IV ZOOM Journal Club 2014

Bologna, 20 Febbraio 2015

Hotel NH De La Gare

Innovazioni tecnologiche e applicazioni nel trattamento radioterapico dei tumori mammari

Bruno Meduri

A.O.U. Policlinico di Modena

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Modena
Policlinico

III ZOOM Journal Club 2013
Bologna

Radioterapia nel trattamento del carcinoma mammario e cardiotossicità

Cardiac dose sparing techniques

352 articles identified

Technique	Cardiac dose reductions
Breath hold	• Decreased cardiac volume in field • Reduced mean, maximum, V5Gy, V15 Gy, V25 Gy, V40 Gy, V50 Gy • Reduced left anterior descending dose • Reduced cardiac mortality probability (4.8% vs. 0.1%)
Prone set-up	• 75–85% of left sided cases reduced cardiac volume in field • Non-significant decrease in mean heart, V40 Gy, V5Gy • Decreased mean cardiac dose (4.6 Gy vs. 3.0 Gy)
IMRT	• Reduction in cardiac NTCP compared with 3D-CRT • Decreased mean dose, V5Gy, V15 Gy, V20 Gy, V30 Gy, Dmax • Reduced dose to left anterior descending, left ventricle
Proton beam irradiation	• Reduction in cardiac dose • Reduction in cardiac NTCP (2.1% vs. 0.5%)
APBI	• Reduction in cardiac dose
IORT	• Maximum heart dose 1 Gy

Shah C., et al., *Radiother Oncol* **2014**; 112: 9-16

Innovazioni tecnologiche e applicazioni nel trattamento radioterapico dei tumori mammari

IMRT/ VMAT and DIBH

Proton beam

IORT

… and issues...

Innovazioni tecnologiche e applicazioni nel trattamento radioterapico dei tumori mammari

IMRT/ VMAT and DIBH

VMAT and DIBH

Breast radiotherapy

Volumetric modulated arc therapy and breath-hold in image-guided locoregional left-sided breast irradiation

Sarah O.S. Osman, Sandra Hol, Philip M. Poortmans, Marion Essers *

Department of Radiation Oncology, Institute Verbeeten, Tilburg, The Netherlands

"…our **hypothesis** is that the **combination of VMAT with vmDIBH** will potentially provide a *cumulative benefit* for this group of patients …

… we *compare* RT planning for left-sided breast cancer and locoregional lymph nodes using conventional *3D-CRT* techniques and using *VMAT* (RapidArc) both in *free-breathing* and in *vmDIBH*…"

Osman S. O., et al., *Radiother Oncol* **2014**; 112: 17-22

VMAT and DIBH

3D-CRT, VMAT, free breathing and vmDIBH

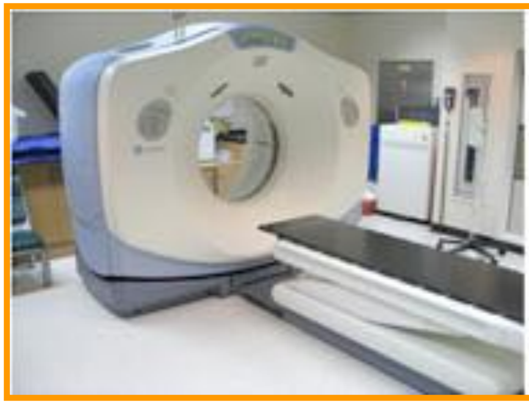
13 pts: RT **WBI + locoregional nodes** (including IMN), left-sided breast

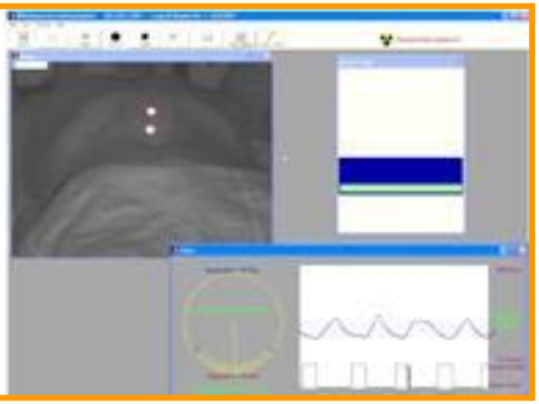
Dose: 42,46 Gy in 16 fr

Treatment plans for each pts: 3D(FB), 3D(vmDIBH), VMAT(FB), VMAT(vmDIBH).

VMAT better: Periclavicular and IMN PTV coverage, PTV Dose conformity, Dmean and V_{20Gy} ipsilateral lung and total lung

3D-CRT better: contralateral lung dose, contralateral breast (0,7 Gy vs 2,7 Gy)

