Role of Tumor Bed Boost in Breast Cancer

Evidence, Localization and Techniques

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Outline

- Rationale of tumor bed boost
- Evidence (Literature)
- Localization of the boost area
- Techniques of boost irradiation
- Dose fraction schedules
- Conclusion

Boost Irradiation: Definition

- Defined as delivering the escalated dose of radiation in the tumor zone that has the highest risk of recurrence

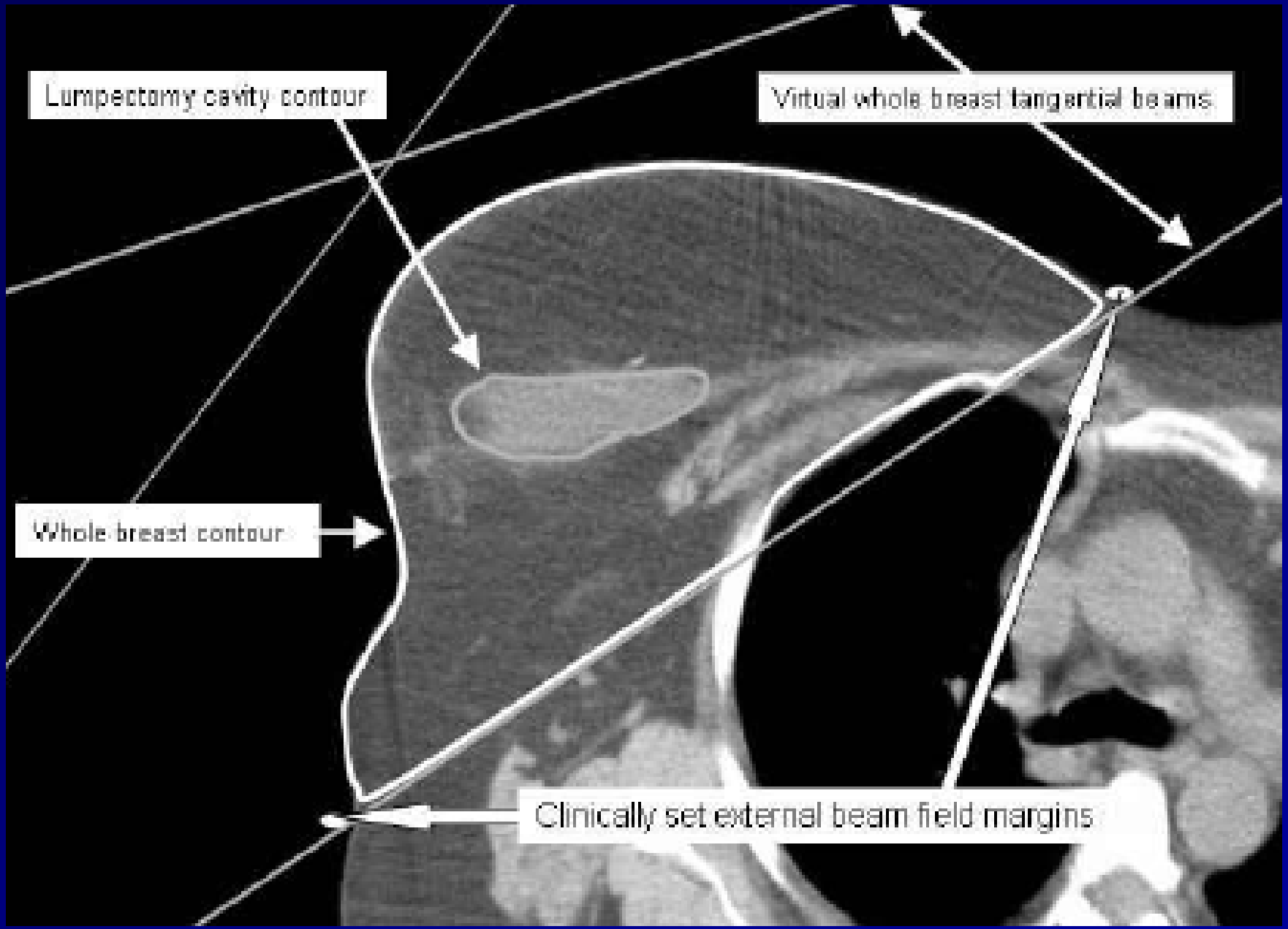
Boost Irradiation: Not a new concept

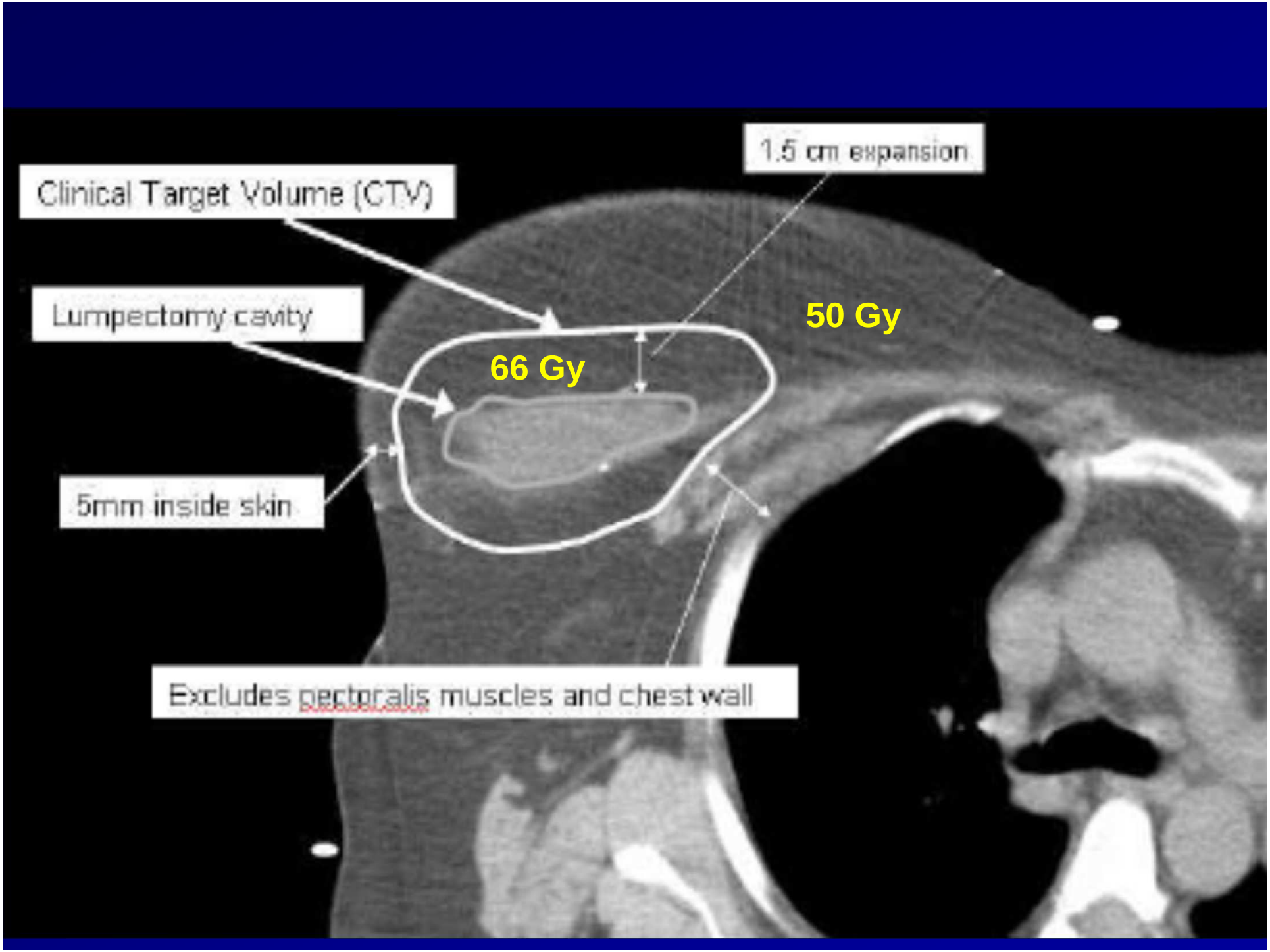
- Practiced for many tumor sites : intact and postoperatively
- Examples: Brain, cervix, H & N, Lung, Sarcomas etc.

Breast Cancer: Tumor Bed Boost

- Early breast cancer: BCS → WBRT + Boost
- Locally advanced breast cancer

  NACT → BCS → WBRT + Boost
- Inoperable LABC: WBRT + Boost
- Post mastectomy RT: Chest wall RT → Boost


Lumpectomy cavity contour
Virtual whole breast tangential beams
Whole breast contour
Clinically set external beam field margins


Clinical Target Volume (CTV)
1.5 cm expansion
Lumpectomy cavity
50 Gy
66 Gy
5mm inside skin
Excludes pectoralis muscles and chest wall

Rationale for the boost

- Even if surgical margins are -ve after the BCS, ~30% risk of microscopic tumor cells in the tumor bed
- Most recurrences (65-80%) are located in the vicinity of the tumor bed
- Boosting the tumor bed aimed to

-reduce the local recurrence and

-reduce the toxicity and improve cosmesis due to reduced dose to OAR

Is boost irradiation a standard practice ?

- Boost vs no Boost
- The literature has shown reduced LR with boost but no survival gain.
- Hypo-fractionated regimes do not involve boost; yet claim similar results
- APBI is replacing WBRT

Landmark Trials

Romestaing P, Lehinge Y, Carrie C, et al. Role of a 10-Gy boost in the conservative treatment of early breast cancer: Results of a randomized clinical trial in Lyon, France. J Clin Oncol 1997;15:963–968.

