Brachytherapy for Breast Cancer

SK Shrivastava, A. Budrukkar, R. Sarin, R. Jalali,
A. Munshi, KA Dinshaw, DD Deshpande
Department of Radiation Oncology & Medical Physics,
Tata Memorial Hospital, Mumbai

Brachytherapy for Breast Cancer

- Boost brachytherapy
- Radical brachytherapy
- Chest wall brachytherapy-recurrences
- Surface mould

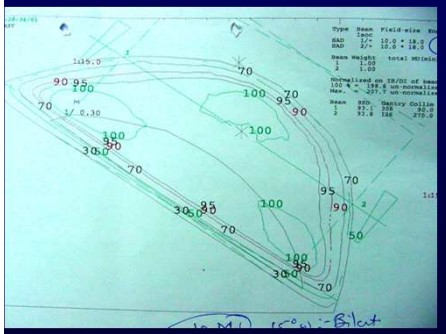
Breast conserving therapy: Standard treatment for early breast cancer

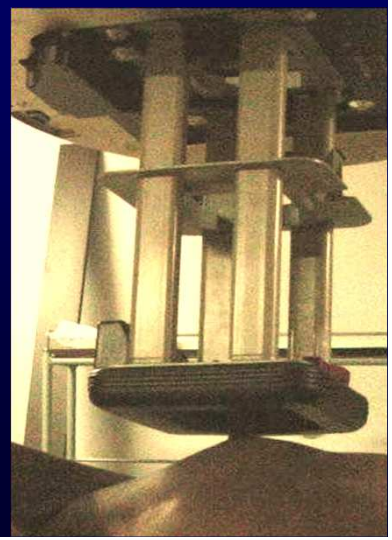
Randomized trials comparing MRM vs BCT:
Comparable outcome

Better cosmetic outcome

Improved psychosocial impact

Critical Role of Radiation Therapy





Tumor Bed Boost

- Current practice
- Rationale for boost
- To boost or not to boost.
- Dose and fractionations.
- Techniques of boost delivery.
- Comparison of above techniques.
- Delineation of boost volume.
- TMH Experience
- Identification of High Risk groups

Rationale for boost..

Pathological basis ..

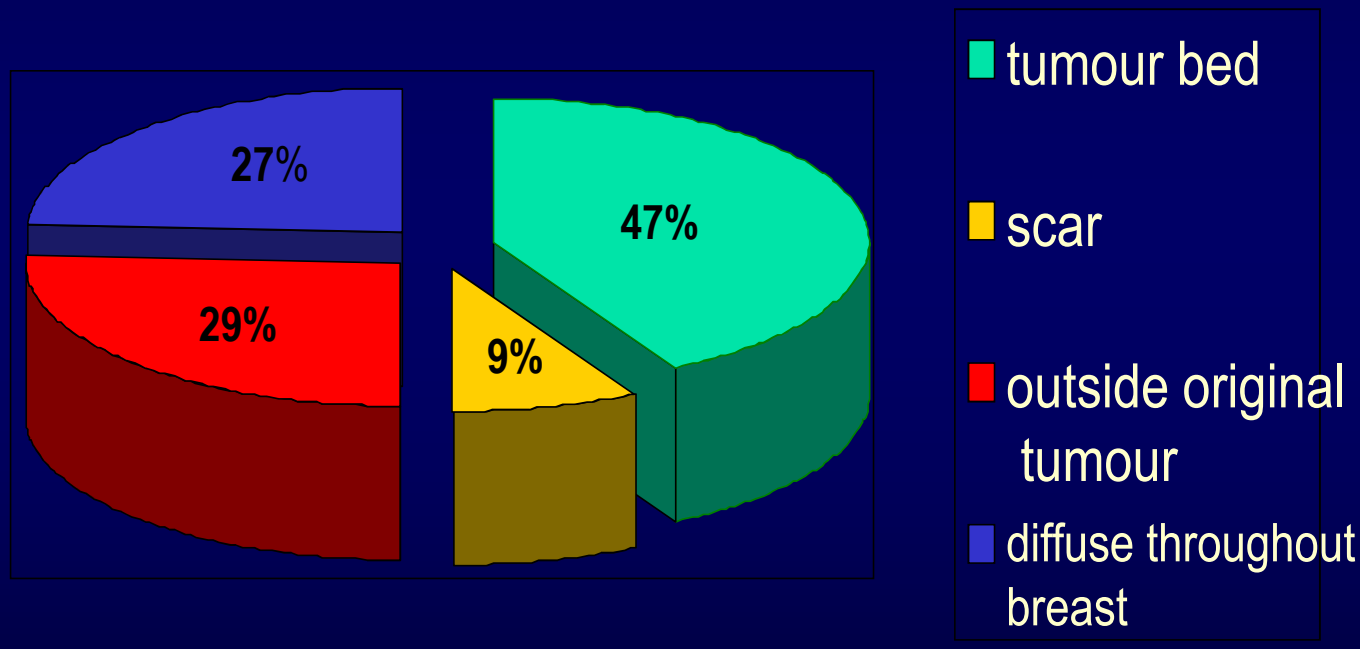
- N =441 pts (333 analysed) of Stage I & II Ca breast
- Aim – to define CTV for PBI
- All the pts underwent re-excision after lumpectomy.

- Results-
  - 35.2% had no residual
  - 20.1% had dis. 0-5 mm from tumour edge
  - 24.9% extended from 5-10 mm
  - 10.2% from 10-15 mm
  - 9% extended > 15 mm
- Conclusion: In ~ 90% of pts margin of 10 mm is adequate.

Frank A. Vicini IJROBP. 60(3) :2004

Clinical basis…

- Recurrence pattern in EORTC trial ...



Harry Bartelink, N Engl J Med ;346(5):388, 2002

Boost Vs No Boost

Boost Vs No Boost

- Recommendations for post-lumpectomy radiotherapy prescription varied.
- This ranged from 50 Gy/25fr to whole breast without a boost to 45 Gy/25fr followed by a 16 Gy tumor bed boost.
- No level 1/ 2 evidence for standardisation of dose schedules.

CMAJ. 1998 Feb 10;158 Suppl 3:S35-42

No boost..

- Compared two short fractionation schedules for post-lumpectomy whole breast irradiation.
- RT schedules:
  - Arm A -Experimental arm (N = 622) -42.5 Gy/ 16 fr
  - Arm B -Standard arm (N = 612) -50 Gy/ 25 fr
- No difference in disease free or overall survival.

	Arm A	Arm B
Local recurrence free survival (5 yr)	97.2 %	96.8 %
Cosmesis (excellent / good)	76.8 %	77.4 %

Whelan T, J Natl Cancer Inst. 2002 Aug 7;94(15):1143-50.

Boost Vs No Boost
RCT in Lyon, France (1986-92)

- Boost arm
- N = 521
- 50 Gy/ 25 fr. Followed by 10Gy/4fr
- LR (5 yr)- 3.6%
- Telangiectasia (Gr 1&2) - 12.4%

