Accelerated Partial Breast Irradiation With Brachytherapy: Evolving Techniques

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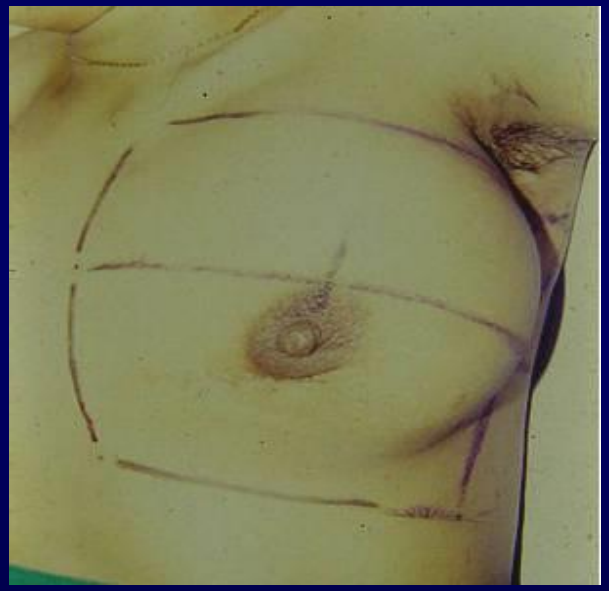
Partial breast irradiation: Attractive alternative

Accelerated RT: shorter treatment duration

APBI: Accelerated Partial Breast Irradiation



5-6 Weeks of RT

Whole breast

1 week of RT

Tumor bed with adequate margin

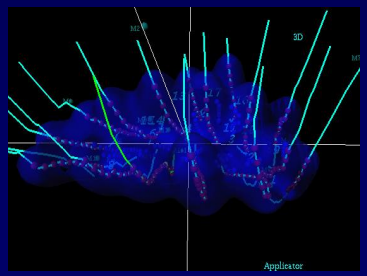
BCT: Patient perspective

- Do not opt for BCT due to inability to stay away from home for 6-8 weeks
- Small percentage of women do not take RT after BCT (14-20%)
- Dependents on other family members
- Some of the patients are earning members to support their families
- Cannot stay away from home

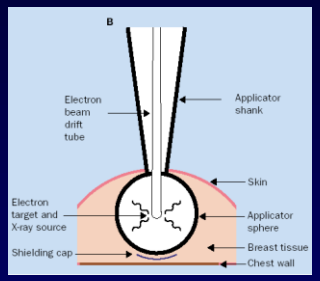
Clinico-pathological basis

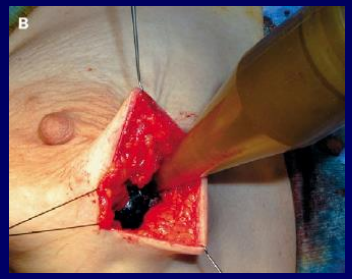
- (70-90%) recurrences after whole breast RT in the tumour bed
- Pattern for site of recurrence same whether RT given or not (NSABP B06 trial)
- Very small percentage of the BCT patients recur outside tumour bed after whole breast RT
- Most of these outside recurrences are in fact New Breast Cancers
- Pathologically: multicentric foci seen away from the tumor bed
- But not all of them turn into cancers
- ? Need to treat whole breast in selected patient population

Methods of APBI



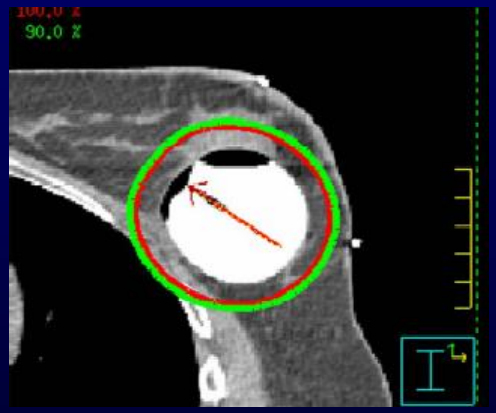
Interstitial brachytherapy



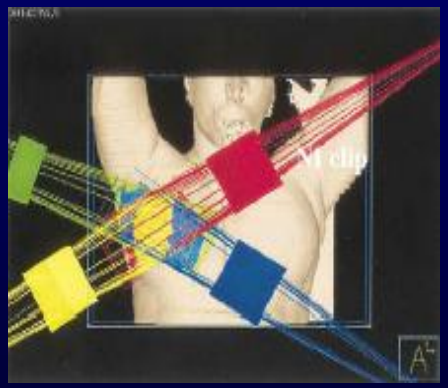


TARGIT

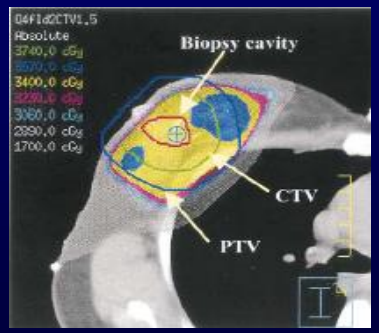
ELIOT



Mammosite

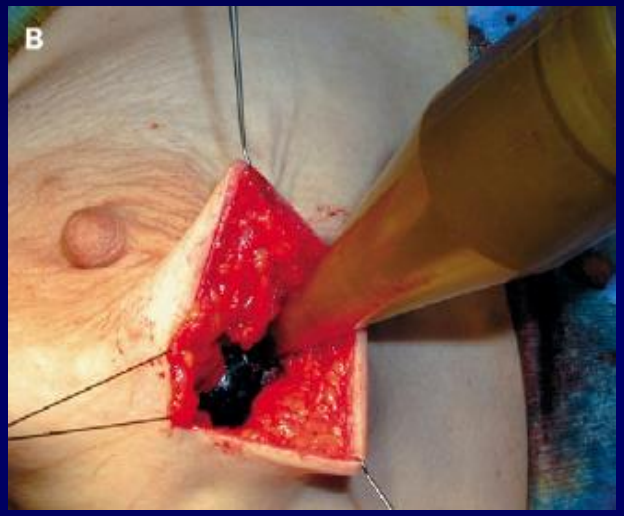


3DCRT



IMRT

Methods of APBI: Intraoperative X rays



TARGIT

Targeted intraoperative therapy

Source: 50KV Xray source

Technique: Intraoperative radiation after wide excision

Dose: 20Gy in 1 fraction at 1mm

Effective dose at 1cm: 5-7Gy

Advantage:

- simple technique
- sparing of normal tissues

Problems:

- Issues of penetration
- Adequacy of cavity wall dose ?

Methods of APBI: Intra-operative Electrons

Machine: Mobile linear accelerator

Electron energy: 3-10MeV

Technique: Wide excision

Placement of shield to protect chest wall

Reconstruction of the tumor bed

Dose: 21Gy at 90% isodose

Advantages: single fraction

Problems: Issues of cavity wall coverage

Set up and expenses

Violation of surgical planes

Methods of APBI: Interstitial Brachytherapy

Brachytherapy

- Oldest method
- Large and encouraging data
- Good target volume coverage with sparing of normal tissues
- Brachytherapy Machines more common
- Requires technical expertise

Methods of APBI: Mammosite

Mammosite

Balloon with single catheter

Dose: 34Gy/10 fraction BID

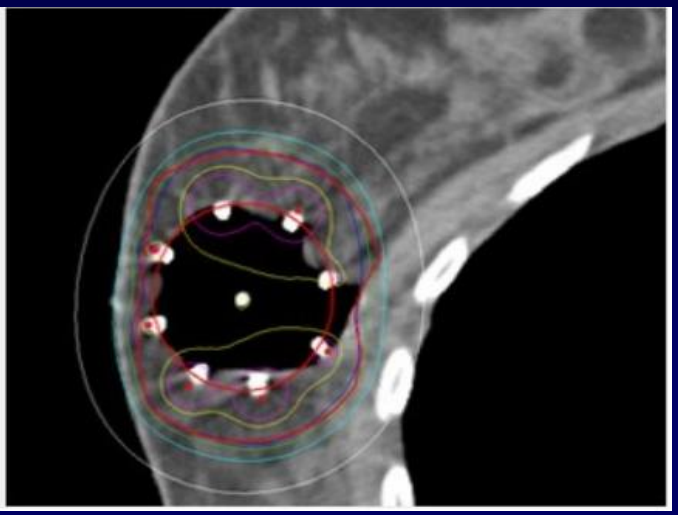
Advantage:

