V ZOOM Journal Club 2015

Bologna, 19 Febbraio 2016

NH Hotel De La Gare

Prevenzione della Cardiotossicità

Contornazione e Tecnica

Fiorenza De Rose

HUMANITAS
CANCER CENTER

BACKGROUND

- Breast cancer is one of the most common malignancies among women (1.4 million cases/year)
- Long-term cause-specific survival has improved significantly over the past few decades
- More patients at risk of developing chronic toxicities associated with their care
- Cardiac toxicity could reduce their survival

Lee MS et al. Cardiovascular complications of radiotherapy. Am J Cardiol 2013;112:1688–96.
Kanapuru B et al. Long-term survival of older breast cancer patients: population-based estimates over three decades. Breast Cancer Res Treat 2012;134:853–7.

BACKGROUND

Accelerated atherosclerosis
Inflammation
Fibrosis
Fibrosis/Damage of the AV node and conduction system

Myocardial infarctions
Pericarditis
Congestive heart disease
Valvular disease
Arrhythmias

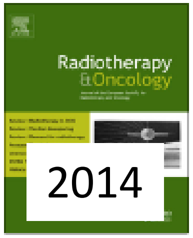
Duma MN et al. From heart to heart for breast cancer patients—cardiovascular toxicities in breast cancer radiotherapy. Strahlenther Onkol 2014 · 190:5–7

Literature Review

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com



Review

Cardiac dose sparing and avoidance techniques in breast cancer radiotherapy

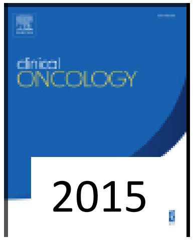
CrossMark

Chirag Shah [a], Shahed Badiyan [b], Sameer Berry [a], Atif J. Khan [c], Sharad Goyal [c], Kevin Schulte [a], Anish Nanavati [d], Melanie Lynch [a], Frank A. Vicini [e,*]

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net



Overview

Cardiac Side-effects From Breast Cancer Radiotherapy

CrossMark

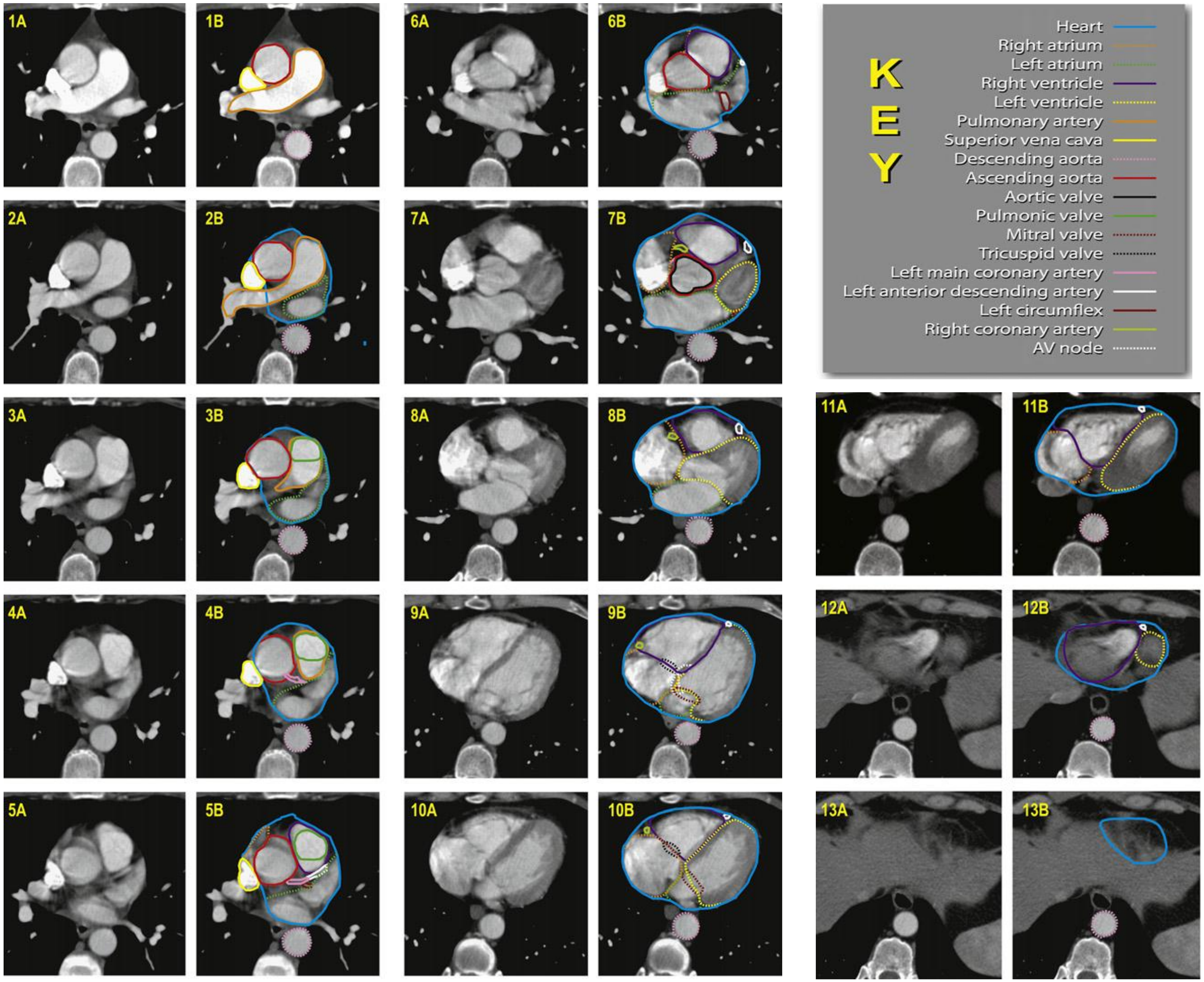
C.W. Taylor [*], A.M. Kirby [†]

OUTLINE

- Heart atlas and Cardiac radiation dose
- Reduction in cardiac exposure:

  Which technique?
  - IMRT and Arc Therapy
  - Proton Beam Therapy
  - Prone breast radiotherapy
  - Deep-inspiratory Breath-hold

Heart Contouring



Feng M et al. Development and validation of a heart atlas to study cardiac exposure to radiation following treatment for breast cancer. J. Radiation Oncology Biol. Phys., Vol. 79, No. 1, pp. 10–18, 2011

Heart Contouring

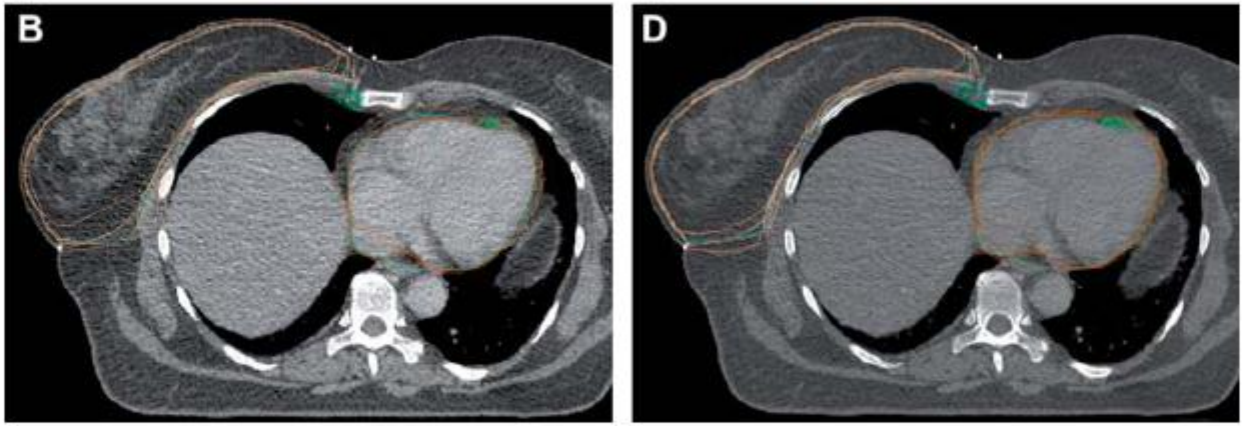


Table III. Mean and ranges of DSC before and after consensus.

