Role of Tumor Bed Boost in Breast Cancer
Evidence, Localization and Techniques

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All India Institute of Medical Sciences, New Delhi
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 $\rightarrow$ WBRT + Boost
- Locally advanced breast cancer
  - NACT $\rightarrow$ BCS $\rightarrow$ WBRT + Boost
- Inoperable LABC: WBRT + Boost
- Post mastectomy RT: Chest wall RT $\rightarrow$ Boost
Clinical Target Volume (CTV)

Lumpectomy cavity

66 Gy

50 Gy

5mm inside skin

1.5 cm expansion

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

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


CLINICAL INVESTIGATION

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 Colleete, 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
EORTC Trial 2001

RECURRENT 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

<table>
<thead>
<tr>
<th></th>
<th>Boost</th>
<th>No Boost</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>2657</td>
<td>2661</td>
</tr>
<tr>
<td>LR</td>
<td>4.3%</td>
<td>7.3%</td>
</tr>
<tr>
<td>LR in &lt;40yrs</td>
<td>10.2%</td>
<td>19.5%</td>
</tr>
<tr>
<td>5-yr Survival</td>
<td>87%</td>
<td>91%</td>
</tr>
<tr>
<td>Good cosmesis</td>
<td>71%</td>
<td>87%</td>
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</table>

*47% recurrences in tumor bed*
### 10-yr FU data (JCO 2007)

<table>
<thead>
<tr>
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<th>Boost</th>
<th>No Boost</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>2657</td>
<td>2661</td>
</tr>
<tr>
<td>LR</td>
<td>6.2%</td>
<td>10.2% (p&lt;.0001)</td>
</tr>
<tr>
<td>10-yr Survival</td>
<td>82%</td>
<td>82%</td>
</tr>
<tr>
<td>Severe fibrosis</td>
<td>4.4%</td>
<td>1.6% (p&lt;.0001)</td>
</tr>
</tbody>
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*47% recurrences in tumor bed*
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**

<table>
<thead>
<tr>
<th>Time (years)</th>
<th>No boost</th>
<th>Boost</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2657</td>
<td>2661</td>
</tr>
<tr>
<td>5</td>
<td>2332</td>
<td>2361</td>
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<tr>
<td>10</td>
<td>1878</td>
<td>1867</td>
</tr>
<tr>
<td>15</td>
<td>1331</td>
<td>1302</td>
</tr>
<tr>
<td>20</td>
<td>241</td>
<td>223</td>
</tr>
</tbody>
</table>

HR 1.05 (99% CI 0.92–1.19)
p=0.323
Figure 3: Ipsilateral breast tumour recurrence

Competing risks HR
HR 0.65 (99% CI 0.52-0.81)
P < 0.0001
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<0.001). The 20-year cumulative incidence of ipsilateral 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<0.001).

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%)
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
  - Images
- For multi catheter brachy: intra-operative, CT scan
- For balloon: with respect to the balloon surface
- New technique: PET scan
## Methods of Cavity Delineation

<table>
<thead>
<tr>
<th>Technique</th>
<th>Delineation</th>
<th>Experience</th>
<th>Availability</th>
<th>Cost effective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scar</td>
<td>poor</td>
<td>wide</td>
<td>easy</td>
<td>+++</td>
</tr>
<tr>
<td>USG</td>
<td>good</td>
<td>-</td>
<td>easy</td>
<td>+++</td>
</tr>
<tr>
<td>CT</td>
<td>excellent</td>
<td>emerging</td>
<td>easy</td>
<td>++</td>
</tr>
<tr>
<td>MRI</td>
<td>excellent</td>
<td>limited</td>
<td>sparse</td>
<td>+</td>
</tr>
<tr>
<td>PET</td>
<td>?</td>
<td>?</td>
<td>scanty</td>
<td>+/-</td>
</tr>
</tbody>
</table>
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

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: $\text{Y}^{90}$ (Eur J Nucl Med Mol Imaging (2010))
EBRT – 3DRT and IMRT
The influence of the boost technique on local control in breast conserving treatment in the EORTC ‘boost versus no boost’ randomised trial

<table>
<thead>
<tr>
<th>Technique</th>
<th>No. of pts</th>
<th>No. of Recurrences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electron</td>
<td>1635 (63%)</td>
<td>74 (4.8%)</td>
</tr>
<tr>
<td>Photon</td>
<td>753 (28%)</td>
<td>28 (4.0%)</td>
</tr>
<tr>
<td>Brachy</td>
<td>225 (9%)</td>
<td>6 (2.5%)</td>
</tr>
</tbody>
</table>
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*
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
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%


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

Daya Nand Sharma¹, SVS Deo², Goura Kisar Rath¹, Nootan Kumar Shukla², Sanjay Thukar³, Renu Madan¹, and Pramod Kumar Julka¹

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

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)