- Ease of application

Problems:

- High skin dose and telengectesia
- Rib fractures
- Problem in non-uniform cavities

Mutli-channel Catheters



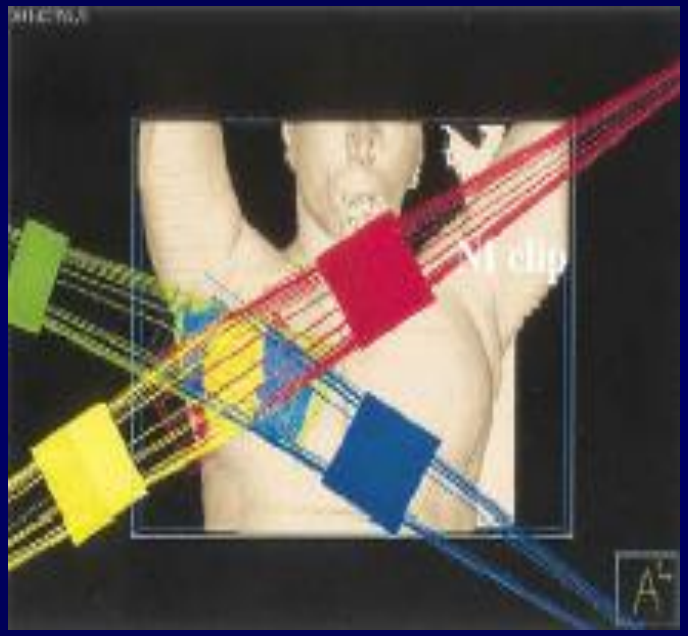
Mutlichannel Balloon based brachytherapy

Single balloon: to be inflated

Coverage better than Mammosite

Issues related to cavity coverage in irregularly shaped cavities

Methods of APBI: External Beam Radiation



Machine: Linear Accelerator

Technique: External Beam RT

3DCRT,IMRT,Tomotherapy

Advantages:

Good coverage of target

Good dose homogeneity

Problems:

Issues of movement with breathing

More margin

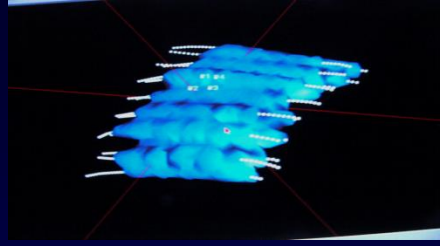
Higher intergral dose-lungs, heart

Comparison between the techniques

	Interstitial Brachytherapy	3DCRT/IMRT	Introperative electrons (ELIOT)	Intraoperative Xrays TARGIT	Mammosite
Coverage of target volume	Variable	Best	Good	Good	Good
Thickness of target treated	1-2cm	2-2.5cm	1-2.5cm	Dose prescribed at 1mm. At 10mm:5-7Gy	1cm
Sparing of normal breast	good	least	good	best	good
Skin dose	Least	High	Least	Least (can shield)	Variable
Technical limitations	Axilla	Almost Nil	Axilla, brachial plexus, skin	Large cavities, irregular cavities	Large cavities, irregular cavities, close to skin, periphery
Drawbacks	Adequacy of target coverage Wider applicability	High dose to normal tissues, motion	Histopathology Wider applicability	Very limited depth of irradiation, cavity shape, size, no hitopathology	Cavity shape and size Skin dose

Sarin R. Nature P Oncology 2005;2 (1): 40-47, Offerson BV. Radiother Oncol 2009;90(1):1-13

Selection Criteria for APBI



Criteria	American Brachytherapy Society recommendation	American Society of Breast Surgeons recommendation
Age	45 years or more	50 years or more
Tumour size	≤3cm	≤2cm
Node	Negative	Negative
Histology	Infiltrating duct carcinoma (IDC)	IDC or DCIS
Margins	Microscopically negative	Microscopically negative (>2mm)

Importance of patient selection
APBI studies in optimally selected patients

Study	N	Median FU (yrs)	Local Rec %
Polgar (2009) NIO, Budapest	45	12	8.9
Johansson (2009) Orebro Medical Centre	51	7.2	5.9
King T (2000) Ochsner Clinic,New Orleans	51	6.25	2
Arthur DW (2008) RTOG 95-17	99	7	6.1
Mark (2009) J Arrington Cancer Centre	192	5.4	4.2
Antonucci (2009) William Beaumont Hospital, Detroit	199	9.6	5

Strnad V. IJROBP 2010, Sarin R Nature Oncol 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%

Sarin R, Nature Oncology 2005

ASTRO Recommendations

Factor	Suitable	Cautionary	Unsuitable
Age	≥ 60 years	50-59 years	< 50 years
BRCA 1/2 mutation	Not present		Present
Tumor size	≤ 2 cms	2.1 -3 cms	> 3 cms
T stage	T1	T0-T2	T3-4
Margins	Negative(by 2 mm)	Close (<2mm)	Positive
LVSI	No	Limited	Extensive
ER status	Positive	Negative	
Multicentricity	Unicentric only		Present
Multifocality	Unifocal	Size 2-3 cms	>3 cm
Histology	IDC and favorable	ILC	
Pure DCIS	Not allowed	≤ 3cms	> 3cms
EIC	Not allowed	≤ 3cms	> 3cms
N stage	pN0 i-,i+		pN1,pN2,pN3
Neoadjuvant therapy	Not allowed		If used

Smith et al, IJROBP 2009

ESTRO Recommendations

Factor	Low risk	Intermediate risk	High risk
Age	> 50 years	40-50 years	≤ 40 years
Tumor size	≤ 3 cms	≤ 3 cms	> 3 cms
Margins	Negative(by 2 mm)	Close (<2mm)	Positive
LVSI	Not allowed	Not allowed	Present
ER status	Any	Any	
Multicentricity	Unicentric only	Unicentric	Multicentric
Multifocality	Unifocal	Within 2 cm	> 2cm
Histology	IDC and favorable	IDC and favorable	
ILC	Not allowed	Allowed	
Associated LCIS	Allowed	Allowed	> 3cms
DCIS	Not allowed	Allowed	
EIC	Not allowed	Not allowed	Present
N stage	pN0	pN1 mi,pN1A	pNx, >pN2a
Neoadjuvant therapy	Not allowed	Not allowed	If used

Polgar et al, Radiother oncol, 2010

Updated ASTRO Recommendation

Factor	Suitable	Cautionary	Unsuitable
Age	**≥ 50 years**	**40-49 years if all other criteria of suitable 50 or more if 1 criteria not matching**	**< 40 years**
BRCA 1/2 mutation	Not present		Present
Tumor size	≤ 2 cms	2.1 -3 cms	> 3 cms
T stage	**Tis** or T1	T0-T2	T3-4
Margins	Negative(by 2 mm)	Close (<2mm)	Positive
LVSI	No	Limited	Extensive
ER status	Positive	Negative	
Multicentricity	Unicentric only		Present
Multifocality	Unifocal	**Microscopic allowed**	>3 cm
Histology	IDC and favorable	ILC	
Pure DCIS	**Allowed**	≤ 3cms	> 3cms
EIC	Not allowed	≤ 3cms	> 3cms
N stage	pN0 i-,i+		pN1,pN2,pN3
Neoadjuvant therapy	Not allowed		If used