- No Boost
- N = 503
- 50 Gy/ 25 fr.
- LR (5 yr)- 4.5% (P= 0.044)
- 5.9 %

ROMESTAING ET AL , J Clin Oncol 15:963-968.1997

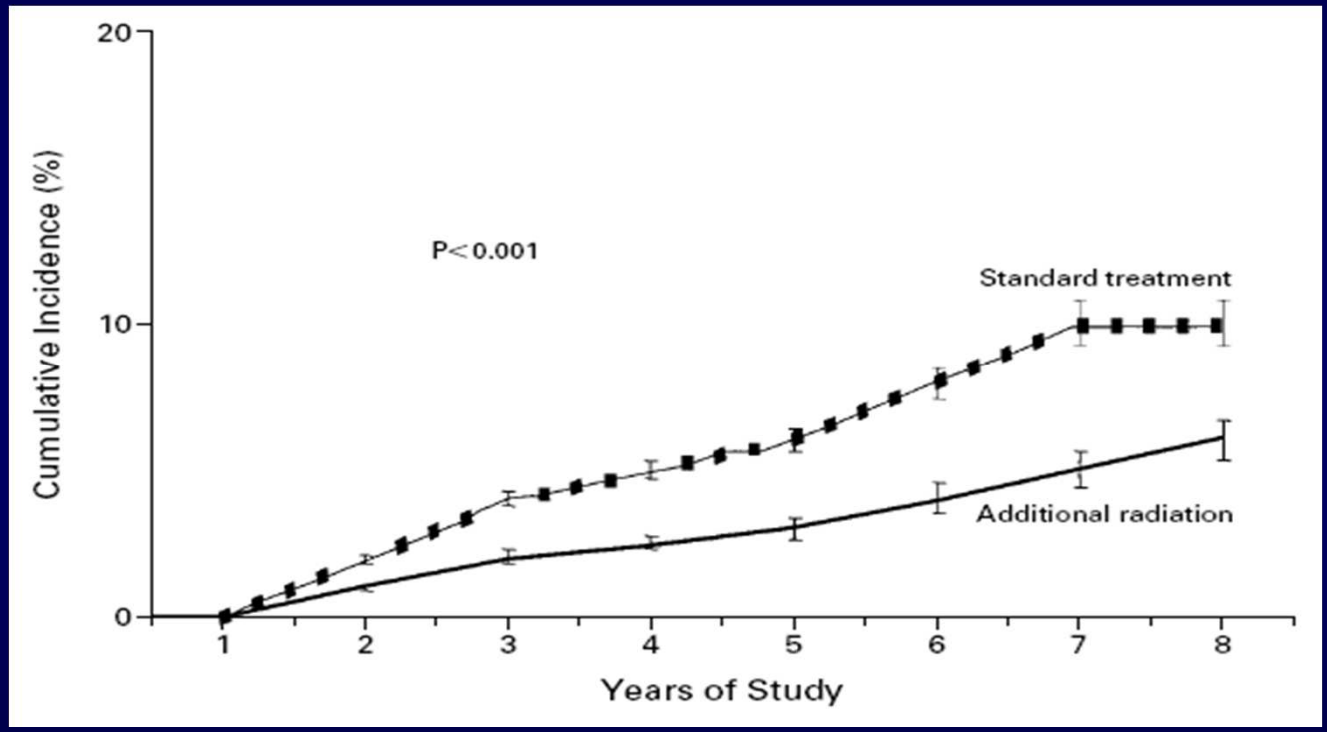
Boost Vs No boost ..EORTC Trial

- Assessed the effect of boost to tumour bed on LR in post-lumpectomy pts (T1-2, N0-1, M0).
- Median f/u – 5.1 yrs
- WBRT to a dose of 50 Gy/25 fr, was followed by a boost of 16 Gy/8 fr. (e- beam)

	WBRT	WBRT + boost
N	2657	2661
LR (5 yrs)	7.3 %	4.3 %
Cosmesis (3yrs- excellent - good)	86 %	71 %

Harry Bartelink, N Engl J Med 2002;346(5):388

Boost Vs No boost ..EORTC Trial



Cumulative incidence of local recurrence

Harry Bartelink, N Engl J Med 2002;346(5):388

Boost Vs No Boost ..

	WBRT	WBRT + Boost	
		HDR BT	Electrons
N	103	52	52
EBRT	50 Gy/ 25 fr	50 Gy/ 25 fr	50 Gy/ 25 fr
Boost (median)	Nil	14.25 Gy/ 3 fr	16 Gy/ 8 fr
Follow up	5.3 yrs	5.3 yrs	5.3 yrs

Polgar C : *Strahlenther Onkol. 2002 Nov;178(11)*

Boost Vs No boost..

	WBRT	WBRT + Boost
Local rec.	15.5 %	6.7 %
LTC	84.9 %	92.7 %
RFS	66.2 %	76.6 %
S/E (Gr. 2-3)	7.8 %	17.3 %
Cosmesis (excellent /good)	91.3 %	85.6 % P - NS

Polgar C *: Strahlenther Onkol. 2002 Nov;178(11)*

RT boost .. Dose & Fractionation

RT boost .. Dose & Fractionation

Trial	N (pts)	EBRT (dose/fr)	Boost (dose/fr)	LR (%)	Med. f/u (yr)
Bartelink et al.	2657 2661	46-50Gy/25 fr 50 Gy/25 fr	- 16 Gy/8 fr	7.3 4.3	5.1
Romestaing et al.	503 521	47-50 Gy/20 fr 50 Gy/20 fr	- 10 Gy/ 4 fr	4.5 3.6	3.3
Teissier et al.	327 337	48-50 Gy/25 fr 50 Gy/25 fr	- 10 Gy/ 5 fr	6.8 4.3	6.1
Polgar et al.	103 104	49-50 Gy/25 fr 50 Gy/25 fr	- 12-16Gy/ 3-8 fr	15.5 6.7	5.3

RT boost .. Dose & Fractionation

Author	TBD (Gy)	LR (%)	p value
Clarke (Int J Radiat Oncol Biol Phys 11:137-145, 1985).	< 60	6.6 (5 yr)	0.003
	> 60	2.3 (5 yr)	
Recht (Int J Radiat Oncol Biol Phys 11:1271-1276, 1985.)	< 60	7 (5 yr)	0.06
	60-70	4 (5 yr)	
	>70	1 (5 yr)	
Van limbergen (Radiother Oncol 8:1-9, 1987.)	40-49	28	0.01
	50-59	15	
	60-69	10	
	70-79	6	
	80-89	2.5	

Margin directed boost..

- N =509; Stage I & II Ca breast.
- Post-lumpectomy, re-excision when margin< 2 mm.
- WBRT -50Gy, followed by e- boost.
- Median f/u – 121 mths.
- No boost when no residual on re-excision (LR-6%).

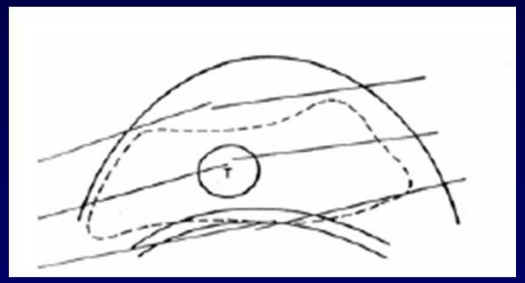
Final margin status	+ve	0-2 mm	2-5 mm	> 5 mm
Boost dose	20 Gy	20 Gy	14 Gy	10 Gy
LR (12 yrs)	17%	9%	5%	0

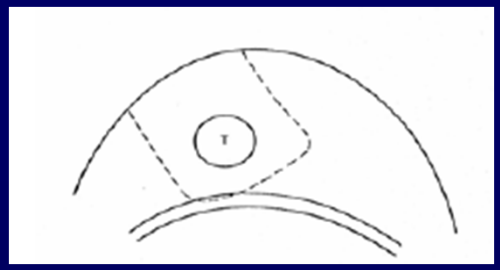
***Neuschatz** et al.* **Cancer** 2003;97:30–9.

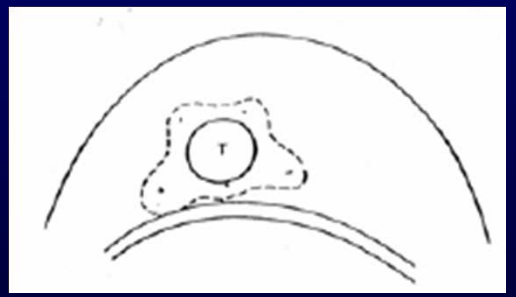
Boost delivery..

Tumor Bed Boost: Techniques

- Photons
- Electrons
- Interstitial Brachytherapy
  - Intraoperative
  - Postoperative
- Mammosite
- Intraoperative Electrons







Comparison of Boost Techniques

Comparison of Boost Techniques.. EORTC Trial

- Assessed the role of RT boost.
- N= 2661; randomized in WBRT & WBRT+ boost
- Median f/u – 5 yrs
- WBRT- 50 Gy was delivered.
- Type of boost on investigator's choice.
- Boost delineation was done clinically (scar & or surgical clips).

