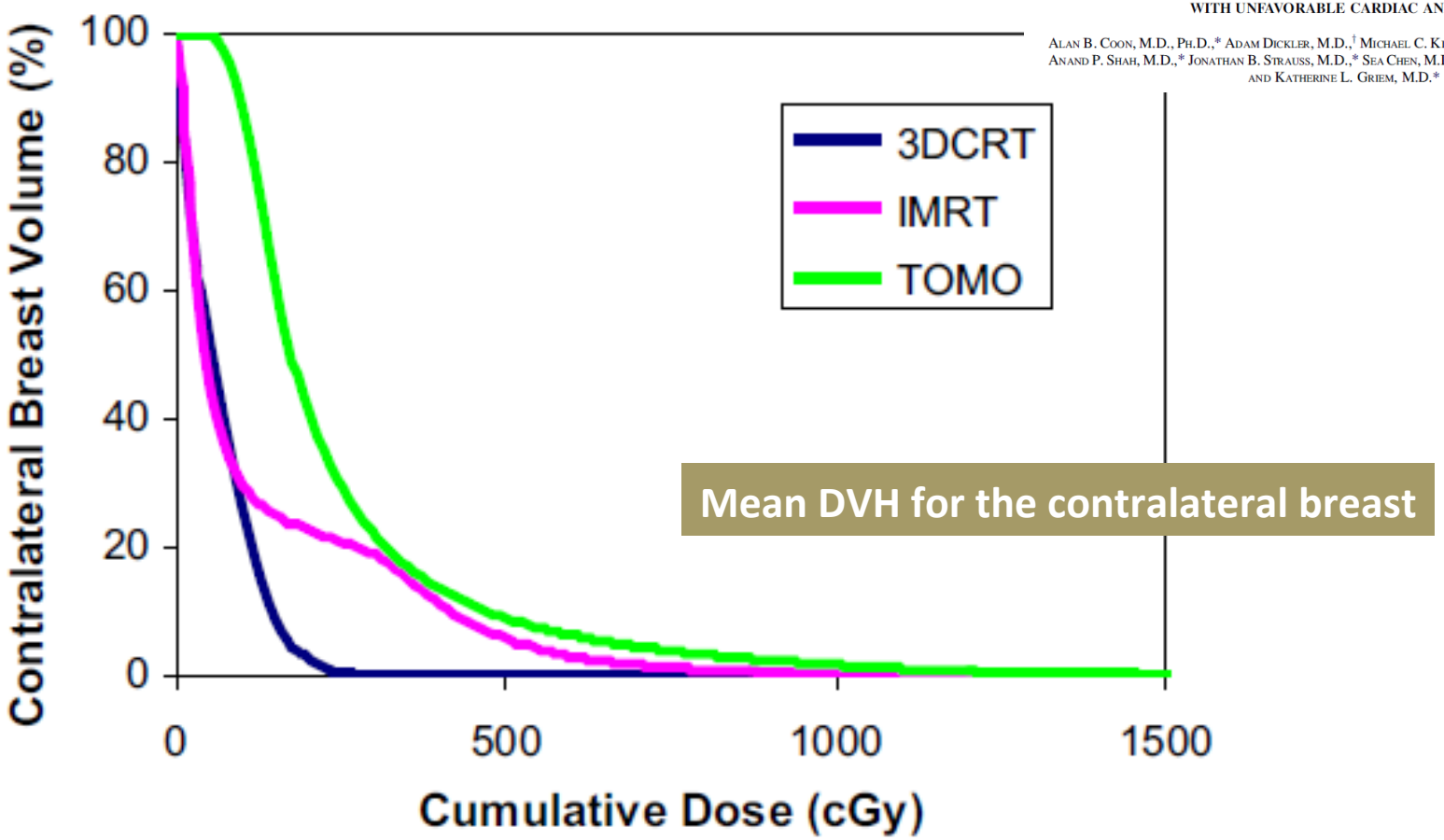


Mean DVH for the contralateral breast

Contralateral breast mean dose for TOMO (2.48 Gy) was higher than for 3D CRT (0.93 Gy) or IMRT (1.38 Gy)