Volume	Consensus volume (ml)	Mean DSC (range) Before consensus	Mean DSC (range) After consensus
Breast	1247	0.93 (0.89–0.96)	0.95 (0.93–0.96)
Boost	40	NA	0.75 (0.60–0.89)
Internal mammary LN	15	0.59 (0.32–0.72)	0.71 (0.63–0.81)
Axillary LN level I	108	0.65 (0.59–0.75)	0.70 (0.60–0.77)
Axillary LN level II	32	0.56 (0.35–0.69)	0.76 (0.67–0.84)
Axillary LN level III	17	0.56 (0.39–0.73)	0.74 (0.66–0.82)
Periclavicular LN	47	0.41 (0.34–0.56)	0.56 (0.43–0.73)
Interpectoral LN	33	0.54 (NA)	0.66 (0.55–0.78)
Heart	731	0.91 (0.88–0.94)	0.94 (0.90–0.96)

DSC, Dice similarity coefficient; NA, not available.

Nielsen MH et al. Delineation of target volumes and organs at risk in adjuvant radiotherapy of early breast cancer: National guidelines and contouring atlas by the Danish Breast Cancer Cooperative Group. Acta Oncologica; 52: 703–710. 2013

Heart Contouring

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ELSEVIER

Radiotherapy & Oncology

2013

Cardiac dosimetry in breast cancer

Inter-observer variation in delineation of the heart and left anterior descending coronary artery in radiotherapy for breast cancer: A multi-centre study from Denmark and the UK

CrossMark

Ebbe L. Lorenzen[a,b,*], Carolyn W. Taylor[c], Maja Maraldo[d], Mette H. Nielsen[e], Birgitte V. Offersen[f], Maria R. Andersen[a], Dean O'Dwyer[a], Lone Larsen[g], Sharon Duxbury[h], Baljit Jhitta[h], Sarah C. Darby[c], Marianne Ewertz[e,b], Carsten Brink[a,b]

Table 1
Measures for heart and LADCA delineations performed without and with common guidelines. *p*-Values are given for difference between without and with guidelines and are bold when significant.

	Units	Without guidelines		With guidelines		p-Value
		Average	Range	Average	Range	
Heart						
Volume	cm^3	**668**	**484–820**	**751**	**553–931**	**<0.0001**
Mean DSI		**0.89**	**0.84–0.93**	**0.93**	**0.91–0.95**	**<0.0001**
Mean JSI		**0.80**	**0.73–0.88**	**0.88**	**0.83–0.90**	**<0.0001**
CV mean dose	%	**7.5**	**3.4–13**	**3.6**	**1.9–8.5**	**<0.0001**
CV maximum dose	%	**8.7**	**2.3–27.8**	**4**	**0.9–10.2**	**0.002**
Mean dose	Gy	**2.0**	**1.1–3.1**	**2.1**	**1.2–3.4**	**0.0008**
Maximum dose	Gy	**39**	**24–48**	**42**	**26–49**	**<0.0001**
LADCA						
CV mean dose	%	27	10–40	29	17–60	0.50
CV maximum dose	%	39	15–63	31	9–49	0.069
Mean dose	Gy	**5.4**	**3.2–11**	**7.0**	**3.0–14**	**<0.0001**
Maximum dose	Gy	**20**	**8.6–33**	**26**	**9.8–42**	**<0.0001**

Cardiac dose constraints

Table II. Constraints for organs at risk in adjuvant radiotherapy of early breast cancer.

Organ at risk	Normofractionation 2 Gy per fraction/ 5 fractions/week
LADCA	$V_{20Gy} = 0\%$
Heart	$V_{20Gy} = 10\%, V_{40Gy} = 5\%$
Ipsilateral lung	$V_{20Gy} = 25\%$ (exclusive periclavicular LN)
	$V_{20Gy} = 35\%$ (inclusive periclavicular LN)
	Mean dose < 18 Gy
Spinal cord	Max. 45 Gy
Plexus brachialis	Max. 54 Gy
Maximal dose of CTV	107% = 53.5 Gy
Maximal dose outside PTV	54 Gy

CTV, clinical target volume; LADCA, left anterior descending coronary artery; LN, lymph nodes; PTV, planning tumor volume.

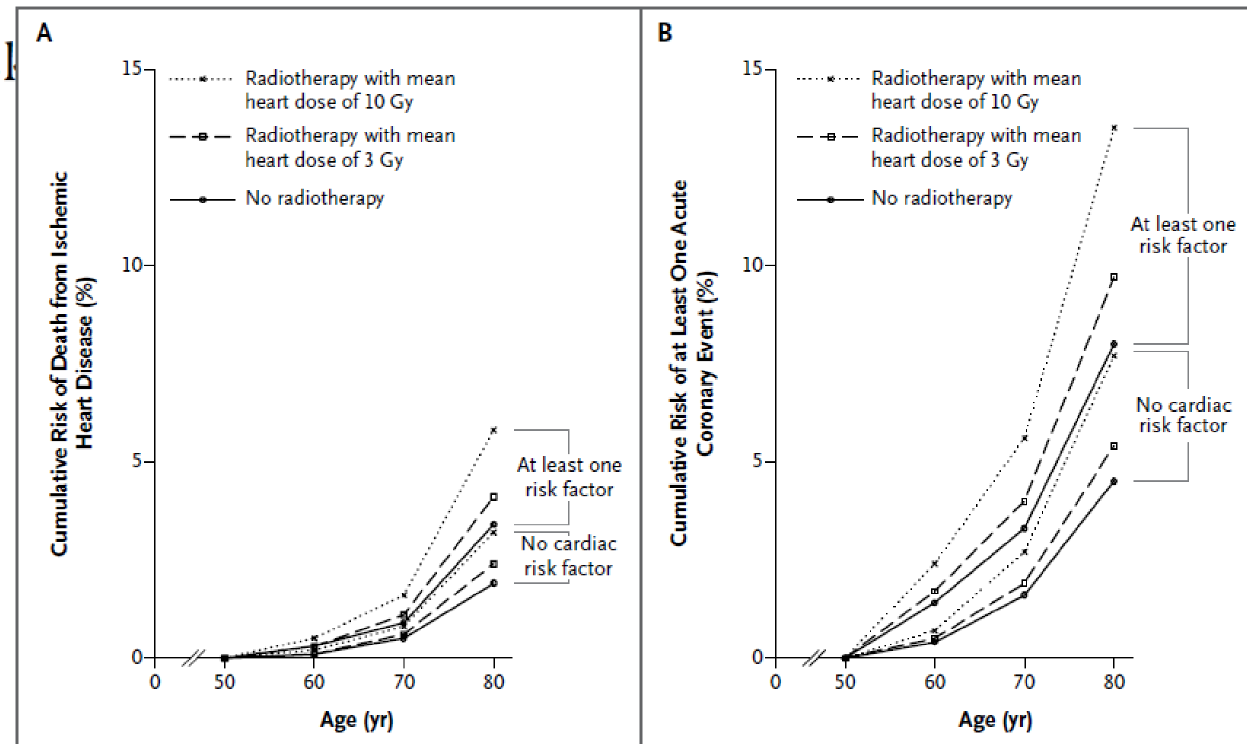
Nielsen MH et al. Delineation of target volumes and organs at risk in adjuvant radiotherapy of early breast cancer: National guidelines and contouring atlas by the Danish Breast Cancer Cooperative Group. Acta Oncologica; 52: 703–710. 2013

Cardiac dose constraints

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 14, 2013 VOL. 368 NO. 11

Risk



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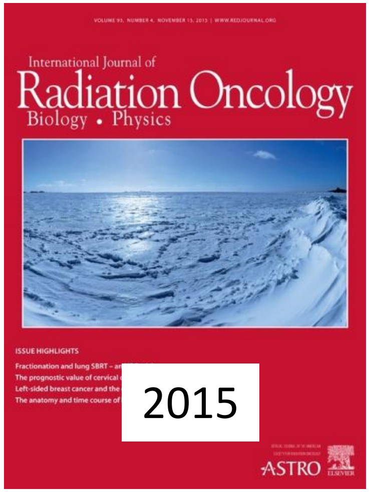
Heart dose from breast cancer RT

Clinical Investigation

Exposure of the Heart in Breast Cancer Radiation Therapy: A Systematic Review of Heart Doses Published During 2003 to 2013

Carolyn W. Taylor, DPhil, FRCR,* Zhe Wang, PhD,*
Elizabeth Macaulay, MSc,† Reshma Jagsi, MD, DPhil,‡
Frances Duane, FFRRCSI,* and Sarah C. Darby, PhD*



