The Evolving Role of Radiotherapy in Treatment of Breast Cancer

Richard L. Crownover, M.D., Ph.D.
Professor and Residency Program Director
Department of Radiation Oncology
UT Health San Antonio MD Anderson Cancer Center
The Evolving Role of XRT in Treatment of Breast Cancer

• The Big Picture: Why XRT?
• Surface-Image Guidance
• Hypofractionation
• Accelerated Partial Breast
• Radiosurgery
• Stereotactic Body Radiotherapy
Why XRT?

70 Gy in 31 fractions

5 year result
Why BCT and Why Include Radiotherapy?

NSABP B-06

Figure 2. Disease-free Survival (Panel A), Distant-Disease-free Survival (Panel B), and Overall Survival (Panel C) among 596 Women Treated with Total Mastectomy, 83 Treated with Lumpectomy Alone, and 628 Treated with Lumpectomy plus Irradiation. In each panel, the P value above the curves is for the three-way comparison among the treatment groups; the P values below the curves are for the two-way comparisons between lumpectomy alone or with irradiation and total mastectomy.

Figure 1. Cumulative Incidence of a First Recurrence of Cancer in the Ipsilateral Breast during 20 Years of Follow-up among 570 Women Treated with Lumpectomy Alone and 567 Treated with Lumpectomy plus Breast Irradiation. The data are for women whose specimens had tumor-free margins.
Survival Benefit  Oxford Meta-Analysis

For every four LR prevented, one death is prevented at 15 years.
Conventional Tangent-Field XRT
Conventional Tangent-Field XRT (circa 1995)
Oxford Overview 1995: Breast Cancer and Overall Mortality

40 randomized trials; 20,000 women

Breast cancer deaths only

4.8% benefit

Non-breast-cancer deaths

4.3% detriment

Points out the importance of reducing toxicity
Radiation-Related Cardiac Impact

Fig 1. Survival curves according to laterality of breast cancer.

Fig 2. Time to occurrence of MI according to laterality of breast cancer.

Vallis et al., JCO 20(4): 1036-1042, 2002
Radiation-Related Cardiac Impact

Based on 300,000 US women with breast cancer (SEER data)
Relative Risk (95% confidence interval) for left versus right sided tumors

<table>
<thead>
<tr>
<th>Time</th>
<th>&lt; 10 years</th>
<th>10-14 years</th>
<th>≥ 15 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>1973 - 1982</td>
<td>1.2 (1.04-1.38)</td>
<td>1.52 (1.11-1.82)</td>
<td>1.58 (1.29-1.95)</td>
</tr>
<tr>
<td>1983 - 1992</td>
<td>1.0 (0.91-1.18)</td>
<td>1.27 (0.99-1.63)</td>
<td>NA</td>
</tr>
<tr>
<td>1993 - 2001</td>
<td>1.0 (0.82-1.12)</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

1 Gy increase in mean heart dose was associated with a 7% relative increase in cardiac events

Darby et. al. NEJM 368: 987-998, 2013
Techniques for Cardiac Avoidance
Deep-Inspiration Breath Hold
Changing Technology and Patient Experience

1995

2019
Deep Inspiration Breath Hold
Surface Monitoring of Breath Hold
DIBH Reduction in Cardiac Dose

<table>
<thead>
<tr>
<th></th>
<th>Free Breathing</th>
<th>DIBH</th>
<th>Ours</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Heart</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median</td>
<td>3.62 Gy</td>
<td>1.86 Gy</td>
<td>1.34 Gy</td>
</tr>
<tr>
<td>2 cm³</td>
<td>45.7 Gy</td>
<td>21.5 Gy</td>
<td></td>
</tr>
<tr>
<td>&gt; 42 Gy</td>
<td>17 pts</td>
<td>4 pts</td>
<td></td>
</tr>
<tr>
<td><strong>Ipsilateral Lung</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median</td>
<td>8.7 Gy</td>
<td>6.3 Gy</td>
<td></td>
</tr>
<tr>
<td>V\textsubscript{20}</td>
<td>17%</td>
<td>12%</td>
<td></td>
</tr>
</tbody>
</table>

Daily median treatment time was 9 minutes

Hepp et al, Strahlenther Onkol 191:710-716 2015
Risk adaptation of breast RT: high risk - simultaneous integrated breast boost (SIB)
RAPID Trial
Randomized Trial of Accelerated Partial Breast Irradiation using 3-Dimensional Conformal Radiotherapy (3D-CRT)


Ontario Clinical Oncology Group
In Breast Tumor Recurrence

<table>
<thead>
<tr>
<th>APBI –</th>
<th>WBI –</th>
</tr>
</thead>
<tbody>
<tr>
<td>37 events</td>
<td>28 events</td>
</tr>
<tr>
<td>HR=1.27 (90%CI, 0.84-1.91)</td>
<td></td>
</tr>
</tbody>
</table>