The New England Journal of Medicine

RECURRENCE RATES AFTER TREATMENT OF BREAST CANCER WITH STANDARD RADIOTHERAPY WITH OR WITHOUT ADDITIONAL RADIATION

Landmark Trials

VOLUME 25 · NUMBER 22 · AUGUST 1 2007

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

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

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 75, No. 4, pp. 1029–1034, 2009

0360-3016/09/$–see front matter

doi:10.1016/j.ijrobp.2008.12.038

CLINICAL INVESTIGATION **Breast**

BENEFIT OF RADIATION BOOST AFTER WHOLE-BREAST RADIOTHERAPY

Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial

Harry Bartelink, Philippe Maingon, Philip Poortmans, Caroline Weltens, Alain Fourquet, Jos Jager, Dominic Schinagl, Bing Oei, Carla Rodenhuis, Jean-Claude Horiot, Henk Struikmans, Erik Van Limbergen, Youlia Kirova, Paula Elkhuizen, Rudolf Bongartz, Raymond Miralbell, David Morgan, Jean-Bernard Dubois, Vincent Remouchamps, René-Olivier Mirimanoff, Sandra Collette, Laurence Collette; on behalf of the European Organisation for Research and Treatment of Cancer Radiation Oncology and Breast Cancer Groups

Lancet Oncol 2015; 16: 47–56

Boost vs No Boost: Trials

- All the trials show consistent reduction in local recurrence
- No difference in the overall survival
- Effect of boost was more evident in younger patients
- Compromised cosmesis in certain subgroup of pts

But …… for a marginal gain

? Is additional dose justified

? Prolongation of treatment by 1.5 wks

? Overburdening of resources

? Inferior breast cosmesis

The New England Journal of Medicine

EORTC Trial 2001

RECURRENCE RATES AFTER TREATMENT OF BREAST CANCER WITH STANDARD RADIOTHERAPY WITH OR WITHOUT ADDITIONAL RADIATION

EBC after lumpectomy + ALND

WBRT 50 Gy

Boost 16 Gy (2657)

No boost (2661)

5-yr FU data

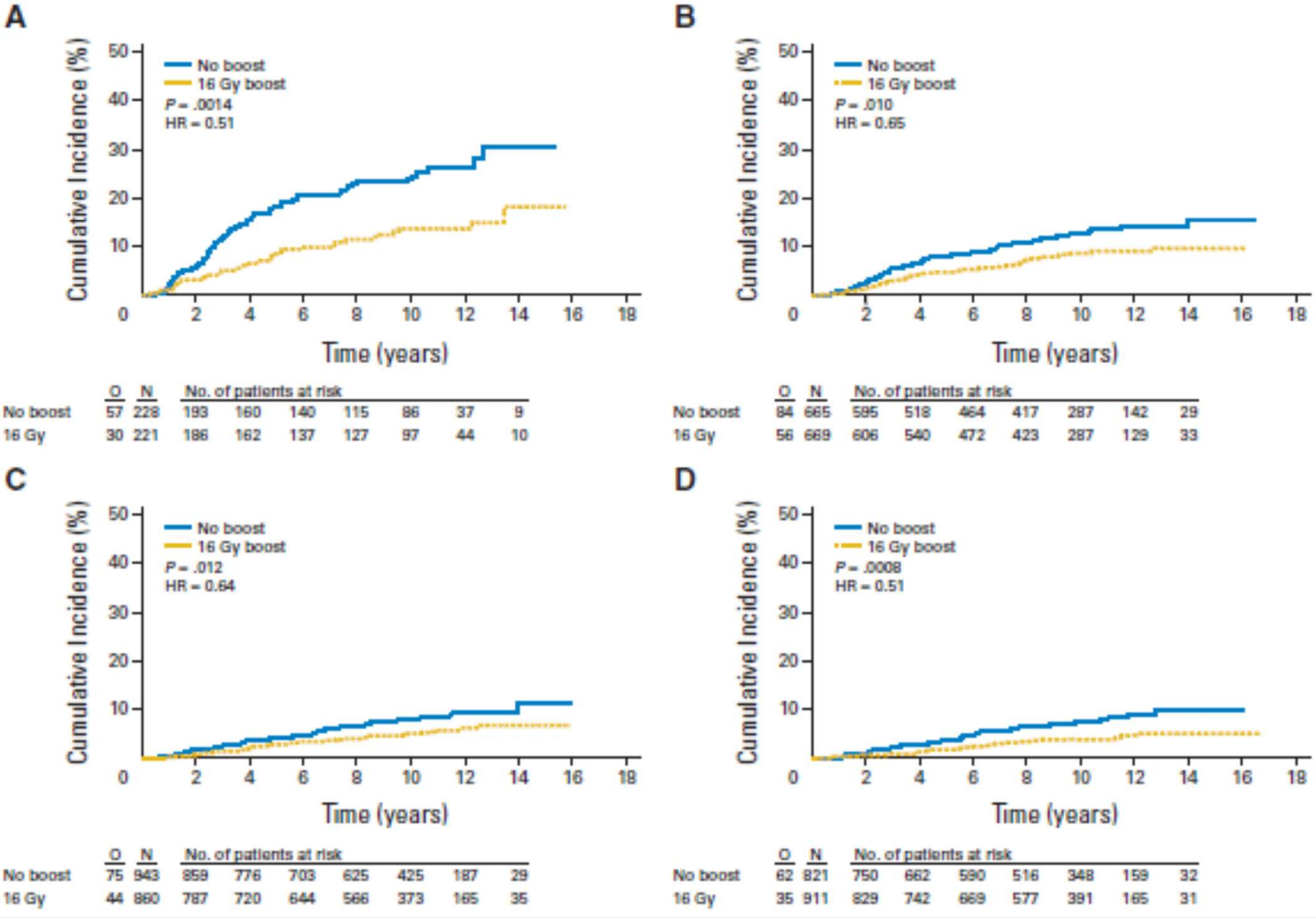
	Boost	No Boost
n	2657	2661
LR	4.3%	7.3%
LR in <40yrs	10.2%	19.5%
5-yr Survival	87%	91%
Good cosmesis	71%	87%

47% recurrences in tumor bed

10-yr FU data (JCO 2007)

	Boost	No Boost
n	2657	2661
LR	6.2%	10.2% **(p<.0001)**
10-yr Survival	82%	82%
Severe fibrosis	4.4%	1.6% **(p<.0001)**

47% recurrences in tumor bed


A
Cumulative Incidence (%)
No boost
16 Gy boost
P = .0014
HR = 0.51
Time (years)
O N No. of patients at risk
No boost 57 228 193 160 140 115 86 37 9
16 Gy 30 221 186 162 137 127 97 44 10
B
Cumulative Incidence (%)
No boost
16 Gy boost
P = .010
HR = 0.65
Time (years)
O N No. of patients at risk
No boost 84 665 595 518 464 417 287 142 29
16 Gy 56 669 606 540 472 423 287 129 33
C
Cumulative Incidence (%)
No boost
16 Gy boost
P = .012
HR = 0.64
Time (years)
O N No. of patients at risk
No boost 75 943 859 776 703 625 425 187 29
16 Gy 44 860 787 720 644 566 373 165 35
D
Cumulative Incidence (%)
No boost
16 Gy boost
P = .0008
HR = 0.51
Time (years)
O N No. of patients at risk
No boost 62 821 750 662 590 516 348 159 32
16 Gy 35 911 829 742 669 577 391 165 31

EORTC 10 yr data: key points

- 47% breast recurrences located in tumor bed
- Significant reduction in I.L. rec. for all age Gps by adding 16 Gy boost
- Similar 10-yr survival rates (82% vs 82%)
- Breast fibrosis significantly more with boost (4.4% vs 1.6%)

- Higher local control rate w/o survival advantage at the cost of increased fibrosis

Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial

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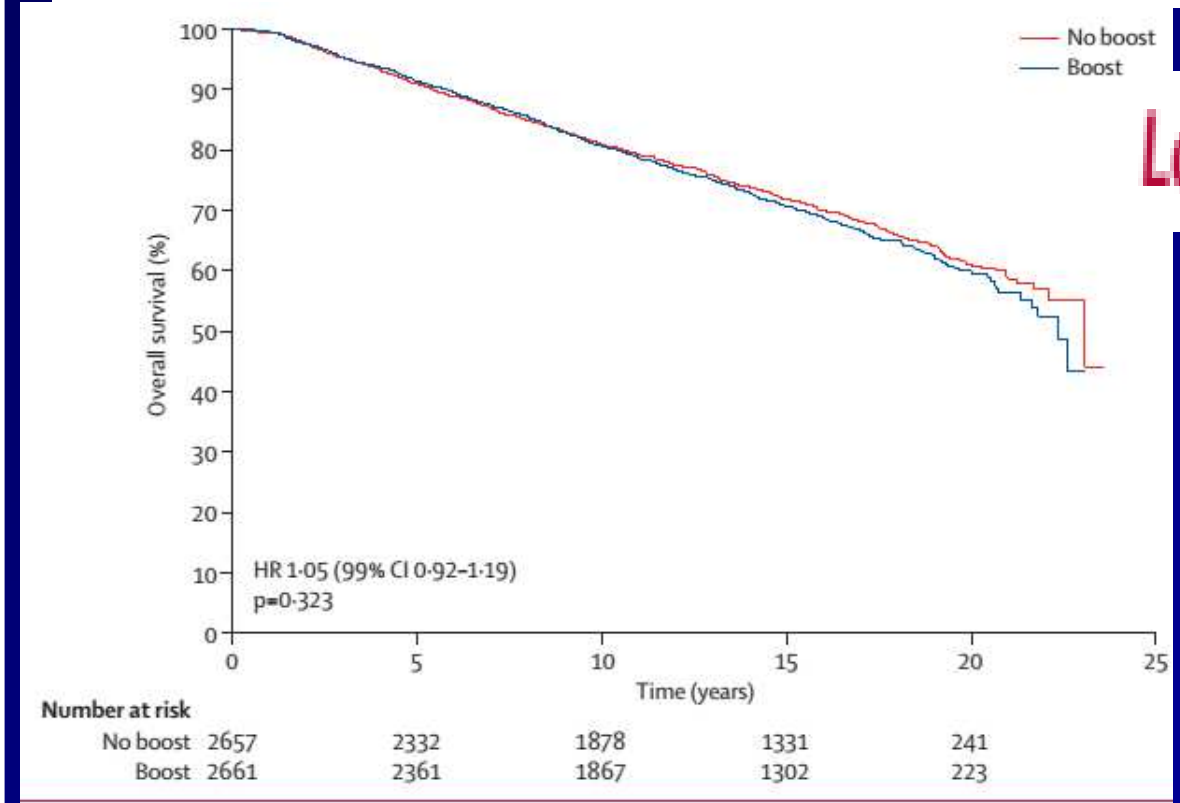