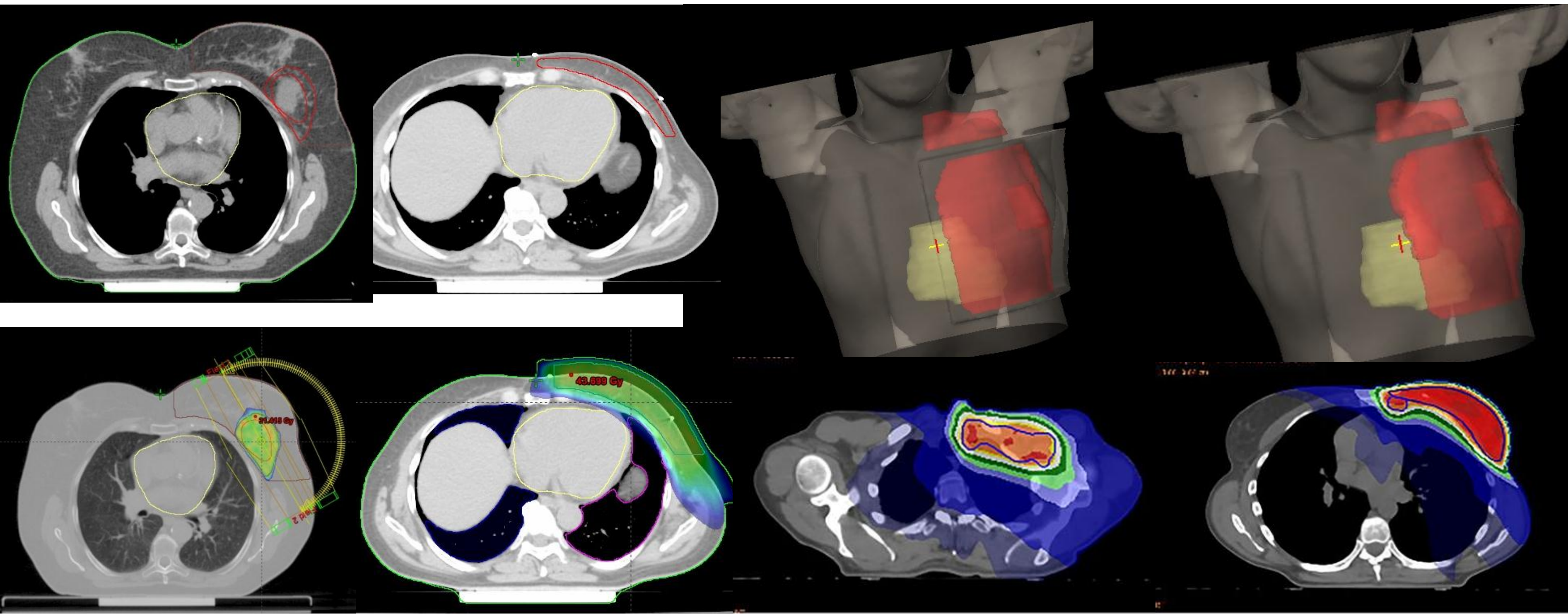
Whole-heart dose: **the most commonly** reported measure

Variability affected by:

- Tecnique
- More extensive targets
- Unfavorable anatomy
- Interobserver variation in cardiac contouring

Heart dose from breast cancer RT

PBI | WBI | WBI+SCF | WBI+SCF+IMC



1.1 Gy | 3.7 Gy | 6.1 Gy | 8.5 Gy

Average mean heart dose

OUTLINE

- Heart atlas and Cardiac radiation dose
- Reduction in cardiac exposure:

  Which technique?

  - IMRT and Arc Therapy
  - Proton Beam Therapy
  - Prone breast radiotherapy
  - Deep-inspiratory Breath-hold

IMRT and Arc Therapy

Zhao *et al. Radiation Oncology* (2015) 10:231
DOI 10.1186/s13014-015-0531-4

RADIATION ONCOLOGY

Table 4 Dose comparison of the heart, coronary artery and heart minus coronary artery in the four plans

Structure	Dose parameter	2FIMRT	4FIMRT	2ArcVMAT	1ArcVMAT
Heart	D_{mean}(Gy)	2.8 ± 1.0 [A]	3.0 ± 1.4 [a]	3.3 ± 1.3 [B]	3.7 ± 1.4 [B,b]
	D_{max}(Gy)	50.2 ± 2.3 [A]	48.2 ± 3.7 [B,a]	44.1 ± 15.7	45.4 ± 5.2 [B,b]
	V5	8.6 % ± 3.8 % [A]	[illegible]	[illegible]	…2 % [B,b]
	V20	3.4 % ± 1.7 % [A]	[illegible]	[illegible]	…5 % [A]
	V40	0.9 % ± 0.5 % [A]	[illegible]	[illegible]	…5 % [B,b]
CA	D_{mean}(Gy)	13.2 ± 3.9	[illegible]	[illegible]	[illegible]
	D_{max}(Gy)	50.2 ± 1.7 [A]	[illegible]	[illegible]	… [B]
	V5	56.4 % ± 15.4 % [A]	[illegible]	[illegible]	…5.2 % [B]
	V20	26.1 % ± 10.5 %	[illegible]	[illegible]	…3.3 % [B]
	V40	7.3 % ± 3.8 % [A]	[illegible]	[illegible]	…5 % [B]
Heart-CA	D_{mean}(Gy)	1.4 ± 0.5 [A]	[illegible]	[illegible]	… [,b]
	V5	2.4 % ± 2.0 % [A]	[illegible]	[illegible]	…5 % [B,b]
	V20	0.3 % ± 0.6 %	[illegible]	[illegible]	…1 %
	V40	0.1 % ± 0.2 %	0.1 % ± 0.2 %	0.1 % ± 0.2 %	0.0 % ± 0.1 %

"A" is statistically significantly different from "B" ($p < 0.05$); "a" is statistically significantly different from "b" ($p < 0.05$). No other statistically significant difference was found between any two ($p > 0.05$)

… "2-F IMRT plan has demonstrated the combined advantages in PTV dose coverage and dose drop to most normal tissue involved in our research, besides for the heart and coronary artery. So **we suggest employing 2 F-IMRT plan for left breast cancer radiotherapy after breast-conserving surgery**".

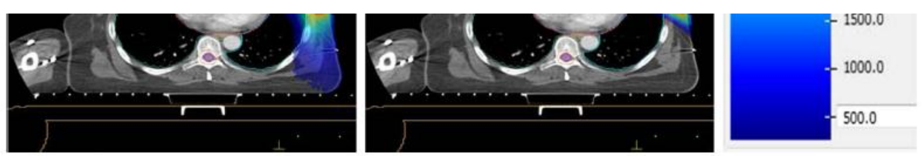
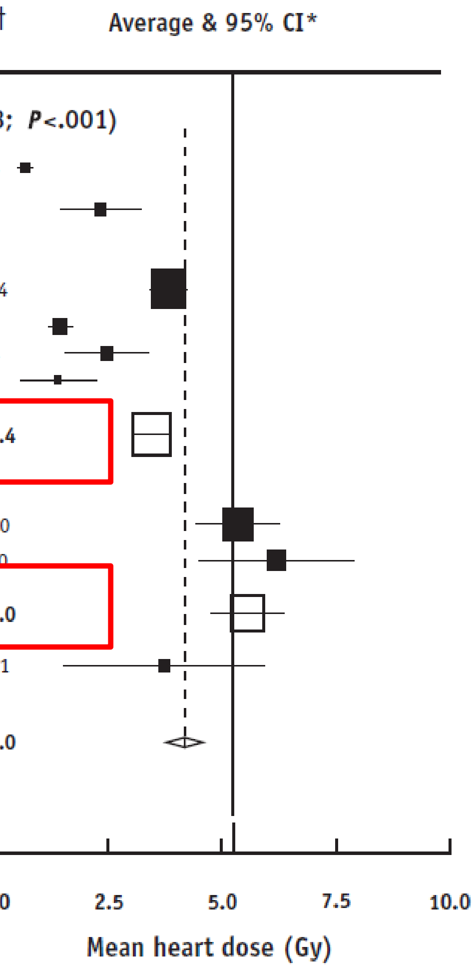