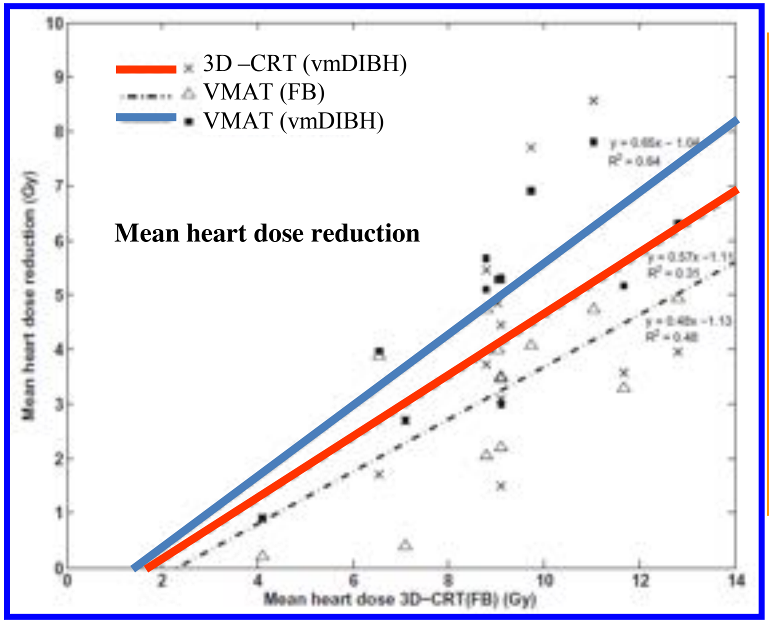




Osman S. O., et al., *Radiother Oncol* **2014**; 112: 17-22

VMAT and DIBH

3D-CRT, VMAT, free breathing and vmDIBH

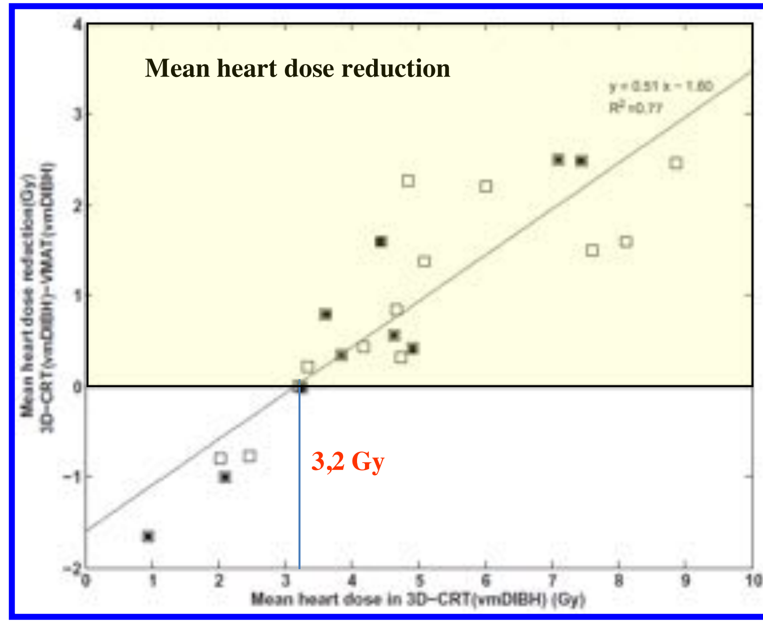


Hearth dose

3D(FB) >
VMAT(FB) >
3D(DIBH) >
VMAT(DIBH)

3D(DIBH) better if mean hearth <3,2 Gy

VMAT(DIBH) better if >3,2 Gy



"… combination of VMAT and vmDIBH … *reducing heart exposure* for pts treated with locoregional RT of left-sided BC when $D_{mean,heart}$ is >3.2 Gy in 3D (vmDIBH)…

…For pts with a $D_{mean,heart}$ <3.2 Gy in 3D(vmDIBH), VMAT(vmDIBH) results in *> heart dose*...

…For pts *<40 years* the advantages of VMAT should be balanced against the *small increase in contralateral breast dose*."

Osman S. O., et al., *Radiother Oncol* **2014**; 112: 17-22

IMRT/ VMAT and DIBH

Accelerated partial breast irradiation (APBI): Are breath-hold and volumetric radiation therapy techniques useful?

MARION ESSERS, SARAH O. S. OSMAN, SANDRA HOL, TANJA DONKERS & PHILIP M. POORTMANS

“ we systematically investigate and compare the dosimetric results of APBI planned with *3D-CRT* and with *VMAT*, both in *free-breathing* and in voluntary moderately deep inspiration breath-hold *vmDIBH*… “

Essers M., et al., *Acta Oncol* **2014**; 53: 788-94

VMAT and DIBH

3D-CRT, VMAT, free breathing and vmDIBH

21 pts: RT **PBI**, left-sided breast **Dose:** 38,5 Gy in 10 fr twice daily

Treatment plans for each pts: 3D(FB), 3D(vmDIBH), VMAT(FB), VMAT(vmDIBH).

VMAT better: PTV coverage, PTV Dose conformity, Dmean ipsilateral lung, $V_{50\%}$ ipsilateral breast, V_{5Gy} heart (D_{mean}: 3D=VMAT)

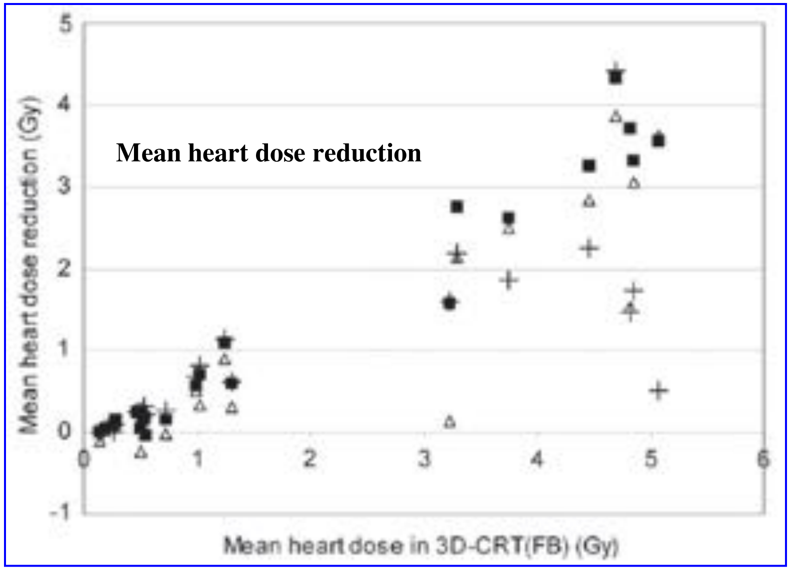
3D-CRT better: contralateral lung dose, contralateral breast (D_{max} > D_{mean})

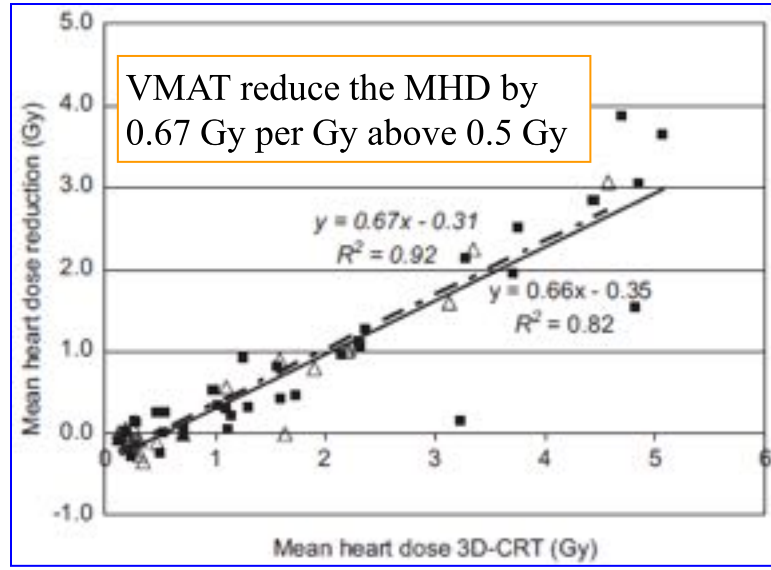
MU	3D-CRT FB 521 (476–617)	3D-CRT vmDIBH 528 (497–611)	VMAT FB 862 (700–1065)	VMAT vmDIBH 843 (701–1065)
Ipsilateral breast (non-PTV)				
$V_{50\%}$ (%)	23.2 (9.8–36.9)**	23.0 (8.0–39.9)**	19.7 (8.2–30.2)	18.0 (2.9–27.0)
V_{5Gy} (%)	48 (23–91)	51 (23–91)	46 (21–92)	47 (21–89)
Heart				
D_{Max} (Gy)	19.8 (0.8–38.3)**	11.2 (0.6–38.6)*	14.3 (0.5–39.7)*	8.5 (0.6–30.9)
D_{Mean} (Gy)	2.0 (0.1–5.1)**	1.0 (0.1–4.6)	1.0 (0.1–3.3)*	0.6 (0.1–1.6)
V_{5Gy} (%)	15.9 (0.0–46.9)**	7.6 (0.0–39.3)*	4.3 (0.0–47.7)*	1.4 (0.0–8.1)
Contralateral breast				
D_{Max} (Gy)	0.7 (0.04–5.8)**	0.4 (0.1–1.4)**	4.6 (0.1–9.4)	4.3 (0.6–8.3)
D_{Mean} (Gy)	0.05 (0.01–0.08)**	0.05 (0.01–0.08)**	0.6 (0.03–1.6)	0.6 (0.03–1.9)
Ipsilateral lung				
Volume (cm^3)	1311 (809–1920)*	2125 (1408–2727)	1311 (809–1920)*	2125 (1408–2727)
D_{Mean} (Gy)	3.7 (0.7–8.7)**	3.4 (1.2–8.0)**	1.9 (0.4–5.5)	1.8 (0.5–4.0)
V_{5Gy} (%)	31.2 (18.7–73.8)**	27.4 (15.0–67.3)**	10.4 (0.0–40.3)	10.6 (0.0–30.8)
Contralateral lung				
D_{Max} (Gy)	2.1 (0.1–8.1)**	2.9 (0.2–12.5)*	4.2 (0.5–15.0)	5.0 (0.3–10.5)
D_{Mean} (Gy)	0.1 (0.01–1.1)**	0.1 (0.01–1.2)**	0.4 (0.02–1.9)	0.4 (0.02–1.0)