Figure 2: **Overall survival**

Lancet Oncol 2015; 16: 47–56

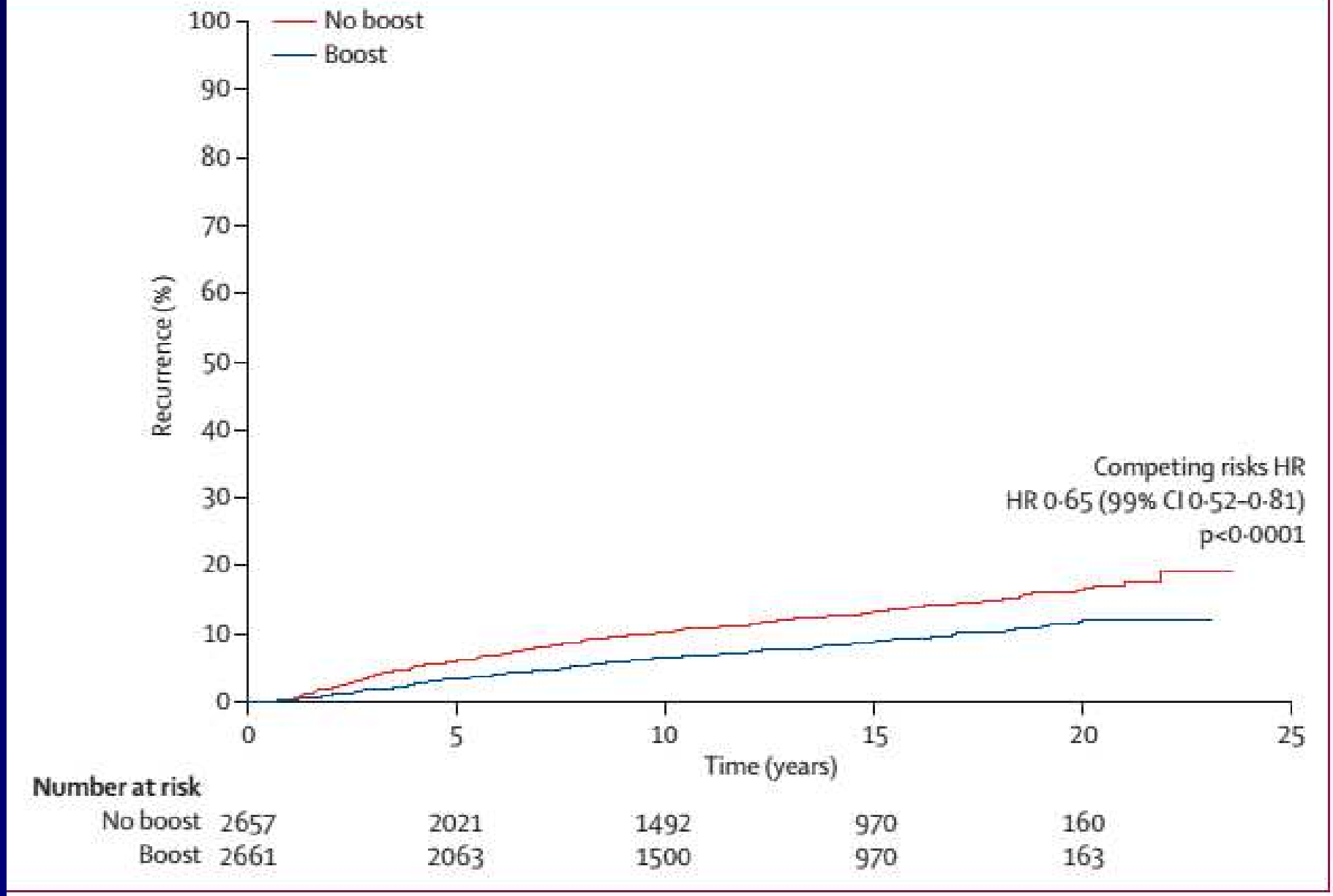

Figure 3: **Ipsilateral breast tumour recurrence**

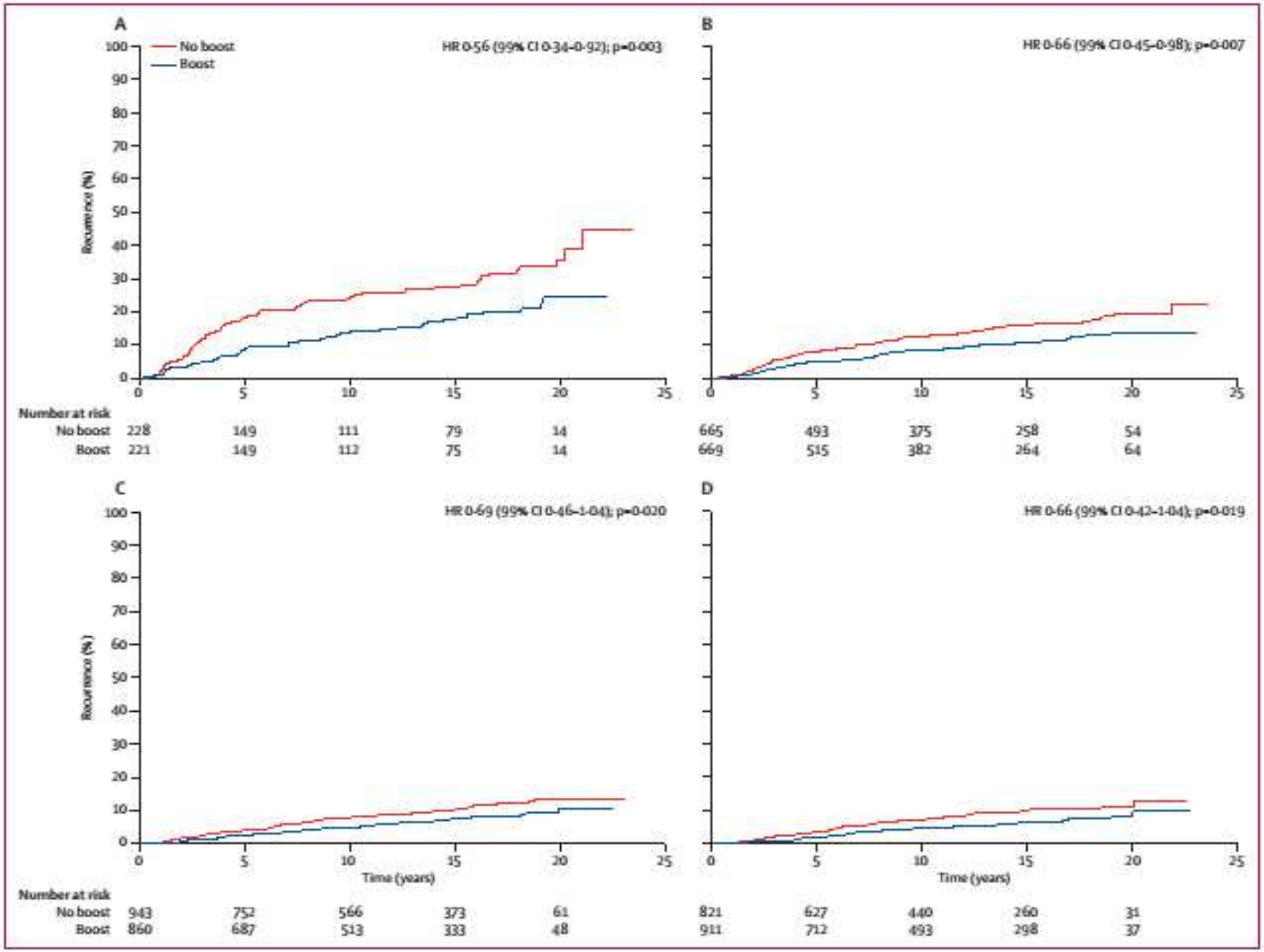

Figure 4: Cumulative incidence of ipsilateral breast tumour recurrence by age

For patients aged ≤40 years, 71 patients in the no boost group versus 42 in the boost group had recurrence (A); for patients aged 41–50 years, 108 versus 74 had recurrence (B); for patients aged 51–60 years, 100 versus 64 had recurrence (C); and for patients aged >60 years, 75 versus 57 had recurrence (D). HR=hazard ratio.

EORTC study: 20 yrs FU

Findings Between May 24, 1989, and June 25, 1996, 2657 patients were randomly assigned to receive no radiation boost and 2661 patients randomly assigned to receive a radiation boost. Median follow-up was 17·2 years (IQR 13·0–19·0). 20-year overall survival was 59·7% (99% CI 56·3–63·0) in the boost group versus 61·1% (57·6–64·3) in the no boost group, hazard ratio (HR) 1·05 (99% CI 0·92–1·19, p=0·323). Ipsilateral breast tumour recurrence was the first treatment failure for 354 patients (13%) in the no boost group versus 237 patients (9%) in the boost group, HR 0·65 (99% CI 0·52–0·81, p<0·0001). The 20-year cumulative incidence of ipsilatelal breast tumour recurrence was 16·4% (99% CI 14·1–18·8) in the no boost group versus 12·0% (9·8–14·4) in the boost group. Mastectomies as first salvage treatment for ipsilateral breast tumour recurrence occurred in 279 (79%) of 354 patients in the no boost group versus 178 (75%) of 237 in the boost group. The cumulative incidence of severe fibrosis at 20 years was 1·8% (99% CI 1·1–2·5) in the no boost group versus 5·2% (99% CI 3·9–6·4) in the boost group (p<0·0001).

Interpretation A radiation boost after whole-breast irradiation has no effect on long-term overall survival, but can improve local control, with the largest absolute benefit in young patients, although it increases the risk of moderate to severe fibrosis. The extra radiation dose can be avoided in most patients older than age 60 years.

Boost or no boost: Yes

- Reduced recurrence will lessen mastectomies
- Indian scenario: still in transition from MRM to BCT
- Higher local control has been proved to lower mortality in other trials.
- *For 4 local recurrences prevented, 1 death from breast cancer would be avoided at 15 years of follow up* (EBCTCG study. Lancet 2005 366:2087)
- Increase in fibrosis not a real concern (1.6% to 4.4%)

Int. J. Radiation Oncology Biol. Phys., Vol. 75, No. 4, pp. 1029–1034, 2009

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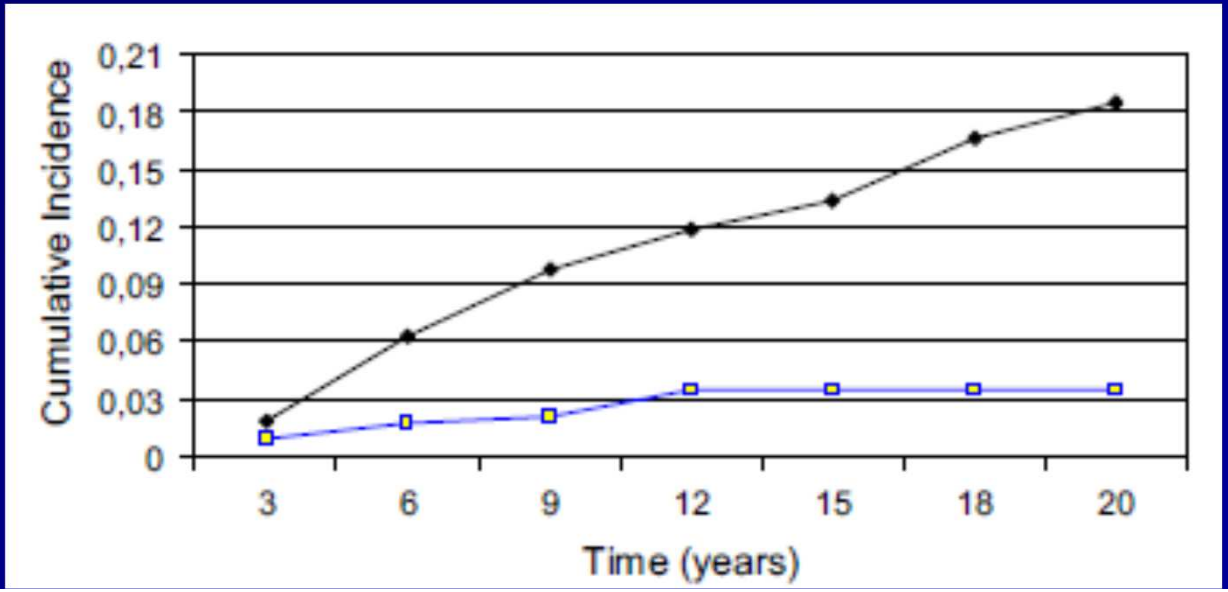
doi:10.1016/j.ijrobp.2008.12.038

