BRACHYTHERAPY FOR BREAST CANCER

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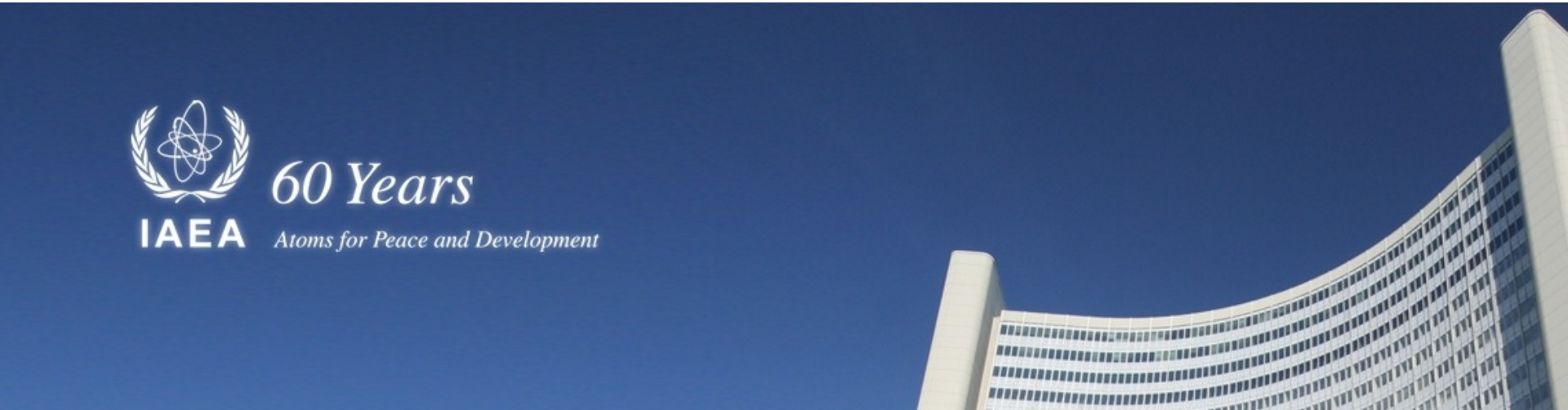
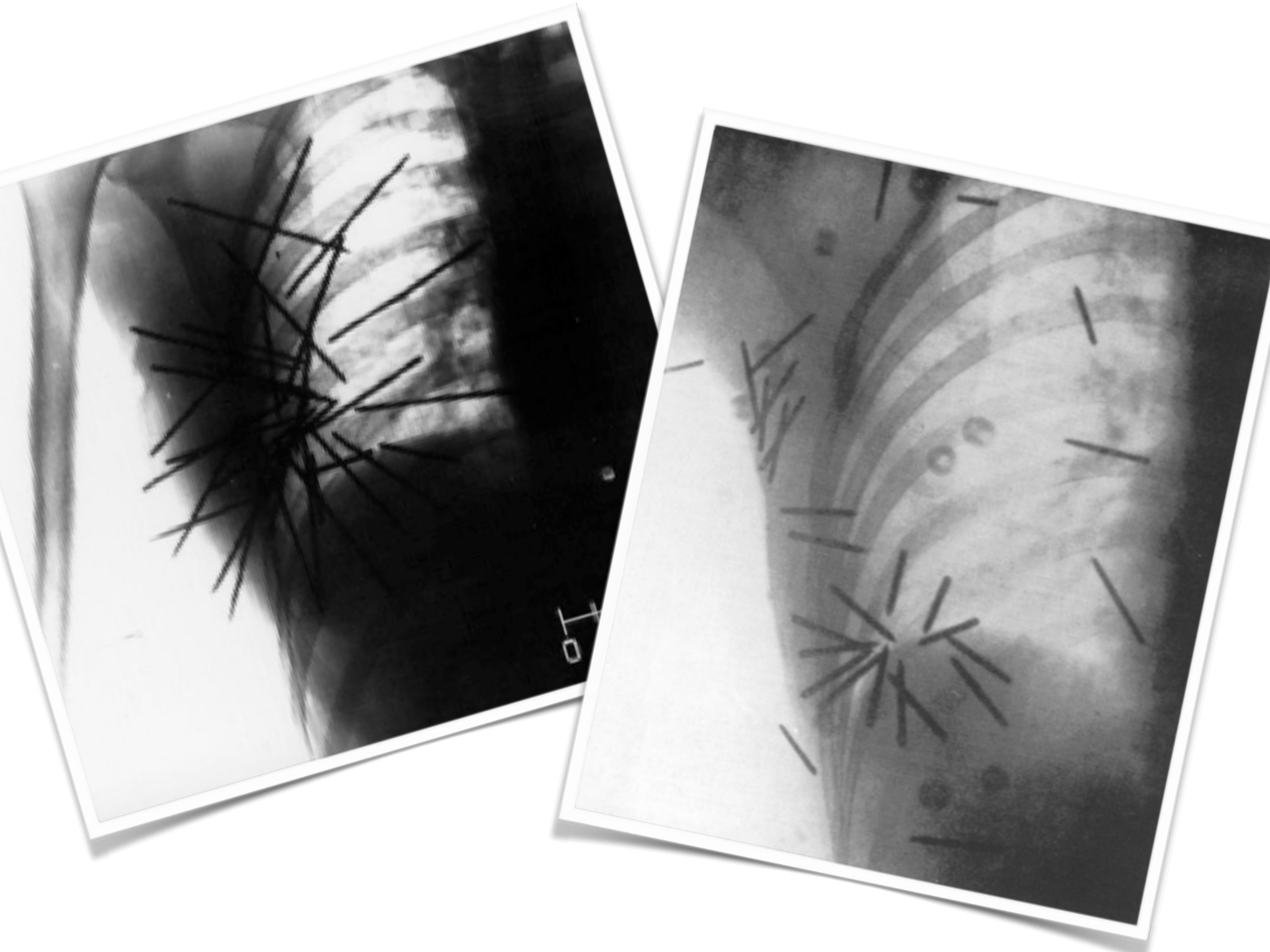
Division of Human Health

International Atomic Energy Agency



THE BOOST TO THE TUMOR BED IN BREAST CANCER RADIOTHERAPY

INTRODUCTION



DOSE - CONTROL

Clinical–Pathologic Study of Early Breast Cancer Treated by Primary Radiation Therapy

By Jay R. Harris, James L. Connolly, Stuart J. Schnitt, Richard B. Cohen, and Samuel Hellman

We performed a clinical-pathologic review of 231 patients with early breast cancer treated by primary radiation therapy. There were 27 patients with infiltrating ductal carcinoma treated with excisional biopsy whose tumors showed a constellation of histologic features: moderate or marked intraductal carcinoma in the tumor, intraductal carcinoma in the adjacent tissue, and high nuclear grade. These patients had a 5-yr local tumor control rate of 61% compared to 96% for similar patients whose tumors did not show all three features. Radiation dose to the primary tumor area influenced the likelihood of local recurrence in these 27 patients: 15 of these patients received 6000 rads or more to the primary tumor area and had a 5-yr local tumor control rate of 84%, compared to 48% for the 12 patients who received less than 6000 rads. These results indicate that a subgroup of breast cancer patients can be identified that has a high risk of local recurrence when an insufficient radiation dose (i.e., less than 6000 rads) is delivered to the primary tumor area.

Table 1. Analysis of Local Recurrence Related to Intraductal Involvement

Group	No. of Patients	True Recurrences		Marginal Miss	Elsewhere in Breast
		Dose < 6000 rads	Dose ≥ 6000 rads		
Both features present*	59	5/22	0/37	2	1
Both features not present	95	0/29	0/66	1	0

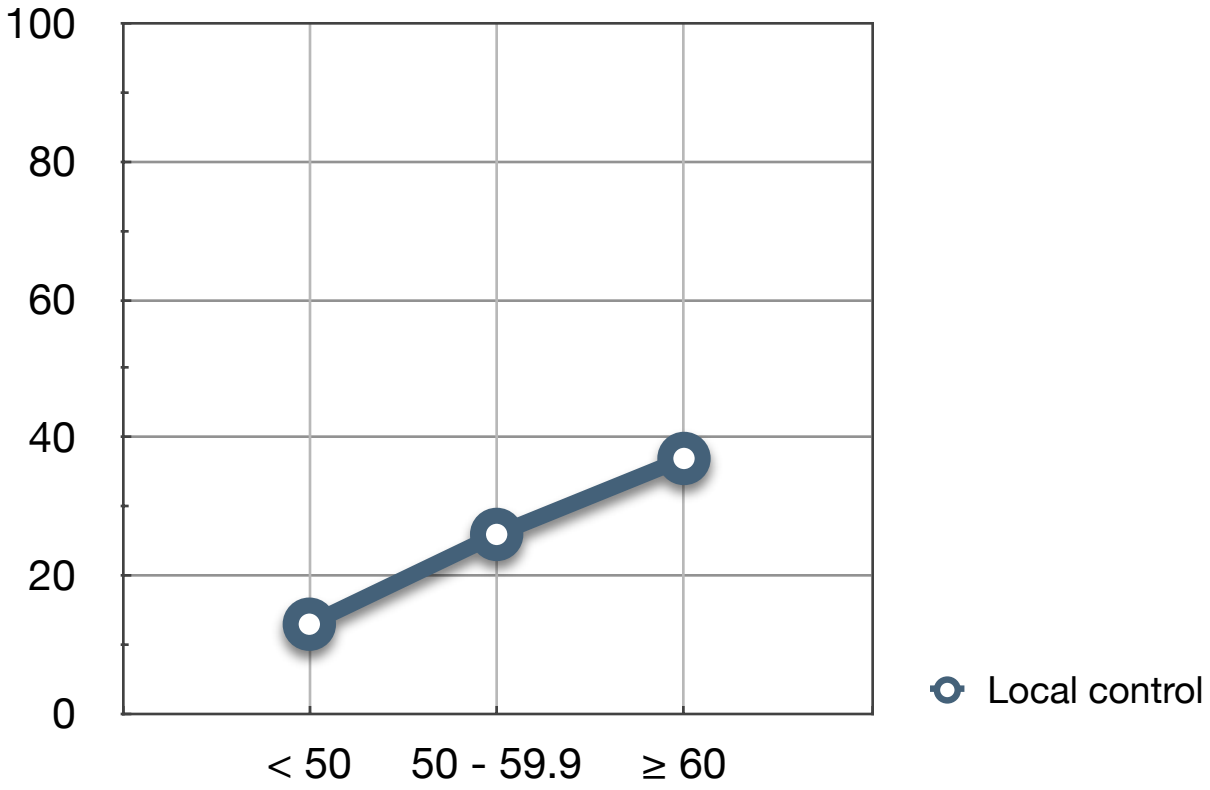
*Moderate to marked intraductal involvement in the primary and present in the adjacent tissues.

Harris JR, Connolly JL, Schnitt SJ, Cohen RB, Hellman S. Clinical-pathologic study of early breast cancer treated by primary radiation therapy. J Clin Oncol. 1983;1:184-189.

RESULTS OF NON-SURGICAL SERIES

	Pfahler 1932	**Keynes 1937**	**Baclesse 1965**
Patients	53	176	142
5yOS	80%	Stage I: 71% Stage II: 29%	•
5yCSS	•	•	Stage A: 54% Stage B: 67%
Comments		As good as mastectomy. Not widely used due to lack of Radium	66 - 70 Gy fractionated over 3months

Price A, Kerr GR, Rodger A. Primary radiotherapy for T4 breast cancer. Clin Oncol (R Coll Radiol). 1992;4:217-221.



Clarke DH, Le MG, Sarrazin D et al. Analysis of local-regional relapses in patients with early breast cancers treated by excision and radiotherapy: experience of the Institut Gustave-Roussy. Int J Radiat Oncol Biol Phys. 1985;11:137-145.