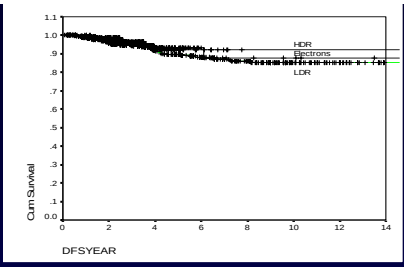
P. Poortmans et al. / Radiotherapy and Oncology 72 (2004) 25–33

Comparison of Boost Techniques.. EORTC Trial..

Boost tech.	Electrons	Photons	Interstitial	Unknown
N	1653	753	225	48
Dose (Gy)	16	16	15	16
T.V.(cm^3)	144	288	60	-
Gap bet WBI &boost (d)	1	1	18	-
Total Tt time	48 days	48 days	54 days	-
LR (%)	4.7	4	2.5	2
Fibrosis (mod –severe)	22.4%	26.3%	27.1%	8.3%

P. Poortmans et al. / Radiotherapy and Oncology 72 (2004) 25–33

Tumor bed boost : TMH data



	LDR	HDR	Electrons	P value
Cosmesis: Good to excellent	301 (79%)	121 (79%)	294 (64%)	LDR vs Electrons: p=0.000003 HDR vs Electrons: p=0.0005
Worsening of the cosmesis	35 (9%)	19 (12%)	45 (10%)	NS
Moderate to late sequelae	49 (13%)	39 (25%)	45 (10%)	LDR vs HDR: p=0.0003, LDR vs Electrons: p=NS HDR vs Electrons: p=0.0000009
5 yr local control	90%	92%	93%	

Budrukkar et al. Clincal Oncology 2008

Delineation of lumpectomy cavity..

Delineation of lumpectomy cavity.. Techniques..

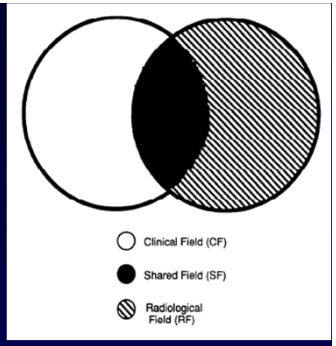
- Clinical (based on surgical scar)
- Surgical clips
- Ultrasound guided
- CT guided
- MRI

Surgical Scar

- Surgical scar at the centre of the tumor
- Simple and non invasive
- No additional costs

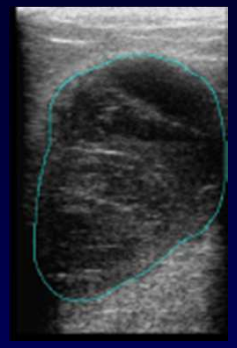
- Highly subjective
- Geographical miss
- Poor cosmetic outcome-Normal tissue irradiation

Surgical Clips



- Radio-opaque clips- 4 corners and centre
- Feasible –surgical cooperation
- Inexpensive
- Detection by fluoroscopy or CT

- Migration of clips
- Change in position over 3-4 months

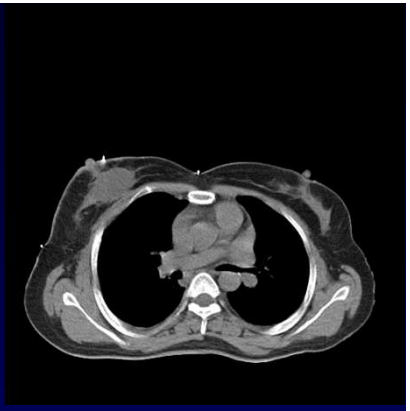


Ultrasonographic Localization

- Intra-operative as well as postoperative
- Images compatible-RT planning systems
- Noninvasive
- Highly reproducible
- Less expensive

- Poor delineation 6-8 weeks postoperatively
- Underestimation of Tumor bed

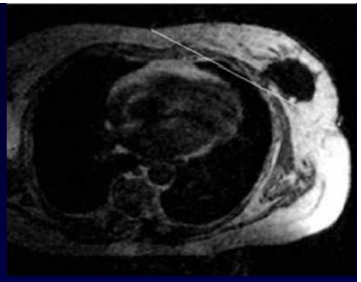
CT Based delineation



- Accurate localization
- Planning in treatment position
- Excellent definition of breast tissue

- Difficult to distinguish glandular breast tissues from surrounding anatomy.
- Surgical clips necessary for delineation.
- Varies with window settings.

MRI



- Accurate delineation of target
- Accurate delineation of critical organs

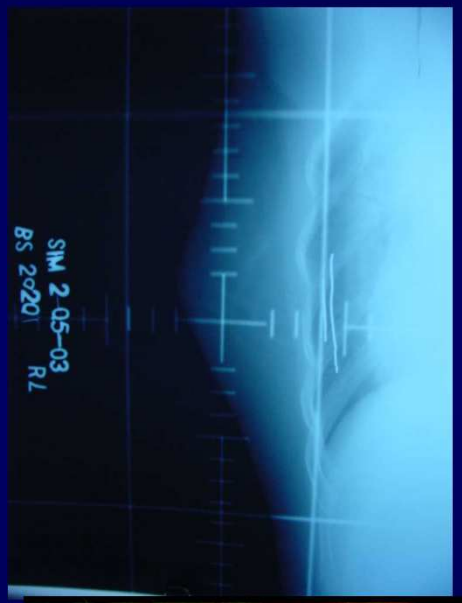
- Expensive
- Difficulty in scanning in treatment position
- Image distortion during co registration of images for RT planning

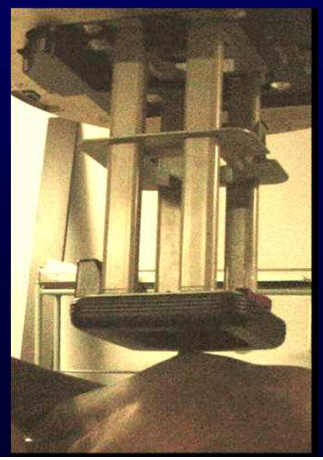
TMH Experience ..

Tata Memorial Hospital

Breast Conserving Therapy: 1980-2000

1022 patients



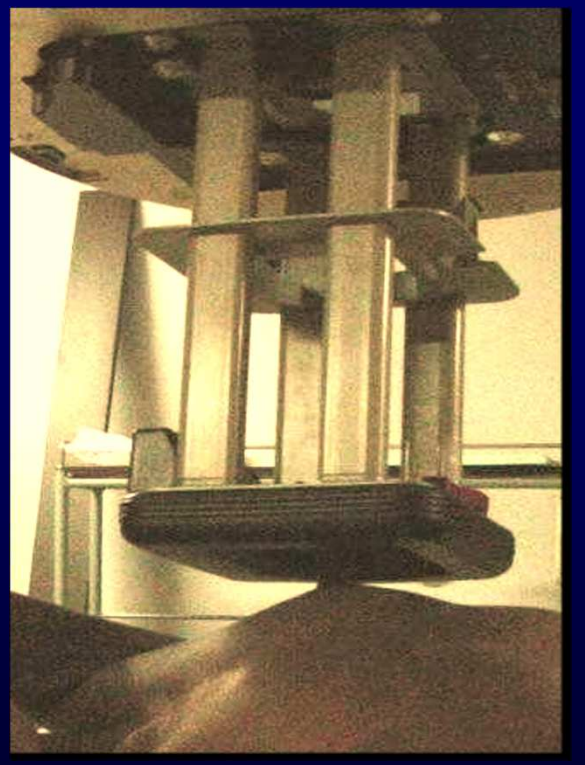


Tumor Bed Boost

Interstitial Brachytherapy (implant):

Low Dose Rate(LDR) ^{192}Ir : 15-20Gy

High Dose Rate (HDR) ^{192}Ir: 10 Gy/1 #



Electron:

Appropriate energy (9 to 16 MeV) according to tumour bed depth (clinical data, mammo, CT) to a dose of 15 Gy/6 #