Correa C. Practical Rad Onco 2017

TARGIT trial

Patients suitable for BCT

Age > 45 years, T size upto 3 cm, unifocal tumors

BCT+ TARGIT

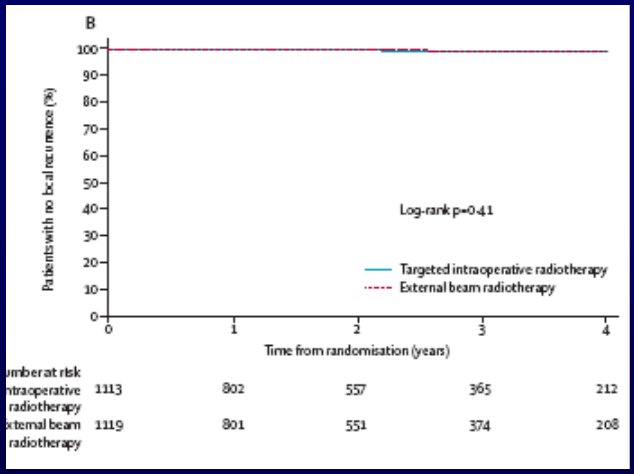
BCT+ External RT

N= 2232

Local recurrence rate at 4 years

TARGIT group: 1.2%

External RT group: 0.95%

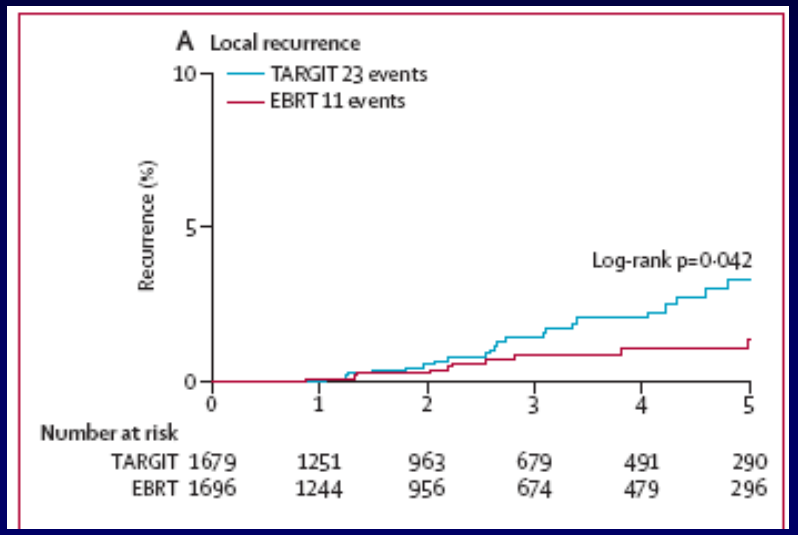


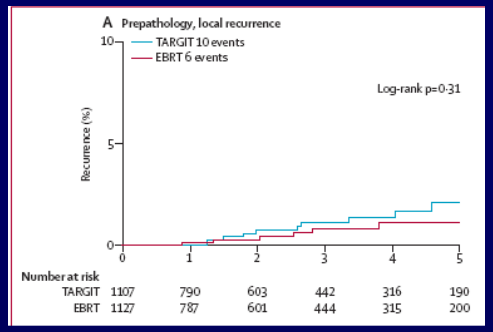
Vaidya JS et al. Lancet 2010;376: 91-102

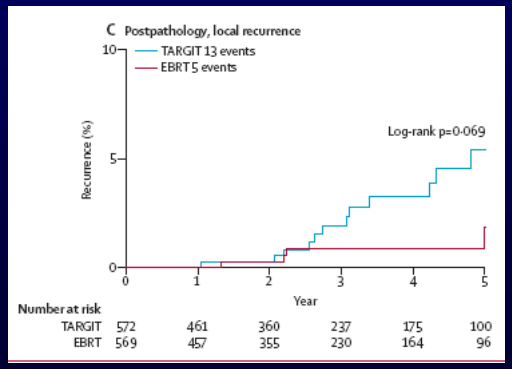
TARGIT: 5 year Outcome

Local Recurrence in TARGIT arm: 3.3%

Local recurrence in EBRT arm: 1.1%







TARGIT inferior to EBRT for Local Control

Vaidya JS. Lancet 2014;383:603-613

ELIOT (Intraoperative Electrons): Outcome

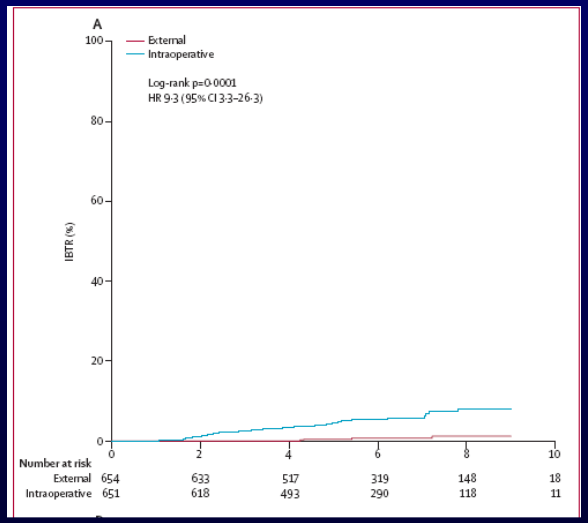
November 2000-December 2007
N=1306
T<2.5CM,Age >48 years

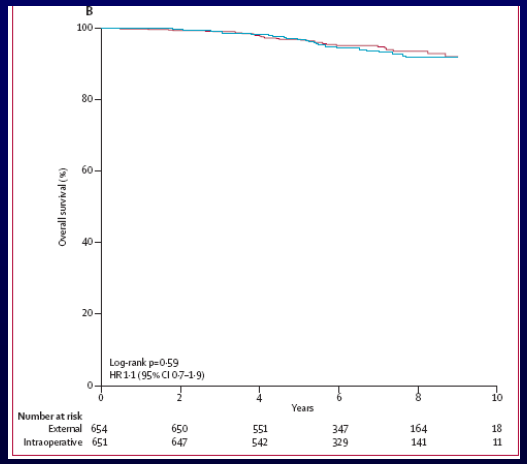
BCT+ Whole Breast RT

(60Gy) N=651

BCT+ ELIOT

(21Gy) N=655

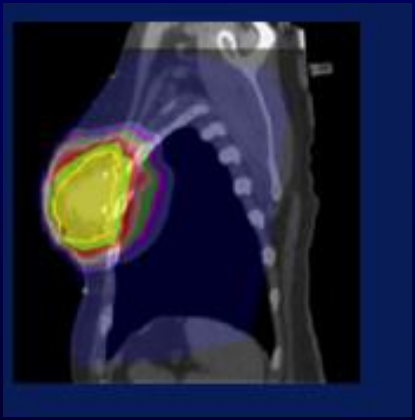




Veronesi U et al. Lancet 2013;14:1269-77

3DCRT Technique: Outcome

- Prospective IRB approved study of Beamlet IMRT with deep aspiratory breath hold method.
- Dose: 38.5Gy in 10 fractions, 3.85Gy with bid regimen.
- 32 patients were enrolled
- With a median follow up of 2.5 years, 7 patients developed unacceptable cosmetic outcome.
- V50 and V100 volumes correlated with cosmetic outcome



Jagsi R. IJROBP2010;76(1):71-78

Mammosite: 5 year outcome (phase II data)

- 1440 women
- Median FU: 53.7 months
- Median age: 65.5
- Median T size 1cm
- Node negative: 83.2%
- ER positive: 62%
- Grade I and II: 76.1%
- 5 year LR control rates: 96.2%
- Symptomatic seroma rates: 13%
- Excellent cosmetic outcome at 5 years: 90.6%
- ER negativity only strong factor affecting LR rates (p=0.0022)

Vicini FA. IJROBP 2010

Phase III data
Hungarian Randomized trial: 5 and 10 year results

1998-2004 (N=258)