IMPACT OF DOSE ESCALATION

	NSD cut-off	Local control	Relative Risk
Whole breast	1530	96.2% vs. 90.8%	2,4
Tumor bed	1840	92.9% vs. 97.6%	3,2

van Limbergen E, van den Bogaert W, van der Schueren E, Rijnders A. Tumor excision and radiotherapy as primary treatment of breast cancer. Analysis of patient and treatment parameters and local control. Radiother Oncol. 1987;8:1-9.

Breast cancer: tumor excision and radiotherapy. Radiotherapy treatment policy.

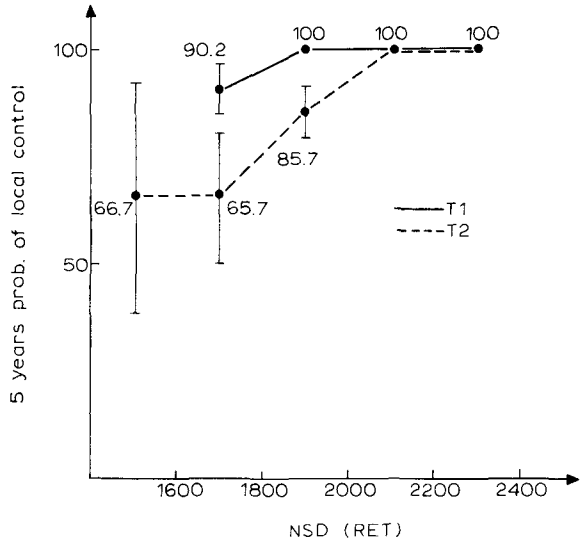
	Dose to the breast (Gy)	Boost (Gy)	Total dose (Gy)	NSD
1966–70	40–45[a]	–	40–45	1450–1500
1970–72[b]	45[a]	8–20[c]	53–65	1580–1760
1972–75	65	12–20[c]	77–85	2055–2120
	45 + 20[c]			
1976	65[a]	–	65	±1760
1977–79	65[a]	–	60–65	1760–1780
	20[a] flash[d] + 40			

[a] Cobalt 60 SSD 60 cm.

[b] Some patients received 2 × 4 Gy on the tumormass as a prebioptic procedure before Vim Silverman Needle biopsy. If this was the case, usually no electron boost was given afterwards, except in 5 cases.

[c] 15 MeV electrons (Brown Boveri Betatron).

[d] Flash: preoperative irradiation of the entire breast 5 × 4 Gy.



Recht A, Silver B, Schnitt S, Connolly J, Hellman S, Harris JR. Breast relapse following primary radiation therapy for early breast cancer. I. Classification, frequency and salvage. Int J Radiat Oncol Biol Phys. 1985;11:1271-1276.

IMPACT OF DOSE ESCALATION

Dose (Gy)	5y Local control (%)
< 60	93
60 - 70	96
> 70	99

Arriagada R, Mouriesse H, Sarrazin D, Clark RM, Deboer G. Radiotherapy alone in breast cancer. I. Analysis of tumor parameters, tumor dose and local control: the experience of the Gustave-Roussy Institute and the Princess Margaret Hospital. Int J Radiat Oncol Biol Phys. 1985;11:1751-1757.

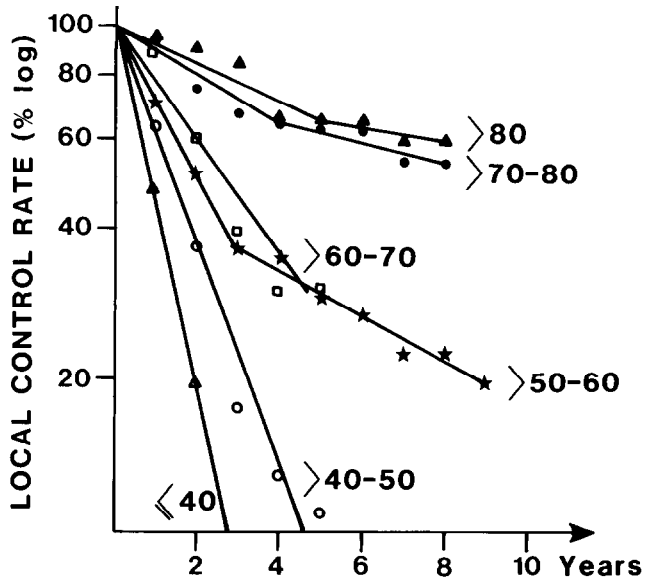


Fig. 3. Local control according to 6 groups of tumor dose (Gy). ▲ = >80 Gy; ⁎ = >50–60 Gy; ● = >70–80 Gy; ○ = >40–50 Gy; □ = >60–70 Gy; △ = ⩽40 Gy.

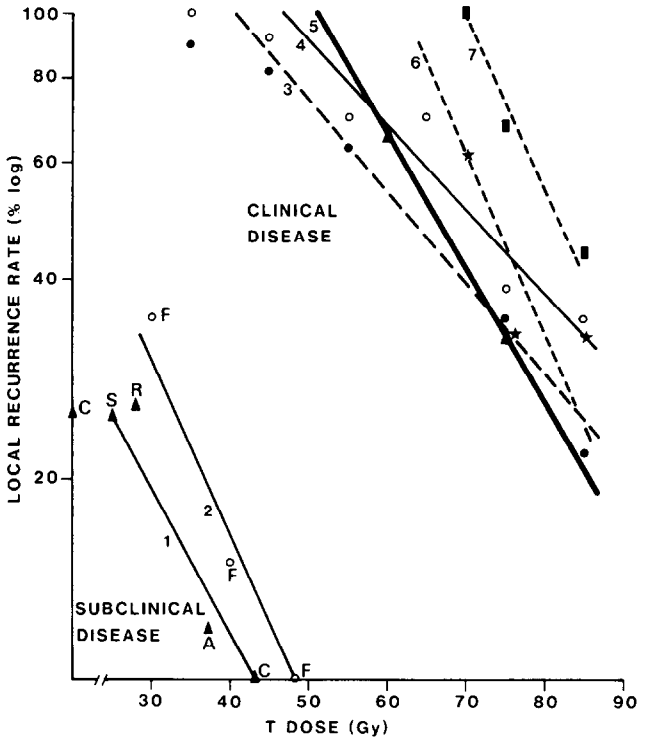


Fig. 8. Tumor (T) dose and local recurrence rate curves: Subclinical disease: 1) After lumpectomy (▲): C: Clark[7]; S: Simon *et al.*[24]; R: Rissanen[19]; A: Atkins *et al.*[2] In fact, Sarrazin *et al.*[21] and Pierquin *et al.*[12,18] report local recurrence rates at 5 years of 4% and 3%, delivering doses of 66 Gy and 70 Gy, respectively. 2) F (○): Fletcher data.[11] Clinical disease: IGR-PMH data: 3) (●): recurrence at 3 years; 4) (○): recurrence at 5 years; and 5) (▲) local recurrence and tumor dose relationship according to the multivariate analysis for a tumor larger than 5 cm, T3bN2 (see text). Calle *et al.*[5,6]: 6) (⁎) Local recurrence at 5 years for tumors ⩽ 5 cm; 7) (■) Local recurrence at 5 years for tumors > 5 cm.

Arriagada R, Bourgier C. Effect of radiation dose on local control in breast cancer. Radiother Oncol. 2008;86:285-6

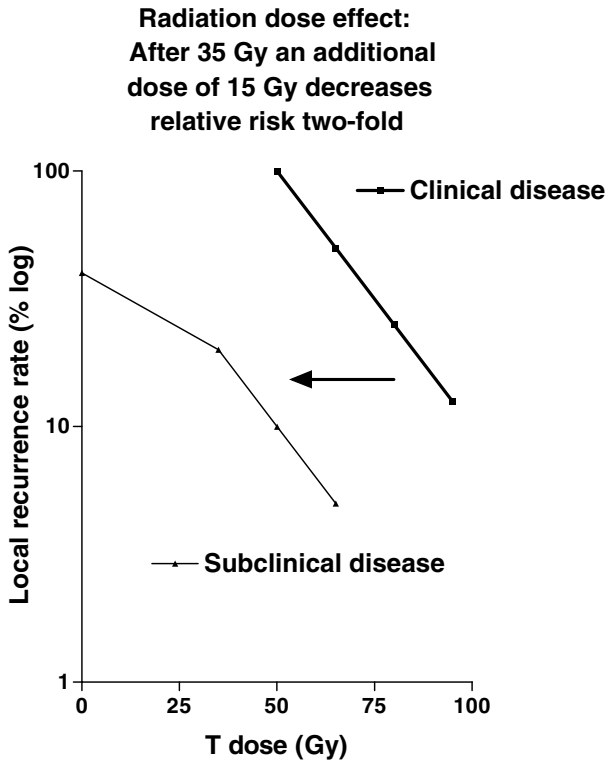
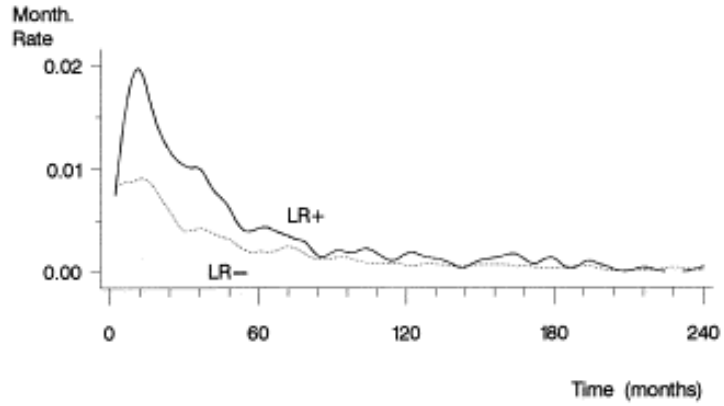


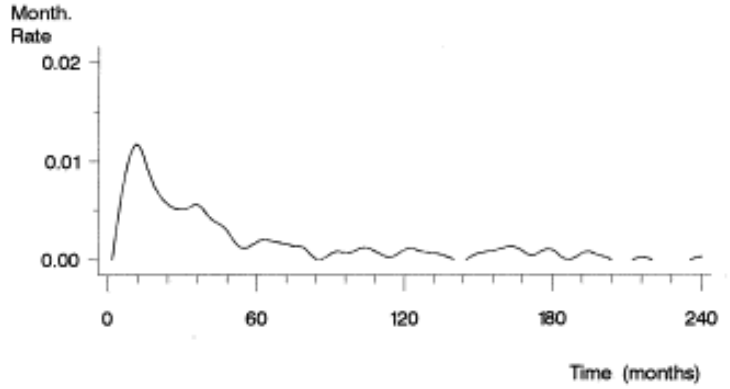
Fig. 1. Radiation dose effect: after 35 Gy an additional dose of 15 Gy decreases twofold the relative risk of local recurrence.

Koscielny S, Tubiana M. The link between local recurrence and distant metastases in human breast cancer. Int J Radiat Oncol Biol Phys. 1999;43:11-24.