Essers M., et al., *Acta Oncol* **2014**; 53: 788-94

VMAT and DIBH

3D-CRT, VMAT, free breathing and vmDIBH





"… we suggest to *always* apply **vmDIBH** and to combine this with VMAT if MHD without VMAT exceeds 0.5 Gy and VMAT is able to provide equal or reduced heart dose…"

Essers M., et al., *Acta Oncol* **2014**; 53: 788-94

Innovazioni tecnologiche e applicazioni nel trattamento radioterapico dei tumori mammari

Proton beam

PBI with proton beam

Clinical Investigation

Partial Breast Radiation Therapy With Proton Beam: 5-Year Results With Cosmetic Outcomes

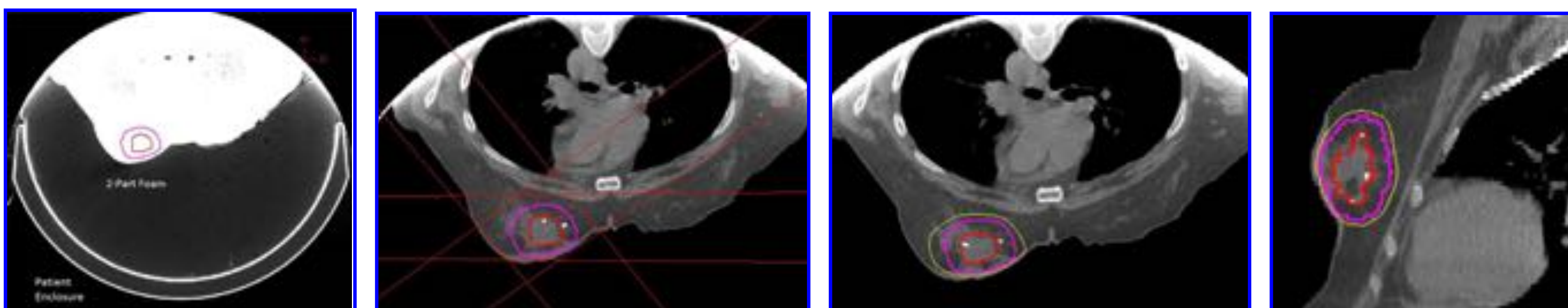
" We initiated a *phase 2 trial* in an effort to demonstrate the *efficacy* and define the *toxicity* of the use of **proton beam therapy** for *PBI*, with the primary endpoint being freedom from breast tumor recurrence…"

Bush D. A., et al., *Int J Radiat Oncol Biol Phys* **2014**; 90: 501-5

PBI with proton beam

Materials and methods

- **Eligible subjects:** invasive carcinoma (no LCI), pN0, R0 (>2mm), surgical clips, T<3cm
- **Treatment**:
  - customized, rigid immobilization device in a prone position (vacuum)
  - <u>CTV</u>: lumpectomy cavity + 1cm (edited from the skin of the breast and chest wall as needed)
  - <u>PTV</u>: CTV + 2 mm
  - multibeam proton <u>plan</u> (2 to 4 separate beam angles)
  - <u>prescribed dose</u>: 40 Gy delivered in 10 fractions over 2 weeks
  - <u>IGRT</u>: daily in-room kilovoltage orthogonal imaging (clips were used as fiducial markers)



Bush D. A., et al., *Int J Radiat Oncol Biol Phys* **2014**; 90: 501-5

PBI with proton beam

Results

100 pts

Table 1 Patient characteristics	
Subjects	Medical follow-up (60 months)
Age (yrs)	
Average	63
Range	41-83
Carcinoma histology type	
Ductal	90
Mucinous	5
Tubular	[illegible]
Medullary	[illegible]
Involved breast	
Right	[illegible]
Left	[illegible]
Tumor size (cm)	
Average	[illegible]
Range	[illegible]
Stage	
T1a	[illegible]
T1b	[illegible]
T1c	34
T2	14
Estrogen receptor status	
ER+	88
PR+	70

Conclusion

"…Proton PBI can provide excellent results in terms of disease control, toxicity profile, and cosmetic results…"

5-y DFS: 94% ; 5-y OS: 95%

Toxicity: No G ≥ 3 acute toxicity; 1 fat necrosis; 7% telangiectasias; no cases of rib fractures, clinical pneumonitis or cardiac events

Cosmetic results: a good to excellent result of 90% was well maintained through 5 years of FUP

Bush D. A., et al., *Int J Radiat Oncol Biol Phys* **2014**; 90: 501-5

Innovazioni tecnologiche e applicazioni nel trattamento radioterapico dei tumori mammari