CLINICAL INVESTIGATION **Breast**

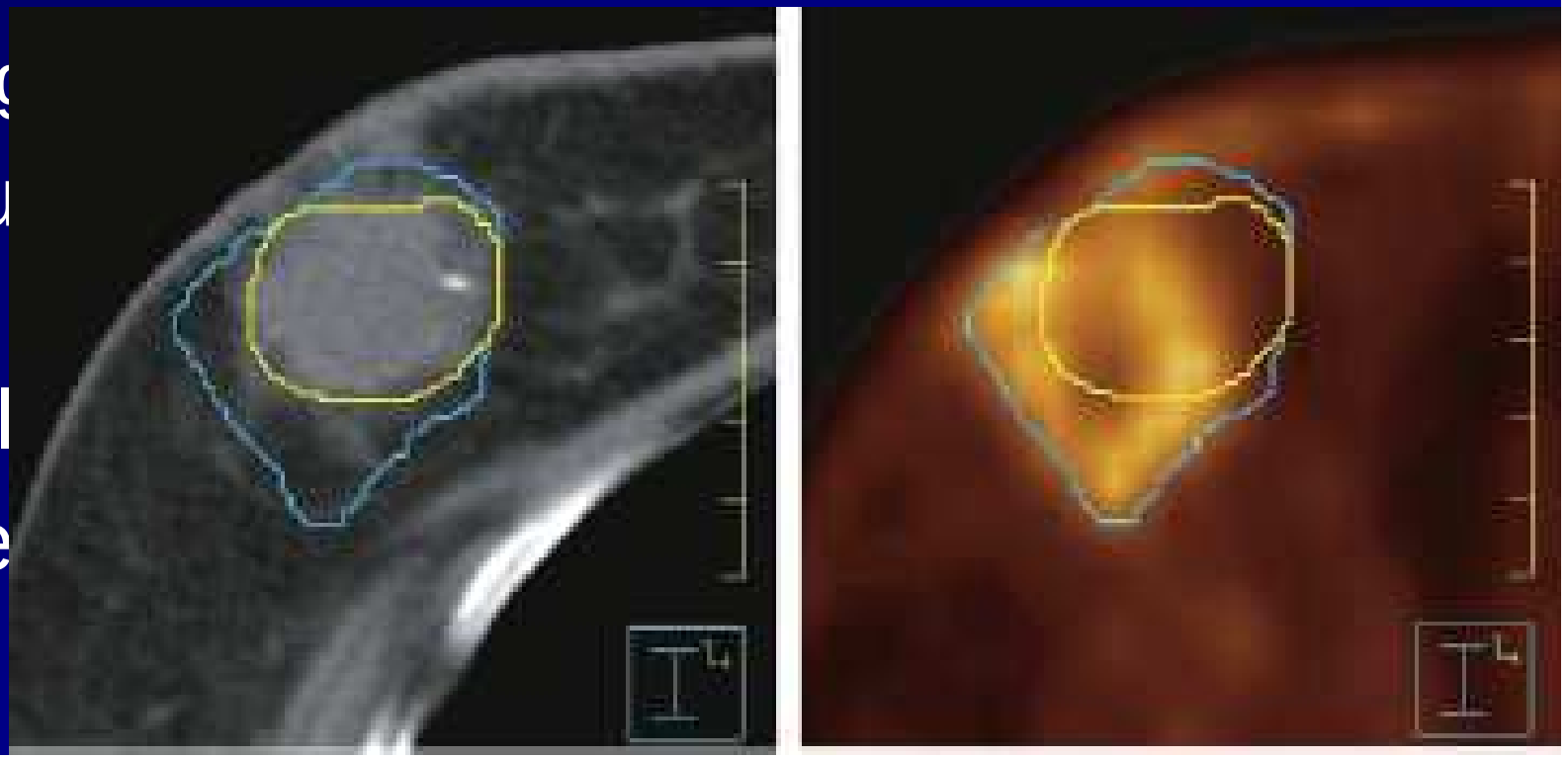
BENEFIT OF RADIATION BOOST AFTER WHOLE-BREAST RADIOTHERAPY

- 1138 patients (boost 739; no boost 399)
- WBRT : 50 Gy followed by Boost dose : 10 Gy/5F/5d



Delineation of the boost volume

- For Photon/electron
  - Scar based
  - Clips
  - Imag
- For mu
  scan
- For bal
- New te



Methods of Cavity Delineation

Technique	Delineation	Experience	Availability	Cost effective
Scar	poor	wide	easy	+++
USG	good	-	easy	+++
CT	excellent	emerging	easy	++
MRI	excellent	limited	sparse	+
PET	?	?	scanty	+/-

Dose prescription point/volume

- 1-2 cm around the lumpectomy cavity
- More in case of boost by photon/electron
- For balloon, 1 cm from the surface
- Distance from the skin : 0.5 cm
- For brachy : CTV=PTV

Dose of radiation for boost

- Usual dose: 15-20 Gy (16 Gy in EORTC trial)
- But it depends on the technique of boost
- LDR: 15 Gy @50cGy/hr
- HDR: 15 Gy/6F/3 days (BD schedule)
- ABS guideline: 10Gy/2F by HDR in 24 to 48 hrs
- IORT: 20 Gy

www.americanbrachytherapy.org/guidelines/abs_breast_brachytherapy_taskgroup.pdf

Boost dose for close or positive margins

- Theoretically require higher dose
- Many trials have used escalated boost dose of upto 20 Gy
  - Ryoo et al. Radiology 1989;172:5559.
  - Neuschatz et al. Cancer 2003;97:309.
  - Poortmans et al.Impact of the boost dose of 10Gy vs. 26Gy in patients with microscopically incomplete lumpectomy. Radiother Oncol 2009;90:80.

However, no benefit has been observed so far with escalated doses for close/positive margins