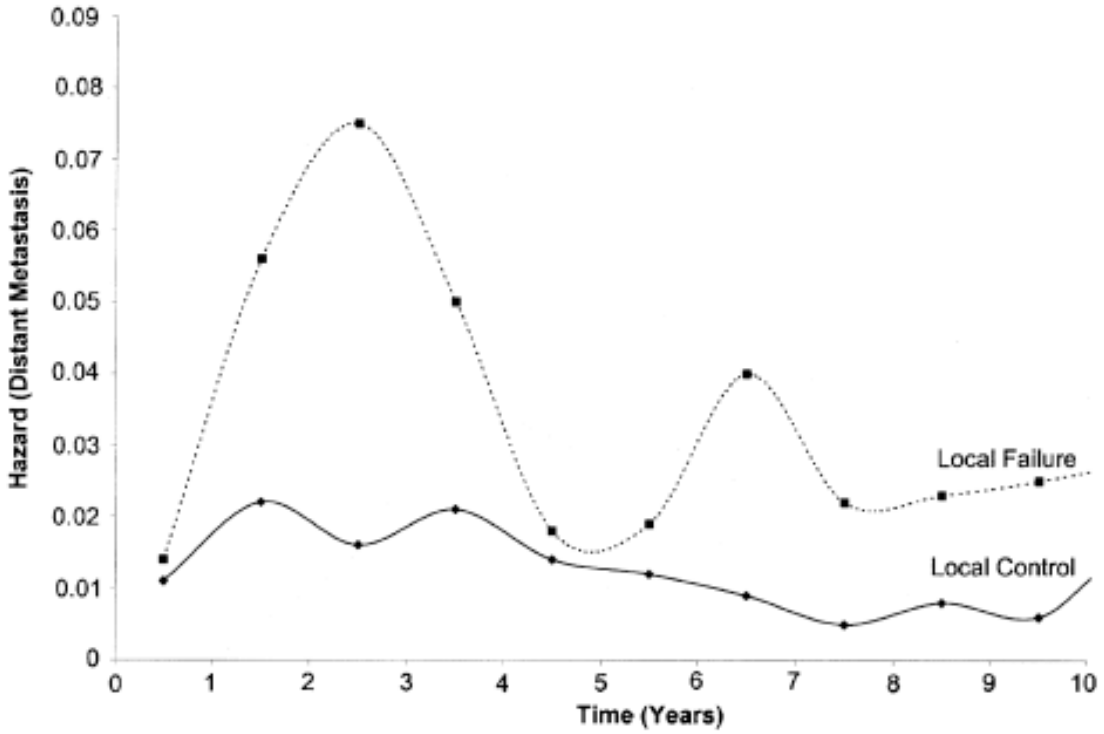
Overall population
A: Monthly rate of metastases in LR− and LR+ patients



Overall population
B: Difference (LR+ − LR−). Monthly rates of met. in excess in LR+ patients



Vicini FA, Kestin L, Huang R, Martinez A. Does local recurrence affect the rate of distant metastases and survival in patients with early-stage breast carcinoma treated with breast-conserving therapy? Cancer. 2003;97:910-919.



RANDOMIZED TRIALS

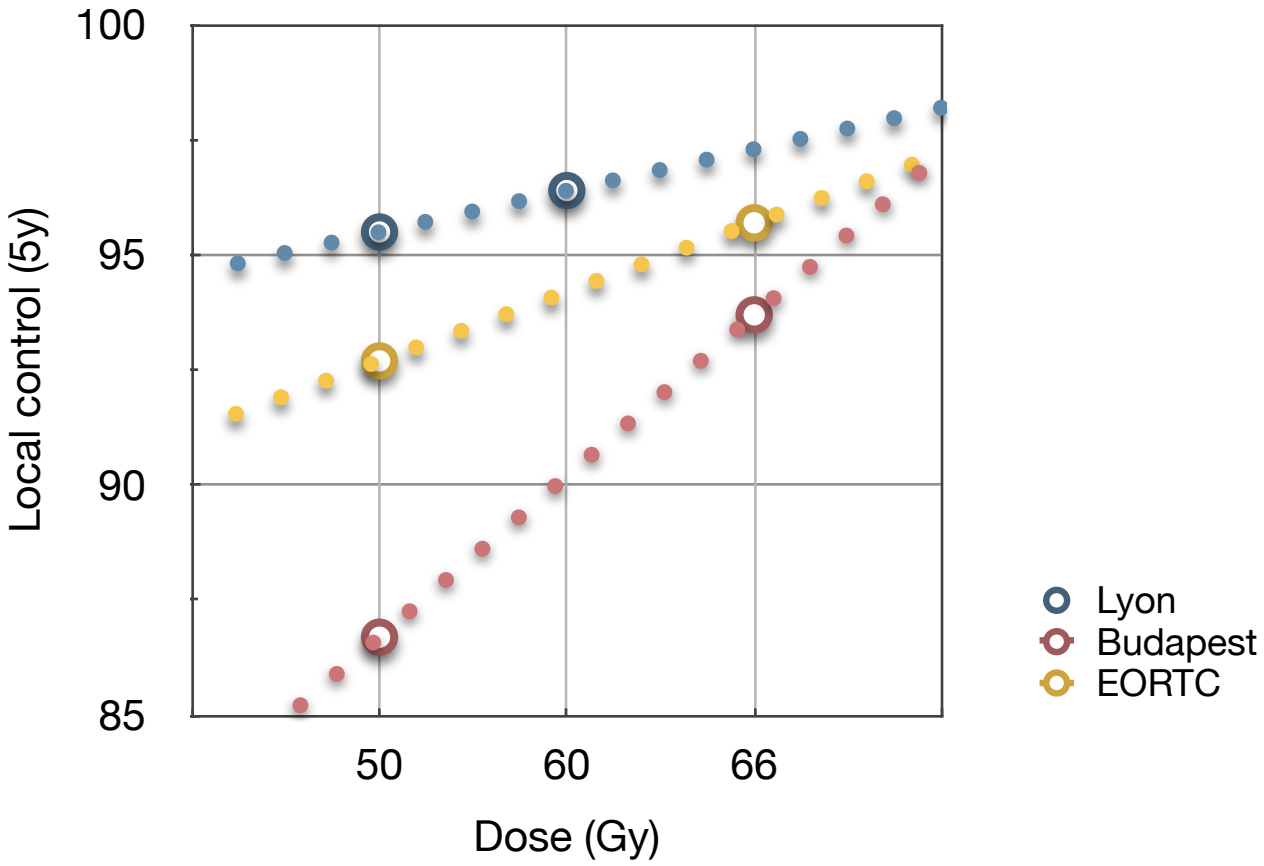
Polgar C, Major T. Current status and perspectives of brachytherapy for breast cancer. Int J Clin Oncol. 2009;14:7-24.

Table 1. Results of randomized "boost versus no boost" trials

Clinical trial	No. of patients	Technique	Boost dose (Gy)	Median FUP (years)	5-year LR Boost vs no boost (%)	10-year LR Boost vs no boost (%)	*P* value
EORTC[28]	5318	EBI/LDR BT	15–16	10.8	4.3 vs 7.3	6.2 vs 10.2	<0.0001
HNIO[3,29,30]	627	ELE/HDR BT	12–16	5	6.3 vs 13.3	NR	0.0017
Lyon[31]	1024	ELE	10	3.3	3.6 vs 4.5	NR	0.044

EORTC, European Organisation for Research and Treatment of Cancer; HNIO, Hungarian National Institute of Oncology; FUP, follow-up period; LR, local recurrence; EBI, external beam irradiation (photons or electrons); ELE, electrons; LDR, low-dose-rate; HDR, high-dose-rate; BT, brachytherapy; NR, not reported

COMPARISON RANDOMIZED TRIALS



Bartelink H, Horiot JC, Poortmans PM et al. Impact of a higher radiation dose on local control and survival in breast-conserving therapy of early breast cancer: 10-year results of the randomized boost versus no boost EORTC 22881-10882 trial. J Clin Oncol. 2007;25:3259-3265.

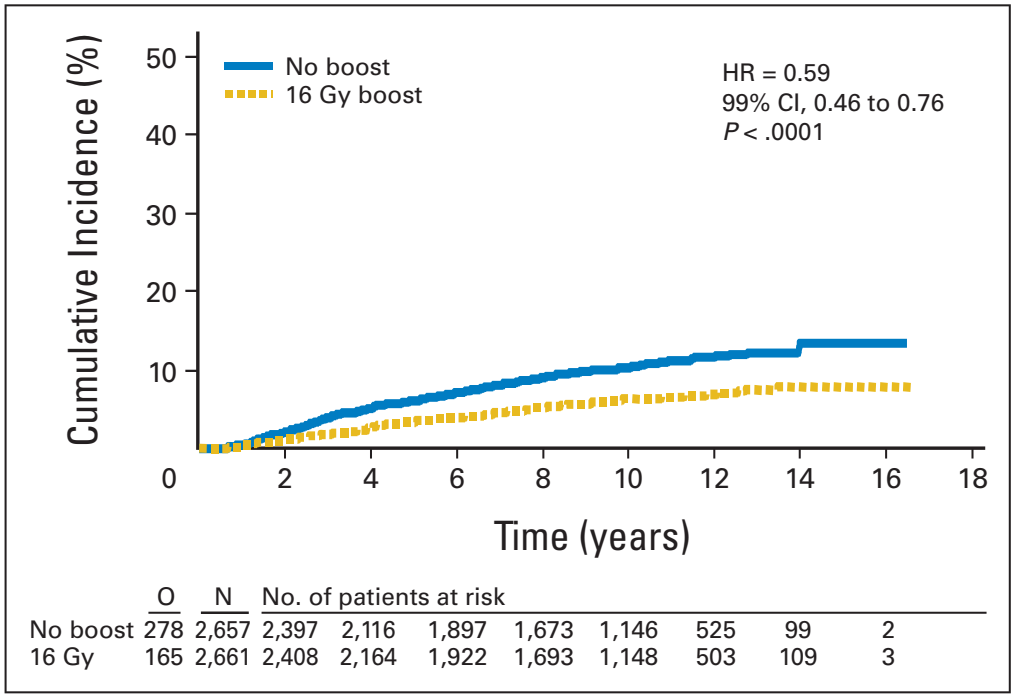


Fig 2. Cumulative incidence of recurrence of tumor as first event in the ipsilateral breast after 50 Gy whole-breast irradiation or 50 Gy whole-breast irradiation and a boost of 16 Gy. HR, hazard ratio; O, occurrences; N, number of patients at risk.

Number needed to treat (NNT): number of patients who need to be treated in order to prevent one additional bad outcome (i.e. the number of patients that need to be treated for one to benefit compared with a control in a clinical trial)

	Experimental group (E)	Control group (C)	
Events (E)	EE	CE	EE + CE
Non-events	EN	CN	EN + CN
	EE + EN	CE + CN	

Event rate (EER) = EE/EN
Event rate (CER) = CE/CN
Absolute risk reduction = EER - CER
NNT = 1/Absolute risk reduction

	Experimental group (E)	Control group (C)	
Events (E)	165	278	443
Non-events	2496	2379	4875
	2661	2657	5318

Event rate (EER) = 0.06610
Event rate (CER) = 0.11685
Absolute risk reduction = [-0.05075]
NNT = 19 (@10y)

Bartelink H, Horiot JC, Poortmans PM et al. Impact of a higher radiation dose on local control and survival in breast-conserving therapy of early breast cancer: 10-year results of the randomized boost versus no boost EORTC 22881-10882 trial. J Clin Oncol. 2007;25:3259-3265.