IORT

TARGIT-A

THE LANCET

Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial

Vaidya J. S., et al., *Lancet* **2014**; 383: 603-13

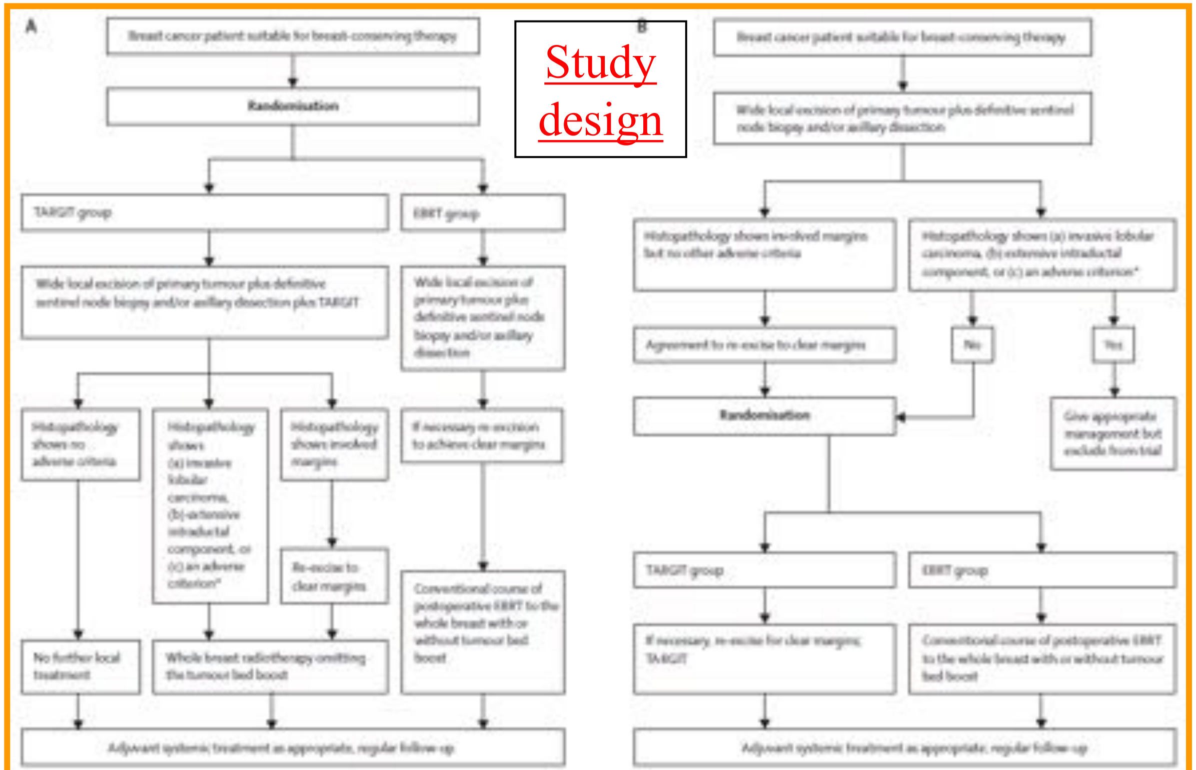
TARGIT-A: 5-year results

Randomised non-inferiority trial

<u>Inclusion criteria</u>

- Age ≥ 45
- CDI suitable for breast conserving surgery (T1 and small T2, N0-1, M0)

<u>Study design</u>



<u>Procedures</u>

Low energy x-rays (50 kV max) at the tip of a 3·2 mm Ø tube

Appropriately sized applicator

Surface of the tumour bed receives 20 Gy that attenuates to 5–7 Gy at 1 cm depth

<u>Primary end point</u>

Local relapse within the treated breast

<u>Secondary end point</u>

Relapse-free survival, OS, toxicity

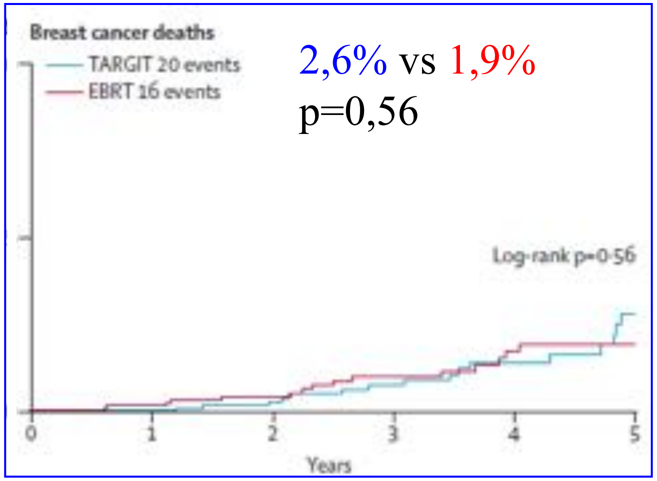
Vaidya J. S., et al., *Lancet* **2014**; 383: 603-13 - Vaidya J. S., et al., *Lancet* **2010**; 376: 91-102

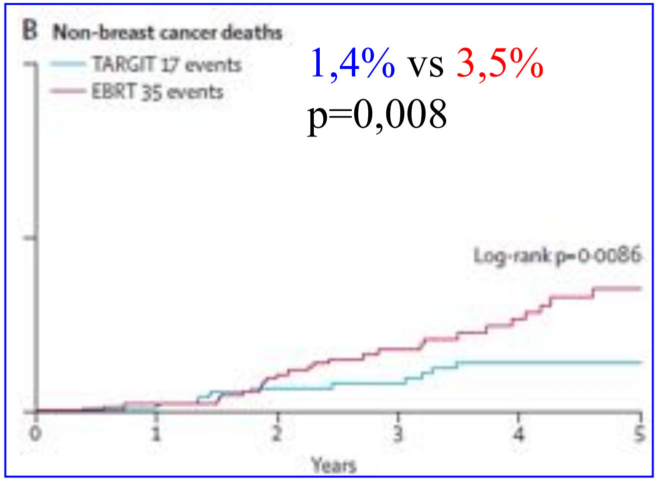
TARGIT-A: 5-year results

3451 pts: 1721 **TARGIT** (15.2% (239 of 1571) TARGIT + EBRT), 1730 **EBRT**

Median FUP: 2,5 years

	Events; 5-year cumulative risk (95%CI)		Absolute difference*
	TARGIT	EBRT	
All patients			
Local recurrence (n=3375)	23; 3·3% (2·1–5·1)	11; 1·3% (0·7–2·5)	12 (2·0%)
Any other recurrence (n=3375)	46; 4·9% (3·5–6·9)	37; 4·4% (3·0–6·4)	9 (0·5%)
Death (n=3451)	37; 3·9% (2·7–5·8)	51; 5·3%(3·9–7·3)	-14 (-1·4%)
Prepathology†			
Local recurrence (n=2234)	10; 2·1% (1·1–4·2)	6; 1·1% (0·5–2·5)	4 (1·0%)
Any other recurrence (n=2234)	29; 4·8% (3·1–7·3)	25; 4·7% (3·0–7·4)	4 (0·1%)
Death (n=2298)	29; 4·6% (1·8–6·0)	42; 6·9% (4·3–9·6)	-13 (-2·3%)
Postpathology‡			
Local recurrence (n=1141)	13; 5·4% (3·0–9·7)	5; 1·7%(0·6–4·9)	8 (3·7%)
Any other recurrence (n=1141)	17; 5·2% (3·0–8·8)	12; 3·7% (1·9–7·0)	5 (1·5%)
Death (n=1153)	8; 2·8% (1·3–5·9)	9; 2·3% (1·0–5·2)	-1 (0·5%)





5-y risk for LR: **3,3**% for TARGIT vs **1,3%** EBRT (p=0,042)