Fig. 2 Isodose distributions for IMRT and VMAT treatment plans

V20
V40

IMRT and Arc Therapy

	Number of regimens	Mean heart dose (Gy) Average* (SE)	Range†
a Internal mammary chain NOT irradiated (χ^2_8 = 420.3; *P*<.001)			
Protons	6	0.5 (0.1)	0.1 – 0.8
Brachytherapy	8	2.2 (0.5)	<0.1 – 3.8
Tangents‡			
Supine + NO breathing control	112	3.8 (0.2)	<0.1 – 12.4
Supine + breathing control	14	1.3 (0.1)	0.4 – 2.5
Prone position	11	2.4 (0.5)	0.4 – 5.4
Lateral decubitus position	2	1.2 (0.4)	0.8 – 1.7
All tangents	**(139)**	**3.4 (0.2)**	**<0.1 – 12.4**
IMRT‖			
Standard	76	5.4 (0.5)	0.5 – 23.0
Rotational fields	26	6.3 (0.9)	<0.1 – 18.0
All IMRT	**(102)**	**5.6 (0.4)**	**<0.1 – 23.0**
Others	9	3.7 (1.2)	0.2 – 10.1
(a) Subtotal	**264**	**4.2 (0.2)**	**<0.1 – 23.0**



Difference between (a) and (b): χ^2_1 = 55.93; *P*<.001

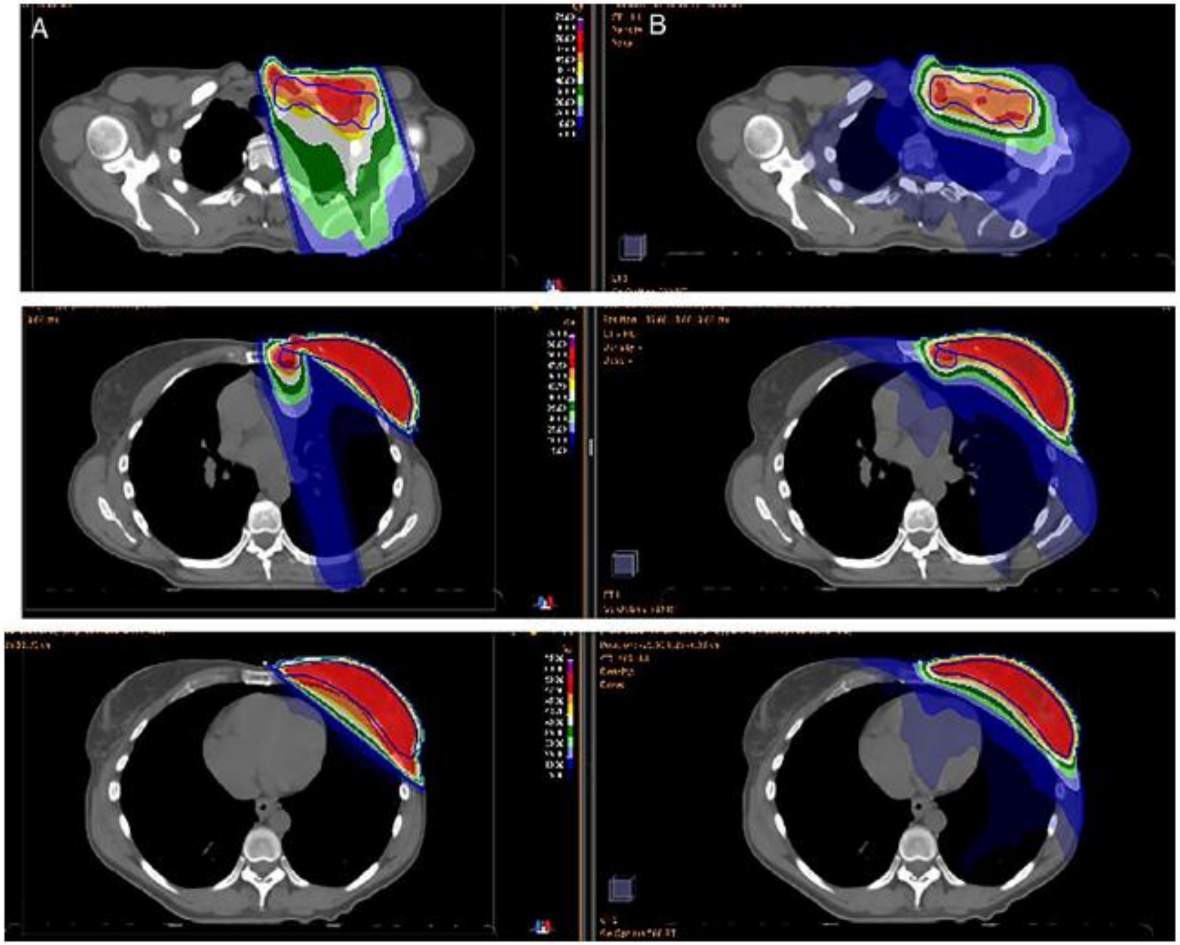
Taylor CW, Wang Z, Macaulay E et al. Exposure of the Heart in Breast Cancer Radiation Therapy: A Systematic Review of Heart Doses Published During 2003 to 2013 .Int J Radiation Oncol Biol Phys, Vol. 93, No. 4, pp. 845e853, 2015

IMRT and Arc Therapy

Journal of Radiation Research, Vol. 56, No. 6, 2015, pp. 927–937
doi: 10.1093/jrr/rrv052
Advance Access Publication: 19 September 2015

Journal of Radiation Research

OXFORD



The **high doses delivered to the heart and the LCA** (illustrated by the D2%) were **reduced using the VMAT plans**. The **mean dose to the heart** was acceptable using the VMAT plans, but this was **even lower using a forward-planned** multi-segment technique with a monoisocenter

IMRT and Arc Therapy

Table 2. Plan comparison parameters, mean values for VMAT and MONOISO for this study and for other studies of the literature concerning similar volumes treated with static and dynamic intensity-modulated radiotherapy

	VMAT (study)	MONO ISO (study)	Popescu [6]		Sakumi [7]		Pasler [16]	Caudrelier [24]	Goddu [23]	Jagsi [31]	Krueger [25]	Dogan [29]	Van der Laan [28]	Beckham [27]	Popescu [26]	Cozzi [30]
n =	10		5		5		10	10	10	10	10	10	10	30	5	10
Technique	VMAT	MONO ISO	Rapid Arc	MWT	VMAT	MWT	VMAT	TOMO	TOMO	IMRT 9 fields	IMRT 9 fields	IMRT 9 fields	IMRT 9 fields	IMRT 11 fields	IMRT 11 fields	IMRT
Target volumes	Left breast supra-clav, II III, IMC		Left breast supra-clav, II III, IMC		Left breast supra-clav, III IMC		Left breast supra-clav, III + tumor bed	Left breast supra-clav, II III, IMC	Left breast supra-clav, II III, IMC	Left chest-wall supra-clav, III, IMC	Left chest-wall supra-clav, II III, IMC	Left chest-wall supra-clav, I II III, IMC	Left chest-wall supra-clav, IMC	Left breast, IMC	Left breast, IMC	Left and right breasts, IMC
Heart																
V30 (%)	1.3	2.7	2.6	16.0	3.0	14.0	2.7	1.5		0.0	0.1		5.3	0.7	3.0	
D2% (Gy)	26.0	32.0					32.0							47.0		53[f]
Dmean (Gy)	8.6	6.7	11.0	11.0	11.0		8.9	7.0	12.0	7.2		4.1	10.0		13.0	9.9
LCA																
Dmean (Gy)	18.0	19.5								11.2						
D2%	34.4	40.3								19.3[d]						

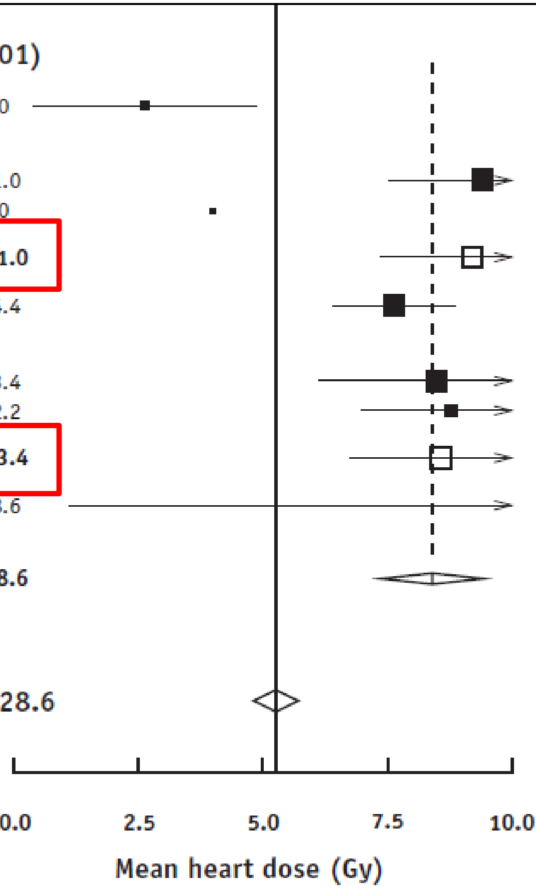
… "VMAT improved PTV coverage and dose homogeneity, but clinical benefits remain unclear. Decreased dose exposure of the LCA may be clinically relevant. VMAT could be used for complex treatments difficult with conventional techniques. Patient age should be considered because of uncertainties concerning secondary malignancies".