CONTROVERSIAL ISSUES

DOSE-ESCALATION
FOR CLOSE OR POSITIVE MARGINS

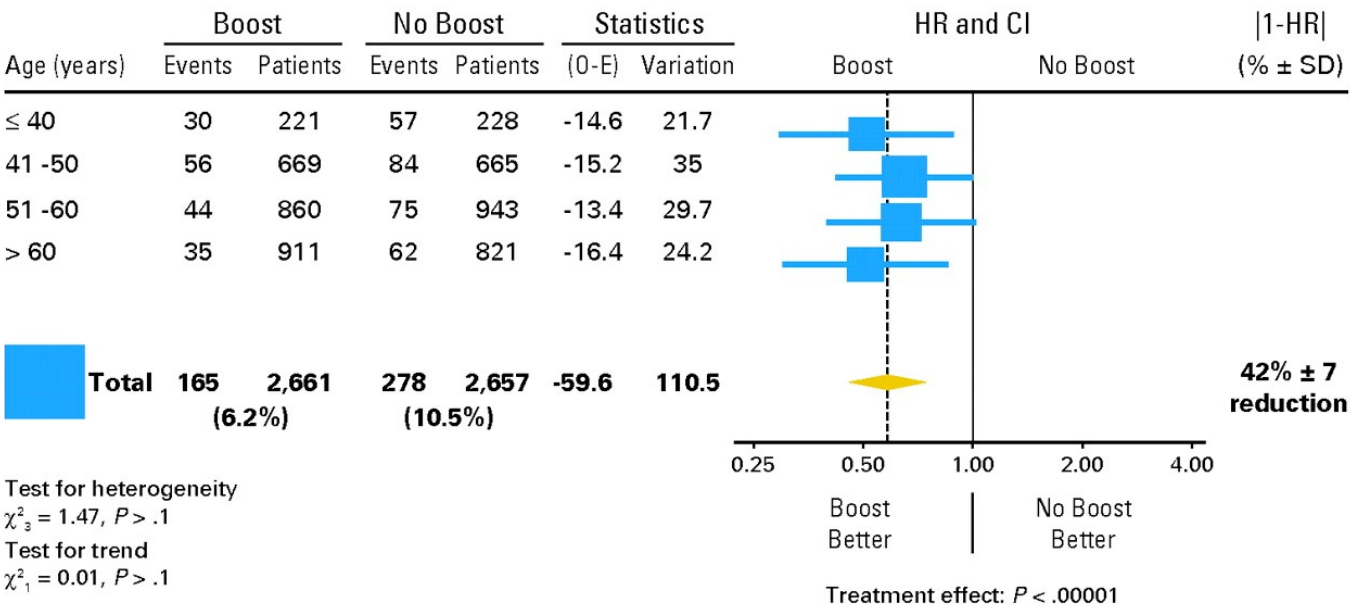
DOSE-ESCALATION BENEFICIAL	DOSE-ESCALATION NEUTRAL
• University of Pennsylvania • Japanese overview • Instituto Valenciano de Oncología • University of Florence	• EORTC trial • Fox Chase Cancer Center • Tufts - New England Medical Center • University of Maryland Medical Center

STUDIES SHOWING BENEFIT FOR DOSE-ESCALATION IN CLOSE OR POSITIVE MARGINS

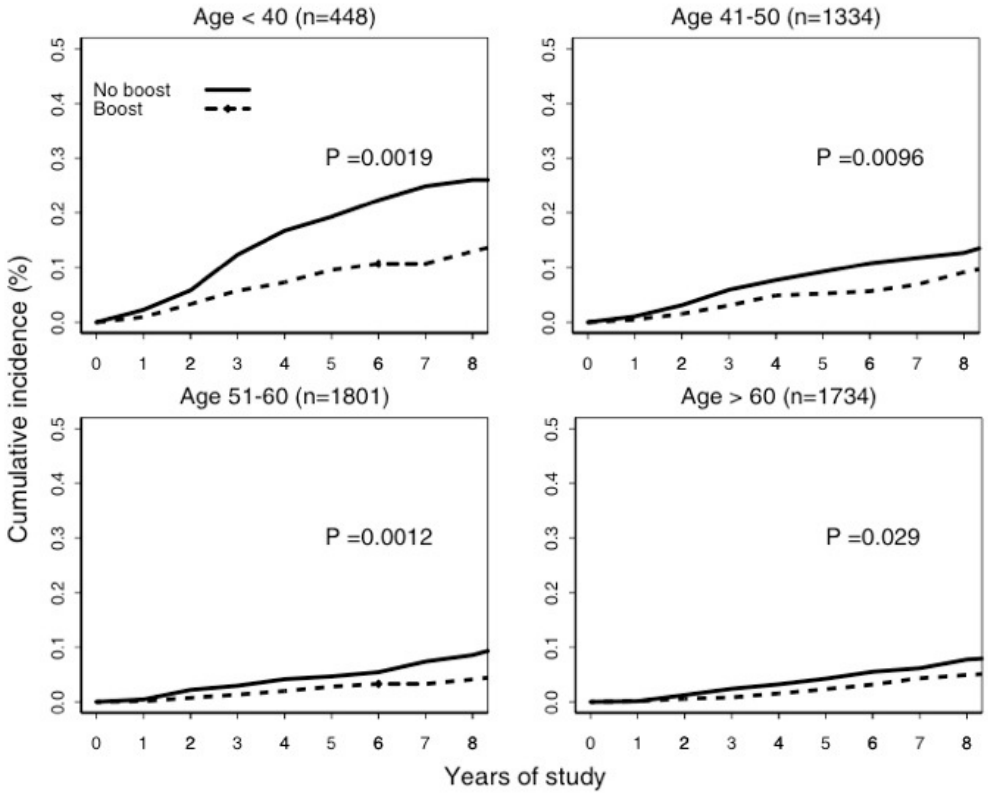
	NEGATIVE MARGINS	CLOSE MARGINS	POSITIVE MARGINS	COMMENTS
University of Pennsylvania {Solin et al., 1991}	>2mm; 60 Gy; 5yRFS=75%	<2mm; 64 Gy; 5yRFS=69%	65 Gy; 5yRFS = 81%	Selected patients with focally positive or close microscopic pathology margins can be adequately treated
IVO {Guinot et al., 2007}		<2mm; HDR 4.4 Gy x 3fr;5yLC = 95%, 9yLC = 76% 2-5mm; 4.4 Gy x 3fr; 5yLC = 100%, 9yLC = 100%	HDR 4.4 Gy x 3fr; 5yLC = 97%, 9yLC = 92.6%	Breast can be preserved in women with high-risk breast cancer due to close or positive margins
University of Florence {Livi et al., 2013}	>5mm; 10 Gy; LR = 1.8%	2-5mm; 16 Gy; LR = 2.6%	<2mm or positive; 20 Gy; LR = 2.3%	A margin-directed boost dose-escalation might reduce the negative impact of margins on early LR

DOSE-ESCALATION
IN YOUNG PATIENTS

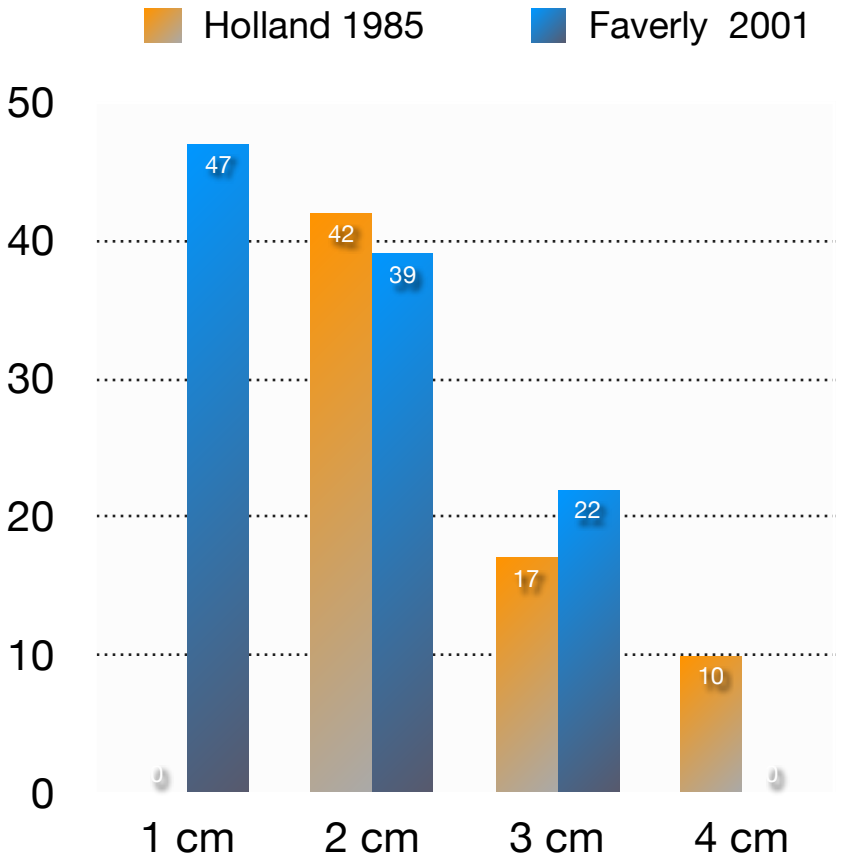
Bartelink H, Horiot JC, Poortmans PM et al. Impact of a higher radiation dose on local control and survival in breast-conserving therapy of early breast cancer: 10-year results of the randomized boost versus no boost EORTC 22881-10882 trial. J Clin Oncol. 2007;25:3259-3265.

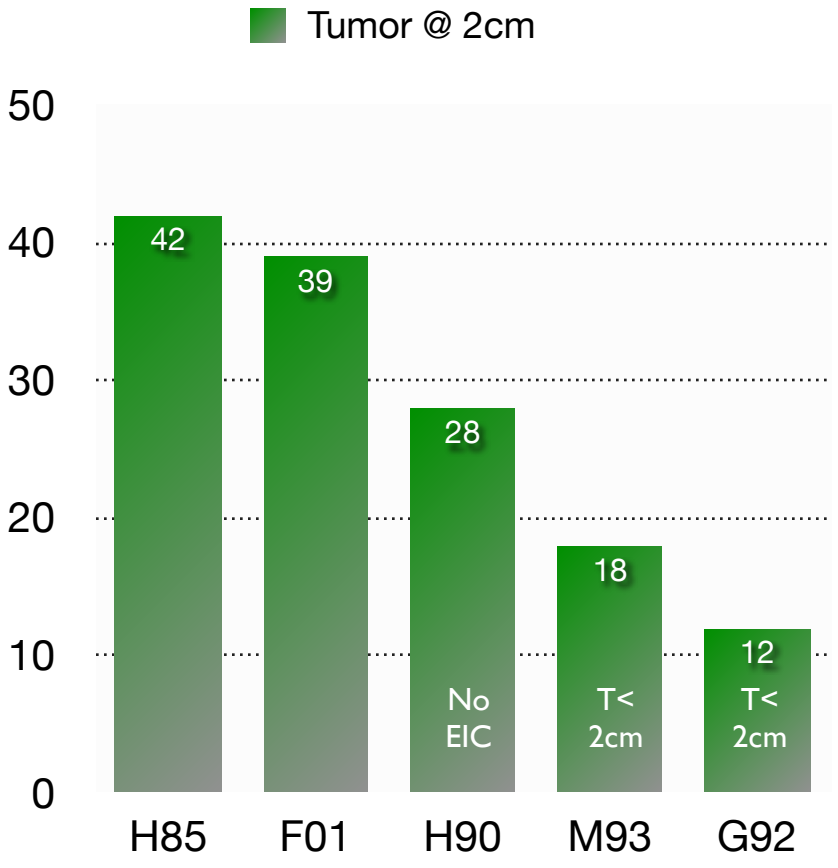


Antonini N, Jones H, Horiot JC et al. Effect of age and radiation dose on local control after breast conserving treatment: EORTC trial 22881-10882. Radiother Oncol. 2007;82:265-271.