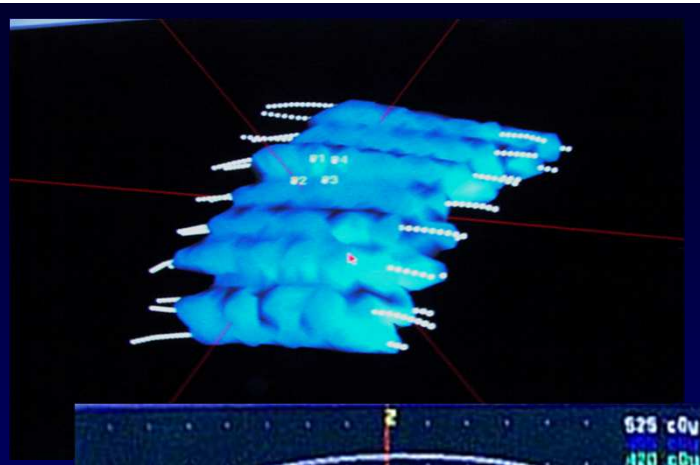
Tumor Bed Boost

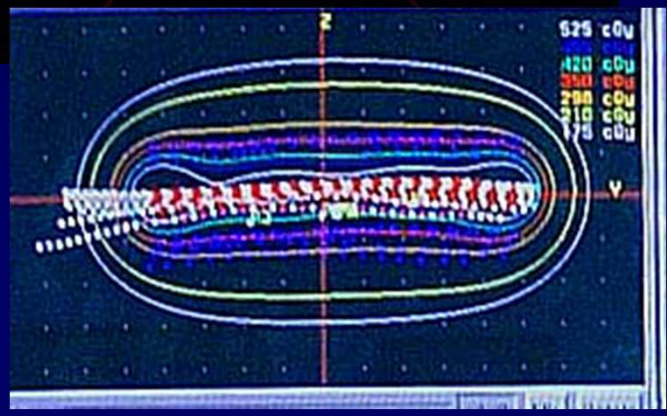
LDR Ir-192 : n = 383 (1980-1996)

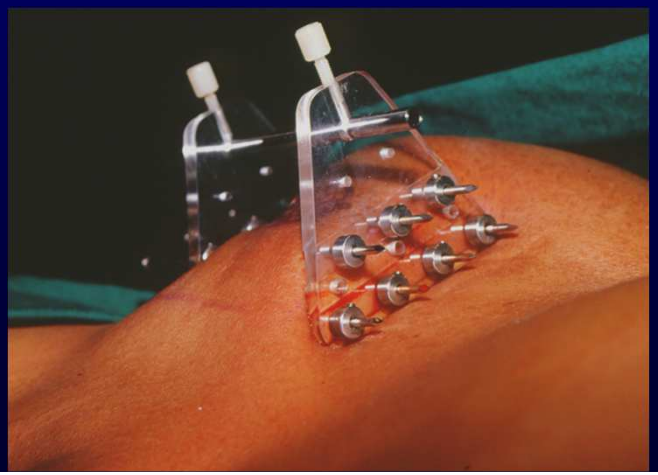
HDR Ir-192 : n = 153 (1996-2000)

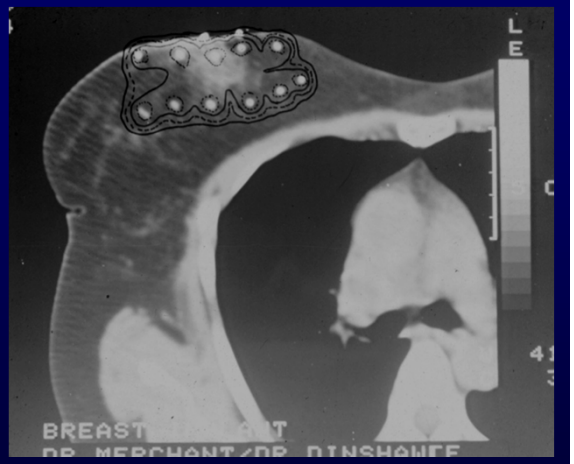
Electron : n = 460 (1996-2000)