Tyran M et al. Volumetric-modulated arc therapy for left-sided breast cancer and all regional nodes improves target volumes coverage and reduces treatment time and doses to the heart and left coronary artery, compared with a field-in-field technique Journal of Radiation Research, Vol. 56, No. 6, 2015, pp. 927–937

IMRT and Arc Therapy

	Number of regimens	Mean heart dose (Gy) Average* (SE)	Range†
b Internal mammary chain irradiated		($\chi^2_5 = 40.2$; $P<.001$)	
Protons	4	2.6 (1.1)	1.0 – 6.0
Tangents‡¶			
Supine + NO breathing control	27	9.4 (1.0)	1.9 – 21.0
Supine + breathing control	1	4.0	4.0 – 4.0
All tangents	**(28)**	**9.2 (0.9)**	**1.9 – 21.0**
Wide tangents	25	7.6 (0.6)	2.5 – 14.4
IMRT‖			
Standard	24	8.5 (1.2)	0.7 – 23.4
Rotational fields	8	8.8 (0.9)	5.4 – 12.2
All IMRT	**(32)**	**8.6 (0.9)**	**0.7 – 23.4**
Others	4	12.0 (5.6)	4.9 – 28.6
(b) Subtotal	**93**	**8.4 (0.5)**	**0.7 – 28.6**
Total	**357**	**5.3 (0.2)**	**<0.1 – 28.6**

Average & 95% CI*



Difference between (a) and (b): $\chi^2_1 = 55.93$; $P<.001$

Taylor CW, Wang Z, Macaulay E et al. Exposure of the Heart in Breast Cancer Radiation Therapy: A Systematic Review of Heart Doses Published During 2003 to 2013 .Int J Radiation Oncol Biol Phys, Vol. 93, No. 4, pp. 845e853, 2015

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- Heart atlas and Cardiac radiation dose
- Reduction in cardiac exposure:

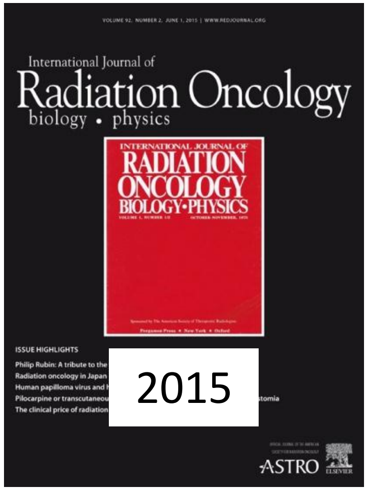
  Which technique?
  - IMRT and Arc Therapy
  - Proton Beam Therapy
  - Prone breast radiotherapy
  - Deep-inspiratory Breath-hold

Proton Beam Therapy

Clinical Investigation

Early Toxicity in Patients Treated With Postoperative Proton Therapy for Locally Advanced Breast Cancer

John J. Cuaron, MD,[*] Brian Chon, MD,[†] Henry Tsai, MD,[†] Anuj Goenka, MD,[†] David DeBlois, MD,[†] Alice Ho, MD,[*] Simon Powell, MD,[*] Eugen Hug, MD,[†] and Oren Cahlon, MD[*,†]



… "These patients were not part of a clinical trial. Patients were generally referred because of **unfavorable cardiopulmonary anatomy.** Postlumpectomy patients were not offered treatment if **large breast size** (defined as having breast anatomy that was prone to significant interfraction mobility) **would preclude accurate setup**".

Proton Beam Therapy

Table 1 Patient characteristics

Age (y), median (range)	49 (29-86)
Stage	
II	8 (26.7)
III	20 (66.7)
Chest wall recurrence	2 (6.7)
Histology	
IDC	27 (90)
ILC	3 (10)
Side	
Left	27 (90)
Right	3 (10)
Chemotherapy	
Neoadjuvant	13 (43.3)
Adjuvant	14 (46.7)
Anthracycline-based	21 (70)
Concurrent herceptin	4 (13.3)
None	3 (10)
Surgery	
Lumpectomy (BCS)	4 (13.3)
Chest wall wide local excision (recurrence)	2 (6.7)
Mastectomy + implant reconstruction	14 (46.7)
Mastectomy + autologous reconstruction	1 (3.3)
Mastectomy + no reconstruction	9 (30)

Table 2 Dosimetry values

PTV	
V100 (%)	89.20 (68.56-96.30)
V95 (%)	96.43 (79.39-99.60)
V110 (%)	13.30 (3.02-34.98)
Max point dose, Gy (RBE)	58.84 (50.8-70.5)
Heart (left-sided tumors, n=27)	
Mean dose, Gy (RBE)	1.0 (0.09-3.20)
V20 (%)	1.16 (0-6.0)
V5 (%)	5.00 (0.17-14.40)
Max point dose, Gy (RBE)	22.80 (2.48-43.70)
Lungs	
Total V20 (%)	7.31 (0.14-13.2)
Ipsilateral V20 (%)	16.50 (6.1-30.3)
Ipsilateral V5 (%)	34.35 (22.5-53.8)
Contralateral V5 (%)	0.34 (0-5.30)
Contralateral breast	
Mean dose, Gy (RBE)	0.29 (0.03-3.50)
V5 (%)	1.46 (0-9.90)
Spinal cord	
Max point dose, Gy (RBE)	1.24 (0-28.1)
Esophagus	
Mean dose, Gy (RBE)	7.50 (0-19.59)
V30 (%)	10.80 (0-37.0)
V40 (%)	3.40 (0-28.9)
Max point dose, Gy (RBE)	45.65 (0-65.4)

Cuaron JJ et al. Early Toxicity in Patients Treated With Postoperative Proton Therapy for Locally Advanced Breast Cancer. Int J Radiation Oncol Biol Phys, Vol. 92, No. 2, pp. 284-291, 2015

Proton Beam Therapy

	Number of regimens	Mean heart dose (Gy)		
		Average* (SE)	Range†	Average & 95% CI*
b Internal mammary chain irradiated		(χ^2_5 = 40.2; *P*<.001)		
Protons	4	2.6 (1.1)	1.0 – 6.0	
Tangents[‡¶]				
Supine + NO breathing control	27	9.4 (1.0)	1.9 – 21.0	
Supine + breathing control	1	4.0	4.0 – 4.0	
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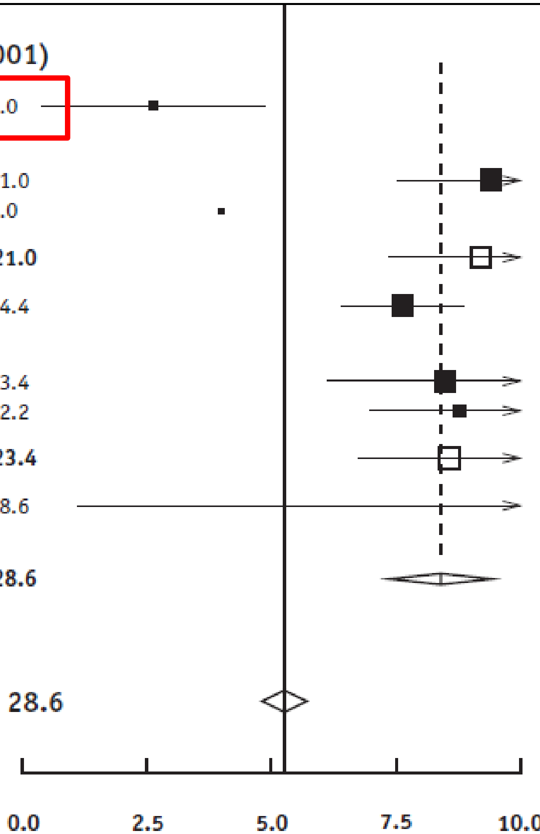