DOSE-ESCALATION AND TARGET MISSING

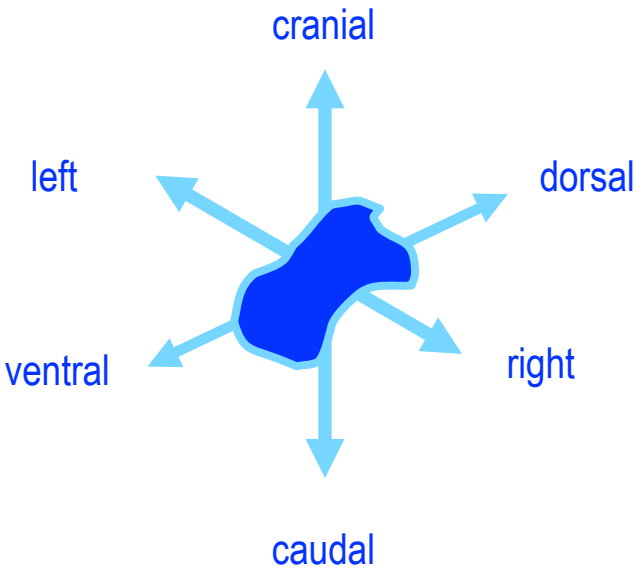




Holland R et al. Cancer 1985; 56: 979-90
Faverlyy D et al. Cancer 2001; 91: 647-59

H85: Holland 1985, F01: Faverly 2001, H90: Holland 1990, M93: Morimoto 1993, G92: Gump 1992

Benda RK, Yasuda G, Sethi A, Gabram SG, Hinerman RW, Mendenhall NP. Breast boost: are we missing the target? Cancer. 2003;97:905-909.


cranial
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ventral
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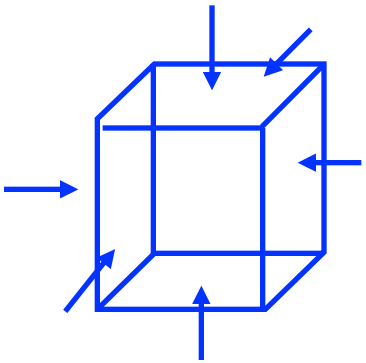
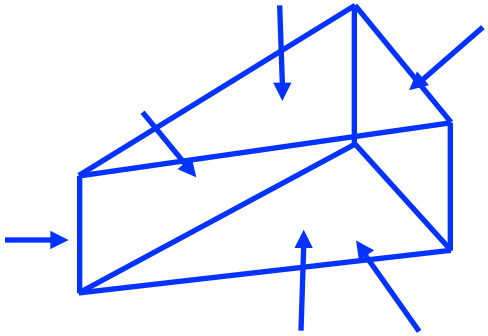
caudal

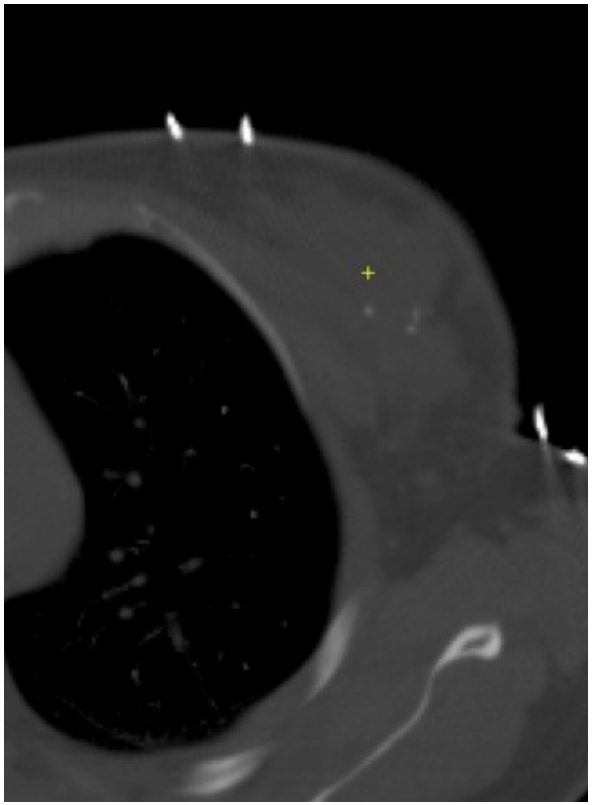




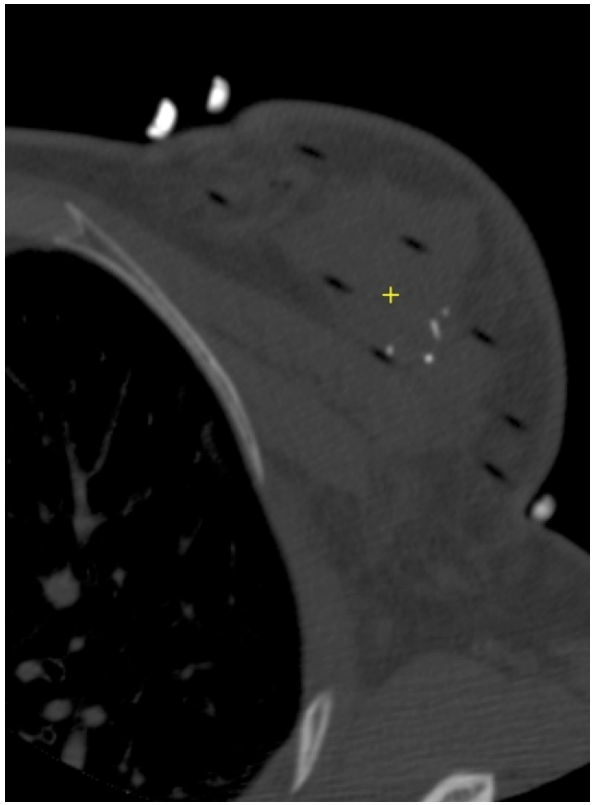
TUMOR BED ASSESSMENT AND TARGET MISS

AUTHOR	ASSESMENT	%MISS
Denham JW. IJRO 1988; 14: 399	Clinical vs. Rx-Clips	37%
Bedwinek J. IJRO 1993; 26: 675	Clinical vs. Rx-Clips	54%
Harrigton KJ. IJRO 1996; 34: 579	Clinical vs. Rx-Clips	68%
Sedlmayer F. IJRO 1996; 34: 1133	Clinical vs. Rx-Clips	52%
Regine WF. IJRO 1991; 20: 121	Clinical vs. CT-Clips	70%
Benda R. Cancer 2004; 97: 905	Clinical vs. CT-Clips	D90 = 51% of PD
Machtay M. IJRO 1994; 30:43	CT	10-88%
DeBiose DA. IJRO 1997; 38:755	Clinical vs. US	87%
Ringash J. R&O 2004; 72: 61	US vs. Rx-Clips	7%
Rabinovitch R. IJRO 2000; 47: 313	US vs. Rx-Clips	55%

Pre-plan



Implant



- It is of critical importance to ensure that the intended dose is delivered to the high risk area, using a rational prescription system

- Retrospective studies and boost trials used to justify dose-escalation focused on the value of intended prescription doses, rather than on the method of dose prescription to the target volume

- New trials have to be considered in the future to assess the value of dose escalation including reliable methods for localizing target volume and rational prescription systems to assure good and reproducible target coverage

CONCLUSIONS

- A dose-response relationship exists in breast conserving therapy
- A dose-boost is recommended for the entire population
- Doses above 66 Gy need to be tested in randomized trials
- Target definition and localization is critical to achieve local control

ACCELERATED PARTIAL BREAST IRRADIATION USING BRACHYTHERAPY

WHOLE BREAST RT MAY NOT BE NEEDED

IN APPROPRIATELY SELECTED PATIENTS

• Elderly patients not so likely to have LR (Milan randomized trials, EORTC trial)

• Recurrences away from tumor bed (‘elsewhere’ failures) are rare after lumpectomy alone or followed by whole breast RT (6 randomized trials plus multiple retrospective BCT studies)

• Some pathological factors increase risk of LR

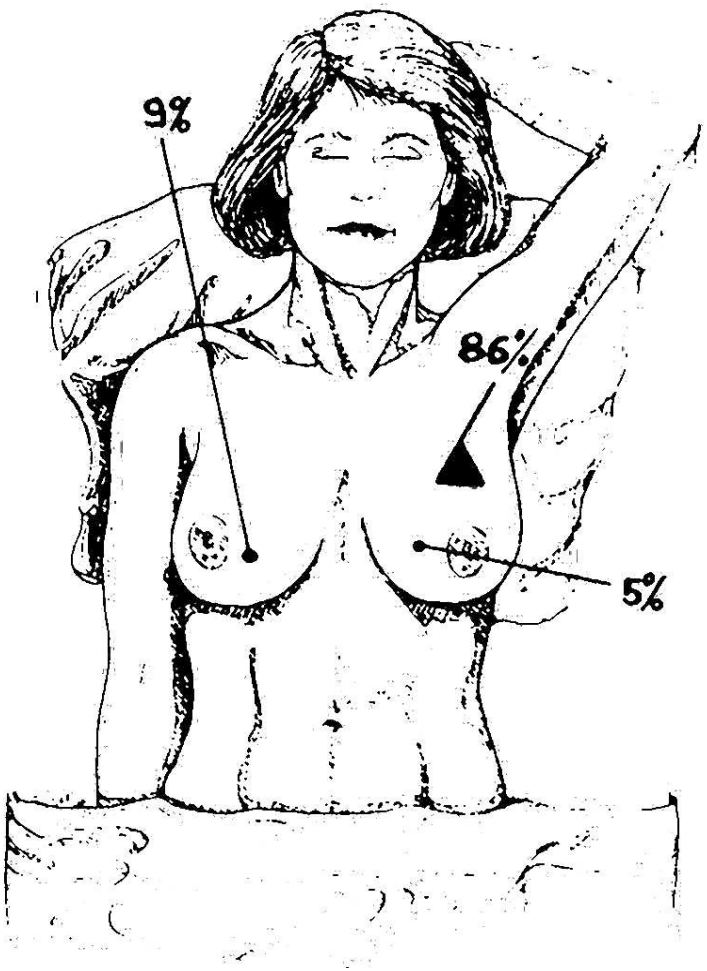
PARTIAL BREAST IRRADIATION
Local relapse according to age groups

MILAN I-II-III RANDOMIZED TRIALS

	< 45	46 - 55	> 55
Halsted	2.6	0.8	3.1
QuaRT	6.7	6.6	1.2
TumRT	12.9	15.8	8.9
Qua	23.8	10.6	5.7

PARTIAL BREAST IRRADIATION
Local relapse according to IQ

Milan III, 12 years follow-up



PARTIAL BREAST IRRADIATION
Local relapse according to IQ

ELSEWHERE FAILURES - RANDOMIZED TRIALS

TRIAL	FU	SURG	SURG+RT
NSABP	144	2,7%	3,8%
Milan III	39	1,5%	0%
Ontario	91	3,5%	1%
W. Beaumont	-	3,3%	0,6%

PARTIAL BREAST IRRADIATION
Local relapse according to Path

Faverly D, Hendriks J, Holland R. Breast carcinoma of limited extent. Cancer 2001; 91:647

BCLE, the proper tumor profile for PBI is defined as having no invasive carcinoma, DCIS and lymphatic emboli beyond 1 cm from the edge of the dominant mass

Mammography: absence of calcifications or tumor density beyond the edge of index tumor

Pathology: 1 cm microscopically tumor free margin (outer rim of 2 cm)

Sensitivity: 89% (disease who have positive test)

Positive predictive value: 89% (positive test who have disease)

False positive: 11% (erroneously suspected BCLE)

PARTIAL BREAST IRRADIATION
Local relapse according to Path

Faverly D, Hendriks J, Holland R. Breast carcinoma of limited extent. Cancer 2001; 91:647