No boost : n = 26







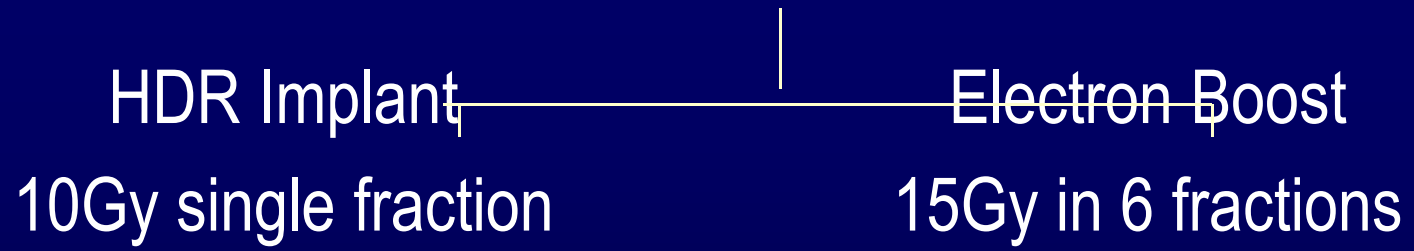


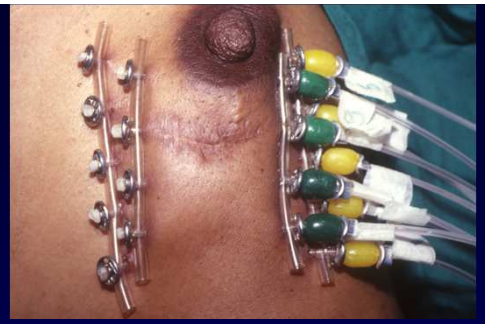
TMH Randomised trial

Stage I and II Breast Cancer

Treated with BCT

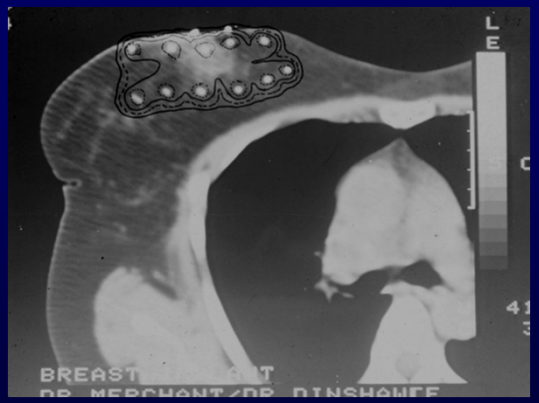
External RT: 45Gy in 25 fractions





LDR Brachytherapy

First BCT patient: 1980



HDR Brachytherapy

Identification of High Risk patients

…

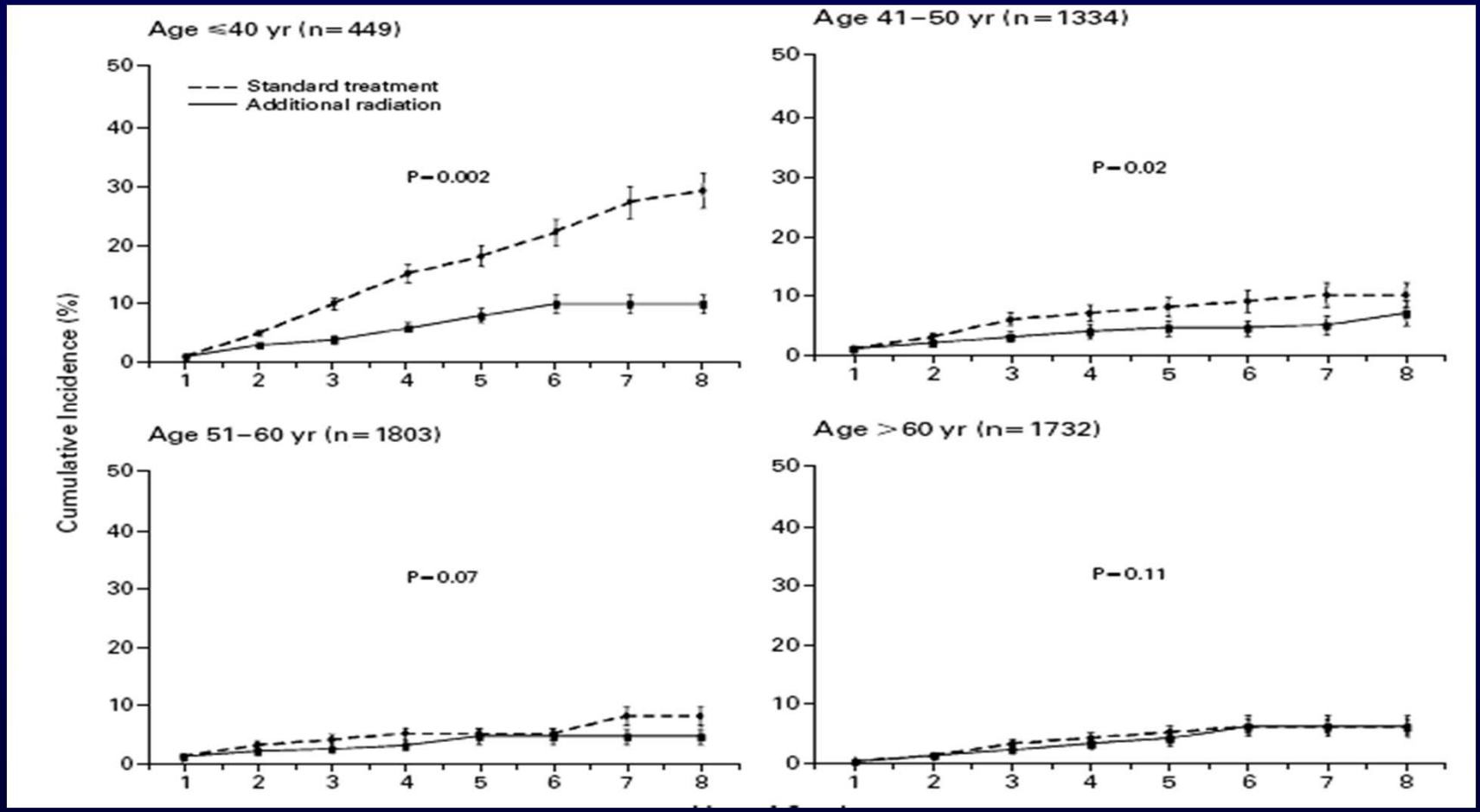
Risk factors for Local Recurrence …

- Age was the only risk factor
- Max. benefit in reduction of LR was seen in young pts.
- Young pts were more radio-responsive.

LR (% at 5 yrs)	WBRT	WBRT+ boost
<40 yrs	19.5	10.2
41-50 yrs	9.5	5.8
51-60 yrs	3.4	5.2
>60 yrs	2.5	4

Harry Bartelink, , N Engl J Med 2002;346(5):388

Risk factors for Local Recurrence …



Harry Bartelink, N Engl J Med 2002;346(5):388

Risk factors for Local Recurrence ..

- Age –
  - Young age pts had higher local failure rates.
  - They had greater reduction in LR %age.
- Positive margin status –Major risk factor for LR
  - No. of positive margins.
  - Width of clear surgical margin.
- EIC – EIC + ve pts had higher residual tumour outside reference tumour.
- Tumour size, LVI, and histological grades - controversial
- Mitotic activity index is investigational.

POLGÁR et al PATHOLOGY ONCOLOGY RESEARCH Vol 7, No 4, 2001

Controversy	Suggested Guidelines	Level of Evidence
To boost or not to boost	To give boost to patients with higher risk of relapse.	I
Boost dose	15-20 Gy	I
Positive margins	Boost dose escalation.	III
Boost fractionation	Electrons: 2–2.5 Gy per fraction HDR Implant : 3-4 Gy per fraction	No definite evidence
Concomitant Boost		II
Technique of Boost delivery	Electrons or HDR Implant	I
Boost delineation	Electrons - CT with surgical clips HDR Implant – Ultrasound	III
Margins to tumour bed	Electrons - 2-3 cm HDR Implant – 1 cm	III
Ideal candidates for boost	Age< 40yrs, EIC, LVI, Axillary nodes positive, Receptor negative	III

Jalali R et al. Acta Oncol 2008

Accelerated Partial Breast Irradiation

Breast Conserving Therapy

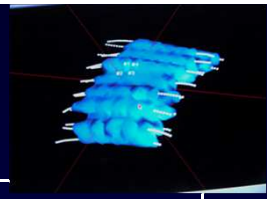
Disadvantages

- Prolonged treatment for 5 weeks followed by boost poses problems for
  - Working women
  - Elderly frail women
  - Patients who live at long distances
- Megavoltage Radiation not easily available at many places and is expensive
- Women with large breasts may have unacceptable toxicity with EBRT
- Around 10-14% of women undergoing BCT do not receive radiotherapy

Concept of Partial breast irradiation

- 70-90% recurrences after whole breast RT in the tumour bed and pattern for site of recurrence same whether RT given or not
- Small percentage of all BCT patients recur outside tumour bed
- Comparable to contralateral breast cancer recurrences
- Most of these outside recurrences are in fact New Breast Cancers
- Hence irradiation of tumor bed with margins
- Smaller volume of Radiation : Higher dose per fraction possible
- Acceleration of treatment over 1 week
- Accelerated Partial Breast Irradiation : APBI

Selection Criteria for APBI



Criteria	American Brachytherapy Society recommendation	TMH
Age	45 years or more	40 years
Tumour size	Up to 3cm	Up to 3 cm
Node	Negative	Negative
Histology	Infiltrating duct carcinoma (IDC)	IDC
Margins	Microscopically negative	Microscopically negative
EIC	-	Negative

APBI studies in optimally selected patients

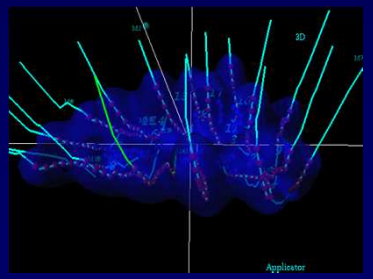
Institution	Number of patients	Median Follow up (yrs)	Breast rec. (anywhere)	Outside the tumor bed
Oshner Clinic	160	7	2.5%	1.2%
NIO Budapest	45	6.7	4.4 %	4.4 %
William Beaumont	199	5.4	1.2 %	0.6 %
Virginia Commonwealth	59	4.2	5.1 %	2.6 %
Orebro	49	4.6	4 %	2 %
RTOG 9517	99	3.7	3 %	NA

R Sarin, Nature Oncology 2005

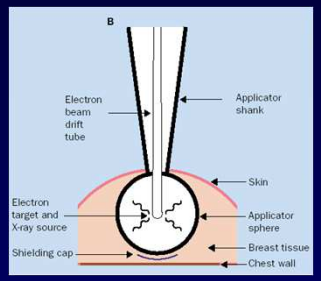
APBI in suboptimally selected patients

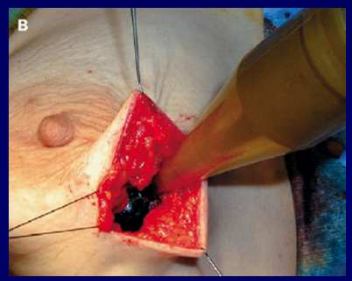
Institution APBI technique	No of patients (Median FU yrs)	Criticism	Breast Recurrence
Christie Hospital RCT External Electrons 40Gy/8#/10days	353 (8)	Lobular ca -15%Margin NK or+ve 19% Inadequate coverage	25%
Guys Hospital LDR 55 Gy over 5 days	27 (6)	Positive margins 55%, EIC+VE 40%	37%
Uzsoki Hospital Budapest LDR 50Gy in 10-22 hrs	70 (12)	Cut margin NK, single plane, unacceptable dose rate	24%
London Regional Cancer Centre Ontario	39 (7.5)	Av. Implant vol:30cc	16%
Tufts New England	33 (5)	55% EIC	6%
University of Kansas	25 (4)	Inadequate LDR dose	0%