Prepathology group: 2,1% vs 1,1% (p=0,31)

Postpathology group (delayed TARGIT): 5,4% vs 1,7% (p=0,06)

Vaidya J. S., et al., *Lancet* **2014**; 383: 603-13

TARGIT-A: 5-year results

	Median follow-up	Number of events	Absolute difference (90% CI) in the binomial proportions of local recurrence* in the conserved breast (TARGIT minus EBRT)	Z score	$P_{non\text{-}inferiority}$
Whole trial					
All patients (n=3451)	2 years 5 months	34	0·72% (0·2 to 1·3)	–5·168	<0·0001
Mature cohort (n=2232)	3 years 7 months	32	1·13% (0·3 to 2·0)	–2·652	0·0040
Earliest cohort (n=1222)	5 years	23	1·14% (–0·1 to 2·4)	–1·750	0·0400
Prepathology†					
All patients (n=2298)	2 years 4 months	16	0·37% (–0·2 to 1·0)	–5·954	<0·0001
Mature cohort (n=1450)	3 years 8 months	14	0·6% (–0·3 to 1·5)	–3·552	0·0002
Earliest cohort (n=817)	5 years	9	0·76% (–0·4 to 2·0)	–2·360	0·0091
Postpathology‡					
All patients (n=1153)	2 years 4 months	18	1·39% (0·2 to 2·6)	–1·503	0·0664
Mature cohort (n=782)	3 years 7 months	18	2·04% (0·3 to 3·8)	–0·429	0·3339
Earliest cohort (n=405)	5 years	14	1·8% (–1·2 to 4·8)	–0·382	0·3511

"TARGIT concurrent with lumpectomy within a risk-adapted approach should be considered as *an option for eligible patients …*

We believe that these data should allow patients and their clinicians to make a *more informed choice* about individualising their treatment"

Vaidya J. S., et al., *Lancet* **2014**; 383: 603-13

Innovazioni tecnologiche e applicazioni nel trattamento radioterapico dei tumori mammari

Issues

SPECT Analysis of Cardiac Perfusion

Clinical Investigation: Breast Cancer

SPECT Analysis of Cardiac Perfusion Changes After Whole-Breast/Chest Wall Radiation Therapy With or Without Active Breathing Coordinator: Results of a Randomized Phase 3 Trial

Zellars R., et al., *Int J Radiat Oncol Biol Phys* **2014**; 88: 778-85

SPECT Analysis of Cardiac Perfusion

Prospective randomized controlled trial

Primary objective: determine whether the ABC prevented deficits in cardiac muscle perfusion as determined by SPECT

Plan: opposed tangents in supine position

ABC with mDIBH technique

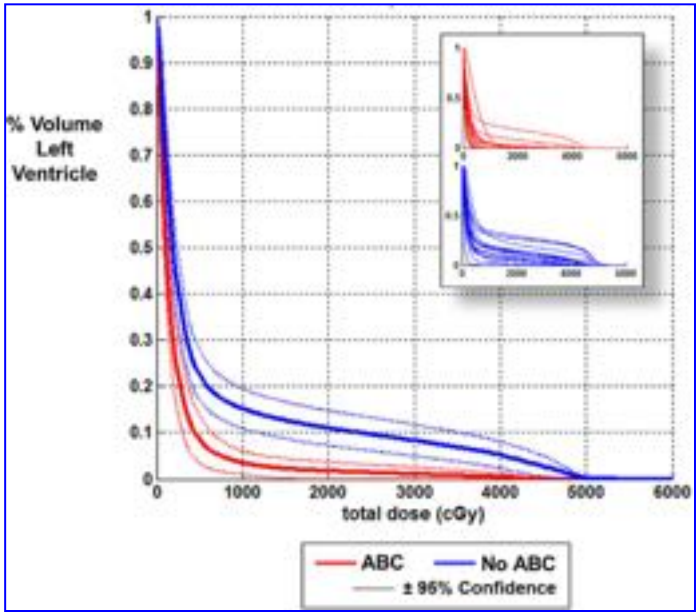
SPECT: regional myocardial perfusion imaging

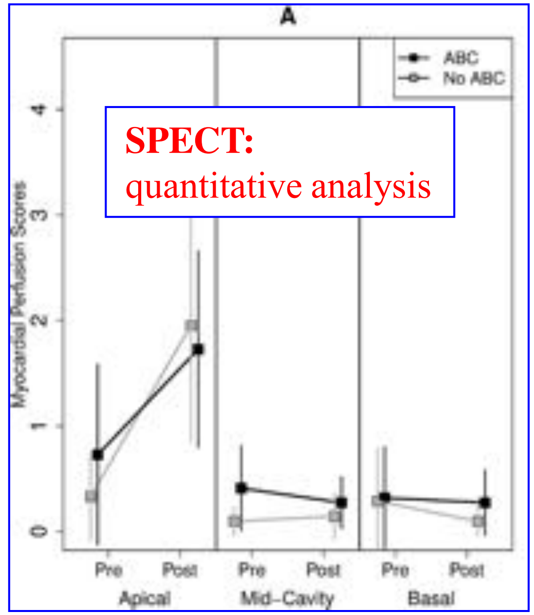
Table 1 Patient characteristics **57 pts**

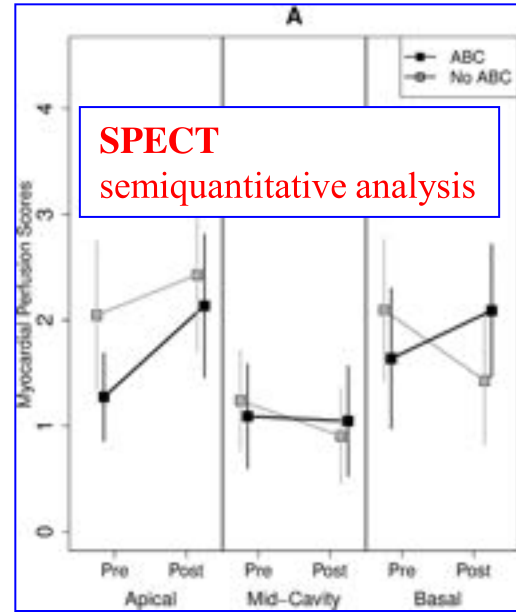
Characteristic	No-ABC (n=29)	ABC (n=28)	*P* value
Age			.07
Mean (SD)	58.7 (12.7)	52.8 (11.9)	
Range	(35-85)	(20-86)	
Tumor size (cm)			.86
Mean (SD)	1.59 (1.23)	1.65 (1.41)	
Range	(0.3, 6.2)	(0.2, 7.0)	
BMI			.99
Mean (SD)	29.2 (7.5)	29.2 (6.4)	
Range	(15.9-49.0)	(18.5-47.9)	
LN positive (%)	32%	36%	1.00
IMLN targeted	24%	36%	.40
Postmenopausal (%)	76%	64%	.40
ER/PR$^+$ (%)	86%	86%	1.00
HER2$^+$ (%)	18%	4%	.19
Chemotherapy (%)	36%	54%	.28
Hormone therapy (%)	69%	67%	1.00