$T_1N_{0\text{-}1mi}$ breast cancer, low risk

Non lobular cancers, Clear margins, No EIC

	Whole Breast RT(N=130) 50Gy/25#	Partial Breast Irradiation (N=128) Interstitial brachytherapy (N=88) Electrons (50Gy/25#) (N=40)
5 yr LR	**3.4 %**	**4.7 %**
5 yr OAS	91.8 %	94.6 %
Cosmesis	62.9%	77.6 %
10 yr LR	**5.1%**	**5.9%**
10 yr OAS	82.1%	79.7%

Median FU: 66 months and 10.2 yrs respectively

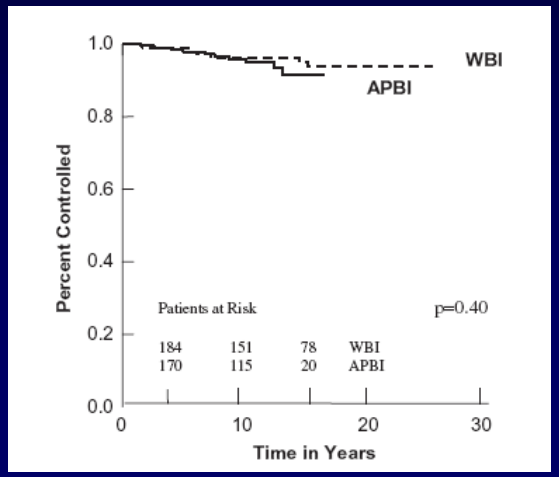
Polgar C et al. Radiother Oncol 2013

Polgar C etal. IJROBP 2007; 69(3):694-702

Phase II Data
12 year outcome of APBI: Match pair analysis

199 patients with interstitial brachytherapy

Matched with 199 women with whole breast RT



	WBI (n = 199)	Interstitial APBI (n = 199)	p-value
Age at diagnosis, mean (years)	63.5	65.1	0.11
Tumor size (mm)	12.3	11.7	0.31
ER+	85%	86%	0.85
PR+	67.5%	69.4%	0.73
Margins			0.05*
Negative	99.5%	97.5%	
Positive	0.5%	0%	
Close	0%	2.5%	
T-Stage			0.10
T1	86.9%	92.0%	
T2	12.6%	8.0%	
T3	0.5%	0%	
Lymph node status			<0.001*
Node negative	88.4%	88.4%	
Node positive	2.0%	11.6%	
Unknown	9.5%	0%	
Adjuvant hormonal therapy	57.3%	39.7%	<0.001*
Adjuvant chemotherapy	3.5%	12.6%	<0.001*
Follow up (years)	14.0	10.4	<0.001*

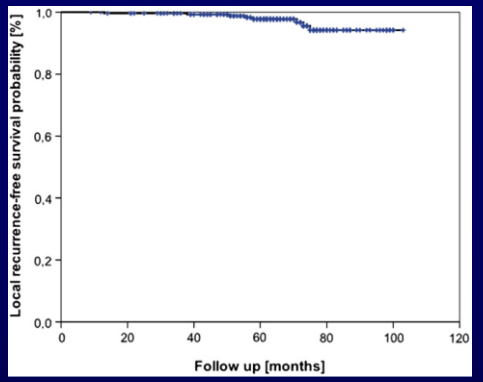
12 yr actuarial	WBI (%)	Interstitial APBI (%)	P value
LR	3.8	5	0.40
RR	0	1.1	0.15
DFS	87	91	0.30
DM	10.1	4.5	0.05
OS	78	71	0.06

William Beaumont Hospital. Dr. Vicini

Shah C et al. Radiother Oncol , 2011;100:210-214

German Austrian multicentric phase II trial

- Eligibility: Age > 35 years, T size <3cm, no lymph nodes, margins >2mm, hormone receptor +ve, histological grade I and II.
- N=274
- Median follow up 63 months
- Median Age: 60.5 years
- Median T size : 12 mm
- Chemotherapy: 6.9%
- 5 year local control rates: 98%
- 5 year DFS and OAS: 96.5% and 97% respectively



Strnad V, IJROBP 2010

GEC-ESTRO Randomized trial of APBI

Stage 0,I and II
Low risk and invasive breast carcinoma
Treated with breast conserving therapy

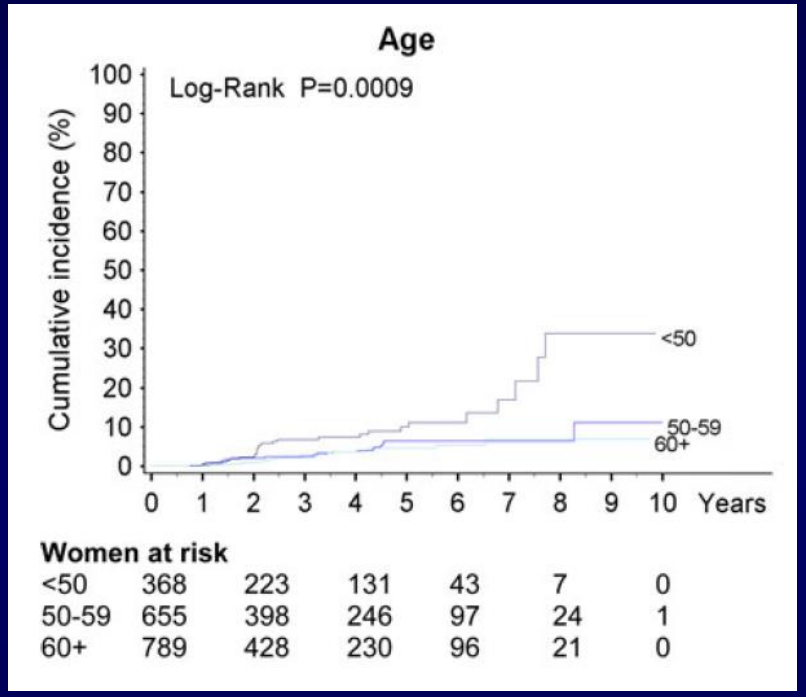
Whole Breast RT + Tumor bed boost
50Gy +10Gy

Interstitial Multicatheter Brachytherapy
HDR:32Gy/8#
PDR: 50Gy in pulses of0.6-0.8Gy/hr given hourly

	WBRT	APBI	P value
5 year Local Recurrence	0.97%	1.38%	0.53
5 year disease free survival	94.45%	95.03%	0.79
5 year overall survival	95.5%	97.25%	0.11

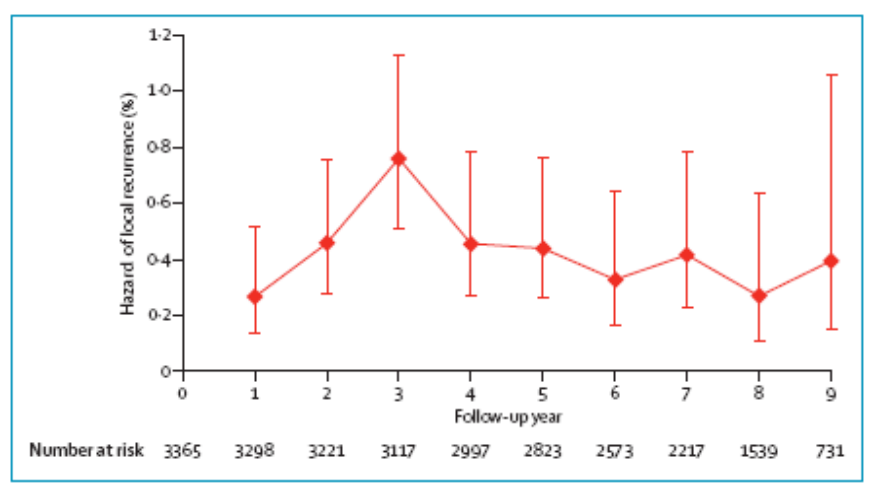
Strnad V. Lancet Oncology 2016

Importance of Long Term Follow up



Intraoperative electrons:
Outside trial

Veronesi et al. Breast Can Research Treat. 2010



START trial data

Haviland JS. Lancet 2010, 376

Interstitial Brachytherapy

- Intra-operative Brachytherapy
- Post operative brachytherapy
  - USG guided
  - CT scan guided
  - Fluoroscopy guided