Methods of APBI



Brachytherapy





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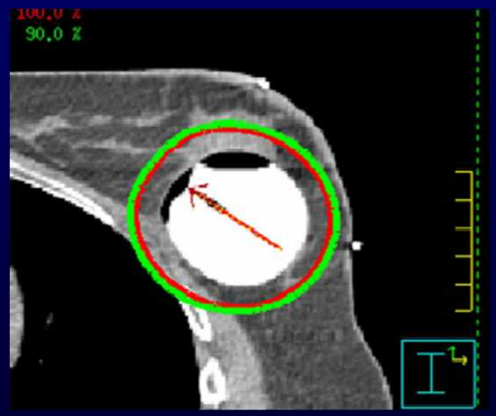
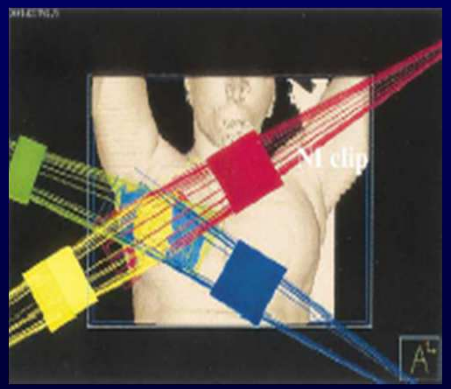
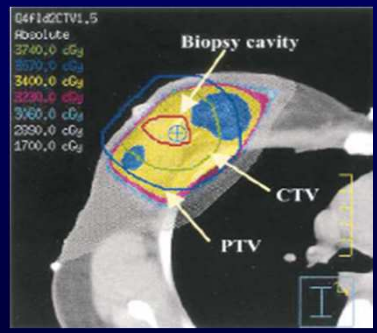


Mammosite



3DCRT



IMRT

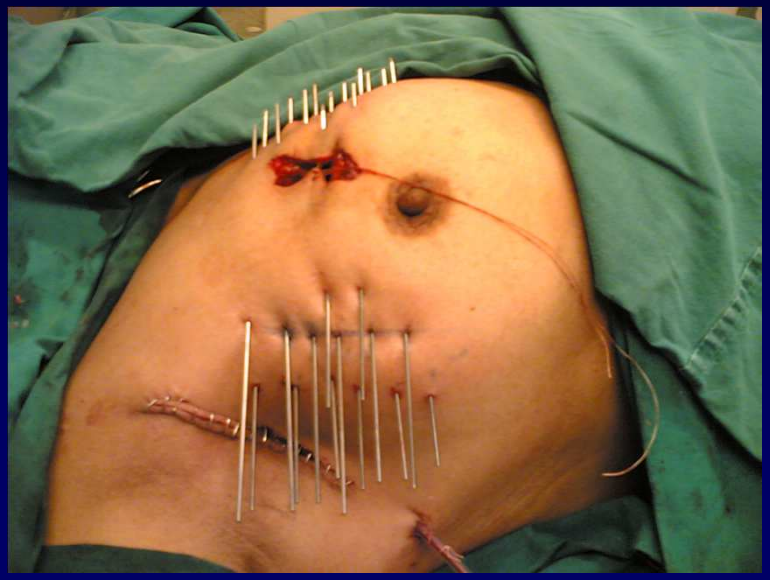
Ongoing Randomized trials

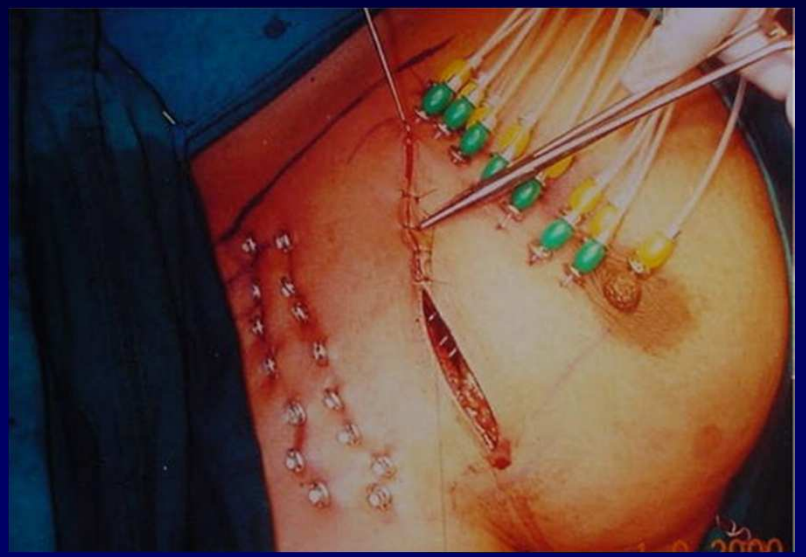
Trial	Technique in APBI arm	Target accrual
National Institute of Oncology, Budapest, Hungary	HDR interstitial implant or electrons	257 patients: published results; comparable outcome
ELIOT, Milan	Intraoperative electrons	824 patients Completed accrual
TARGIT, Multicentric trial	Intraoperative 50 KV Xray	1700 Patients Ongoing
European Multicentre trial	interstitial implant	Target accrual-1170 patients Ongoing
NSABP, USA	Interstitial or MammoSite or 3D CRT	Target accrual-3000 patients Accrual closed for postmenopausal women

Procedure

- Intra-operative Brachytherapy
- Post operative brachytherapy
  - USG guided
  - CT scan guided
  - Fluoroscopy guided
    - ❖Template Guided
    - ❖Free Hand