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Prone breast radiotherapy

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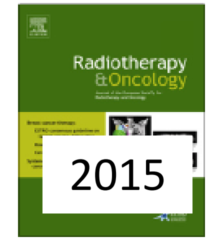
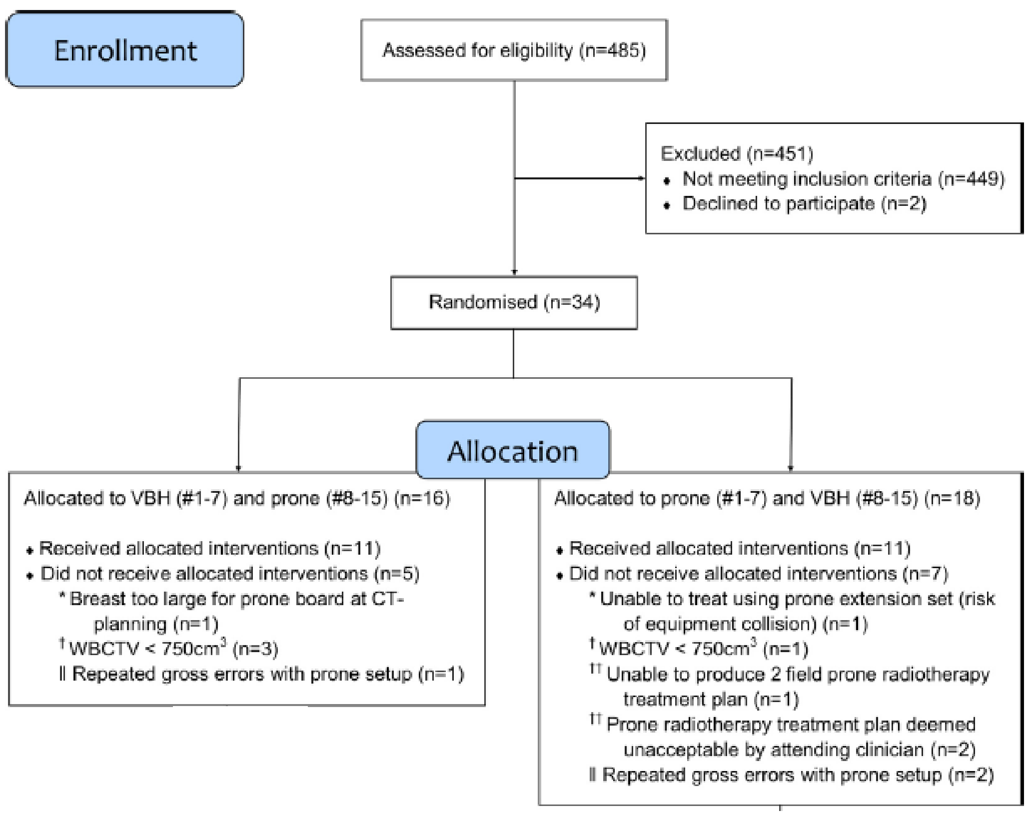


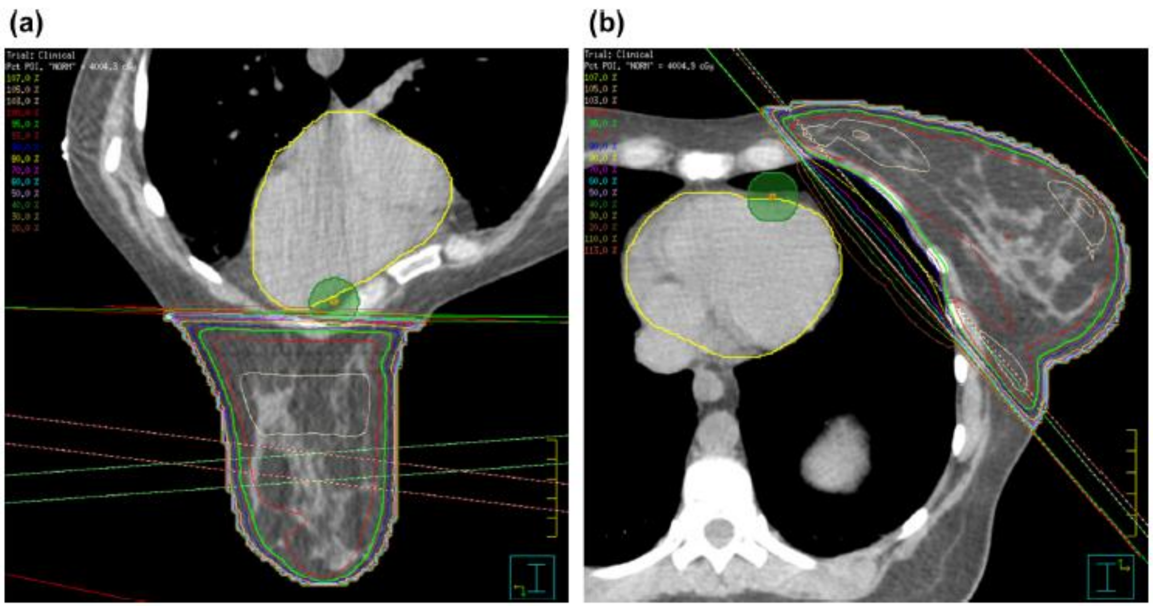
Phase III randomised trial

The UK HeartS… of a voluntary … breast conserv…

Frederick R. Bartle… Carr [a],
Philip M. Evans [b,c], … Anna M. Kirby [a]



Prone breast radiotherapy



Results (sVBH vs. pFB)

- Heart NTDmean 0.44 vs. 0.66 ($p < 0.001$)
- LAD NTDmean 2.9 vs. 7.8 ($p < 0.001$)
- LAD max 21.0 vs. 36.8 ($p < 0.001$)

“Our data suggest that, in **larger-breasted women, supine VBH treatment is better at sparing cardiac tissues and more reproducible** than treatment using a free-breathing prone technique. Patients find VBH more comfortable than the prone position. Treatment setup and total treatment session times are shorter with VBH”.

Bartlett FR et al. The UK HeartSpare Study (Stage IB): Randomised comparison of a voluntary breath-hold technique and prone radiotherapy after breast conserving surgery. Radiotherapy and Oncology 114 (2015) 66–72

Prone breast radiotherapy

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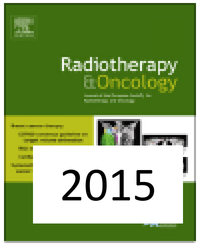


Avoidance of cardiac toxicity

Heart dose reduction by prone deep inspiration breath hold in left-sided breast irradiation

CrossMark

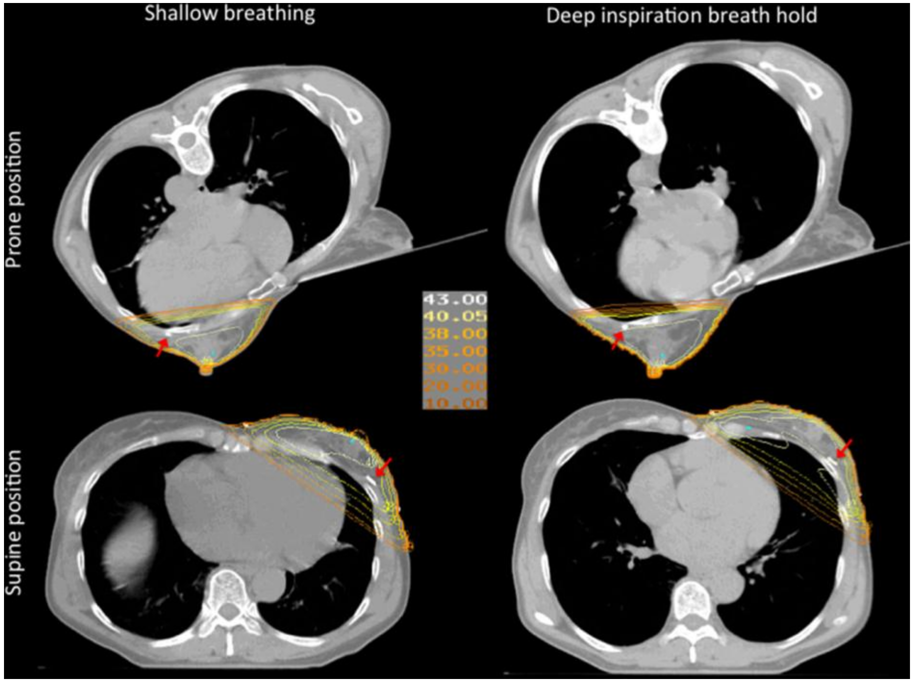
Thomas Mulliez [a,b,*], Liv Veldeman [a], Bruno Speleers [a], Khalil Mahjoubi [b], Vincent Remouchamps [b], Annick Van Greveling [a], Monique Gilsoul [b], Dieter Berwouts [a], Yolande Lievens [a], Rudy Van den Broecke [c], Wilfried De Neve [a]