Template guided

Free Hand

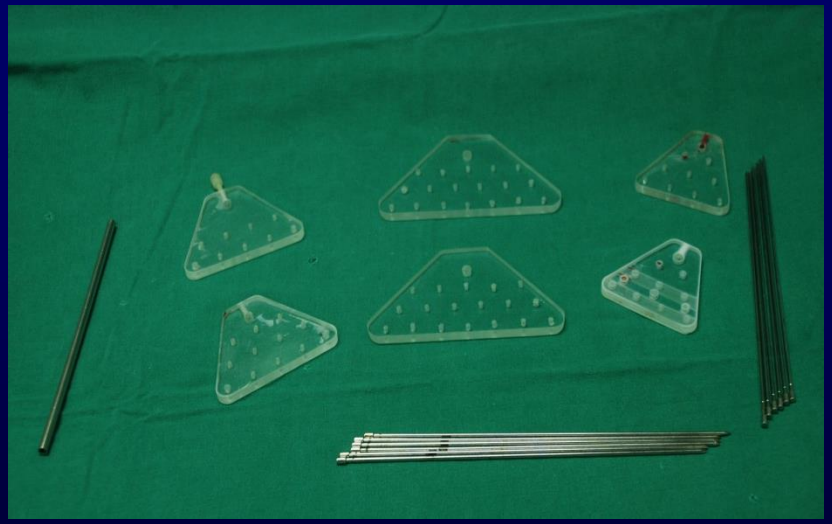
Intra-operative Brachytherapy

- Clinical examination, Mammography, CT scan
- Brachytherapy done at the time of lumpectomy
- Pre-surgical assessment important
- Close collaboration with surgeon, pathologist, medical physicist

Lumpectomy cavity after wide excision and axillary clearance

Placement of radio-opaque markers at four corners and centre of the cavity

Procedure: Instruments



- Radio-opaque clips
- Marking Ink
- Scale
- Needles
- Plastic tubes
- Beads
- Buttons
- Templates

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

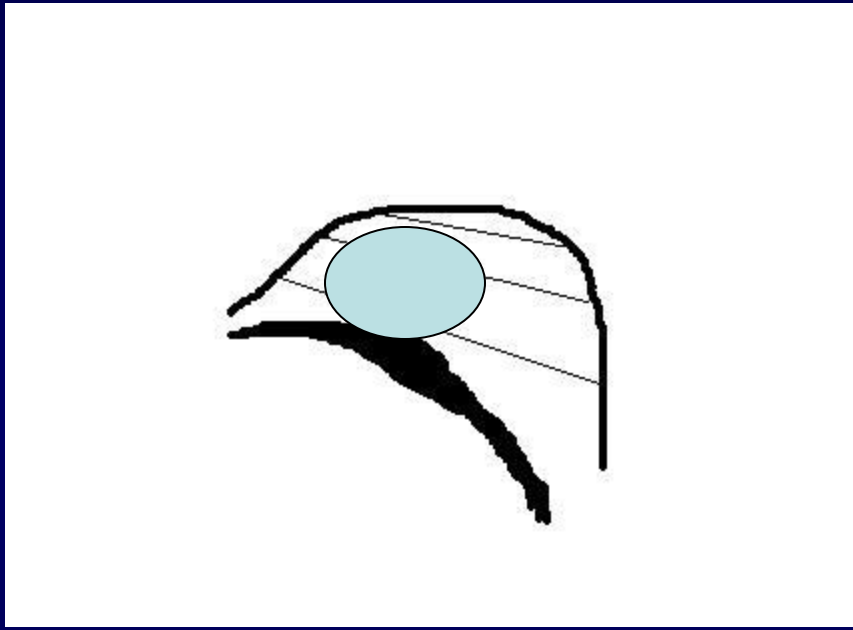
↙ ↘

Favorable: continue brachy

Unfavorable: convert to boost

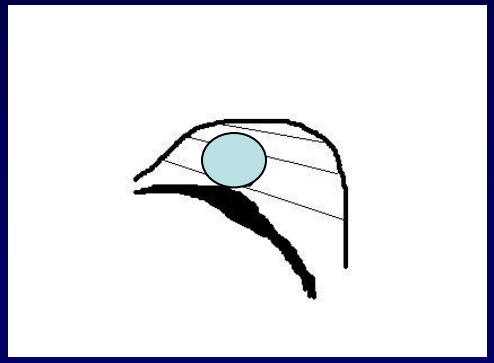
Ext RT to be followed

APBI: Needle entry and exit points



Implanted volume may be larger than the treated volume

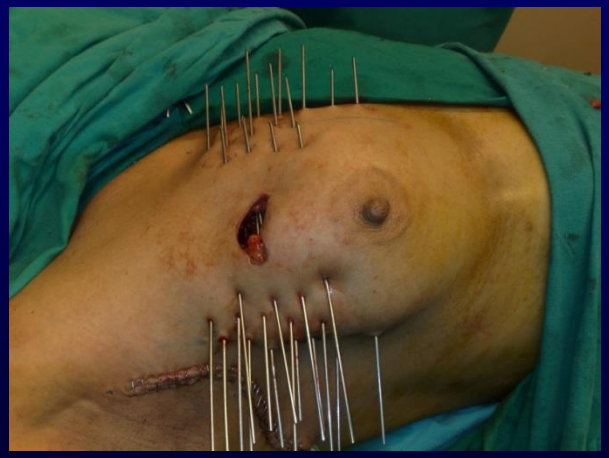
Intra-operative Brachytherapy



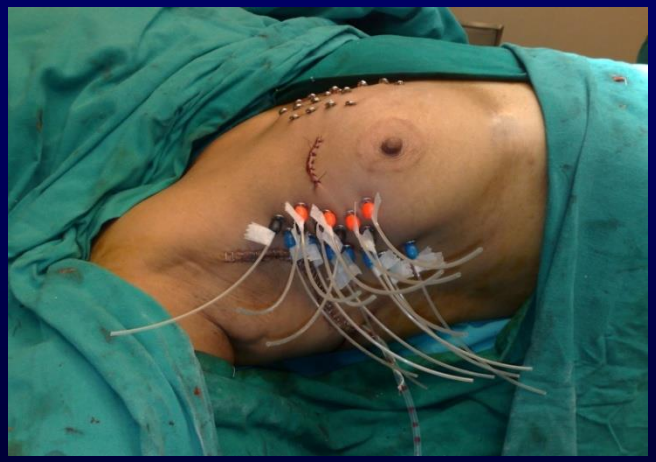
Implant volume may appear larger than the treated volume