VALIDATION OF THE MODEL

SELECTED CASES
Early breast cancer

Schnitt S et al JCO 1996
LR (4.7y FU) = 16%

Expected non-BCLE
(applying Faverly criteria)
15%

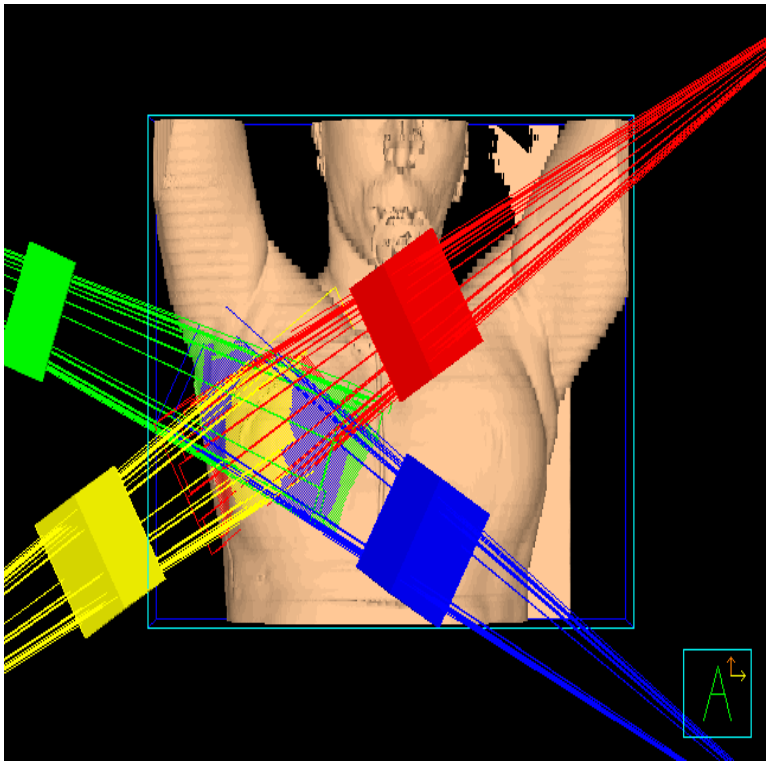
NON-SELECTED CASES
NSABP-06

Fisher R et al NEJM 1995
LR (5y FU) = 37%

Crude rate of non-BCLE
(Faverly series)
47%

PARTIAL BREAST IRRADIATION
Definitions and indications

- Breast cancer of limited extent
- Age group
- PBI may be defined as any scheme that delivers radiotherapy to the clinical target volume (CTV) over a short period of time
- CTV is defined as the tumor bed plus 1-2 cm margin
- Various techniques: BT, IORT, EBRT




Viewing Window [4]
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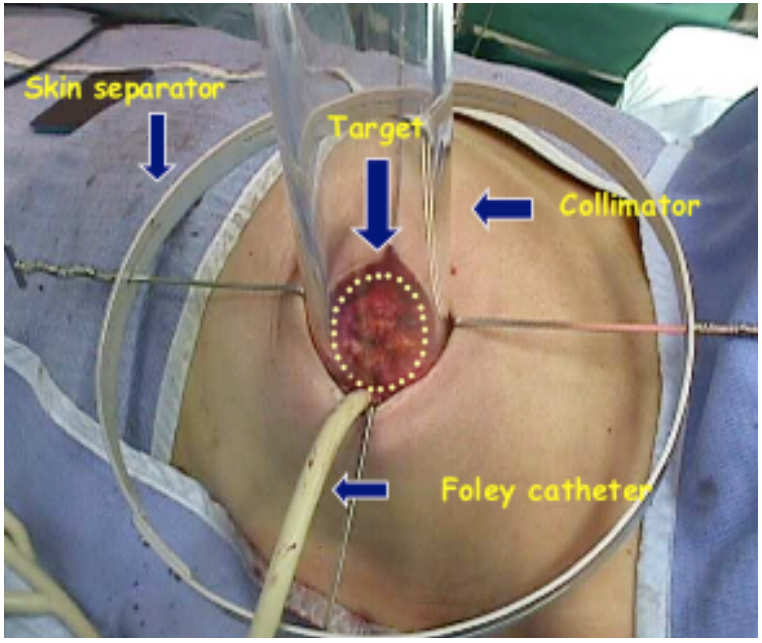
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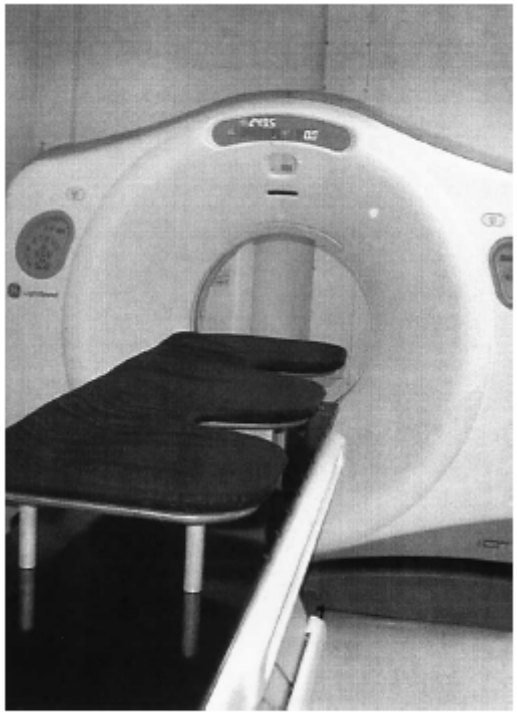
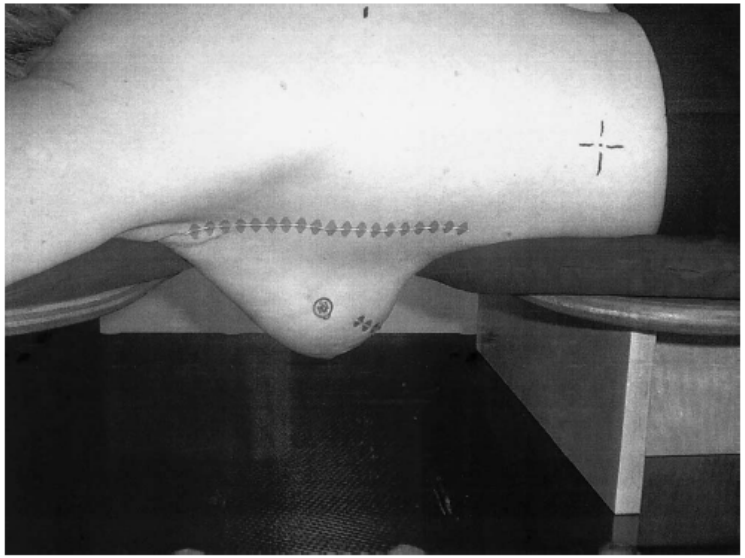
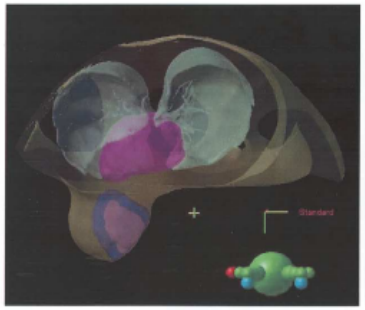
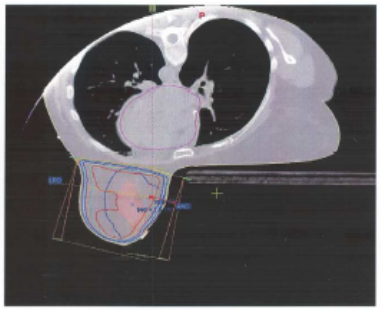
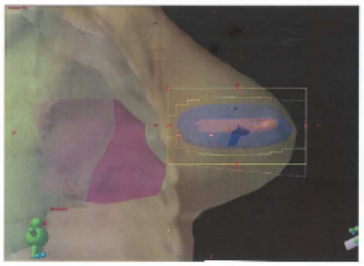
Target
Collimator
Foley catheter