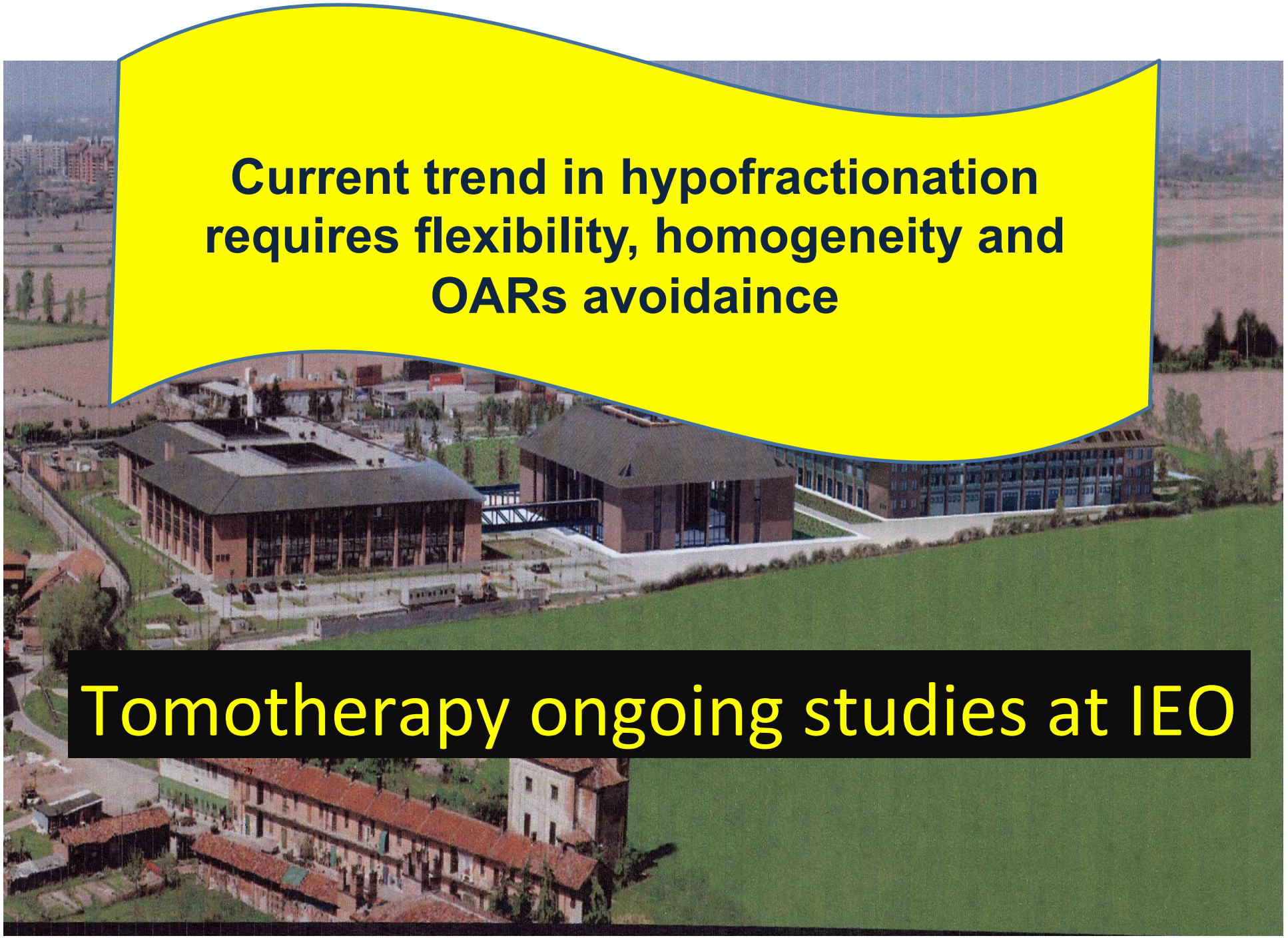
Ongoing Breast cancer IMRT studies

Study name	Principle research question	Number of patients	Status	Trial sponsor	Code
A clinical trial to reduce skin burn induced by breast radiotherapy using intensity-modulated radiation therapy	Phase III RCT of 2DRT versus IMRT	340	Completed	Sunnybrook Health Centre, Canada	NCT 00187343
Prospective randomised clinical trial testing 5.7 Gy and 6.0 Gy fractions of whole breast radiotherapy in terms of late normal tissue responses and tumour control (FAST)	Phase III RCT of standardly versus hypofractionated IMRT	900	Completed	Institute of Cancer Research, UK	ISRCTN 62488883
A randomised phase II trial comparison of radiation therapy techniques in the management of node-positive breast cancer	Phase I/II RCT of 2DRT versus IMRT	Not stated	Recruiting	University of Michigan Cancer Center, USA	NCT 00581256
Randomised trial testing intensity-modulated radiotherapy and partial organ radiotherapy following breast conservation surgery for early breast cancer (IMPORT LOW)	Phase III RCT of standard radiotherapy versus partial breast IMRT	1935	Recruiting	Institute of Cancer Research, UK	ISRCTN 12852634
Randomised trial testing dose escalated intensity-modulated radiotherapy in women with higher than average local tumour recurrence risk after breast conservation therapy for early breast cancer (IMPORT HIGH)	Phase III RCT of standard IMRT versus concomitantly boosted ± dose-escalation IMRT	840	In set-up	Institute of Cancer Research, UK	ISRCTN 4743744