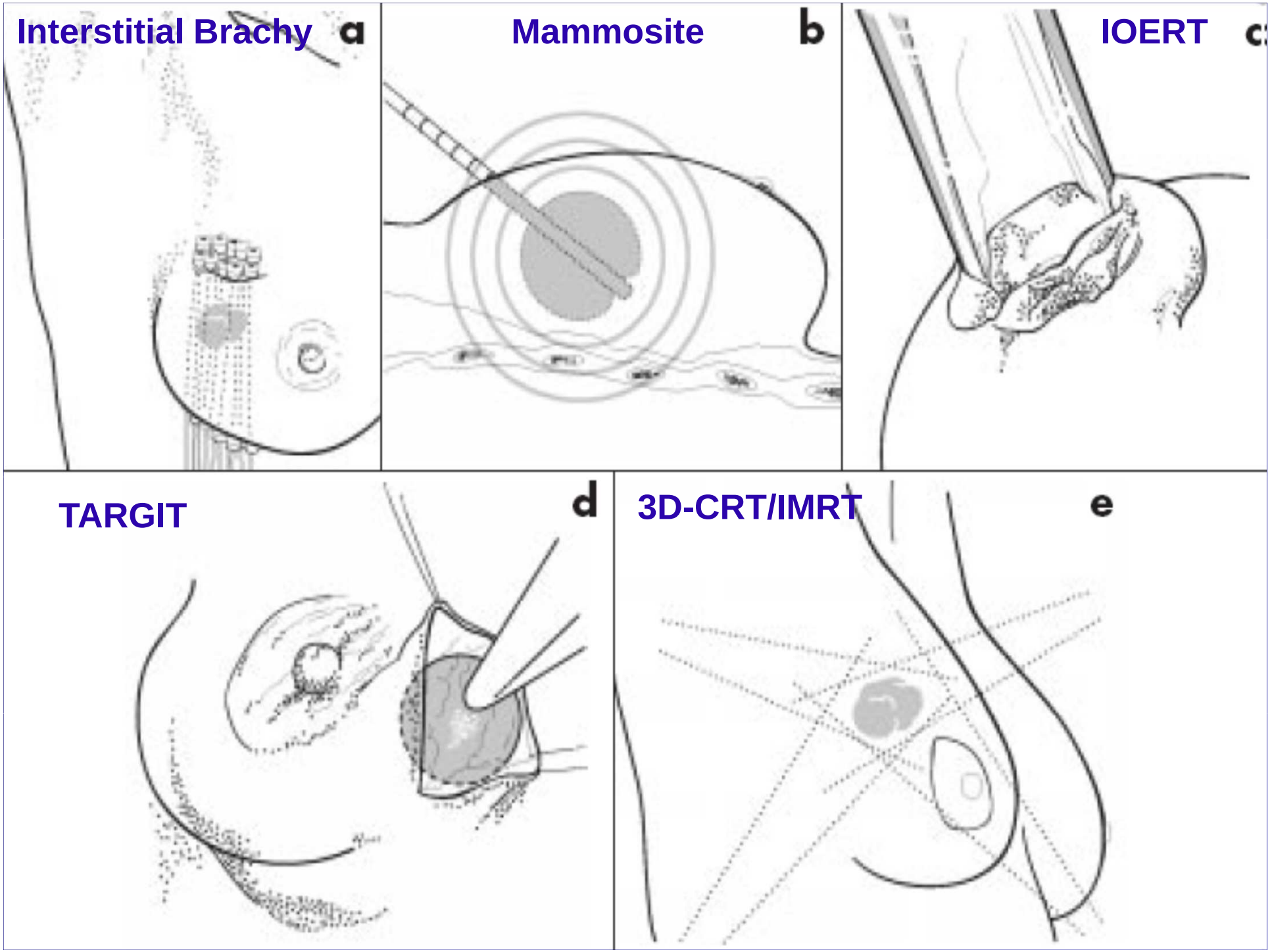
Techniques of boost irradiation

Common techniques

- Photons: Cobalt, X-rays
- Electrons : 9-15 MeV
- Interstitial brachytherapy

Newer techniques

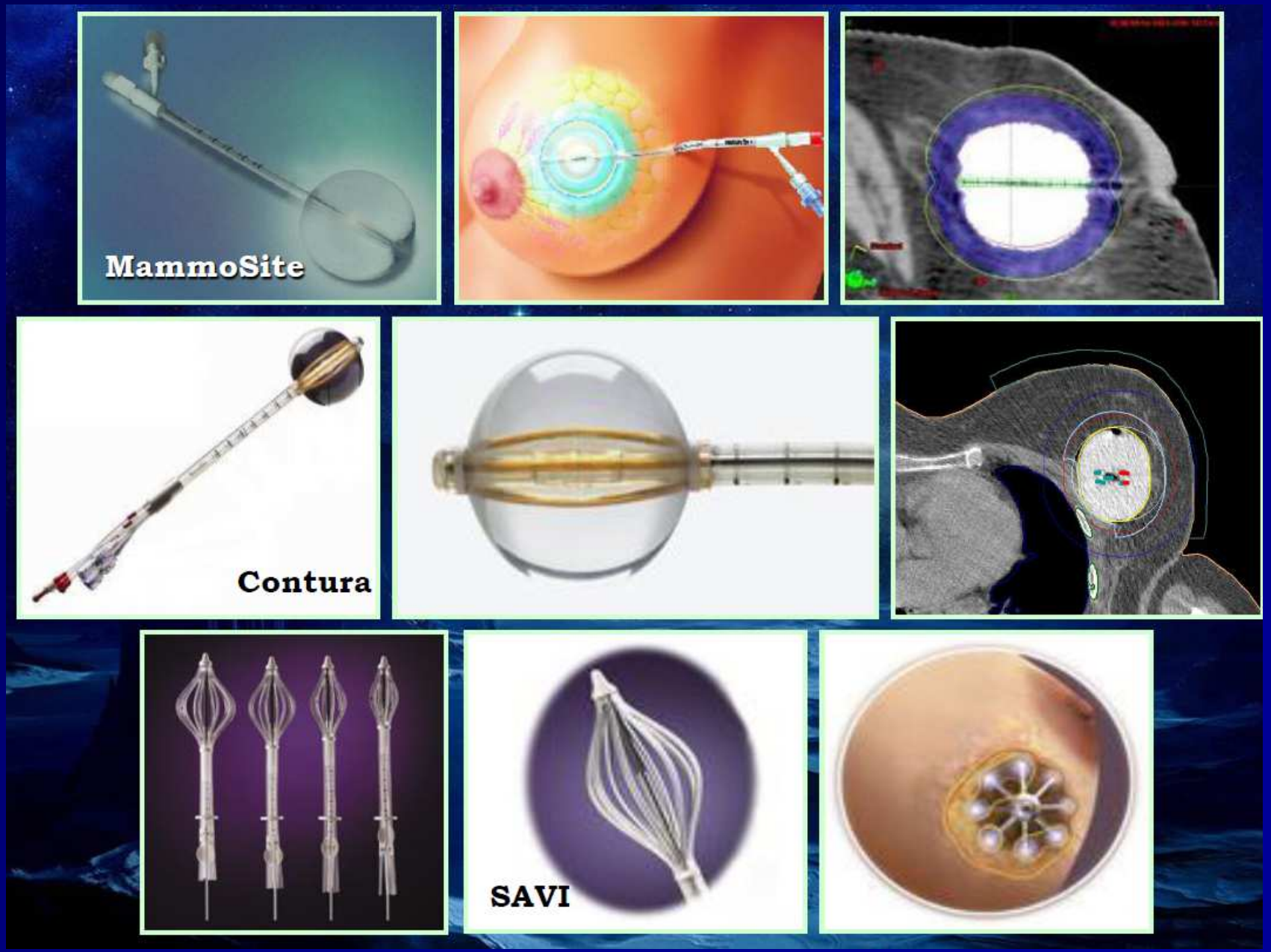
- Protons
- Permanent seed implants
- Mammosite
- IORT
- IMRT
- Radionuclide therapy : Y^{90} (Eur J Nucl Med Mol Imaging (2010)