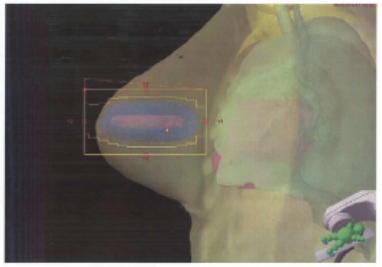


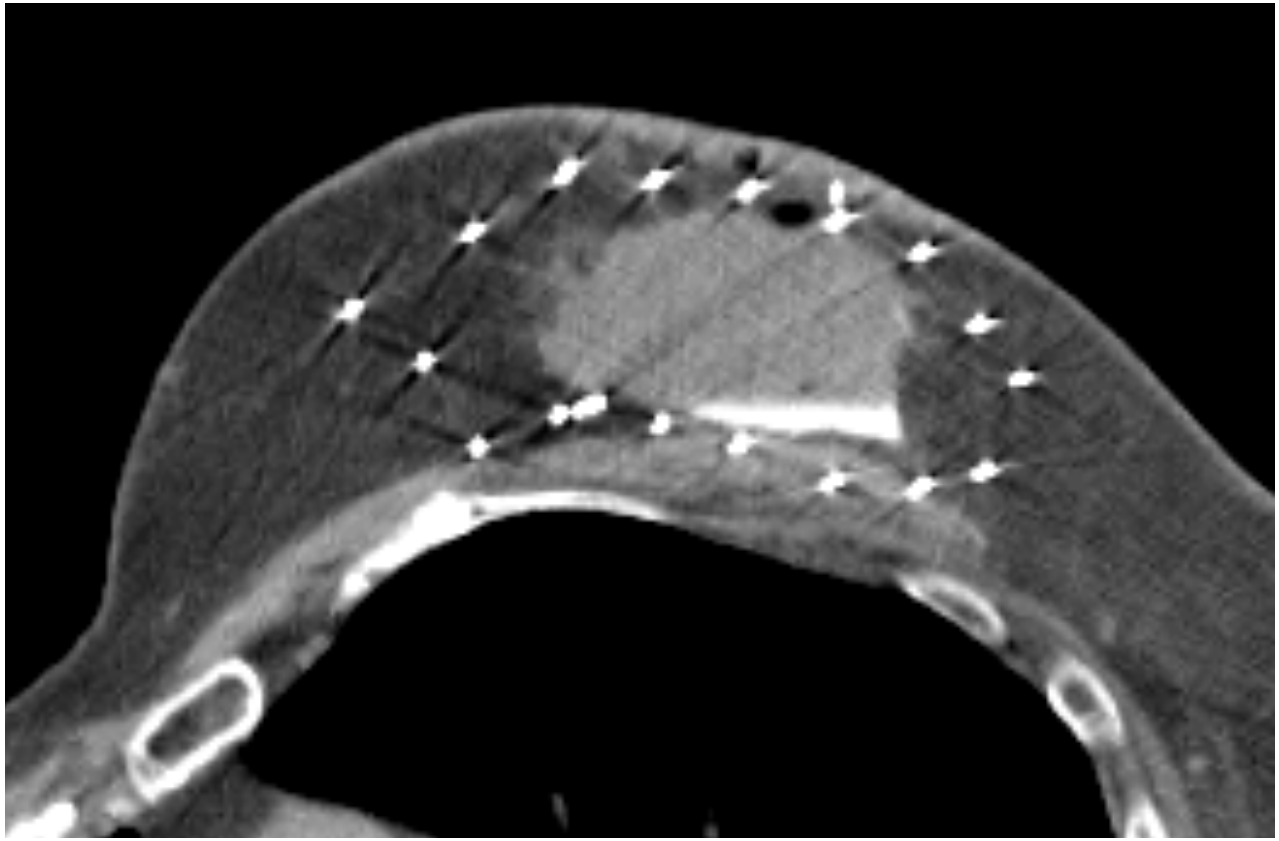



Standard





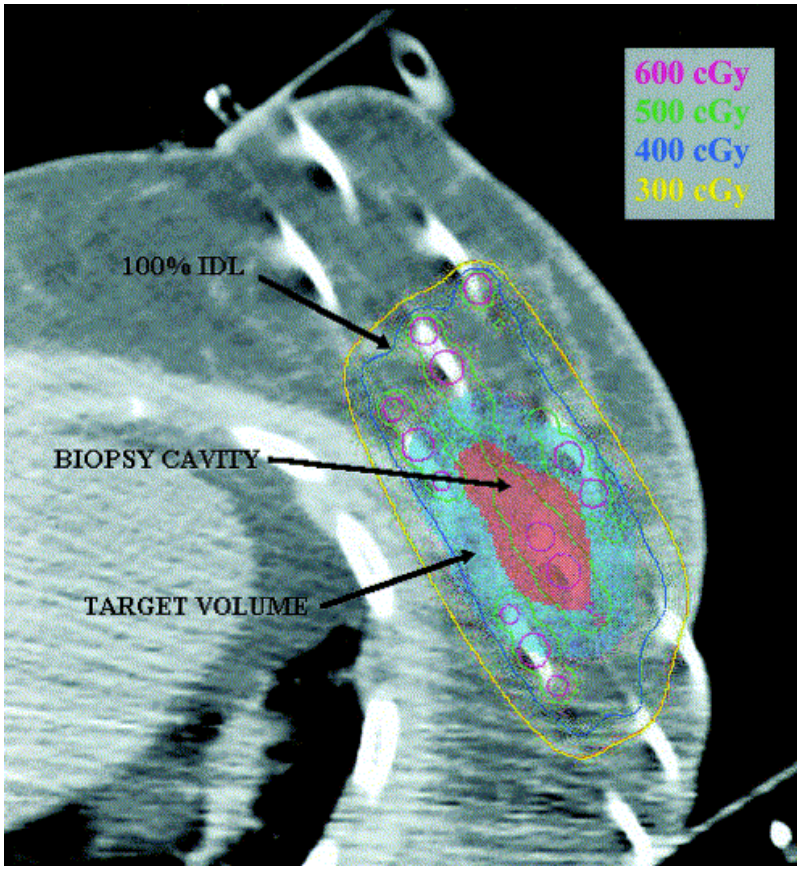


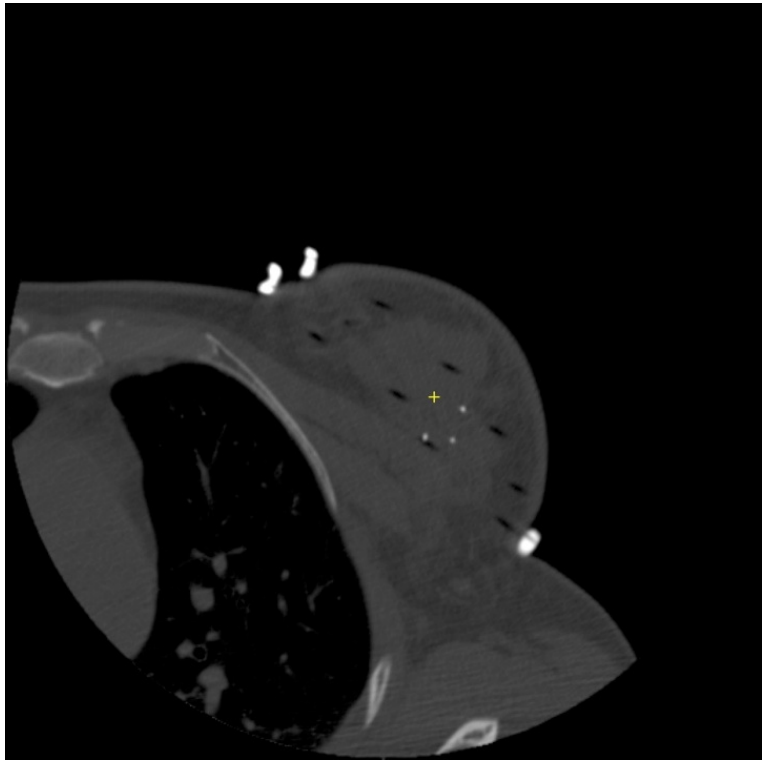


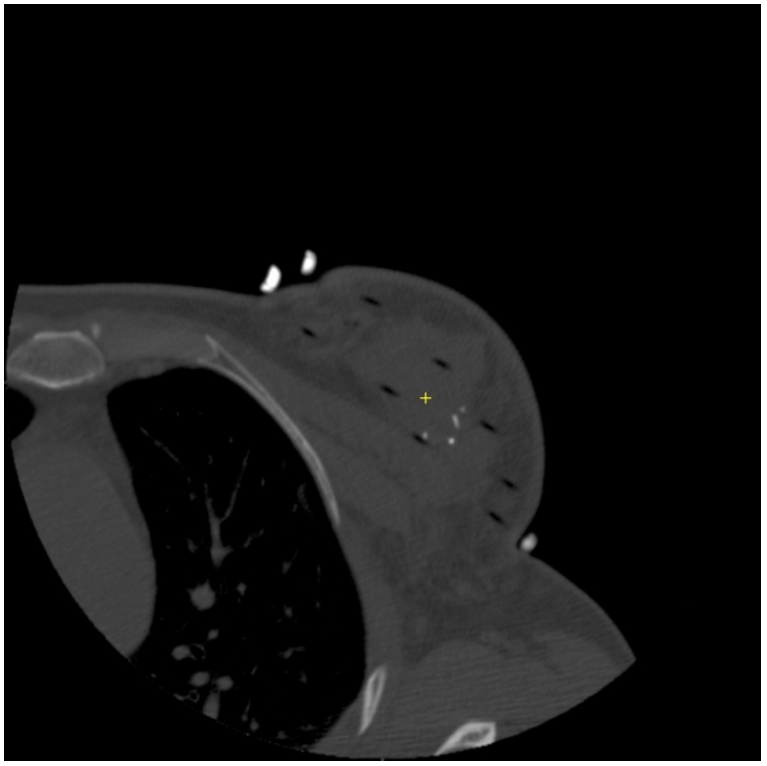
Courtesy Douglas Arthur, M.D.

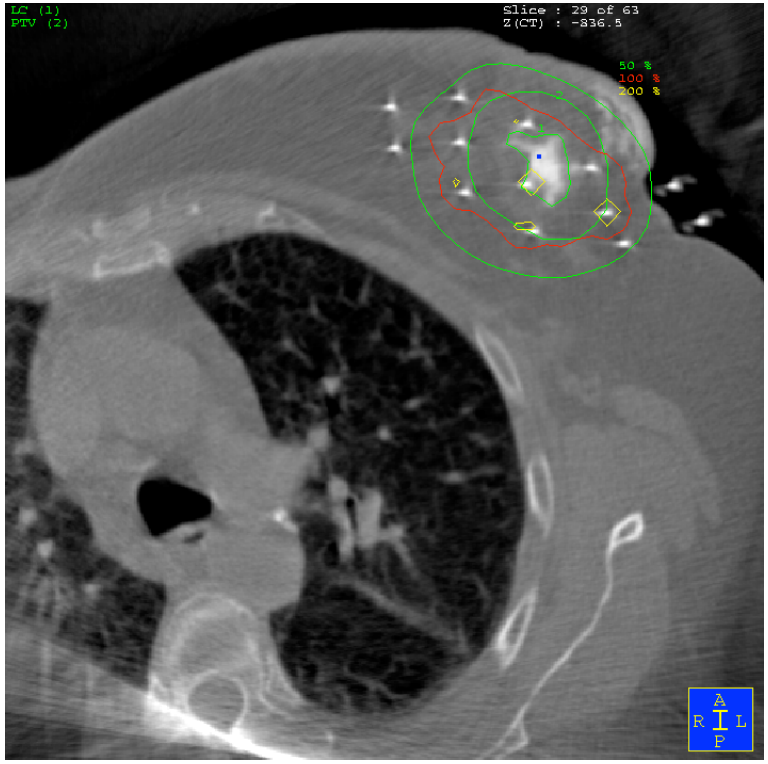
PARTIAL BREAST IRRADIATION
Quadrant brachytherapy: rationale

- Conform RT to cover lumpectomy cavity plus 1-2 cm margin (Clinical Target Volume)
- Sparing normal tissues (normal breast, skin, rib, heart)
- Optimize cosmetic result
- Accelerated radiotherapy (increased tumoricidal effect?)
- Dose-intensity





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PTV (2)
Slice : 29 of 63
Z(CT) : -836.5
50 %
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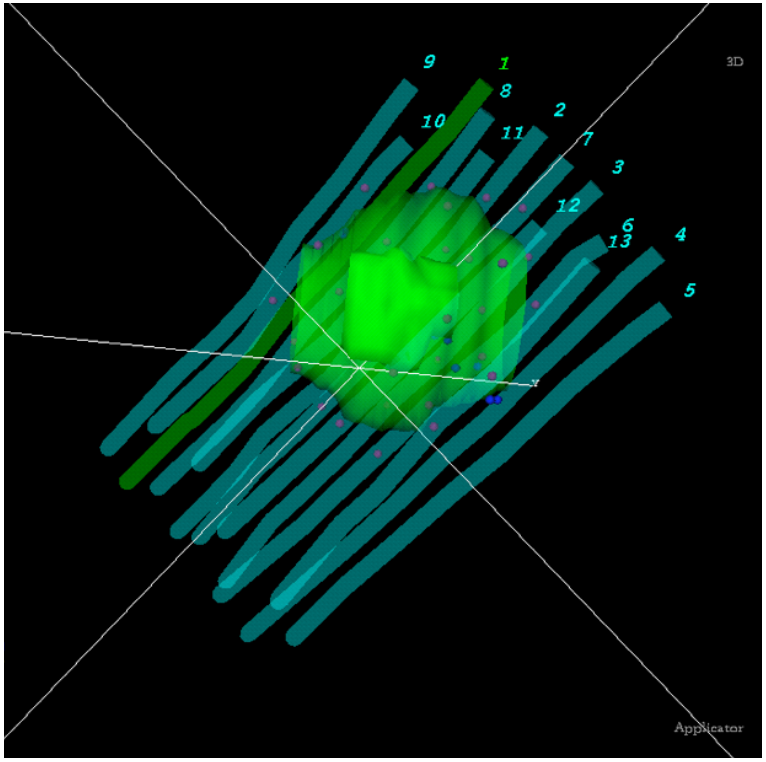
3D
9
1
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Applicator

PARTIAL BREAST IRRADIATION
Advantages over conventional treatment

- Improve documented underutilization of BCT
- Reduce time, cost and inconvenience of BCT
- Potentially reduce acute and chronic toxicity
- Improve QoL
- Eliminate scheduling problems with chemotherapy
- Potentially improve outcome? (reduce delays)

Table 1
Results of APBI studies using suboptimal patient selection criteria with adequate ($\geqslant$4 years) follow-up.