Different endpoints studied

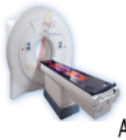
Background on Hypofractionation

- Since 1999 PBI, mainly with ELIOT
- Since 2003 WBI hypofractionated scheme (45 Gy to the whole breast plus and 5 Gy, concomitantly, to the tumor bed in 20 fractions, using 3 D-CRT)
- Since 2004, combination b/n ELIOT boost (12 Gy) and WBI (37.05 Gy/2.85 fraction/13 sessions)
- Since february 2012, starting with TomoDirect modality programs


Current trend in hypofractionation requires flexibility, homogeneity and OARs avoidaince
Tomotherapy ongoing studies at IEO

New irradiation schedules

- **Adiuvant hypofractionated radiotherapy+ simultaneous integrated boost after BCS**
- **Locoregional hypofractionated EBRT**
- **Partial breast reirradiation (APBReI)**
- **Whole Breast after PBI (POLO Study)**
- **Ultra-fast WBI after ELIOT boost (Aftereight Study)**



IEO Arc

Advanced Radiotherapy Center

Il meglio della cura con i raggi intelligenti

ELIOT boost 12 Gy + WB irradiation

FAST
3DCRT

ULTRA-FAST
TomoDirect

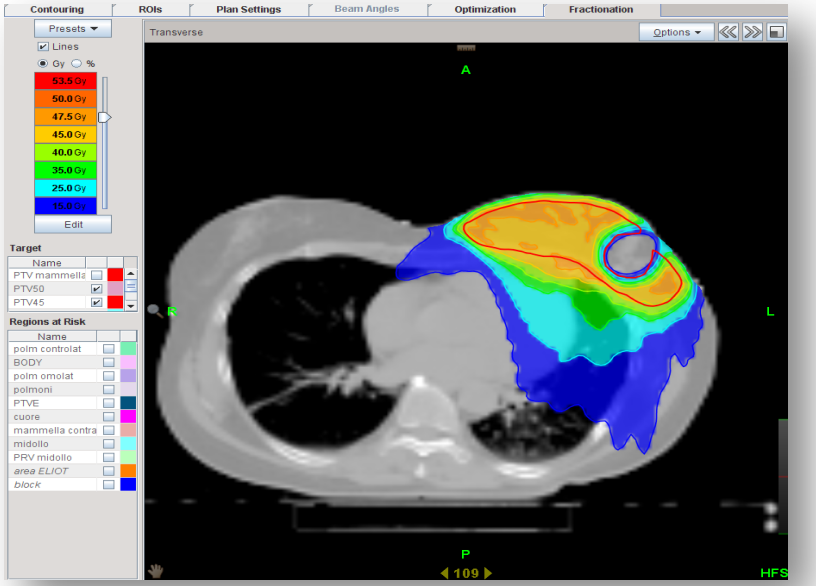
2.85 Gy x 13 fractions
37.05 Gy

4 Gy x 8 fractions
32 Gy

Alfa/beta	2.85 Gy x 13 WBI	4 Gy x 8 WBI
2	90	96
3	72	75
4	63	64
10	48	45

IEO Arc
Advanced Radiotherapy Center
Il meglio della cura con i raggi intelligenti