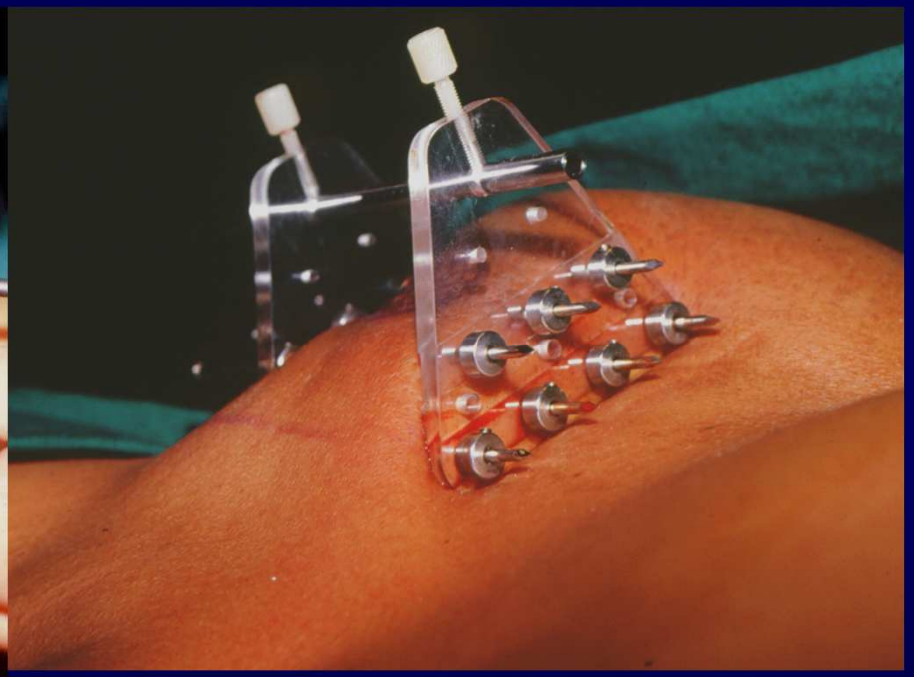
APBI: Intraoperative Procedure



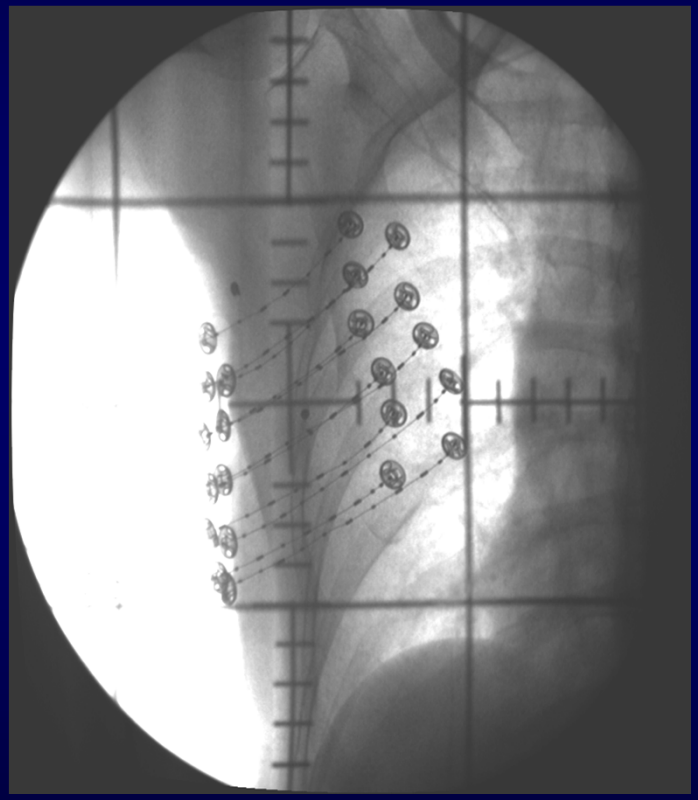


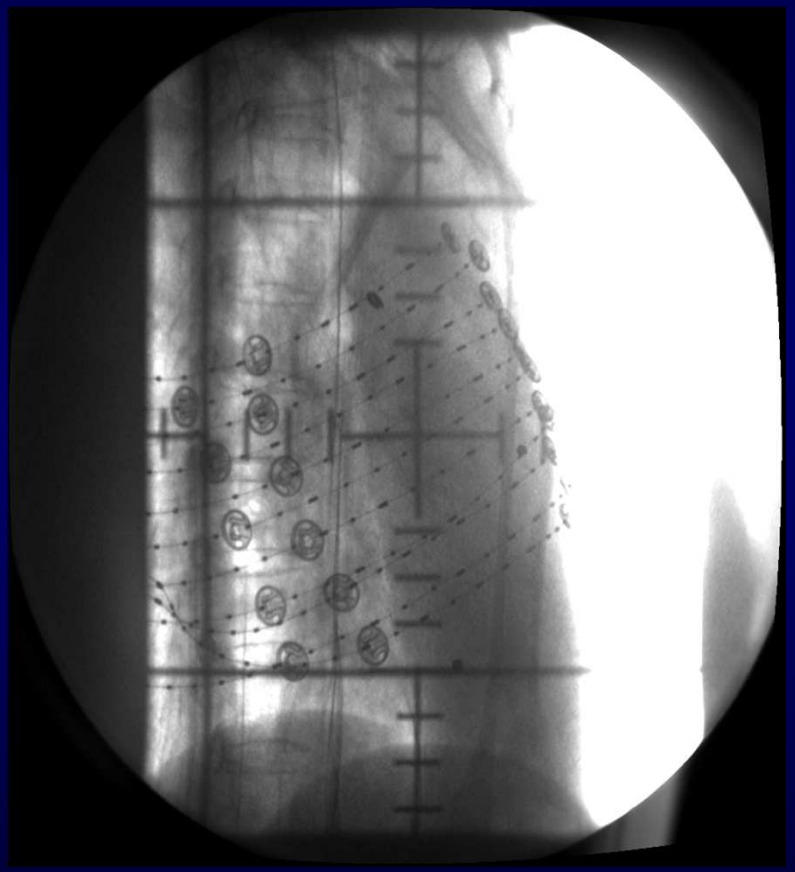
APBI: Post-operative Procedure

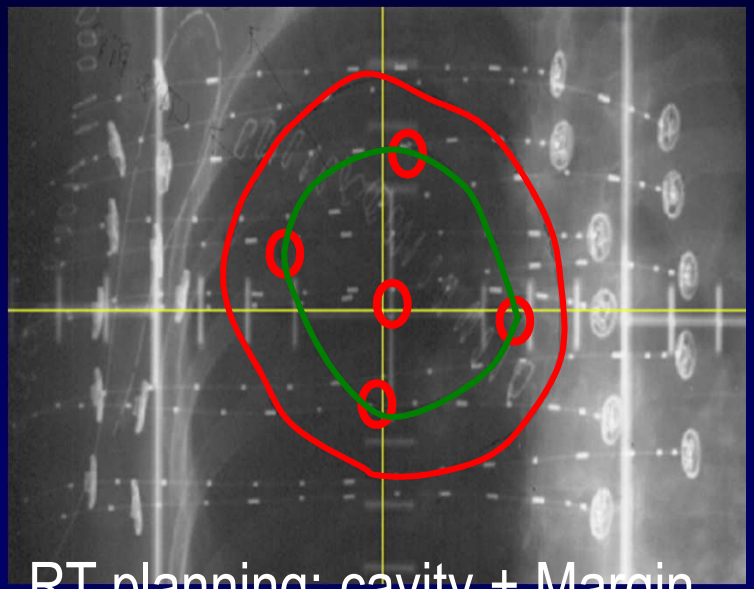
APBI: Intraoperative Template guided procedure



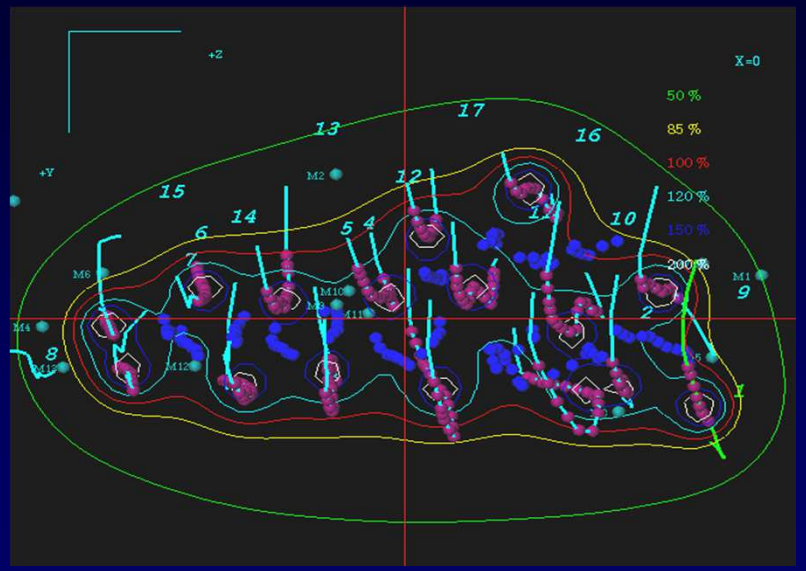
Brachytherapy Planning
Orthogonal X rays (2D brachytherapy)