Zellars R., et al., *Int J Radiat Oncol Biol Phys* **2014**; 88: 778-85

SPECT Analysis of Cardiac Perfusion







"ABC limits the volume of the myocardium exposed to higher doses of radiation …

ABC ***did not prevent*** cardiac muscle perfusion deficits…

Although, our study suggests that ABC may not be as effective as hypothesized, we believe further evaluation of this potentially useful tool is warranted …"

Zellars R., et al., *Int J Radiat Oncol Biol Phys* **2014**; 88: 778-85

PBI with proton beam

Long-term Cosmetic Outcomes and Toxicities of Proton Beam Therapy Compared With Photon-Based 3-Dimensional Conformal Accelerated Partial-Breast Irradiation: A Phase 1 Trial

"…The present study compares the *long-term outcomes* and *toxicities* of patients treated with either **PBT** or photon-based **3D-APBI** in the 32-Gy cohort.…"

Galland-Girodet S., et al., *Int J Radiat Oncol Biol Phys* **2014**; 90: 493-500

PBI with proton beam

Materials and methods and pts characteristics

- **Eligible subjects:** invasive carcinoma, pN0, R0 (>2mm), surgical clips, pT1
- **Treatment**:
  - 79 pts 3D-APBI and 19 PBT
  - PTV: lumpectomy cavity + 1,5-2 cm (edited from the skin and chest wall as needed)
  - PBT plan: 1 to 3 fields (only *1 field was treated per fraction*)
  - prescribed dose: 32 Gy delivered in 8 fractions twice daily

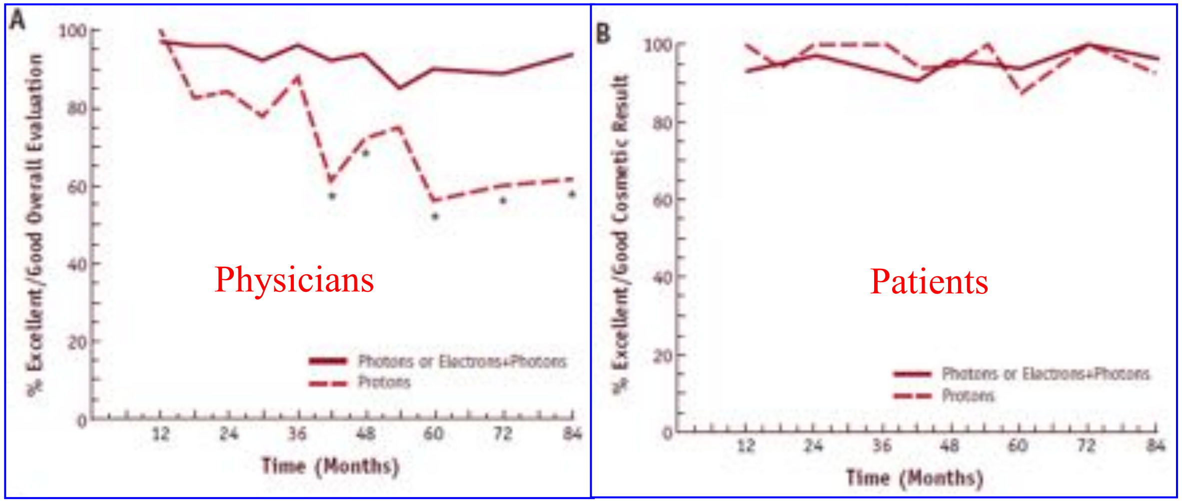
Characteristic	Entire cohort	Photons	Protons	*P*
Patients	98 (100)	79 (81)	19 (19)	—
Median age (y)	61	60	63	.3543
Median tumor size (cm)	0.9	0.9	0.8	.3399
Tumor side				.2466
Right	40 (41)	30 (38)	10 (53)	
Left	58 (59)	49 (62)	9 (47)	
Histology				.9432
IDC no DCIS	89 (91)	72 (91)	17 (89)	
Tubular	5 (5)	3 (4)	2 (11)	
Mucinous	3 (3)	3 (4)	0	
IDC with DCIS	1 (1)	1 (1)	0	
Grade				.4595
1	46 (47)	36 (46)	10 (53)	
2	42 (42)	36 (46)	6 (32)	
3	10 (10)	7 (8)	3 (15)	
ER status				.6487
Positive	87 (89)	71 (90)	16 (84)	
Negative	11 (11)	8 (10)	3 (16)	
PR status				.9873
Positive	76 (79)	62 (80)	14 (78)	
Negative	20 (21)	16 (20)	4 (22)	
Triple negative				.4023
Yes	10 (10)	7 (9)	3 (16)	
No	88 (90)	72 (91)	16 (84)	

Galland-Girodet S., et al., *Int J Radiat Oncol Biol Phys* **2014**; 90: 493-500

PBI with proton beam

Results

Parameter	Photons (79)	Protons (19)	P
Ipsilateral lung (n=98; mean)			
Mean dose (Gy)	2.2	0.5	<.0001
Maximum dose (Gy)	28.9	20.4	<.0001
D20% (Gy)	3.2	0	<.0001
D10% (Gy)	5.2	0.6	<.0001
D5% (Gy)	7.6	2.7	<.0001
V20 Gy (%)	2.0	0.7	NS
V10 Gy (%)	3.8	1.8	NS
V5Gy (%)	13.1	3.1	.001
Contralateral lung (n=98)			
Mean dose (Gy)	0.2	0.2	<.0001
Maximum dose (Gy)	2.1	0	<.0001
Mean D20% (Gy)	0.5	0	<.0001
Mean D10% (Gy)	0.7	0	<.0001
Mean D5% (Gy)	0.8	0	<.0001
Mean V5Gy (%)	1	0	NS
Heart (left-sided only, n=58)			
Mean dose (Gy)	0.9	0	<.0001
Maximum dose (Gy)	7.7	3.8	.001
Mean D20% (Gy)	1.4	0	<.0001
Mean D10% (Gy)	2.2	0	<.0001
Mean D5% (Gy)	3.1	0.1	<.0001
Mean V20 Gy (%)	0.1	0	NS
Mean V10 Gy (%)	2.2	0.1	NS
Mean V5Gy (%)	3.8	0.4	NS



Overall cosmesis

7-year cumulative incidence of local failure rate

Entire population: 6% (5 local recurrences outside the original site)

Proton group: 11% (2 local recurrences)