Marking of the planes on the skin

Insertion of needles in first plane

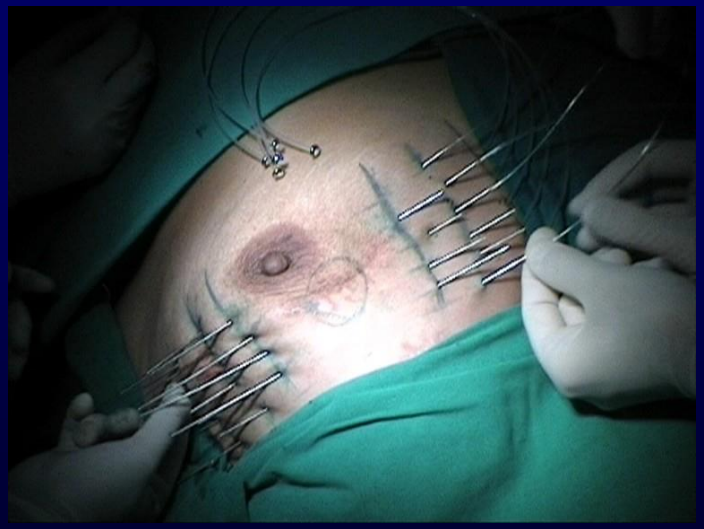


Insertion of second and third plane

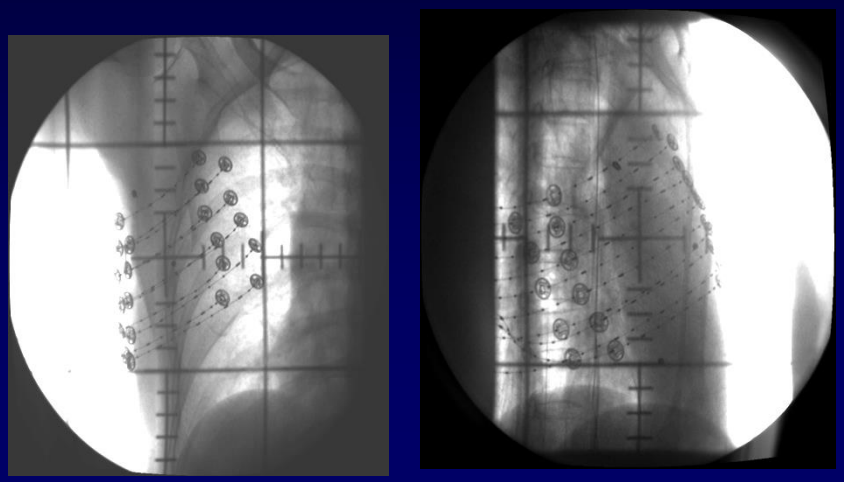


Replacement of needles with tubes

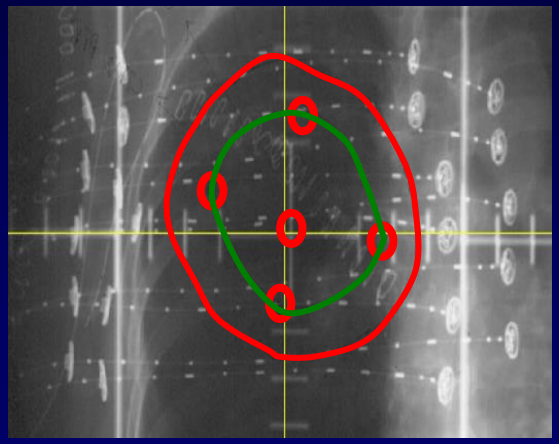
Post-operative Brachytherapy



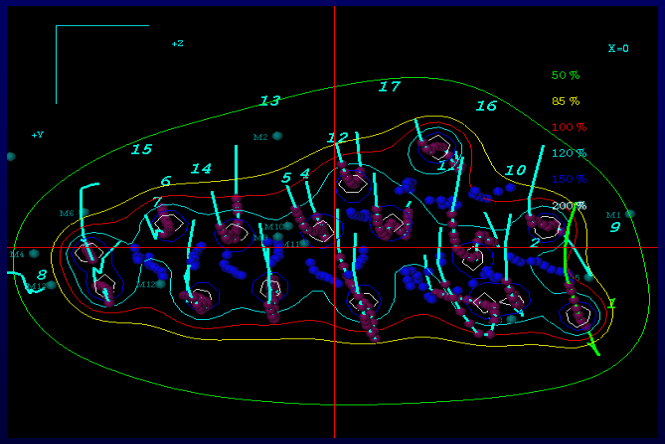
Brachytherapy Planning



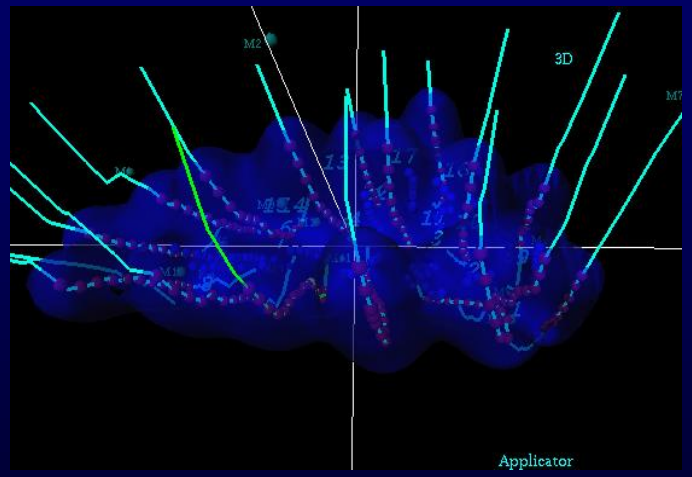
Orthogonal X rays



Identification of clips



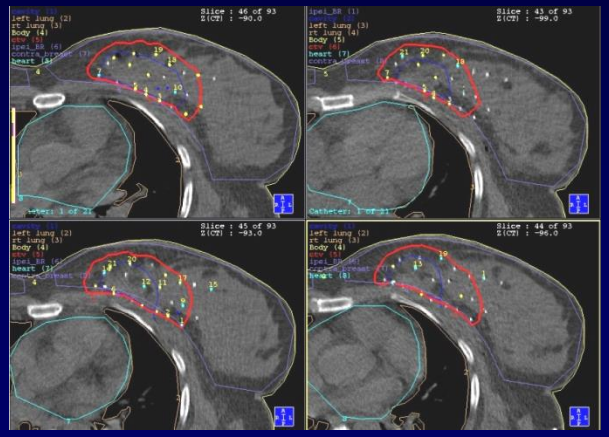
Planning



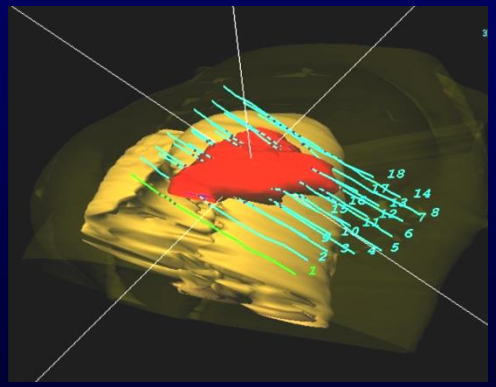
3D Dose distribution

3D Brachytherapy planning

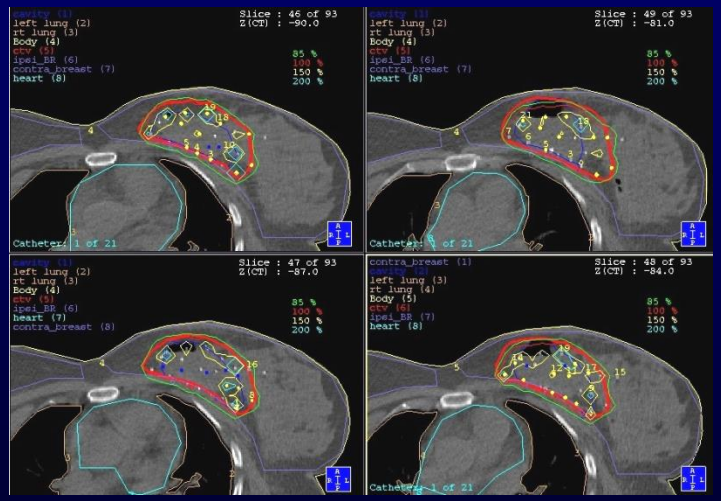
RT planning CT scan



Contouring



Determination of source loading



Slice by slice coverage evaluation

Treatment Delivery

Dose prescription: 340cGy/fraction at 85% basal dose

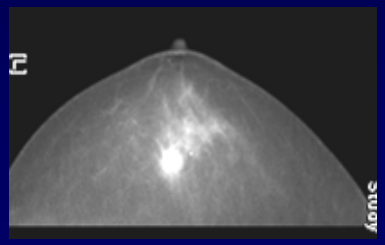
Total dose: 34Gy in 10 fractions bid

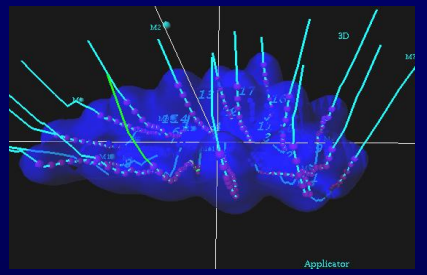
32Gy in 8 fractions bid

APBI: TMH data: 2D Planning

- May 2000- September 2005 (N=118) (X ray based)