Materials and methods

12 pts (EC) received four computed tomography (CT) scans:
supine and prone position, both with and without the DIBH maneuver
These pts were treated in supine position with the breath hold maneuver if indicated.
38 pts (VC) received only two planning CT scans:
prone SB and prone DIBH.
8 were treated in prone SB, the last 30 patients were accepted for prone DIBH treatment.

Prone breast radiotherapy

	Supine SB	Supine DIBH	Prone SB			Prone DIBH		
	EC	EC	EC	VC	All	EC	VC	All
Heart								
D_{mean} (Gy)	4.0 ± 1.8	2.2 ± 1.2	*2.5 ± 1.1*	*2.1 ± 0.7*	2.2 ± 0.8	*1.4 ± 0.4*	*1.3 ± 0.3*	1.3 ± 0.3
D_{max} (Gy)	29.3 ± 10.6	14.6 ± 12.0	*19.6 ± 13.1*	*15.1 ± 8.6*	16.2 ± 9.9	*5.3 ± 2.0*	*5.6 ± 3.6*	5.5 ± 3.3
LAD								
D_{mean} (Gy)	17.6 ± 7.2	10.9 ± 7.8	*12.0 ± 7.1*	*7.1 ± 3.9*	8.3 ± 5.3	*4.1 ± 1.6*	*3.1 ± 1.9*	3.3 ± 1.8
D_{max} (Gy)	36.1 ± 7.5	25.5 ± 12.4	*29.8 ± 8.0*	*25.6 ± 10.5*	26.6 ± 10.0	*14.9 ± 6.6*	*12.2 ± 9.1*	12.9 ± 8.7
Lung								
volume (cc)	1235 ± 485	2090 ± 557	*1258 ± 310*	*1159 ± 226*	1182 ± 249	*1839 ± 509*	*1848 ± 426*	1845 ± 442
D_{mean} (Gy)	5.5 ± 1.8	5.0 ± 1.8	*0.8 ± 0.3*	*0.9 ± 0.7*	0.9 ± 0.6	*0.7 ± 0.2*	*1.0 ± 0.7*	0.9 ± 0.4
D_{max} (Gy)	35.6 ± 4.1	33.5 ± 10.3	*6.1 ± 7.1*	*6.2 ± 7.4*	6.2 ± 7.3	*4.7 ± 3.8*	*7.7 ± 6.5*	7.0 ± 6.1

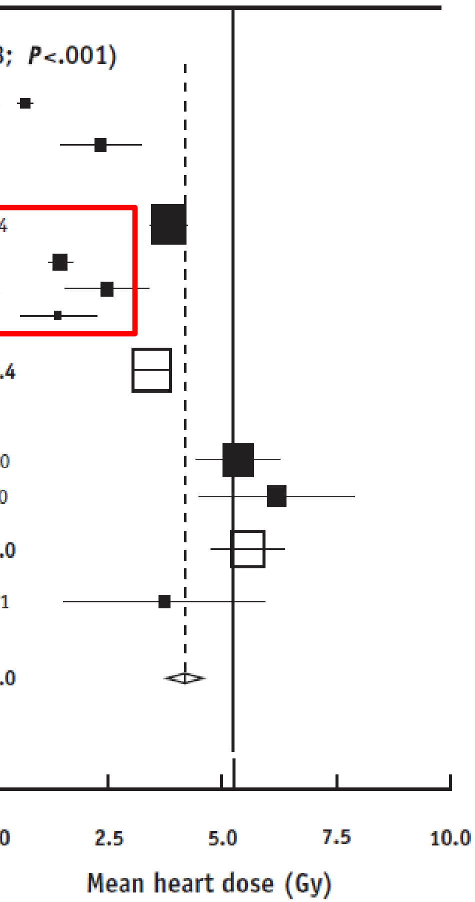


Reductions in heart Dmean with prone DIBH compared to prone SB according to **breast volume <750 cc** (18 patients), 750–1500 cc (22 patients) and >1500 cc (10 patients) were **1.3**, 0.7 and 0.4 Gy, respectively.

Conclusion: Prone position has already shown to be superior for heart sparing in the majority of patients, but **prone DIBH seems to even further reduce the heart dose.** This opens the **window for prone treatment in a specific subgroup of (small breasted)** patients in which higher heart doses in prone than supine position were observed.

Prone breast radiotherapy

	Number of regimens	Mean heart dose (Gy): Average* (SE)	Mean heart dose (Gy): Range†	Mean heart dose (Gy): Average & 95% CI*
a Internal mammary chain NOT irradiated (χ^2_8 = 420.3; P<.001)				
Protons	6	0.5 (0.1)	0.1 – 0.8	
Brachytherapy	8	2.2 (0.5)	<0.1 – 3.8	
Tangents‡				
Supine + NO breathing control	112	3.8 (0.2)	<0.1 – 12.4	
Supine + breathing control	14	1.3 (0.1)	0.4 – 2.5	
Prone position	11	2.4 (0.5)	0.4 – 5.4	
Lateral decubitus position	2	1.2 (0.4)	0.8 – 1.7	
All tangents	**(139)**	**3.4 (0.2)**	**<0.1 – 12.4**	
IMRT‖				
Standard	76	5.4 (0.5)	0.5 – 23.0	
Rotational fields	26	6.3 (0.9)	<0.1 – 18.0	
All IMRT	**(102)**	**5.6 (0.4)**	**<0.1 – 23.0**	
Others	9	3.7 (1.2)	0.2 – 10.1	
(a) Subtotal	**264**	**4.2 (0.2)**	**<0.1 – 23.0**	



Difference between (a) and (b): χ^2_1 = 55.93; P<.001

Taylor CW, Wang Z, Macaulay E et al. Exposure of the Heart in Breast Cancer Radiation Therapy: A Systematic Review of Heart Doses Published During 2003 to 2013 .Int J Radiation Oncol Biol Phys, Vol. 93, No. 4, pp. 845e853, 2015

OUTLINE

- Heart atlas and Cardiac radiation dose
- Reduction in cardiac exposure:

  Which technique?
  - IMRT and Arc Therapy
  - Proton Beam Therapy
  - Prone breast radiotherapy
  - Deep-inspiratory Breath-hold

Deep-inspiratory Breath-hold

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REVIEW ARTICLE

2015

The cardiac dose-sparing benefits of deep inspiration breath-hold in left breast irradiation: a systematic review

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Table 2. Studies reporting mean heart dose and mean LADCA dose for free breathing versus DIBH plans for left breast irradiation.