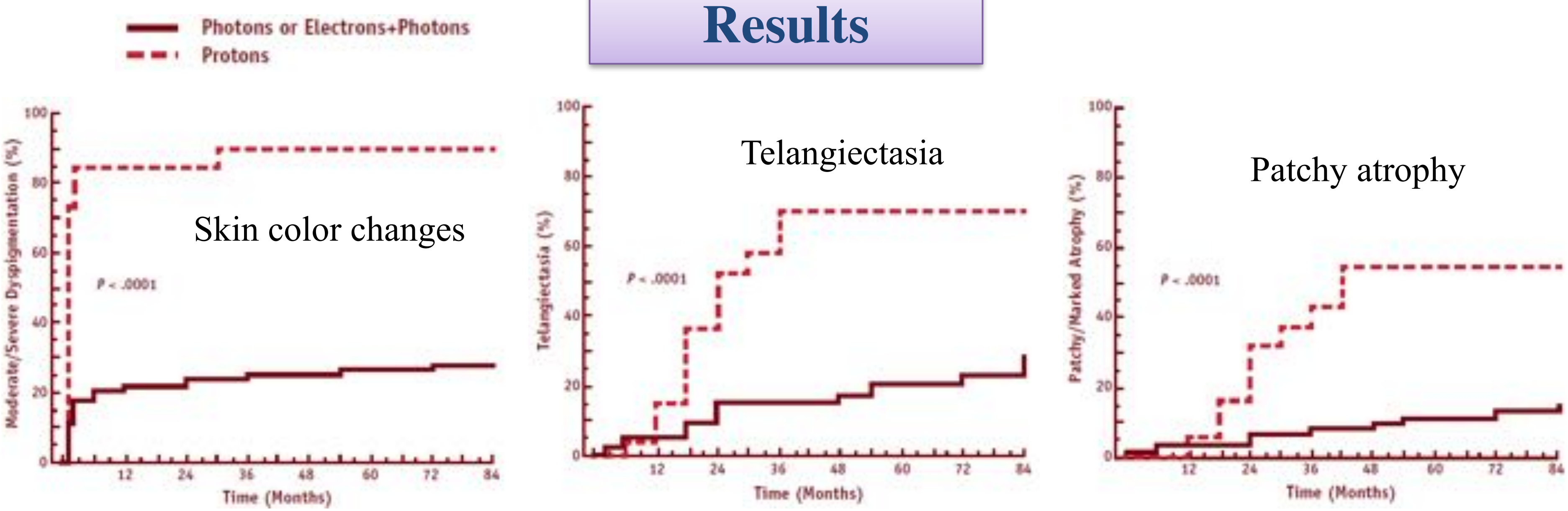
3D-APBI group: 4% (3 local recurrences)

P=.22

Galland-Girodet S., et al., *Int J Radiat Oncol Biol Phys* **2014**; 90: 493-500

PBI with proton beam

Results



Conclusions

"We recommend the use of *multiple beams* for a 3-dimensional conformal PBT plan or the use of proton beam scanning to minimize skin/entry dose…

…Despite our *less-favorable cosmetic results*, we believe proton APBI may be a very useful approach for *selected patients* who may otherwise have a nonoptimal plan using photon-based APBI... deep seromas or unfavorable cardiac anatomy"

Galland-Girodet S., et al., *Int J Radiat Oncol Biol Phys* **2014**; 90: 493-500

IORT and Cost-Effectiveness Analyses

Evaluating Radiotherapy Options in Breast Cancer: Does Intraoperative Radiotherapy Represent the Most Cost-Efficacious Option?

"…the purpose of this study was to evaluate the **cost-efficacy of IORT** via *a cost-minimization analysis*, an *ICER analysis*, …. based on local recurrence data from 2 recently updated randomized trials comparing IORT with WBI.…"

Shah C., et al., *Clin Breast Cancer* **2014**; 14: 141-6

IORT and Cost-Effectiveness Analyses

Cost-efficacy of IORT

- Cost-minimization analysis
    - reimbursement only (professional and facility)
    - reimbursement with *additional medical costs* (increased operative time with IORT, fraction of IORT patients requiring additional radiation)
    - reimbursement with *nonmedical costs* (round-trip travel, time per treatment including travel)
    - reimbursement with *costs associated with recurrences*
- ICER analysis (Incremental Cost Effectiveness Ratios) : increased reimbursement required to use WBI or APBI compared with IORT per percentage point of improvement in local recurrence

Shah C., et al., *Clin Breast Cancer* **2014**; 14: 141-6

IORT and Cost-Effectiveness Analyses

Reimbursements by treatment technique

Technique	Total Reimbursement	Reimbursement Including Additional Medical Costs[a]	Reimbursement Including Medical and Nonmedical Costs[a]	Reimbursements Including Medical, Nonmedical, and Recurrence Costs[a] (TARGIT)	Reimbursements Including Medical, Nonmedical, and Recurrence Costs[a] (ELIOT)
IORT	$3094	$8003-$8706	$8192-$8971	$9399-$10179	$9230-$10,009
WBI 3D-CRT	$11,726	$11,726	$12,985	$13,743	$13,122
APBI 3D-CRT	$6578	$6578	$7028	$7786	$7165
APBI IMRT	$10,547	$10,547	$10,997	$11,755	$11,134
APBI SL	$12,602	$12,602	$13,052	$13,810	$13,189
APBI ML	$16,439	$16,439	$16,889	$17,646	$17,025
APBI Interstitial	$11,765	$11,765	$12,215	$12,974	$12,353

When factoring the costs associated with the higher rates of recurrence as well as medical and non-medical costs, standard modalities including **WBI** and **APBI** are ***cost effective*** compared to IORT

WBI and APBI remain ***standards*** for breast radiation while IORT should be considered investigational at this time

ICER based on local control

	TARGIT	
	Reimbursement Only	Reimbursements Including Medical, Nonmedical, and Recurrence Costs[a]
WBI 3D-CRT	$4316	$1782-$2172
APBI 3D-CRT	$1742	—
APBI IMRT	$3727	$788-$1178
APBI SL	$4754	$1816-$2205
APBI ML	$6672	$3734-$4123
APBI Interstitial	$4336	$1398-$1787

	ELIOT	
	Reimbursement Only	Reimbursements Including Medical, Nonmedical, and Recurrence Costs[a]
WBI 3D-CRT	$1877	$677-$846
APBI 3D-CRT	$757	—
APBI IMRT	$1620	$244-$433
APBI SL	$2067	$691-$861
APBI ML	$2901	$1525-$1694
APBI Interstitial	$1885	$509-$679

Shah C., et al., *Clin Breast Cancer* **2014**; 14: 141-6

Second cancer risk

Secondary cancer

Second cancer risk after 3D-CRT, IMRT and VMAT for breast cancer

Yasser Abo-Madyan[a,b,1], Muhammad Hammad Aziz[a,c,1], Moamen M.O.M. Aly[d,e], Frank Schneider[a], Elena Sperk[a], Sven Clausen[a,d], Frank A. Giordano[a], Carsten Herskind[a], Volker Steil[a], Frederik Wenz[a], Gerhard Glatting[a,d,*]