Interstitial Brachy
a
Mammosite
b
IOERT
c
TARGIT
d
3D-CRT/IMRT
e

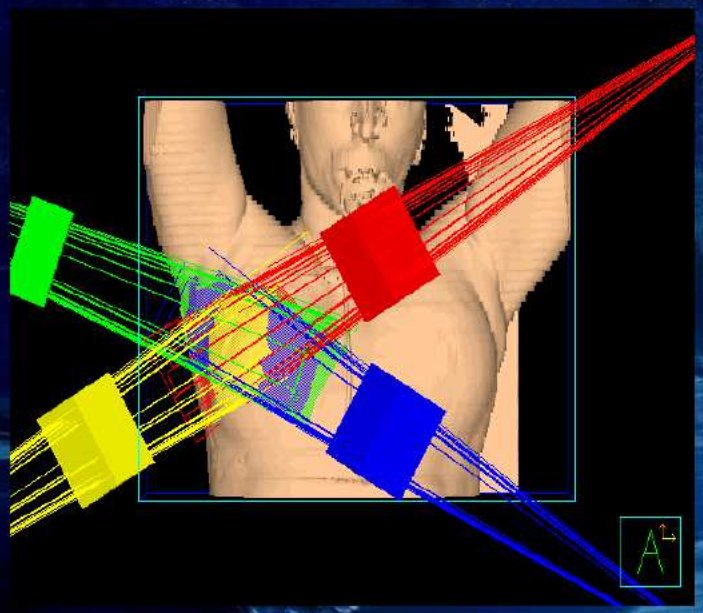

INTRABEAM

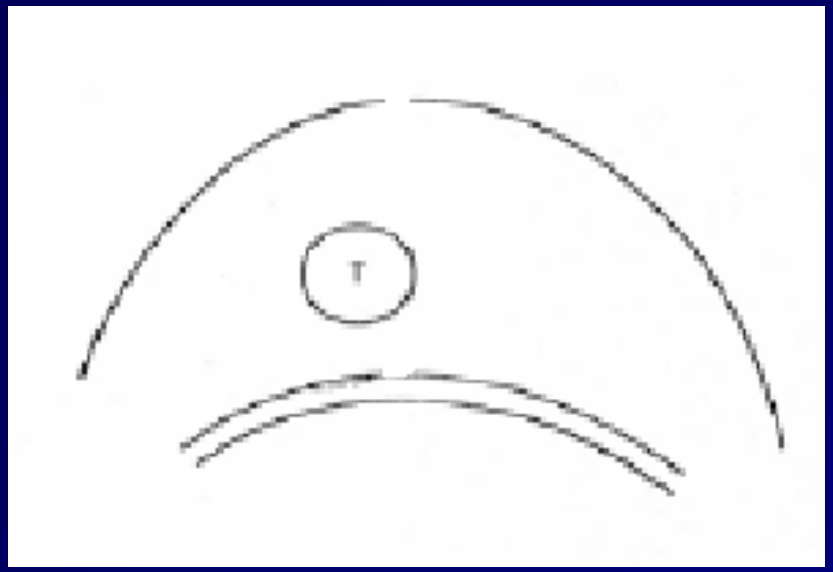

B
INTRAOP


A

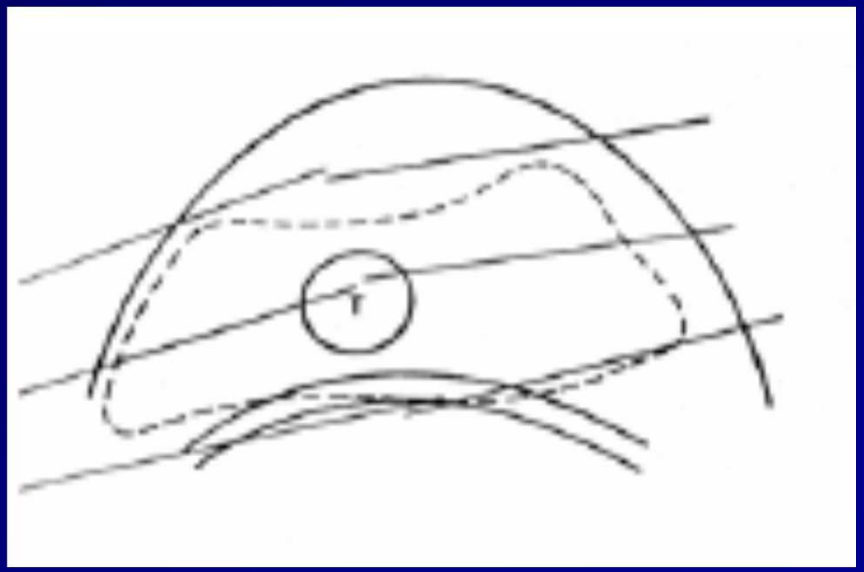

MammoSite
Contura
SAVI

EBRT – 3DRT and IMRT

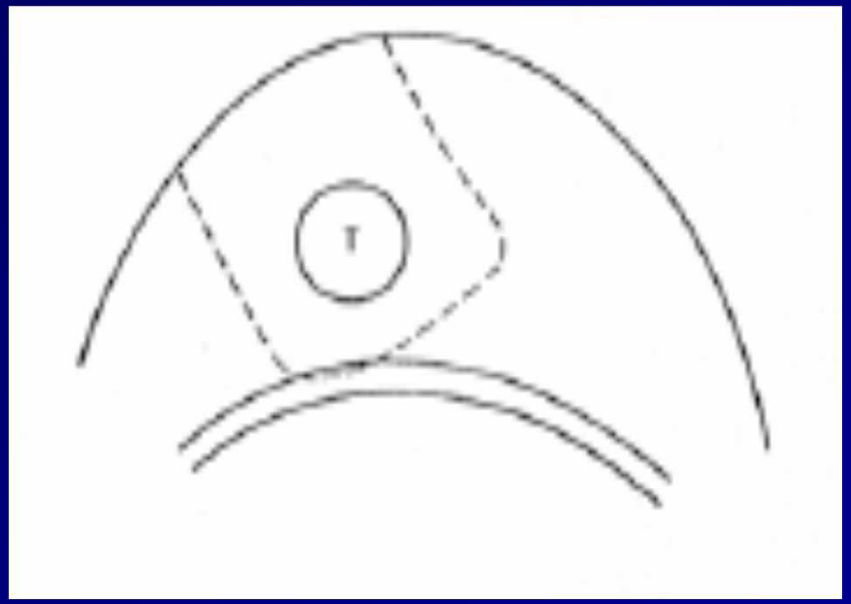




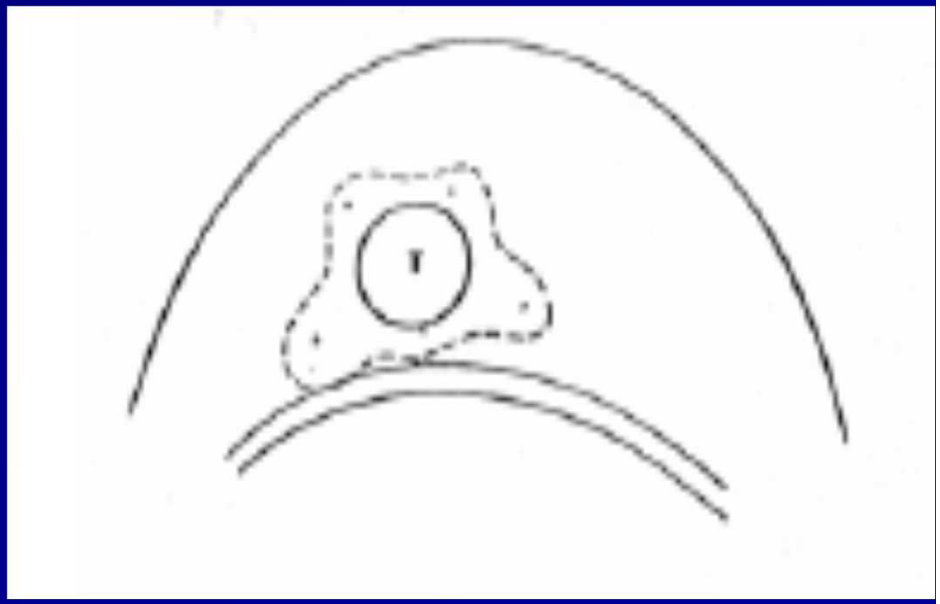
Boost Planning



Photons



Electrons



Interstitial Brachytherapy

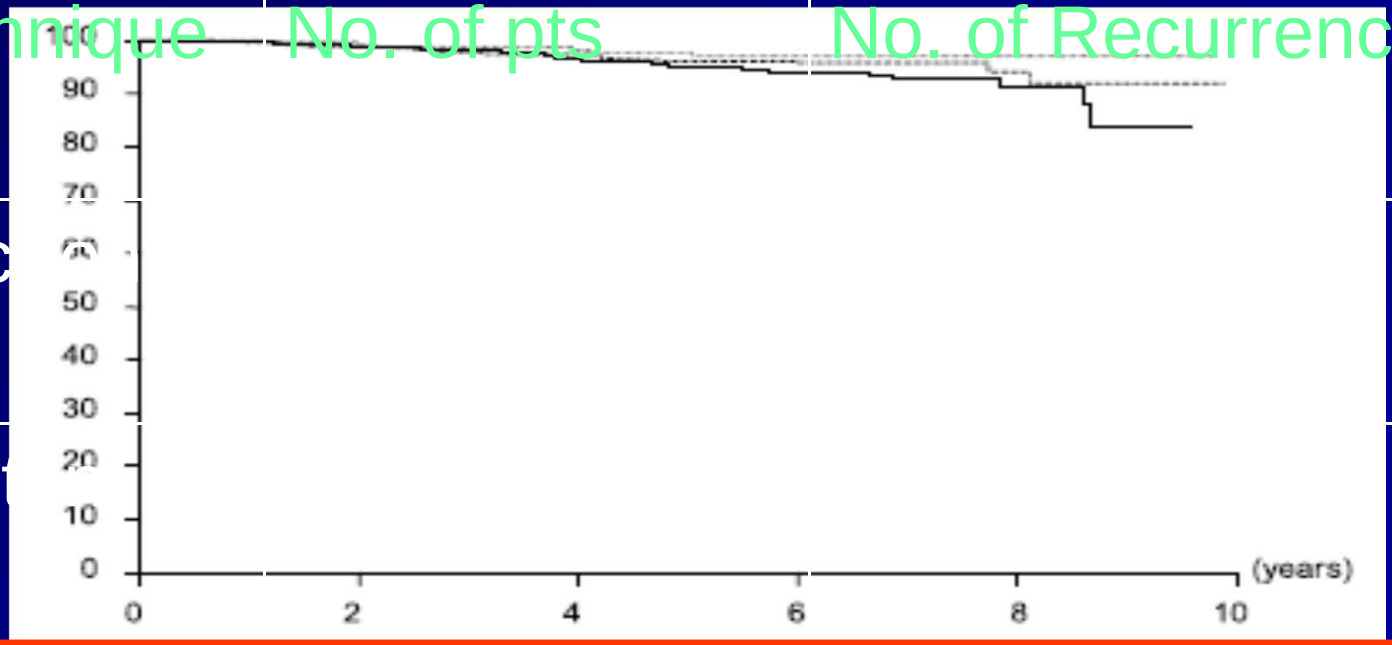
ELSEVIER

Radiotherapy and Oncology 72 (2004) 25–33

RADIOTHERAPY & ONCOLOGY

www.elsevier.com/locate/radonline

The influence of the boost technique on local control in breast conserving treatment in the EORTC 'boost versus no boost' randomised trial



Technique	No. of pts	No. of Recurrences
Elec		
Phot		
Brachy	225 (9%)	6 (2.5%)

Sequence

In relation to WBRT

- WBRT --------→ Boost
- WBRT + Boost (SIBIMRT)
- Boost --------→WBRT (Peri-operative)

In relation to Surgery

- Intra-operative
- Peri-operative
- Post-operative

Peri-operative Brachytherapy for boost

- Brachytherapy catheters implanted at the time of surgery (per-op implant).
- Treatment is started 48-72 hrs later (peri-op)
- Better appreciation of tumor location & dimensions
- Vascularity is maintained
- Gain of 1.5 wks (WBRT 5 wks + boost 1.5 wks)
- Avoid re-hospitalization. Re-anesthesia, stress
- Reducing the burden of resources and waiting list
- ?Delayed wound healing, infection etc. (minimal)
- *Good coordination between surgeon and radiation oncologist*

AIIMS Brachy Protocol for Early Ca Breast

Day 0: surgical resection + Per-op Brachy

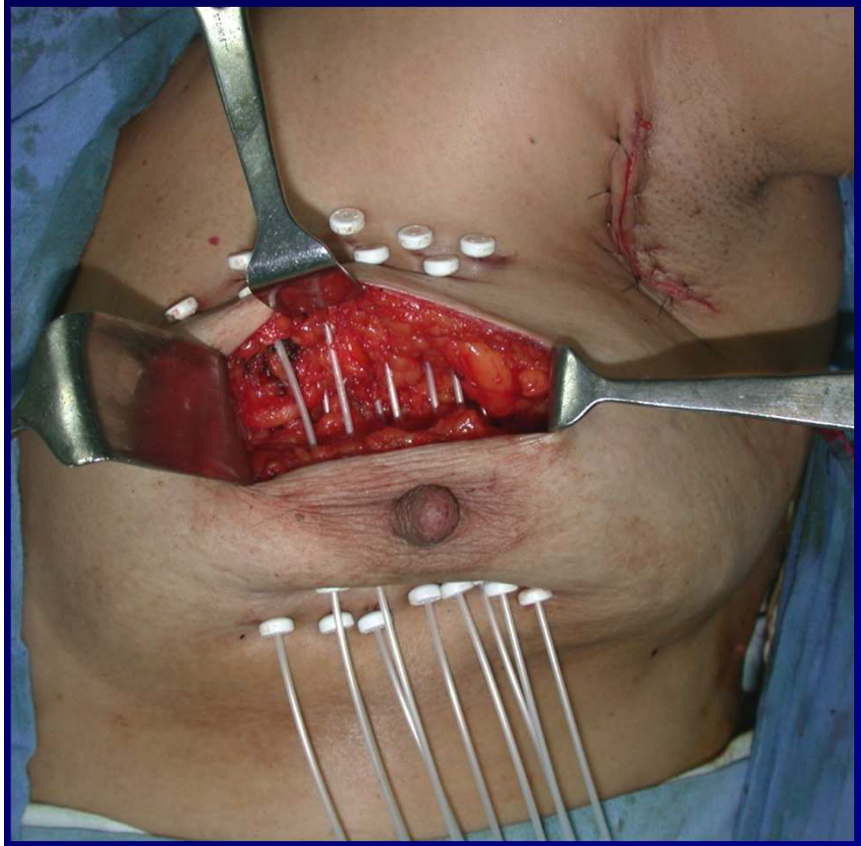
Day 2: CT simulation, planning

Day 3-5: HDR-BT with 3.5 Gy twice daily (14Gy)

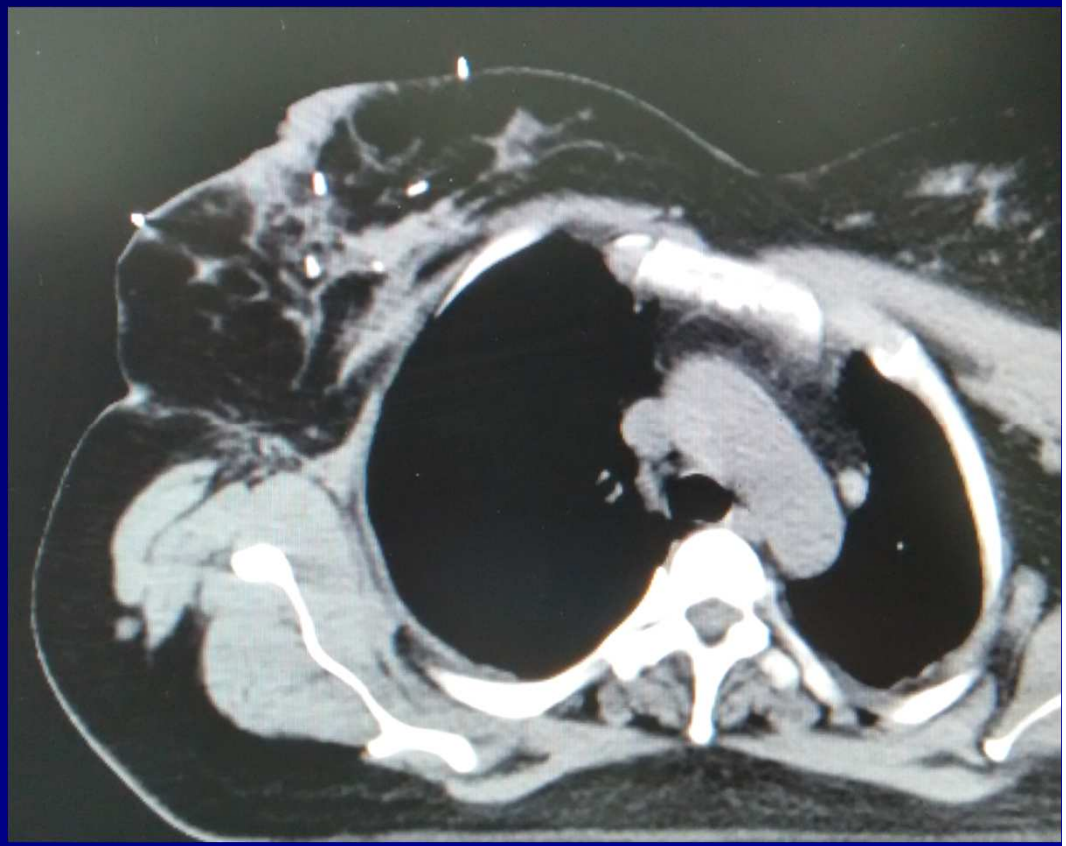
Day 28: EBRT 50 Gy/25F/5 wks

APBI (35Gy/10F/5d)