	Mean heart dose (Gy)			Mean LADCA dose (Gy)		
Study	FB	DIBH	Reduction Gy (%)	FB	DIBH	Reduction Gy (%)
Lee et al.[12†]	4.5	2.5	2.0 (44%)***	26.3	16.0	10.3 (39%)***
Mast et al.[13]	3.3†	1.8†	1.5 (45%)**	18.6†	9.6†	9.0 (48%)**
	2.7‡	1.5‡	1.2 (44%)**	14.9‡	6.7‡	8.2 (55%)**
Swanson et al.[14‡]	4.2	2.5	1.7 (40%)****	–	–	–
Hayden et al.[15‡]	6.9	3.9	3.0 (43%)****	31.7	21.9	9.8 (31%)****
Hjelstuen et al.[16†]	6.3	3.1	3.2 (51%)***	23.0	10.9	12.1 (53%)***
Wang et al.[17‡]	3.2	1.3	1.9 (59%)***	20.0	5.9	14.1 (71%)***
Vikström et al.[18†]	3.7	1.7	2.0 (54%)*	18.1	6.4	11.7 (65%)*
Borst et al.[19‡]	5.1	1.7	3.4 (67%)***	11.4	5.5	5.9 (52%)***
Stranzl et al.[20†]	4.0	2.5	1.5 (38%)**	–	–	–
Stranzl et al.[21†]	2.3	1.3	1.0 (43%)***	–	–	–

Deep-inspiratory Breath-hold

- There are **no studies to date investigating the clinical outcomes of using DIBH for left breast irradiation**. Therefore, there are no data available to assess the impact of DIBH on the rate of late cardiac toxicities
- The mean heart dose in the DIBH plans ranged from 1.3 Gy to 3.9 Gy which may equate to an increased heart disease risk of only 5.2–15.6%
- The **dosimetry of these plans must be accurately translated to the delivered dosimetry during treatment** in order for these benefits to be realised
- A **limited number of studies** reporting on small cohorts have investigated the reproducibility and stability of DIBH. These studies **agree that the inter-fraction and intra-fraction variability in set up position when using DIBH is small**

Smyth LM et al. The cardiac dose-sparing benefits of deep inspiration breath-hold in left breast irradiation: a systematic review. J Med Radiat Sci 62 (2015) 66–73

Deep-inspiratory Breath-hold

Table 1 Baseline demographic and radiotherapy treatment parameters for left-sided breast cancer patients by treatment cohort

Characteristics	WBRT ($n = 11$) (%)	B/CWRT + RNI ($n = 9$) (%)
Median age (years), range	47 (39–54)	51 (34–69)
AJCC Stage		
DCIS	3 (27)	0 (0)
I	5 (45)	0 (0)
II	3 (27)	5 (55)
III	0 (0)	4 (44)
ER/PR positive (for invasive disease)	7/8 (88)	7/9 (78)
HER 2+ (for invasive disease)	2/8 (25)	2/9 (22)
Sur		
B		
M		
RT		
RT		
Bre		
(Gy/# fraction)		

RADIATION ONCOLOGY

Table 3 Average patient percent relative reduction in dose parameters with DIBH compared to FB for left-sided breast cancer patients by treatment cohort. Significant *p*-values after adjusting for multiple testing are indicated by a double asterisk (**)

Parameter	WBRT	B/CWRT + RNI	*p*-value*
D_{mean} Heart	29.2 %	55.9 %	0.003**
D_{mean} LAD	43.5 %	72.1 %	0.014**
V_{20} Left Lung	8.9 %	6.6 %	0.305

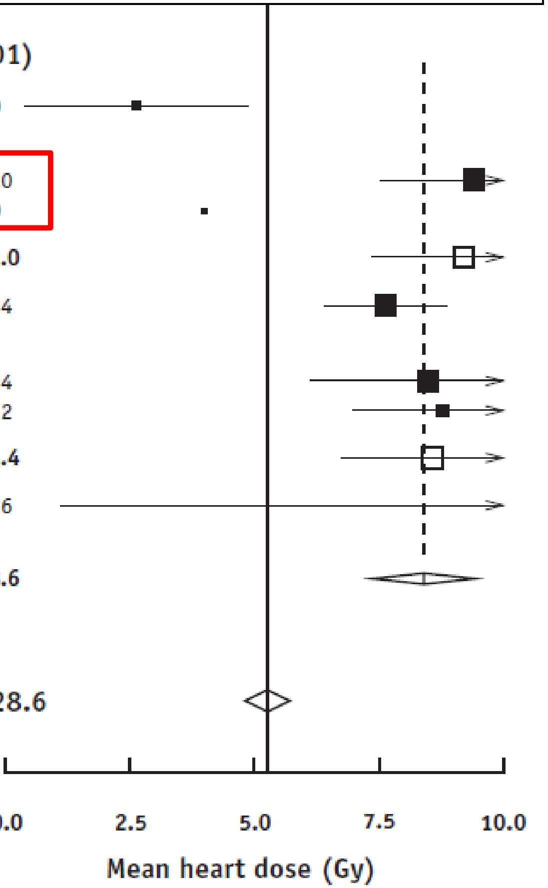
Table 2 Comparison of average dose parameters for targets a

Parameter	WBRT	WBRT FB vs. DIBH *p*-value*	B/CWRT + RNI	B/CWRT FB vs. DIBH *p*-value***	All Patients	FB vs. DIBH *p*-value*
D_{mean} < 4Gy (fraction, %)						
FB	11/11 (100)	N/A	5/9 (56)	0.134	16/20 (80)	0.134
DIBH	11/11 (100)		9/9 (100)		20/20 (100)	

All patients receiving WBRT alone met the mean heart dose constraint of <4 Gy on free breathing planning, while only slightly over half of patients receiving regional nodal irradiation were able to meet this constraint in free breathing. **DIBH is justified for all patients receiving RT for left-sided breast cancer, but as a minimum, should be used regularly for all left-sided breast cancer patients receiving breast/chest wall RT plus nodal RT.**

Deep-inspiratory Breath-hold

	Number of regimens	Mean heart dose (Gy) Average* (SE)	Range†
b Internal mammary chain irradiated		(χ^2_5 = 40.2; *P*<.001)	
Protons	4	2.6 (1.1)	1.0 – 6.0
Tangents‡¶			
Supine + NO breathing control	27	9.4 (1.0)	1.9 – 21.0
Supine + breathing control	1	4.0	4.0 – 4.0
All tangents	**(28)**	**9.2 (0.9)**	**1.9 – 21.0**
Wide tangents	25	7.6 (0.6)	2.5 – 14.4
IMRT‖			
Standard	24	8.5 (1.2)	0.7 – 23.4
Rotational fields	8	8.8 (0.9)	5.4 – 12.2
All IMRT	**(32)**	**8.6 (0.9)**	**0.7 – 23.4**
Others	4	12.0 (5.6)	4.9 – 28.6
(b) Subtotal	**93**	**8.4 (0.5)**	**0.7 – 28.6**
Total	**357**	**5.3 (0.2)**	**<0.1 – 28.6**



Difference between (a) and (b): χ^2_1 = 55.93; *P*<.001

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Risks against benefits

Benefits
After BCS, RT reduces
the absolute risk of
breast cancer death
at 15 years by 4%

Benefits
In node-positive disease,
PMRT reduces
the absolute risk of
breast cancer death
at 15 years by 7%

Risks
50 years of age at RT ,
no cardiac risk factors
mean heart dose of 4 Gy
the absolute risk of
radiation-related ischemic
heart disease would be 0,6%
for mortality

Risks
50 years of age at RT ,
no cardiac risk factors
mean heart dose of 8 Gy (including IMC)
the absolute risk of
radiation-related ischemic
heart disease would be 1,2%
for mortality

Taylor CW, Wang Z, Macaulay E et al. Exposure of the Heart in Breast Cancer Radiation Therapy: A Systematic Review of Heart Doses Published During 2003 to 2013 .Int J Radiation Oncol Biol Phys, Vol. 93, No. 4, pp. 845e853, 2015

Risks against benefits

… "However, the risk-benefit analysis may not be favourable for all women".

DCIS
Elderly patients

Taylor CW, Wang Z, Macaulay E et al. Exposure of the Heart in Breast Cancer Radiation Therapy: A Systematic Review of Heart Doses Published During 2003 to 2013 .Int J Radiation Oncol Biol Phys, Vol. 93, No. 4, pp. 845e853, 2015

Conclusions

- Even in modern studies **cardiac dose is often substantial**
- Cardiac dose is **affected by tecnique, targets irradiated and interobserver heart contouring**
- In different studies, **whole heart dose** is the most commonly reported measure
- **Breathing control** seems to be the best tecnique to reduce mean heart dose mostly for patients with LA BC

Open issues

- **Other cardiac constraints** (LAD, Mean dose or Dmax?)
- **Patients selection for heart-sparing radiotherapy tecniques** (unfavorable anatomy, individual cardiac risk factors)
- **Risk adapted breast radiotherapy** (NO radiotherapy or PBI in Low risk patients)