"…to calculate and compare solid **second cancer risk** after 3DCRT, tangential IMRT, multibeam IMRT and VMAT for breast cancer using the *concept of organ equivalent dose* (OED) for *linear, linear-exponential and plateau dose response models* …"

Abo-Madyan Y., et al., *Radiother Oncol* **2014**; 110: 471-6

Second cancer risk

Materials and methods

- Planning CT datasets of *10 different female breast cancer* (5 right sided and 5 left sided)
- *4 different plans*: 3D-CRT, t-IMRT (tangential intensity modulated beams), m-IMRT (multi-beam step and shoot IMRT) and VMAT
- $EAR = EAR_0 \cdot OED$ (EAR: excess absolute risk per 10,000 persons-years; EAR_0: EAR per Gy; OED: organ equivalent dose)

- The OEDs for contralateral breast, ipsilateral and contralateral lung were calculated for the linear, linear-exponential and plateau dose–response models

DVH(D_i): volume receiving dose D_i and the summation runs over all voxels of organ T with volume V_T. The model parameters α and δ were estimated from a combined fit to the Japanese A-bomb and Hodgkin cohorts by Zwahlen et al.

$$OED_{T,linear} = \frac{1}{V_T}\sum_i \{DVH(D_i) \cdot D_i\}$$

$$OED_{T,linear-exp} = \frac{1}{V_T}\sum_i \{DVH(D_i) \cdot D_i \cdot e^{-\alpha D_i}\};$$

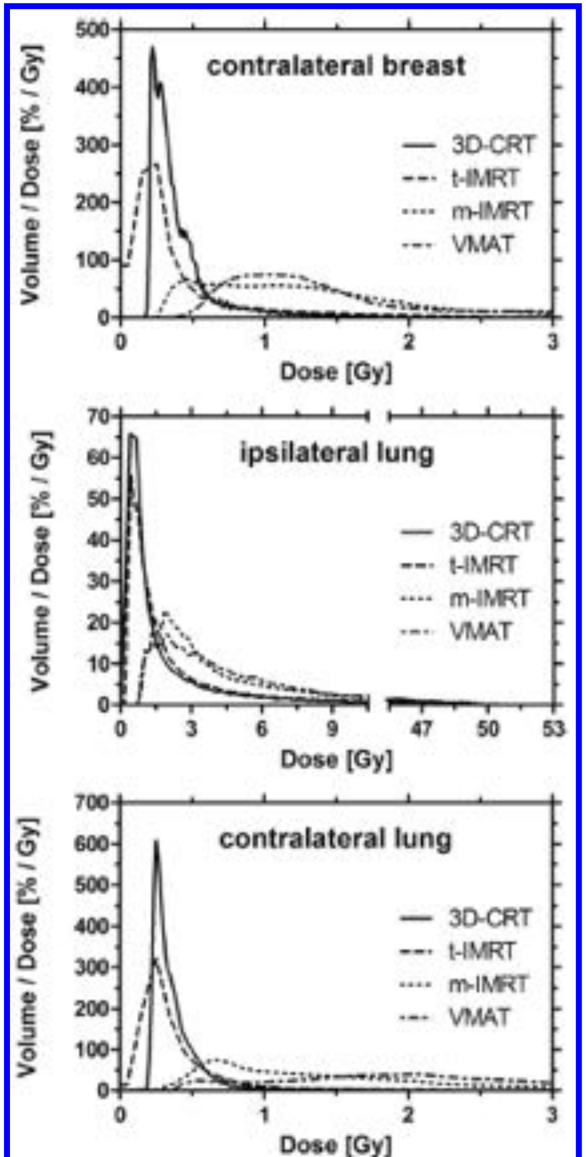
$$\alpha = 0.044\ Gy^{-1}$$

$$OED_{T,plateau} = \frac{1}{V_T}\sum_i \{DVH(D_i) \cdot (1 - e^{-\delta D_i})/\delta\};$$

$$\delta = 0.139\ Gy^{-1}$$

Abo-Madyan Y., et al., *Radiother Oncol* **2014**; 110: 471-6

Second cancer risk



Results

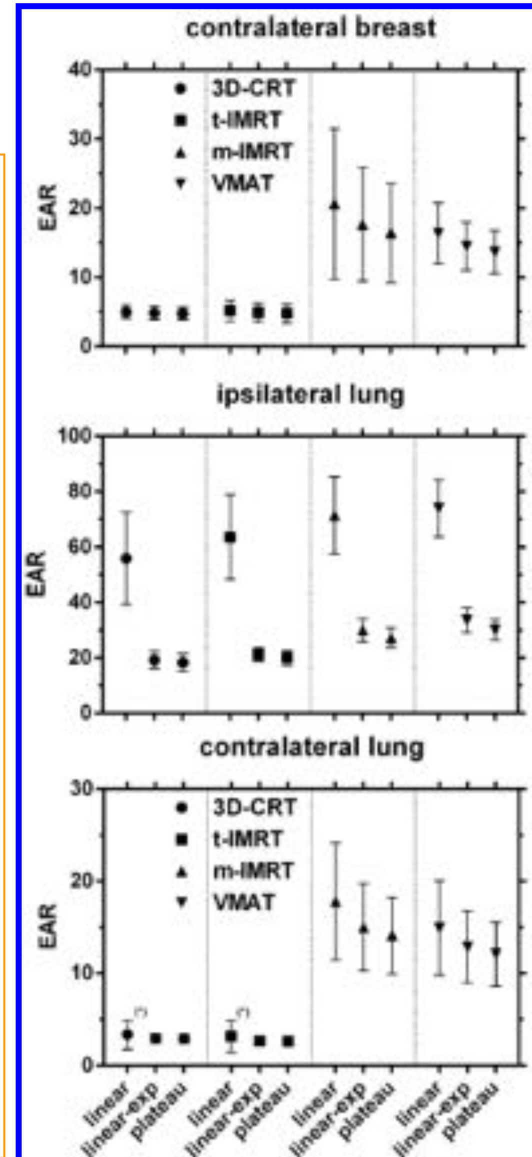
Cumulated EAR (contral breast + ipsil + contral lung) per Gy at an age of 70 yrs after RT at an age of 30:

3D-CRT: 29 ± 7; 70 ± 24; 27 ± 6
(linear-exponential, linear, plateau model)

Increase for:	t-IMRT,	m-IMRT,	VMAT
(LE model)	2 ± 15%	131 ± 85%	123 ± 66%
(L model)	9 ± 22%	82 ± 96%	71 ± 82%
(Pl model)	3 ± 14%	123 ± 78%	113 ± 61%

compared to 3D-CRT
small increase for t-IMRT
increase of 96–280% for m-IMRT
and VMAT

"This risk difference would only be clinically relevant if m-IMRT or VMAT were adopted as *a routine method* for RT of young patients"



Abo-Madyan Y., et al., *Radiother Oncol* **2014**; 110: 471-6

Conclusions