Aftereight study: 21 Gy IORT boost + 8 fraction- whole breast irradiation

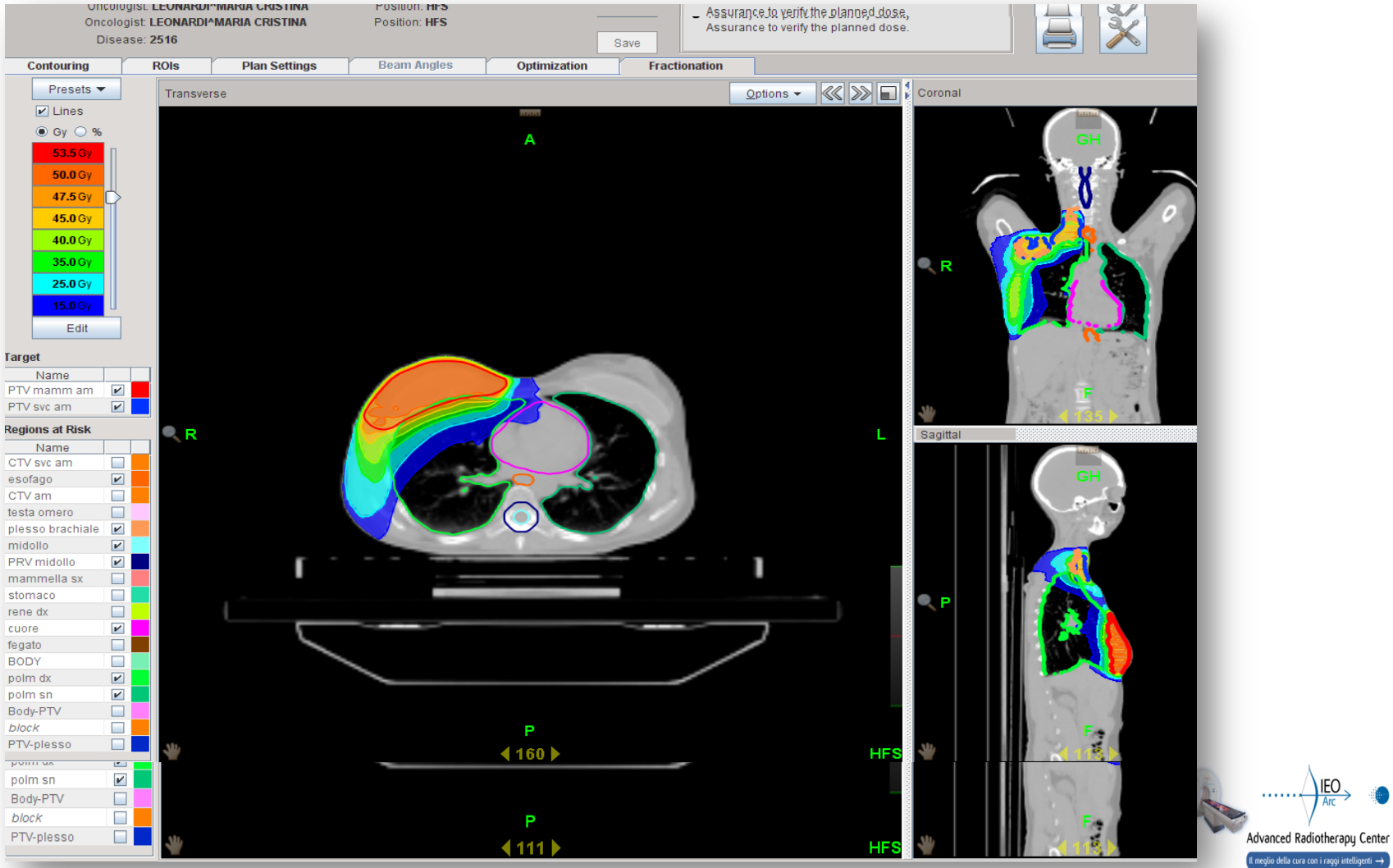


PTV

	Mean (%)	Median (%)	Range (%)
V95% ≥ 95% (V90% ≥ 90%)	98.6	98.6	97.7-99.5
V100% dose boost ≤ 30% (35%)	-	-	-
D50% ≤ 108% (112%)	100	100	100
Dmax ≤ 115% (120%)	113	113	112-114

Aftereight study	Ideal	Acceptable		Dosimetric report		
				Mean	median	range
Heart	D_{max} < 14 Gy	D_{max} < 18 Gy	Gy	-	-	-
Right breast	V_{7Gy} < 10 %	V_{7Gy} < 15 %	%	-	-	-
Heart	$D_{5\%}$ < 14 Gy	$D_{5\%}$ < 18 Gy	Gy	11.5	11.5	7.5-15.5
Left breast	V_{7Gy} < 30 %	V_{7Gy} < 35 %	%	7.2	7.2	5-9.3
heart	D_{mean} < 2,8 Gy	D_{mean} < 3,6 Gy	Gy	1.4	1.4	0.4-2.4
Ipsilateral lung	V_{14Gy} < 15%	V_{14Gy} < 20%	%	12.9	12.9	11-14.8
	V_{6Gy} < 35%	V_{6Gy} < 40%	%	19.1	19.1	17-21.2
	$V_{3,6Gy}$ < 50%		%	23.2	23.2	21-25.4
Contralateral lung	$V_{3,6Gy}$ < 10%	$V_{3,6Gy}$ < 15%	%	0	0	0
Contralateral breast	D_{max} < 2,1 Gy	D_{max} < 2,35 Gy	Gy	2.3	2.2	1.4-3.2
Spinal cord	D_{max} < 3,6 Gy		Gy	0.2	0.2	0.14-0.3
Liver	V_{11Gy} < 10%		%	0	0	