Institution	Technique	Median FUP (years)	LR% (n)	Annual LR% (n)	Comments on patient selection
Uzsoki hospital [37]	MDR	12	24 (17 of 70)	2	Max. tumour size: 5 cm; 100% unknown margins; 30% unknown pathological axillary status (pNx); 4% node positive; 10% lobular ca.; multifocal tumours, LVI and EIC allowed; no patient age limitation
Christie hospital[a] [20]	EBI	8	20 (69 of 353)	2.5	Max. tumour size: 4 cm; 100% unknown margins; no surgical axillary staging; lobular ca., LVI and EIC allowed; no patient age limitation
Cookridge hospital[a] [11]	EBI	8	12 (10 of 84)	1.5	Max. tumour size: 4.5 cm; 41% node positive; lobular ca., LVI and EIC allowed; no patient age limitation
London Reg. Ca. C. [30]	HDR	7.6	15 (6 of 39)	2	Max. tumour size: 4.5 cm; 31% close margins; 15% node positive; 5% pNx; 8% EIC pos.; no patient age limitation
Tufts university [16]	HDR	7	9.1 (3 of 33)	1.30	45% Close margins; 9% node positive; 55% EIC pos.; no patient age limitation
Guy's hospital I [12]	LDR	6	37 (10 of 27)	6.2	Max. tumour size >4 cm; 56% positive margins; 44% node positive, 41% EIC positive; lobular ca. and LVI allowed; patient age >40 years
Guy's hospital II [13]	MDR	6.3	18 (9 of 49)	2.9	Max. tumour size: 4 cm; 43% positive margins; 45% node positive; 14% lobular ca., LVI and EIC allowed, no patient age limitation
Osaka Med. center [26]	HDR	4.3	5.0 (1 of 20)	1.15	15% Positive margins; 35% EIC pos.; 5% lobular ca.; 10% DCIS; no patient age limitation (25% with age $\leqslant$45 years)
Florence hospital [10]	LDR	4.2	6 (7 of 115)	1.4	Max. tumour size: 5 cm; 8% positive and 7% unknown margins; 38% node positive; 20% lobular ca.; LVI and EIC allowed, no patient age limitation
All patients		4.2–12	17 (132 of 790)	1.15–6.2	

APBI = accelerated partial-breast irradiation; FUP = follow-up period; LR = local recurrence; EIC = extensive intraductal carcinoma; LVI = lympho-vascular invasion; EBI = external beam irradiation; MDR = medium-dose rate; LDR = low-dose-rate; HDR = high-dose-rate.

[a] Randomized trial.

Table 2
Results of APBI studies using stringent patient selection criteria with adequate (⩾4 years) follow-up.

Institution/study	Technique	Median FUP (years)	LR% (*n*)	Annual LR%	Comments on patient selection
HNIO, Budapest I [32,33,35,36]	HDR	11.1	8.9 (4 of 45)	0.80	Max. tumour size: 2 cm; clear margins; unifocal tumour; grade I–II; pN0 or pN1mi; no patient age limitation. *Excluded:* lobular ca., DCIS and EIC
WBH, Michigan [5,44]	LDR/HDR	9.7	5.0 (10 of 199)	0.52	Max. tumour size: 3 cm; margins ⩾ 2 mm; pN0; patient age >40 years. *Excluded:* lobular ca., DCIS, and EIC
Örebro Med. Centre [15]	PDR	7.2	5.9 (3 of 51)	0.83	Max. tumour size: 4.2 cm; clear margins; unifocal tumour; 12% node pos. (1–3 nodes); 8% lobular ca.; patient age ⩾ 40 years. *Excluded:* DCIS and EIC
RTOG 95–17 [7]	LDR/HDR	7	6.1 (6 of 99)	0.91	Max. tumour size: 3 cm; clear margins; unicentric tumour; 20% node positive (1–3 pos. nodes without ECE); no patient age limitation. *Excluded:* lobular ca., DCIS, and EIC
HNIO, Budapest II[a] [33–36]	HDR/EBI	6.8	4.7 (6 of 128)	0.69	Max. tumour size: 2 cm; margins ⩾ 2 mm; unifocal tumour; grade I–II; pN0 or pN1mi; patient age >40 years. *Excluded:* lobular ca., DCIS, and EIC
Ochsner clinic [17]	LDR/HDR	6.25	2 (1 of 51)	0.32	Max. tumour size: 4 cm; clear margins; unicentric tumour; 18% node positive (1–3 nodes); 10% DCIS; 14% EIC; no patient age limitation
Ninewells hospital [38]	LDR	5.6	0 (0 of 11)	0	Max. tumour size: 3.5 cm; unifocal tumour, pN0 or pN1a (only 1 pt. node pos.); patient age >40 years. *Excluded:* lobular ca., DCIS, and EIC
Germany–Austria [28,41]	PDR/HDR	5.25	2.9 (8 of 274)	0.55	Max. tumour size: 3 cm; margins ⩾2 mm; unifocal tumour; grade I–II; pN0 or pN1mi; ER or PgR pos.; 16% lobular ca.; patient age >35 years. *Excluded:* DCIS, EIC and LVI
FDA Trial, USA [9]	MammoSite	5.2	0 (0 of 43)	0	Max. tumour size: 2 cm; clear margins; unifocal tumour; pN0; patient age ⩾45 years. *Excluded:* lobular ca., DCIS, and EIC
Kiel-HNIO [25,36]	MammoSite	5	0 (0 of 11)	0	Max. tumour size: 2 cm; margins ⩾5 mm; unifocal tumour; grade I–II; pN0; ER or PgR pos.; patient age ⩾60 years. *Excluded:* lobular ca., DCIS, EIC and LVI
University Navarra [14]	HDR	4.4	3.8 (1 of 26)	0.86	Max. tumour size: 3 cm; margins ⩾2 mm; unicentric tumour; pN0; no patient age limitation *Excluded:* lobular ca., DCIS, and EIC
Wisconsin university [29]	HDR/ MammoSite	4	2.9 (8 of 273)	0.72	Max. tumour size: 3 cm; margins ⩾ 2 mm; unicentric tumour; 7% node positive (1–3 nodes without ECE); 13% DCIS; no patient age limitation. *Excluded:* lobular ca. and EIC.
Kansas university [19]	LDR	4	0 (0 of 25)	0	Max. tumour size: 2 cm; clear margins; grade I–II, pN0; 12% (classical) lobular ca.; patient age ⩾60 years. *Excluded:* non-classical lobular ca., DCIS and EIC
All patients		4–11.1	3.8 (47 of 1236)	0–0.91	

APBI = accelerated partial-breast irradiation; FUP = follow-up period; LR = local recurrence; EIC = extensive intraductal carcinoma; LVI = lympho-vascular invasion; DCIS = ductal carcinoma in situ; ECE = extracapsular extension; ER = estrogen receptor; PgR = progesterone receptor; LDR = low-dose-rate; HDR = high-dose-rate; EBI = external beam irradiation; FDA = food and drug administration; HNIO = Hungarian National Institute of Oncology; RTOG = Radiation Therapy Oncology Group; WBH = William Beaumont hospital.

[a] Randomized trial.

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Review

Accelerated partial breast irradiation as part of breast conserving therapy of early breast carcinoma: A systematic review

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ABSTRACT

New strategies for adjuvant radiotherapy of early breast cancer are being investigated in several phase III randomised trials at the present time. Accelerated partial breast irradiation (APBI) is a way to offer an early breast cancer patient, who has had breast conservative surgery, an adjuvant radiotherapy of short duration aimed at the tumour bed with a certain margin. The rationale of this strategy is that most local recurrences appear close to the tumorectomy cavity and a wish to spare the patient late radiation morbidity. This review discusses the background for APBI, the different techniques, and we highlight possible pitfalls using these techniques. A systematic overview of all phase I and II studies is provided. Patient selection for this therapy is pivotal and based on evidence from previous studies on patient/tumour characteristics and pattern of local recurrences we propose inclusion criteria for patients in APBI protocols.
 Radiotherapy and Oncology xxx (2008) xxx–xxx

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ELSEVIER

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CONSENSUS STATEMENT

ACCELERATED PARTIAL BREAST IRRADIATION CONSENSUS STATEMENT FROM THE AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO)

Benjamin D. Smith, M.D.,[*†] Douglas W. Arthur, M.D.,[‡] Thomas A. Buchholz, M.D.,[†] Bruce G. Haffty, M.D.,[§] Carol A. Hahn, M.D.,[‖] Patricia H. Hardenbergh, M.D.,[¶] Thomas B. Julian, M.D.,[#] Lawrence B. Marks, M.D.,[**] Dorin A. Todor, Ph.D.,[‡] Frank A. Vicini, M.D.,[††] Timothy J. Whelan, M.D.,[‡‡] Julia White, M.D.,[§§] Jennifer Y. Wo, M.D.,[‖‖] and Jay R. Harris, M.D.[¶¶]

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FACTORS		SUITABLE	CAUTIONARY	UNSUITABLE
PATIENT FACTORS	Age	≥ 60	50 - 59	≤ 50
	BCRA1/2 mutation	Not present		Present
PATHOLOGIC FACTORS	Tumor size	≤ 20mm	21 - 30mm	≥ 30mm
	T stage	T1	T1 - T2	T3 - T4
	Margins	Negative (≥ 2mm)	Close (≤ 2mm)	Positive
	Grade	Any		
	LVSI	No	Limited/Focal	Extensive
	ER status	Positive	Negative	
	Multicentricity	Unicentric only		Present
	Multifocality	Clinically unifocal ≤ 20mm	Clinically unifocal 21 - 30mm	Clinically multifocal or microscopically > 30mm
	Histology	Ductal invasive, mucinous, tubular, colloid	Invasive lobular	
	Pure DCIS	Not allowed	≤ 30mm	> 30mm
	EIC	Not allowed	≤ 30mm	> 30mm
	Associated LCSI	Allowed		
NODAL FACTORS	N stage	pN0 (i-, i+)		pN1, pN2, pN3
	Nodal surgery	SNBx, ALND		None performed
TREATMENT FACT.	Neoadjuvant CT	Not allowed		If used

{Smith et al., 2009, Int J Radiat Oncol Biol Phys, 74, 987-1001}

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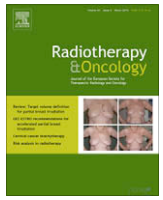

GEC-ESTRO Recommendations

Patient selection for accelerated partial-breast irradiation (APBI) after breast-conserving surgery: Recommendations of the Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) breast cancer working group based on clinical evidence (2009)

Csaba Polgár [a,*], Erik Van Limbergen [b], Richard Pötter [c], György Kovács [d], Alfredo Polo [e], Jaroslaw Lyczek [f], Guido Hildebrandt [g], Peter Niehoff [h], Jose Luis Guinot [i], Ferran Guedea [j], Bengt Johansson [k], Oliver J. Ott [l], Tibor Major [a], Vratislav Strnad [l], On behalf of the GEC-ESTRO breast cancer working group

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FACTORS		LOW RISK	INTERMEDIATE RISK	HIGH RISK
PATIENT FACTORS	Age	≥ 50	40 - 50	≤ 40
PATHOLOGIC FACTORS	Tumor size	≤ 30mm	≤ 30mm	≥ 30mm
	T stage	T1 - T2	T1 - T2 (≤ 30mm)	T2 (> 30mm), T3, T4
	Margins	Negative (≥ 2mm)	Close (≤ 2mm)	Positive
	Grade	Any	Any	
	LVSI	Not allowed	Not allowed	Present
	ER status	Any	Any	
	Multicentricity	Unicentric only	Unicentric only	Multicentric
	Multifocality	Unifocal	Multifocal ≤ 20mm index lesion	Multifocal ≥ 20mm index lesion
	Histology	Ductal invasive, mucinous, tubular, colloid	Invasive lobular	
	Pure DCIS	Not allowed	Allowed	Allowed
	EIC	Not allowed	Not allowed	Allowed
	Associated LCSI	Allowed	Allowed	
NODAL FACTORS	N stage	pN0	pN1mi, pN1a (ALND)	pNx, ≥pN2a (≥4poitive nodes)
	Nodal surgery	SNBx, ALND		None performed
TREATMENT FACT.	Neoadjuvant CT	Not allowed	Not allowed	If used

{Polgar et al., 2010, Radiother Oncol, 94, 264-73}

CONCLUSIONS

PARTIAL BREAST IRRADIATION
Sources of error

- Patient indication: proper patient selection is critical to the successful application of PBI. Patients who may harbor disease a significant distance from the edge of the resection cavity or potentially have multicentric disease should not be treated with PBI (Vicini 2003)

- Treatment technique: basic underlying principle of PBI is to providing and documenting the delivery of a tumoricidal dose of RT to the CTV, considered as the tumor bed plus a 1-2 cm margin

Making no mistakes is what establishes the certainty of victory, for it means conquering an enemy that is already defeated.

Sun Tzu. The Art of War