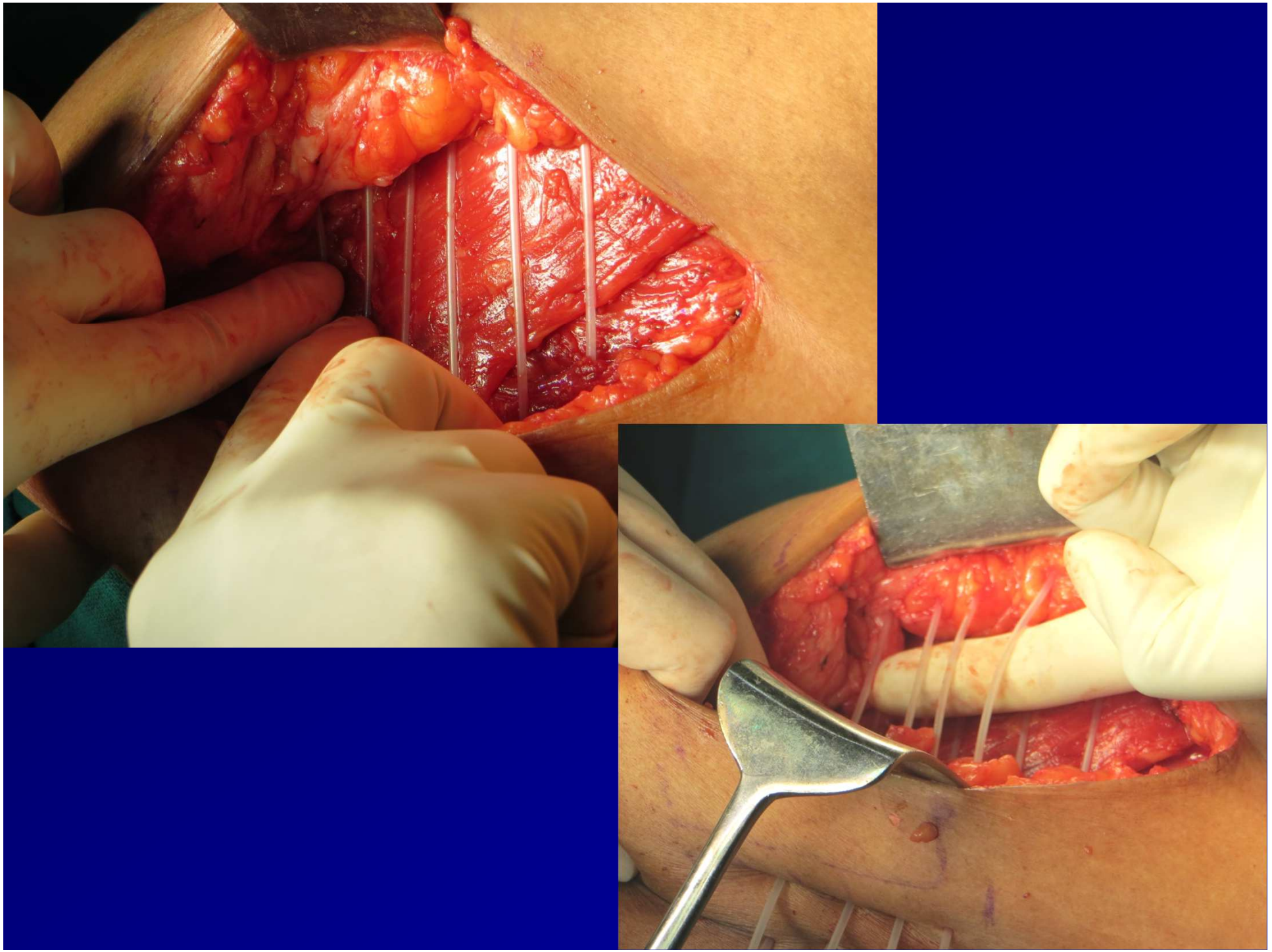
Interstitial Brachytherapy: Techniques

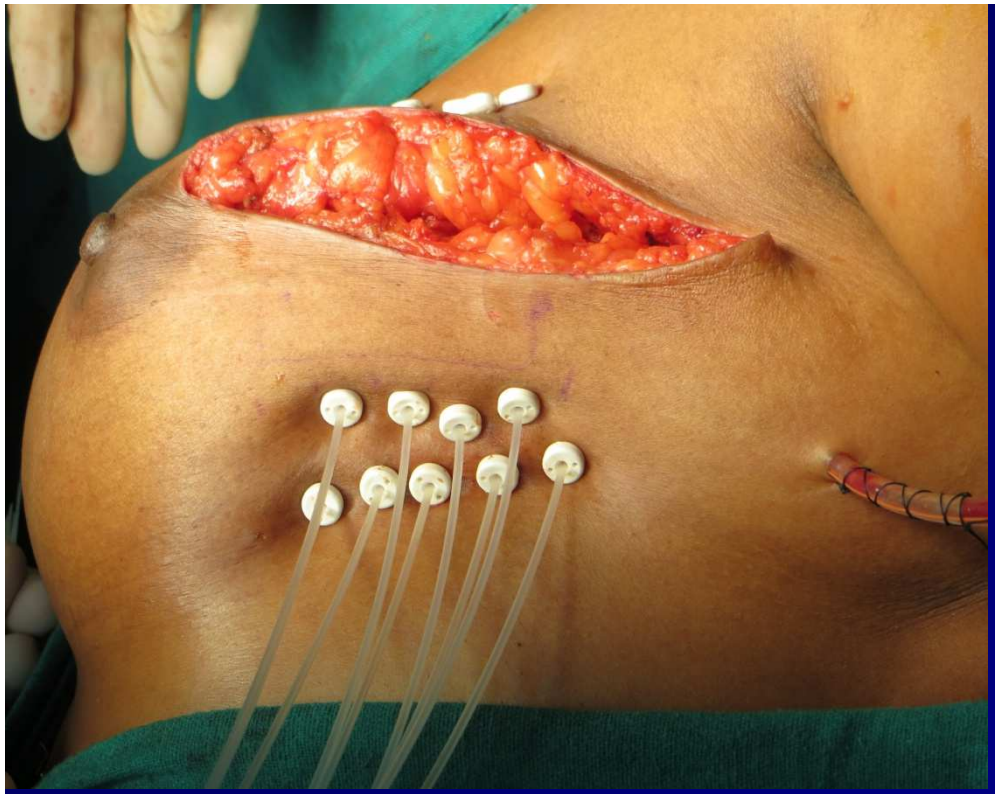


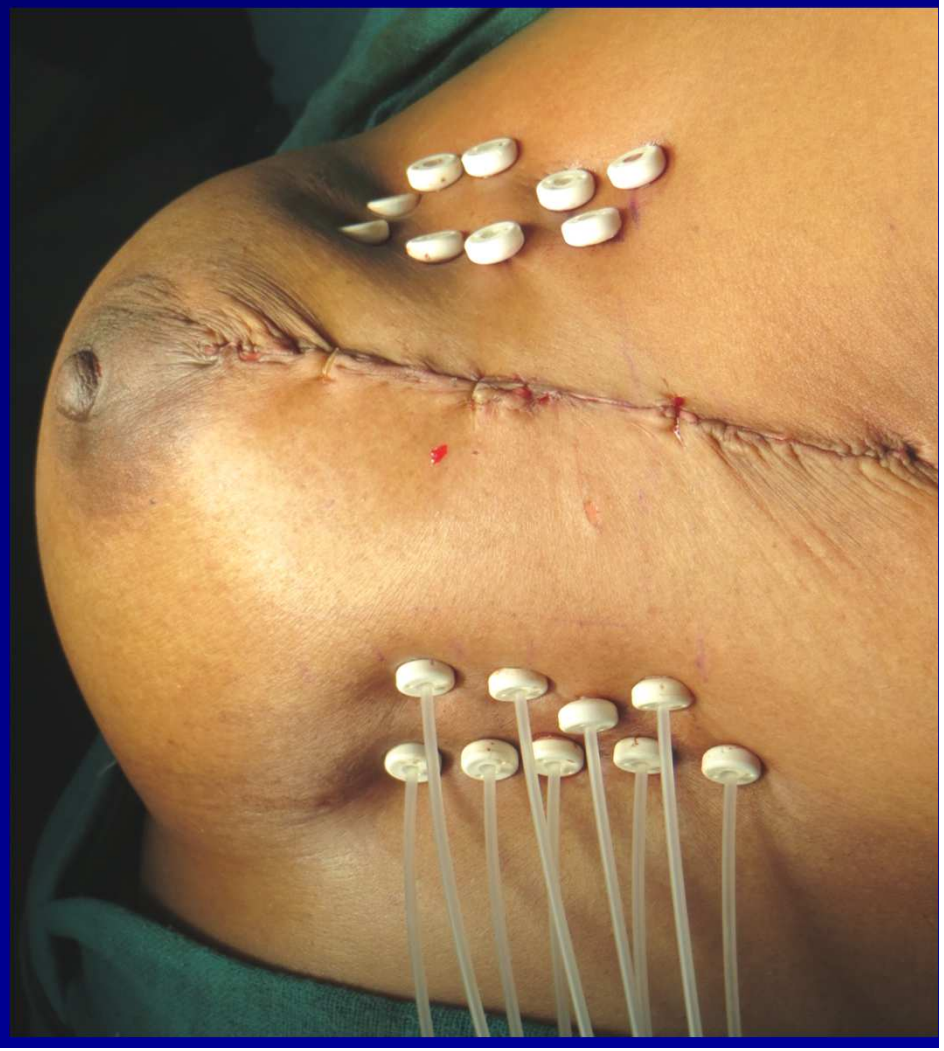
Peri-operative

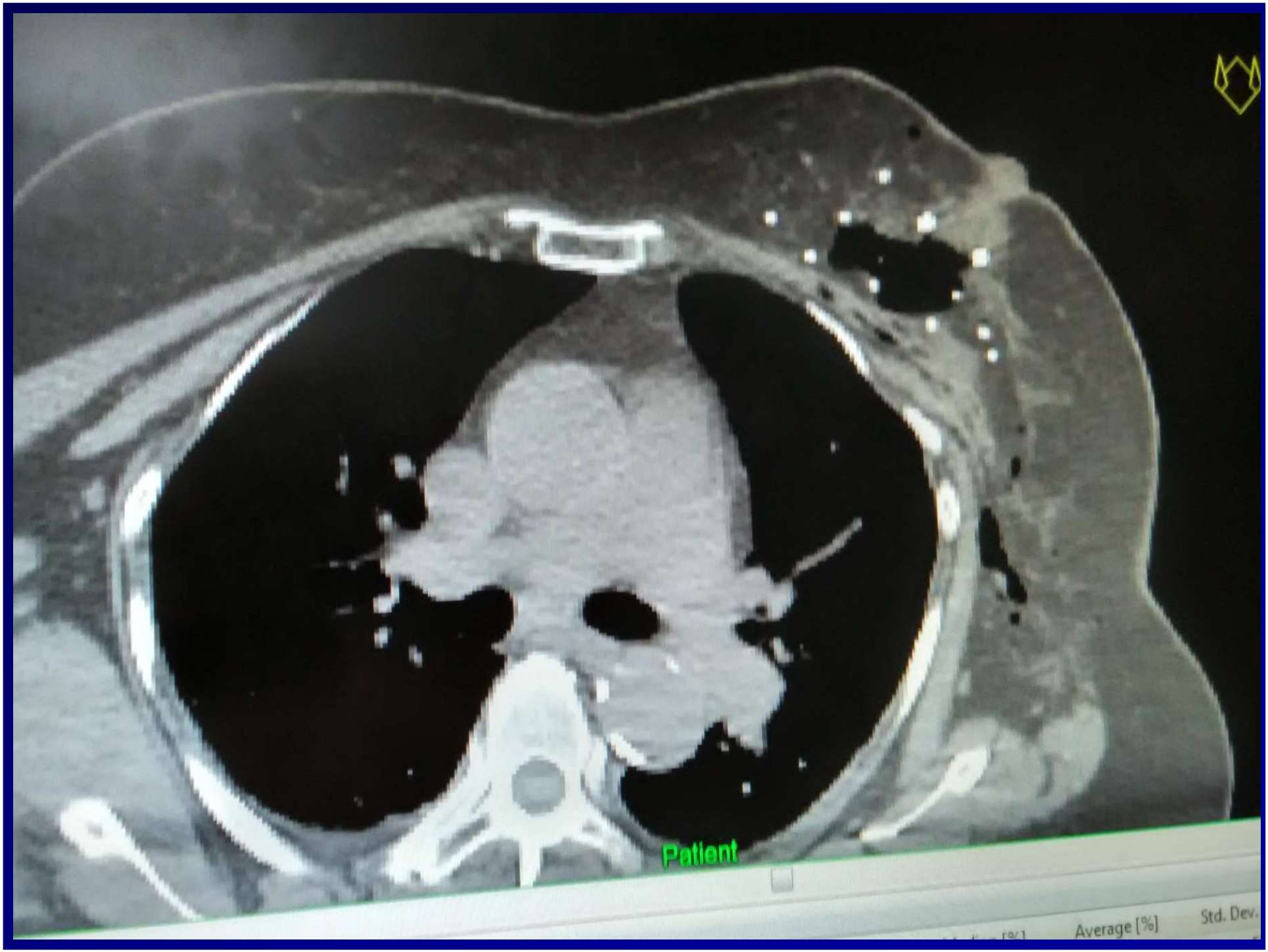


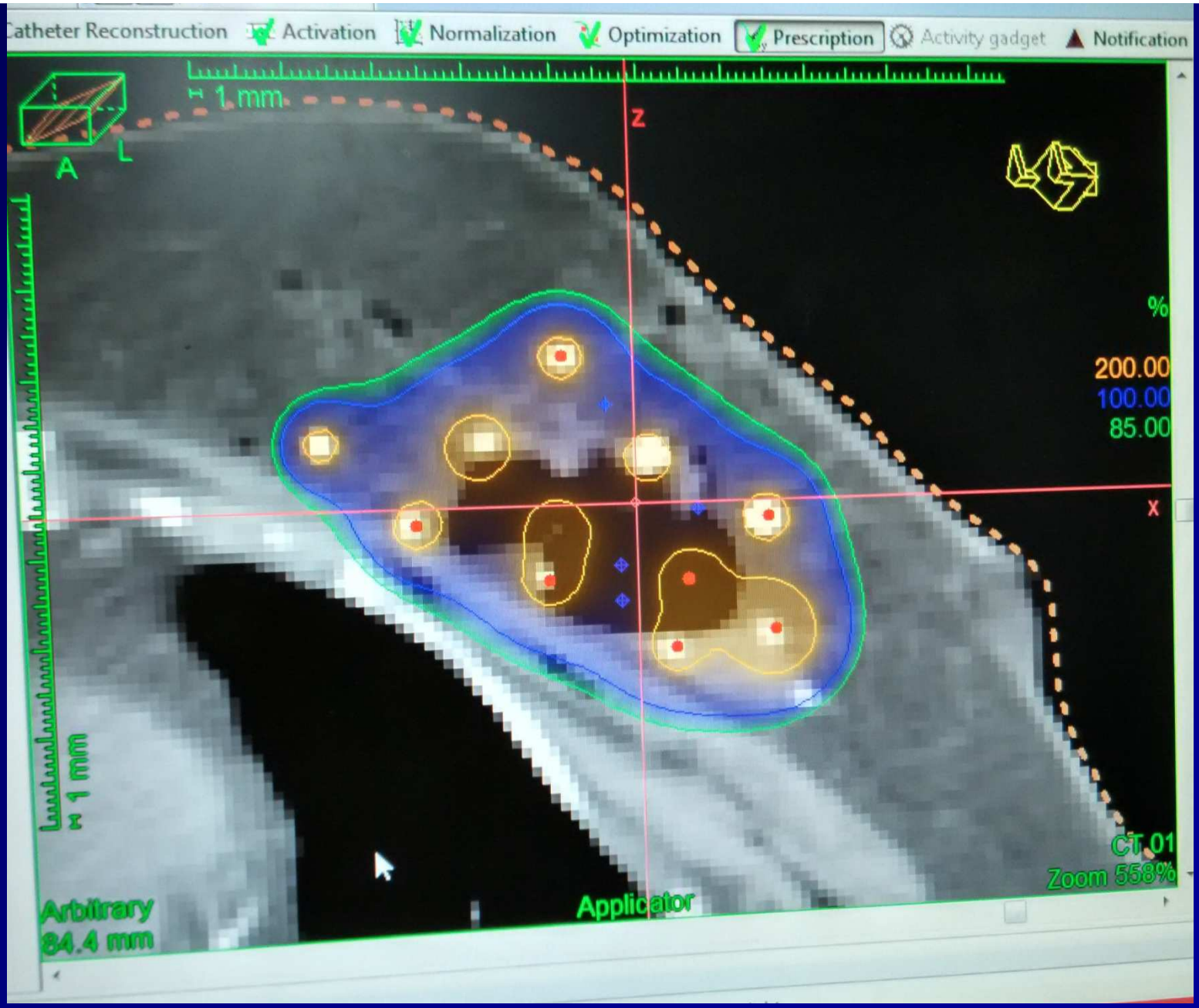
Post-operative








Patient
Average [%]
Std. Dev.


Catheter Reconstruction
Activation
Normalization
Optimization
Prescription
Activity gadget
Notification
H 1 mm
A
L
Z
X
%
200.00
100.00
85.00
H 1 mm
CT 01
Zoom 558%
Arbitrary
84.4 mm
Applicator

Results : Clinical outcome

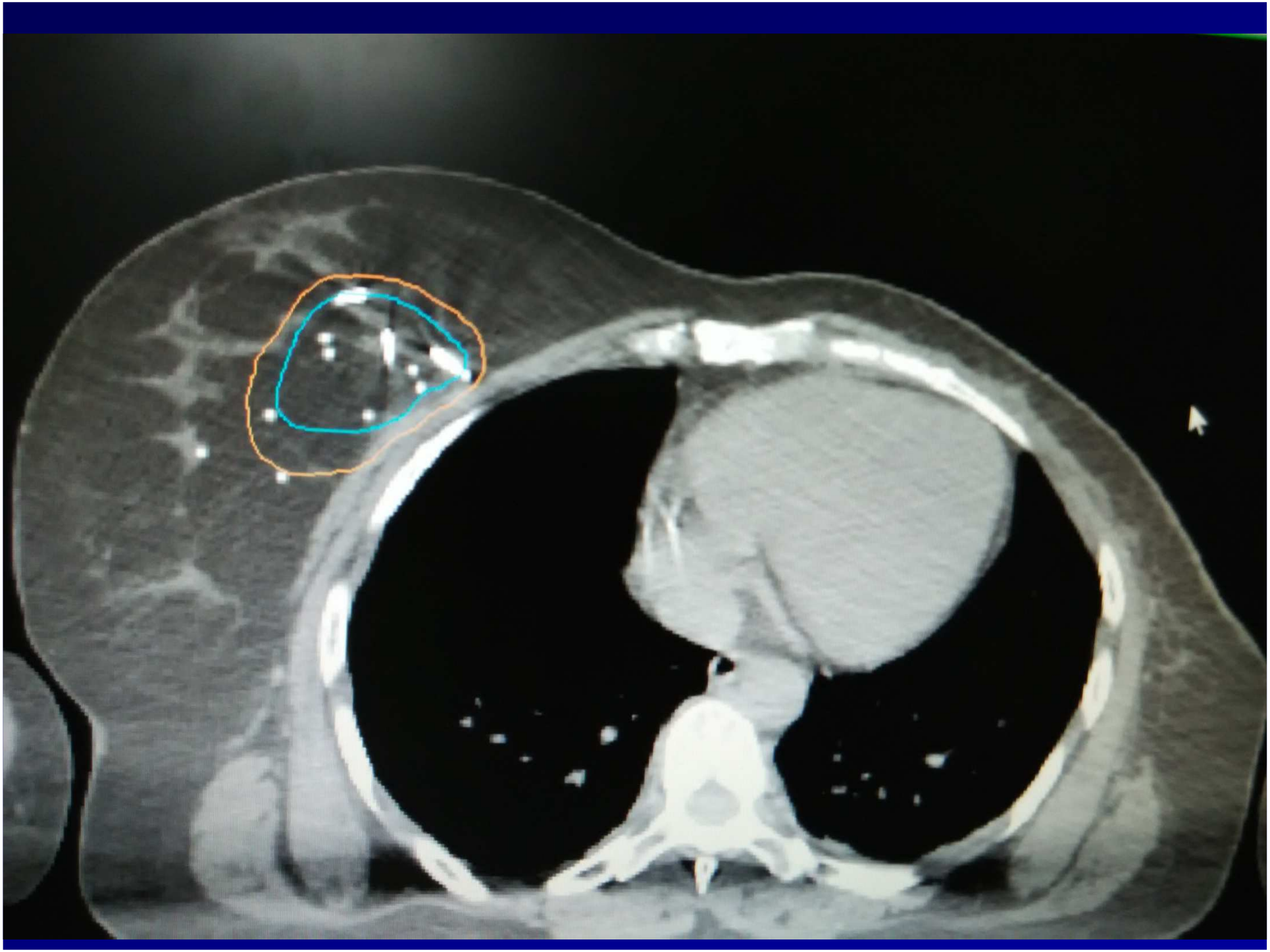
- Total no. of patients: 100
- Median follow up : 32 months (6-54)
- LR:0% ; LC 100%
- 5 Year OS: 86%, 5 Year DFS :77%

Tumori, 99: 650-656, 2013

Perioperative high-dose-rate interstitial brachytherapy boost for patients with early breast cancer

Daya Nand Sharma[1], SVS Deo[2], Goura Kisor Rath[1], Nootan Kumar Shukla[2], Sanjay Thulkar[3], Renu Madan[1], and Pramod Kumar Julka[1]

[1]Department of Radiation Oncology, [2]Surgical Oncology, and [3]Radiodiagnosis, All India Institute of Medical Sciences, New Delhi 110029 India



Cosmetic outcome

- Budrukkar et al. Clin Oncol 2007;19(8):596-603
- 1022 pts; 3 gps – LDR Brachy, HDR brachy; Electron
- 77% had good/excellent cosmesis
- Almost similar in 3 gps.

Tumor Bed Boost: Conclusion

- Tumor bed must be boosted in all BCT patients
- Except in >60 yrs of age
- Technique of boost RT: photon/Electron/brachy
- Brachy ideal for deep seated lesions
- Use of newer technique like SIBIMRT on the rise
- CT scan imaging for boost delineation
- Peri-operative brachy for Indian setup
- Boost dose: 16 Gy (EBRT); ~15 Gy (Brachy)