	D_{mean} < 3,6 Gy		Gy	0.2	0.2	0.09-0.22
Stomach	D_{mean}		Gy	0.6	0.6	

Locoregional hypofractionated EBRT



LOCOREGIONAL HYPOFRACTIONATED EBRT

2.67 Gy in 15 fr ***Total dose 40.05 Gy***

3 WEEKS

Target volumes coverage

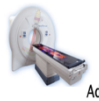
PTV breast/chest wall

% dose	% volume
95%	90%
90%	95%
107%	< 30%
D_{Mean} ≥ 99%	
$D_{0,03cc}$ <110%	

PTV supraclavicular

% dose	% volume
95%	90%
90%	95%
107%	< 30%
D_{Mean} ≥ 99%	
$D_{0,03cc}$ < 110%	

Delivery Mode: TomoHelical



IEO Arc
Advanced Radiotherapy Center
Il meglio della cura con i raggi intelligenti

Dosimetric reports: locoregional hypofractionated RT

Chest wall

Ideal	Acceptabie	UM	Dosimetric report		
			Mean (%)	Median (%)	Range (%)
$V_{95\%} \geq 90\%$	$V_{90\%} \geq 90\%$	%	95.2	96.2	87-100
$V_{90\%} \geq 95\%$	$V_{90\%} \geq 90\%$	%	99.2	99.6	97-100
$D_{mean} \geq 99\%$	$D_{mean} \geq 95\%$	%	99.8	99.9	95-104
$D_{0,03cc} \leq 110\%$	$D_{0,03cc} \leq 115\%$	%	107	107.4	101.3-110
$V_{107\%} \leq 30\%$		%	0.2	0.1	0-1.2