- Median age: 56 years (30-78yrs)
- Median T size : 2cm
- IDC: 112 (97%)
- Grade III: 75 (65%)
- EIC positive: 8 (7%)
- Margin positive: 1 (1%)
- LVI: 13 (11%)
- Node positive: 12 (10%)
- ER positive:62 (55%)
- Intra-op: 69 (60%)
- Chemotherapy: 55 (46%)

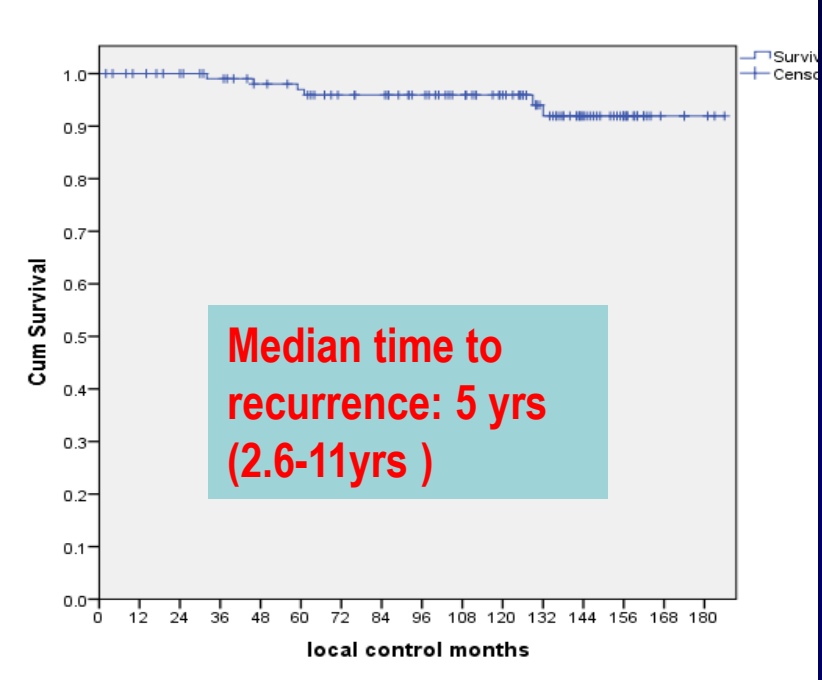


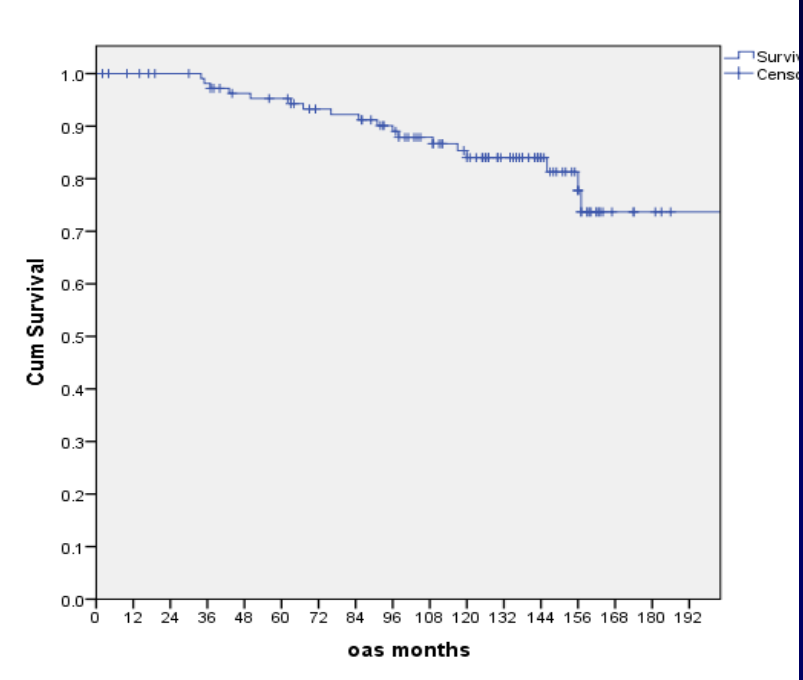


9 patients received WBRT

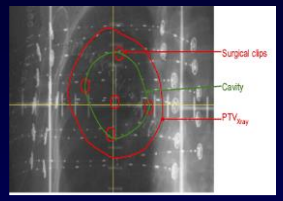
due to adverse prognostic factors

Clinical Outcome: > 10 year follow up





Median follow up 126 months		
	5 yr	10 yr
Local Control	97%	96%
Disease free survival	92%	83%
Overall survival	95%	84%



Clinical Oncology (2008) **20**: 46–52
doi:10.1016/j.clon.2007.09.006

Original Article

Dosimetric Comparison of Conventional Radiograph- and Three-dimensional Computed Tomography-based Planning using Dose Volume Indices for Partial Breast Intraoperative Implants

S. D. Sharma*, A. Budrukkar†, R. R. Upreti*, A. Munshi†, R. Jalali†, D. D. Deshpande*

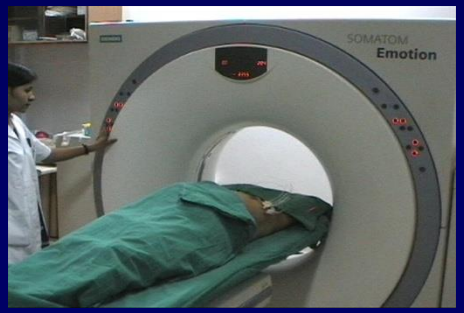
18 patients-treated with APBI

	P_{xray}	P_{CT}	$P_{CT+graphical}$	P value
CI Cavity	0.80	0.82	0.92	<0.001 (gr)
CI of PTV	0.69	0.71	0.85	<0.001 (gr)
DHI	0.81	0.81	0.71	<0.001 (gr)
OI	0.041	0.047	0.087	<0.0001 (gr)
EI	44	25	30	0.013 (CT)
COIN	0.48	0.58	0.68	<0.001 (gr)

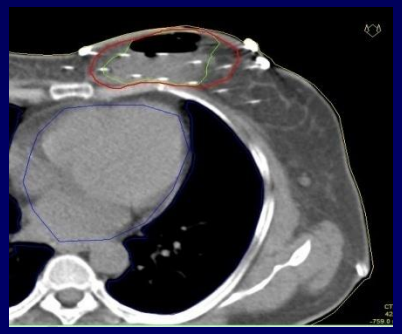
Conclusion: CT better than X ray for planning

APBI using 3D CT Based Brachytherapy

- Prospectively collected data: Between August 2005 to January 2013
- **Number: 140**



Planning CT scan



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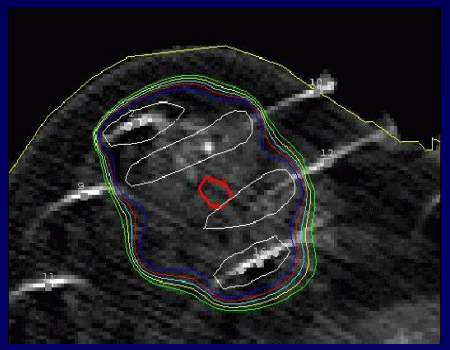
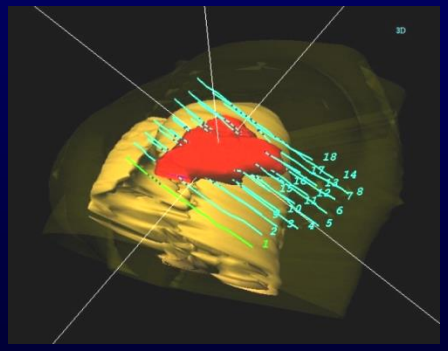