Years Since Randomization

- 0% - 1% - 2% - 3% - 4% - 5% - 6% - 7% - 8% - 9%
Radiation Toxicity ≥ Grade 2

**Acute**
- Grade 2: 26%
- Grade 3: 44%

**Late**
- Grade 2: 28%
- Grade 3: 12%
Cosmetic Rating (Nurse) by Treatment and Time

**APBI**

<table>
<thead>
<tr>
<th></th>
<th>Fair/Poor</th>
<th>Excellent/Good</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base 81%</td>
<td>17%</td>
<td>81%</td>
</tr>
<tr>
<td>3 Year 71%</td>
<td>17%</td>
<td>83%</td>
</tr>
<tr>
<td>5 Year 68%</td>
<td>16%</td>
<td>84%</td>
</tr>
<tr>
<td>7 Year 64%</td>
<td>19%</td>
<td>81%</td>
</tr>
</tbody>
</table>

**WBI**

<table>
<thead>
<tr>
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<th>Excellent/Good</th>
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<tr>
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<tr>
<td>3 Year 17%</td>
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<td>84%</td>
<td></td>
</tr>
<tr>
<td>7 Year 19%</td>
<td>81%</td>
<td></td>
</tr>
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</table>

* p < 0.001
Cosmetic Rating (Patient) by Treatment and Time

**APBI**
- Base: 76% Fair/Poor, 24% Excellent/Good
- 3 Year: 74% Fair/Poor, 26% Excellent/Good
- 5 Year: 70% Fair/Poor, 30% Excellent/Good
- 7 Year: 69% Fair/Poor, 31% Excellent/Good

**WBI**
- Base: 79% Fair/Poor, 21% Excellent/Good
- 3 Year: 82% Fair/Poor, 18% Excellent/Good
- 5 Year: 82% Fair/Poor, 18% Excellent/Good
- 7 Year: 85% Fair/Poor, 15% Excellent/Good

* p < 0.001
Brachytherapy for Breast Cancer
Primary Results of NSABP B-39
A Randomized Phase III Study of
Conventional WBRT vs. PBI
for Women with Stage 0, I, or II Breast Cancer

F Vicini (NSABP PI), R Cecchini, J White (RTOG PI), T Julian, D Arthur,
R Rabinovitch, R Kuske, D Parda, P Ganz, M Scheier, K Winter, S Paik, H Kuerer,
L Vallow, L Pierce, E Mamounas, J Costantino, H Bear, I Germain,
G Gustafson, L Grossheim, L Petersen, R Hudes, W Curran, N Wolmark
NSABP B-39/RTOG 0413 Schema

STRATIFICATION
- Disease Stage (DCIS; Invasive N0; Invasive N1)
- Menopausal Status (pre- and post-)
- Hormone Receptor Status (ER and/or PR+; ER and PR-)
- Intention to Receive Chemotherapy

RANDOMIZED

Whole Breast Irradiation after Adjuvant Chemotherapy
- 50 Gy (2.0 Gy/fraction) or 50.4 Gy (1.8 Gy/fraction) to whole breast, followed by optional boost to ≥ 60 Gy

Partial Breast Irradiation prior to Adjuvant Chemotherapy
- For a total of 10 treatments given on 5 days over 5 to 10 days:
  - 34 Gy in 3.4 Gy fractions Interstitial Brachytherapy or Mammosite Balloon Catheter
  - or 38.5 Gy in 3.85 Gy fractions
  - 3D Conformal External Beam

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Ipsilateral Breast Tumor Recurrence (IBTR)

Hazard Ratio and 90% CI for IBTR

WBI Inferior

Equivalence Margin for IBTR

PBI Inferior

0.94 1.22 1.58

0 0.2 0.4 0.6 0.8 1 1.2 1.4 1.6 1.8 2
Cumulative Incidence per 100 Months Since Randomization

Absolute difference in 10-yr rate of IBTR between PBI and WBI was 0.7%
## In-Breast Tumor Recurrence by PBI Method

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th># of Pts</th>
<th># of Events</th>
<th>Hazard Ratio (HR)</th>
<th>HR 95% Confidential Interval</th>
<th>10-yr Cum Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBI</td>
<td>2,011</td>
<td>67</td>
<td>REF</td>
<td></td>
<td>3.8%</td>
</tr>
<tr>
<td>PBI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi-catheter brachytherapy</td>
<td>130</td>
<td>9</td>
<td>2.21</td>
<td>1.10 – 4.46</td>
<td>7.7%</td>
</tr>
<tr>
<td>Single-entry brachytherapy device</td>
<td>358</td>
<td>24</td>
<td>2.15</td>
<td>1.34 – 3.44</td>
<td>7.8%</td>
</tr>
<tr>
<td>3DCRT (external beam)</td>
<td>1,535</td>
<td>55</td>
<td>1.04</td>
<td>0.73 – 1.49</td>
<td>3.7%</td>
</tr>
</tbody>
</table>
Shrinking Indications for Whole Brain Radiotherapy

- Patient with Limited Life Expectancy, < 3 months*
- Patient with Very Poor Performance Status, KPS < 70*
- Patient with a Very Large Number of Lesions
- Patient with High “Metastatic Velocity”

*Exception may be pt with new diagnosis who has never received effective systemic therapy
Multiple Metastases: BrainLab Elements
Spine SBRT: Novalis Elements
Spine SBRT: Novalis Elements
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- The Big Picture: Why XRT?
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