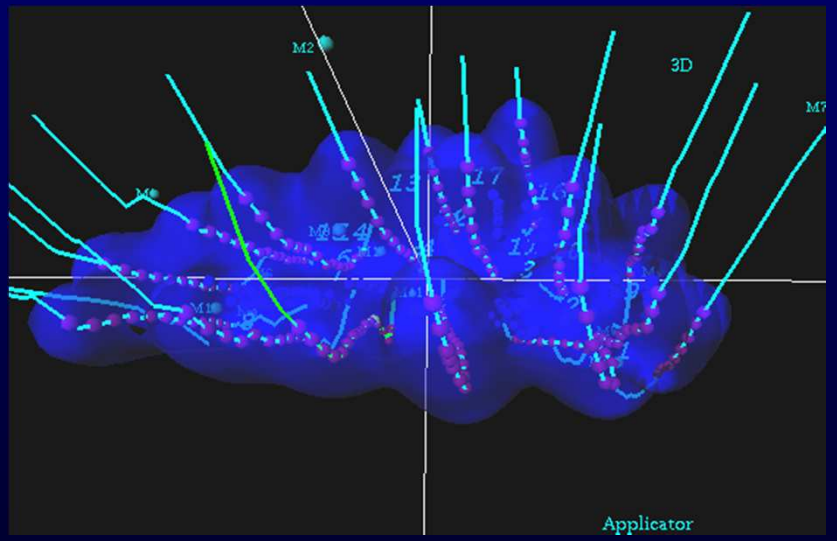




RT planning: cavity + Margin



Dose distribution



Dose distribution

Dose prescription and Treatment delivery

- Dose: 34Gy in 10 fraction two fractions per day, 6 hrs apart
- Dose per fraction: 340cGy

Intraoperative Brachytherapy

W/E+ Axillary dissection

↓

Confirmation of basic histopathological features on Frozen section

↓

If suitable: Intraoperative placement of catheters in 2-4 planes

↓

Radiotherapy planning X rays and CT scans on day 2/3

↓

Treatment starts: day 3/4

↓

Confirmation of final HPR before 5th fraction

↙ ↘

Favorable: continue brachy

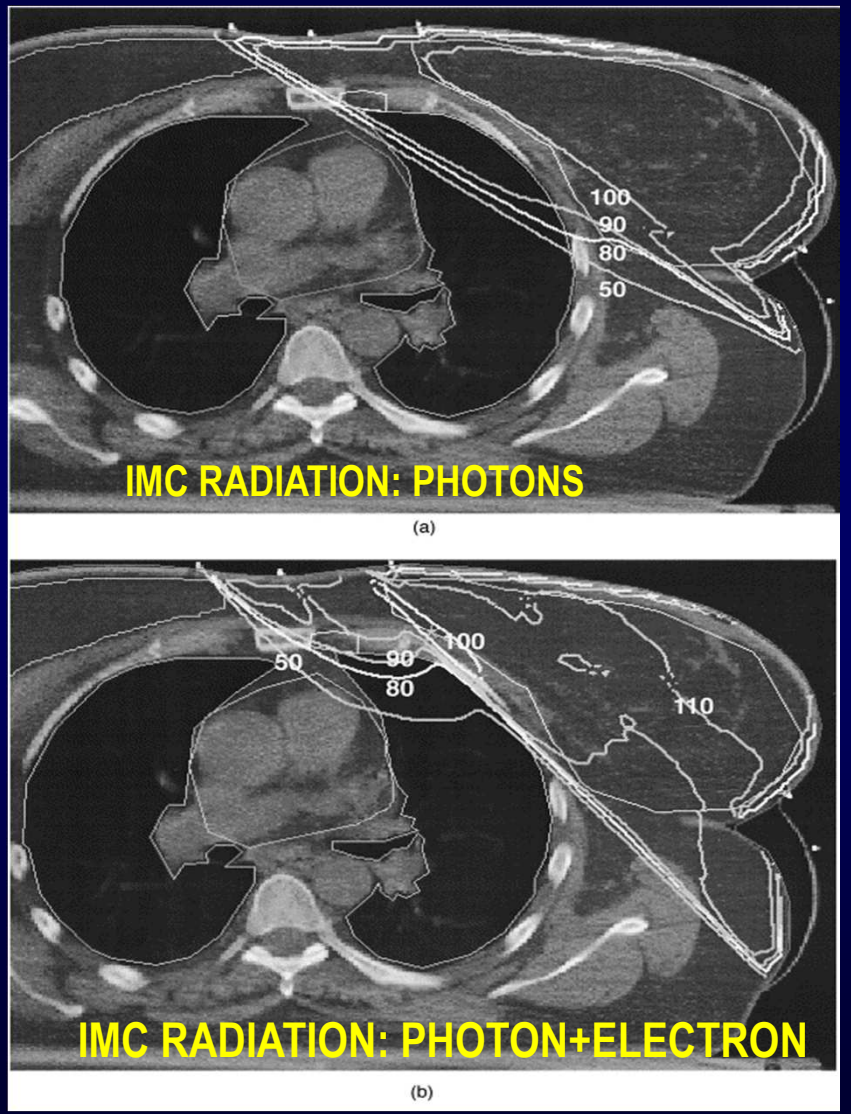
Unfavorable: convert to boost

Ext RT to be followed

Immediate Post Treatment Pictures

Treatment of Regional Nodes
Internal Mammary Chain (IMC) Irradiation

- Involves external RT with mixed photon electron combination
- EORTC has conducted a randomized trial : IMC RT vs No IMC RT (results awaited)
- Disadvantages of external beam
  - Complex planning for photon /electron combinations
  - Use of Linear accelerators
  - Increased risk to heart and lungs due to photons



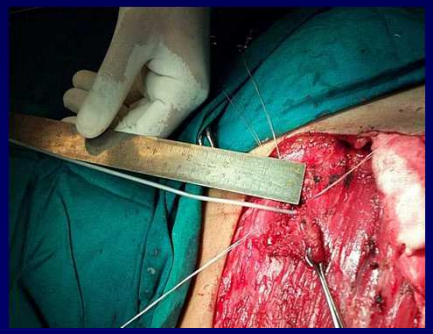
IMC Brachytherapy: A Novel Approach

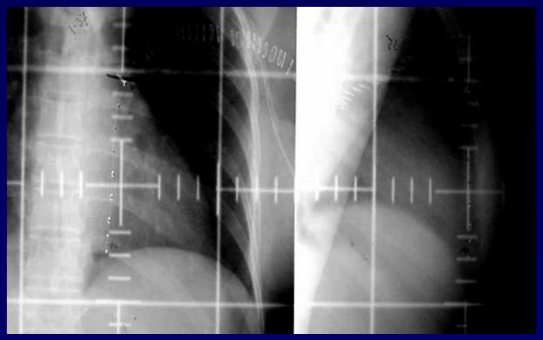
Potential advantages:

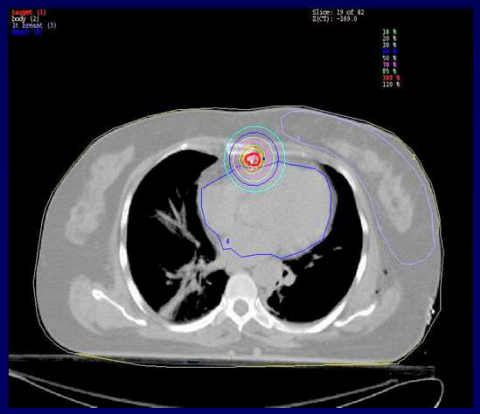
- Rapid fall off of the dose to the cardiac and other structures
- IMC nodes lie around the vessels, which are anyway dispensable
- Brachytherapy machine relatively more common and available (in developing countries)

Internal Mammary Chain Brachytherapy

Tumours more than 3 cms in central / inner quadrants with or without axillary nodes







High Dose Rate Ir-192 brachytherapy

34Gy in 10 fraction (BD) over 5 days starting on 3rd -5th post op day.

Dose prescribed at 1cm off axis.

Sarin R. IJROBP 2003 (abst) ;57:363

TATA MEMORIAL EXPERIENCE
IRIDIUM-192 HDR BRACHYTHERAPY FOR IMC IN BREAST CANCER

Initiated in June 2001

>350 patients (June 2001- Dec06)

- Procedure failed in 3 initial patients (Learning curve)
- Vessel not identified (1), lumen too small to pass catheter (1), Catheter displaced (1)

Immediate complications

7 patients : minimal, asymptomatic, self limiting pleural collection

1 patient : mild self-limiting pneumothorax.

Small Learning Curve: All complications observed in the initial 10 patients

RECURRENCES :

1- Chest wall + Neck+ distant (Died); 2- Distant (alive)

SURFACE MOULD BRACHYTHERAPY FOR CHEST WALL

Brachytherapy for recurrent lesions: Surface mould