Supraclavicular region

Ideal	Acceptable	UM	Dosimetric reports		
			Mean (%)	Median (%)	Range (%)
$V_{95\%} \geq 85\%$	$V_{90\%} \geq 80\%$	%	73.4	76	44-100
$V_{90\%} \geq 90\%$	$V_{90\%} \geq 85\%$	%	92.3	95.6	50-100
$D_{mean} \geq 95\%$	$D_{mean} \geq 90\%$	%	95.5	95.4	85-108
$D_{0,03cc} \leq 110\%$	$D_{0,03cc} \leq 115\%$	%	105.7	106.3	95-113
$V_{107\%} \leq 30\%$		%	0.2	0	0-1.2

ADIUVANT HYPOFRACTIONATED RADIOTHERAPY
+
SIMULTANEOUS INTEGRATED BOOST (SIB)

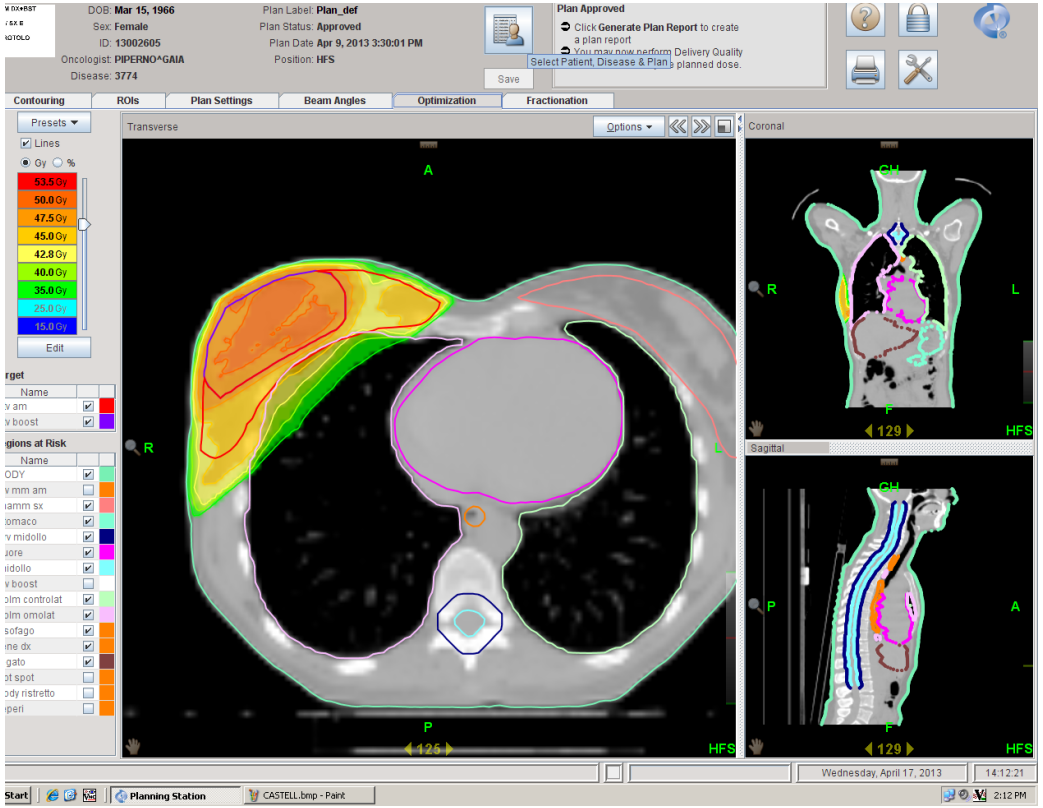
Target volumes coverage

PTV breast

% dose	% volume
95%	95%
50%	< 108%
100% boost dose	< 30%