Multiplanar reconstruction



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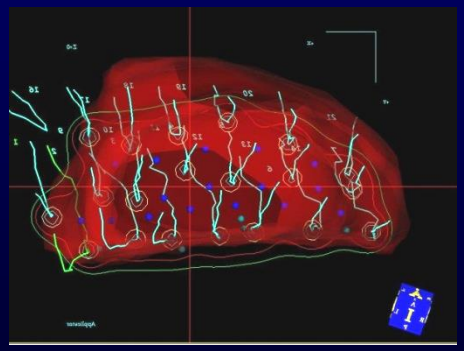


Dose points

3D Visualization

Radiotherapy and Oncology 115 (2015) 349–354

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Partial breast brachytherapy

Clinical outcomes of prospectively treated 140 women with early stage breast cancer using accelerated partial breast irradiation with 3 dimensional computerized tomography based brachytherapy

Ashwini Budrukkar [a,*], Lavanya Gurram [a], Ritu Raj Upreti [b], Anusheel Munshi [a], Rakesh Jalali [a], Rajendra Badwe [c], Vani Parmar [c], Tanuja Shet [d], Sudeep Gupta [e], Tabassum Wadasadawala [a], Rajiv Sarin [a]

[a] Department of Radiation Oncology; [b] Department of Medical Physics; [c] Department of Surgical Oncology; [d] Department of Pathology; and [e] Department of Medical Oncology, Tata Memorial Hospital, Mumbai, India

- Median Age: 57 years (40-79)
- Postmenopausal: 109 (77.5%)
- Intra-operative brachytherapy: 80 (57%)
- Median T size: 2 cm (0.6-3.2cm)
- IDC: 140 (100%)
- Chemotherapy: 73 (52%)

Grade III: 115 (82%)

LVI: 11 (7.4%)

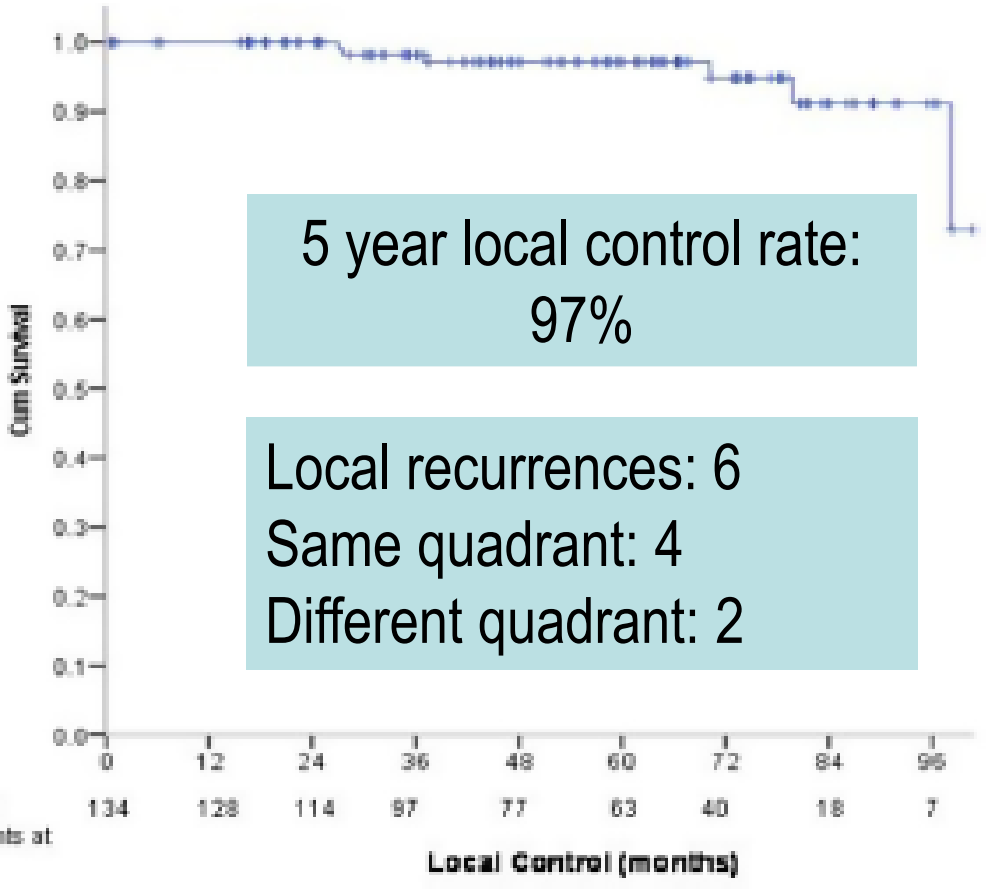
Margin positive: 1 (0.7%)

ER positive: 84 (60%)

Her2 positive: 23 (16%)

3DCT Based brachytherapy: Clinical Outcome

Median follow up : 60months (Range: 1-102months)



5 year local control rate: 97%

Local recurrences: 6
Same quadrant: 4
Different quadrant: 2

Median time to recurrence: 4.4 years

(2.2-6.5 years)

5 year OAS: 97%

Prognostic factors

Factor	5 yr Local control (%)	P value
Age		
<50	100	0.75
≥50	97	
Pathological T size		
≤2	98.5	0.79
>2	95	
Grade		
II	100	0.34
III	98	
Ductal carcinoma in situ		
Yes	96	0.25
No	98.2	
Estrogen receptor status		0.16
Positive	100	
Negative	92.4	
Her2		
Negative	99	0.01
Positive	88	
Vol 340		
≤140 cc	98	0.5
>140cc	100	
Implant		
Intra-op	96	0.07
Post-op	100	

Cosmesis

Good to excellent cosmetic outcome: 77%

Radiotherapy and Oncology 103 (2012) 161–165

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Late sequelae of APBI brachytherapy

Fat necrosis in women with early-stage breast cancer treated with accelerated partial breast irradiation (APBI) using interstitial brachytherapy

Ashwini Budrukkar [a,*], Vikas Jagtap [a], Seema Kembhavi [b], Anusheel Munshi [a], Rakesh Jalali [a], Tanuja Seth [c], Vani Parmar [d], Ritu Raj Upreti [e], Rajendra Badwe [d], Rajiv Sarin [a]

[a] *Department of Radiation Oncology;* [b] *Department of Radiology;* [c] *Department of Pathology;* [d] *Department of Surgery; and* [e] *Department of Medical Physics, Tata Memorial Hospital, Mumbai, India*

- 2000-2008; 170 women treated with APBI
- Median FU: 48 months
- 20 women developed fat necrosis
- Median time to development: 24 months
- 5 year actuarial fat necrosis rate: 18%

Clinical Oncology (2009) **21**: 668–675
doi:10.1016/j.clon.2009.07.014

Original Article

Quality of Life after Accelerated Partial Breast Irradiation in Early Breast Cancer: Matched Pair Analysis with Protracted Whole Breast Radiotherapy

T. Wadasadawala*, A. Budrukkar*, S. Chopra*, R. Badwe†, R. Hawaldar‡, V. Parmar†, R. Jalali*, R. Sarin§

- EORTC QLQ & BR 23
- 48 patients-study period: May 2006-December 2006
- 23 APBI & 25 WBRT
- Median FU: 3 years
- **APBI better than WBRT**
  - QLQ C30
    - Social functioning (p=0.025)
    - Financial difficulties (p=0.019)
  - BR 23
    - Body Image (p=0.005)

APBI Team

- **Radiation Oncology**
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  - Rakesh Jalali
  - Ashwini Budrukkar
  - Tabassum Wadasadawala
  - Santam Chakraborty
- **Surgical Oncology**
  - Rajendra Badwe
  - Vani Parmar
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  - Shalaka Joshi
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  - Seema Gulia
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  - Asawari Patil
- **Medical Physics**
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  - Satish Kolhe
  - Sudershan Kadam
- **Residents**
  - Vikas Jagtap
  - Lavanya Naidu
  - Prakash Pandit
  - Many more..