115 %	0,03 cc

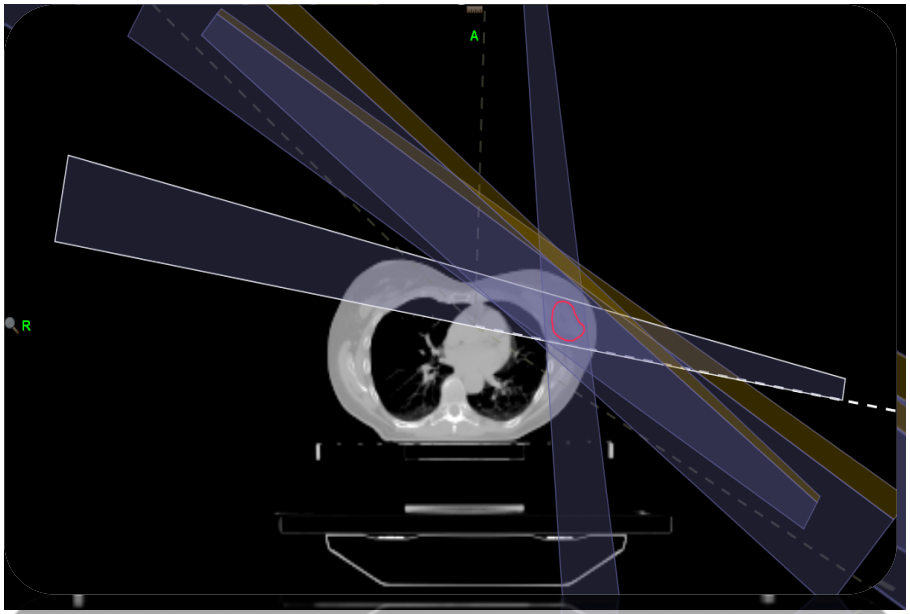
PTV boost

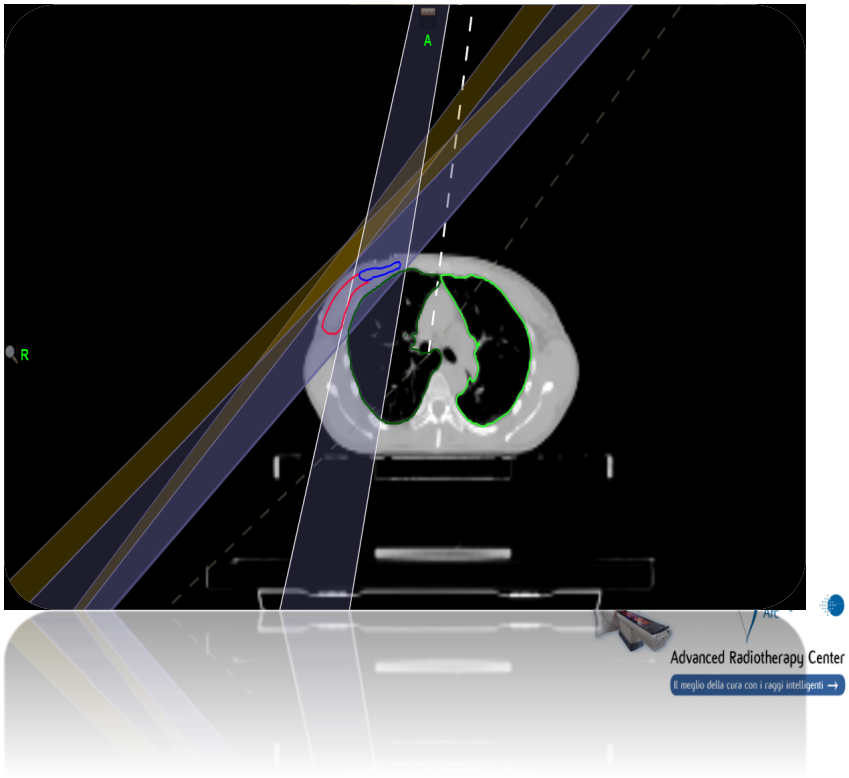
% dose	% volume
95%	95%
50%	< 100%
110%	5%
115 %	0,03 cc



ADIUVANT HYPOFRACTIONATED RADIOTHERAPY
+
SIMULTANEOUS INTEGRATED BOOST (SIB)

Whole breast	*Tumor bed*	
2.25 Gy x 20 fr	*2.50 Gy x 20 fr*	4weeks





Dosimetric report: SIB study

PTV breast

	Media (%)	Mediana (%)	Range (%)
$V_{95\%} \geq 95\%$ ($V_{90\%} \geq 90\%$)	98.8	99.3	93.2-102
$V_{100\%\ dose\ boost} \leq 30\%$ (35%)	0.5	0.1	0-13.6
$D_{50\%} \leq 108\%$ (112%)	101.1	101	96-107.2
$D_{max} \leq 115\%$ (120%)	113.3	113	102-119.5

PTV boost

	Media (%)	Mediana (%)	Range (%)
$V_{95\%} \geq 95\%$ ($V_{90\%} \geq 90\%$)	99.7	100	95-101.5
$V_{110\%} \leq 5\%$ (10%)			
$D_{max} \leq 115\%$ (120%)	103	103.6	101-116

SIB study -OARs	Ideal	Acceptable	UM	Dosimetric reports		
				Mean	Median	Range
Heart	D_{max} < 16 Gy	D_{max} < 20 Gy	Gy	2.5	2.1	0.5-9
Right breast	V_{8Gy} < 10 %	V_{8Gy} < 15 %	%	0.04	0	0-1
Heart	$D_{5\%}$ < 16 Gy	$D_{5\%}$ < 20 Gy	Gy	6	4.7	1-19
Left breast	V_{8Gy} < 30 %	V_{8Gy} < 35 %	%	4.7	4.7	0-16
Heart	D_{mean} < 3,2 Gy	D_{mean} < 4 Gy	Gy	1.4	0.7	0.2-14
Ipsilateral lung	V_{16Gy} < 15%	V_{16Gy} < 20%	%	12.3	13	1.8-23.6
	V_{8Gy} < 35%	V_{8Gy} < 40%	%	17.2	17.4	2.9-29.3
	V_{4Gy} < 50%		%	24.2	24	7.3-44
Contralateral lung	V_{4Gy} < 10%	V_{4Gy} < 15%	%	0.2	0	0-1.8
Contralateral breast	D_{max} < 2,4 Gy	D_{max} < 2,64 Gy	Gy	1.7	1.4	0-7
Stomach	Dmax		Gy	2.2	0.7	0.06-22.6
	Dmedia		Gy	0.4	0.4	0.05-1.2
Esofagus	Dmax		Gy	0.5	0.5	0.18-2

Heart constraints

TomoDirect

OAR	ideal	acceptable	UM	mean	median	range
Heart right breast	D_{max} < 16 Gy	D_{max} < 20 Gy	Gy	2.5	2.1	0.8 - 9
	V_{8Gy} < 10 %	V_{8Gy} < 15 %	%	0	0	0 - 1
Heart Left breast	$D_{5\%}$ < 16 Gy	$D_{5\%}$ < 20 Gy	Gy	8	7	1 - 18
	V_{8Gy} < 30 %	V_{8Gy} < 35 %	%	4.6	5	0 - 16
Heart	**D_{mean} < 3,2 Gy**	**D_{mean}< 4 Gy**	**Gy**	**1.4**	**0.7**	**0.2 - 14**

3D conformal

OAR	Ideal	UM	mean	median	range
Heart	**Dmean < 5 Gy**	**Gy**	**4.57**	**4.70**	**2-11.3**

Lung constraints

TomoDirect

OAR	ideal	aceeptable	UM	mean	median	range
ipsilateral lung	$V_{16Gy} < 15\%$	$V_{16Gy} < 20\%$	%	12.3	12.2	1.8 – 19.7
	$V_{8Gy} < 35\%$	$V_{8Gy} < 40\%$	%	17	17	2.9 - 29
	$V_{4Gy} < 50\%$		%	24	24	7.3 - 44
Contra.lung	$V_{4Gy} < 10\%$	$V_{4Gy} < 15\%$	%	0.2	0	0 – 1.8

3D conformal

OAR	Ideal		UM	mean	median	range
Ipsialteral lung	$V_{20Gy} < 20\%$		%	11.1	11.3	2.7-21.7

Contralateral breast

TomoDirect

OAR	ideal	acceptable	UM	mean	median	range
Contralat breast	D_{max} < 2,4 Gy	D_{max} < 2,64 Gy	Gy	1.7	1.7	0.47 – 5.1

3D conformal

OAR	Ideal		UM	mean	median	range
Contralat breast	< 10% prescription dose		Gy	4.83	4.70	0 – 10

Hypofractionation

Left side breast

Inadeguate standard treatment

When?