Whole Breast Radiation Is The Standard of Care For Breast Cancer Treatment

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History of Breast Cancer Treatment

- **Radical Mastectomy:**
  - Prior to 1894 treatment was wide local excision with high local recurrence rates (LRR).
  - W. Halsted developed in 1894.
  - *Included:* Excision of breast tissue, skin, pectoralis major and minor and level I, II, and III axillary nodes.
  - Significant decrease in LRR and became standard of care.
  - 57% of patients died of breast cancer (BC).
- **Modified Radical Mastectomy (MRM):**
  - Varying procedures:
    - Simple Mastectomy
    - Skin-sparing Mastectomy
  - *Included:* Excision of breast tissue, underlying fascia of pectoralis major muscle, and level I and II axillary nodes.
  - Equivalent survival rates with MRM vs. RM.
History of Breast Cancer Treatment

- Simple Mastectomy:

- Skin-Sparing Mastectomy:

- Modified Radical Mastectomy:
History of Breast Cancer Treatment

• **Breast Conserving Surgery (BCT):**
  – *Definition:* excision of breast tissue including the tumor and a margin of healthy tissues.
  – *Goals:* survival equivalent of mastectomy with cosmetically acceptable breast.
  – *NSABP B-06* showed that patients with Stage I and II BC who had lumpectomy with axillary dissection and irradiation was equivalent to individuals who had MRM.
    • Overall survival (OS) and disease free survival (DFS) were equivalent at 5, 8, 12 and 20 year follow up.
    • Local recurrence risk (LRR) was less in the irradiated breast after lumpectomy (14%) vs. lumpectomy alone (39%) at 20 years.
    • Better cosmetic outcomes.
What is Whole Breast Radiation

• **Technique:**
  – Radiation delivered to breast (s/p BCT) or chest wall (s/p MRM).
  – Borders of the radiation field:
    • *Medial* – midline of the patient (middle of the sternum)
    • *Lateral* – 2cm beyond breast tissue (mid-axillary line)
    • *Inferior* – 2cm below the breast (inframammary fold)
    • *Superior* – above all palpable tissue or the base of the head of the clavicle.

• **Dosage:**
  – Total of 45 to 50 Gy
    • *Fractionated*: 1.8-2.0 Gy/day x 5 weeks (5 days a week).
  – Boost: 10-18 Gy to the tumor bed.
    • 10 Gy for negative margins.
    • 18 Gy for close or positive margins.
    • Controversial but several studies show decreased LRR.
What is Whole Breast Radiation

- **Planning:**
  - *Immobilization* of the patient.
  - *Simulation:* CT scanner used to visualize the chest wall, breast contour, lung and cardiac border.
  - *Planning:* The area to receive radiation is identified and borders created to allow appropriate and reproducible radiation fields.
  - New equipment allows for minimizing radiation to heart and lungs.

- **Timing of RT used in BC treatment regimen:**
  - Neoadjunctive chemotherapy → excision of the primary tumor → WBI started 3 weeks after surgery.
  - Excision of tumor → adjunctive chemotherapy → WBI started after chemotherapy.
Who Receives Whole Breast Radiation

**Who receives WBI:**
- After mastectomy (chest wall irradiation):
  - Tumor size > 5cm; invasion of skin, pectoralis muscle or chest wall.
  - Tumors < 5cm and with > 4 positive axillary lymph nodes.
  - Unclear recommendations: Tumors < 5cm and with 1-3 positive axillary lymph nodes.
- After BCT (irradiation of conserved breast):
  - All BCT patients receive WBI.

**Who receives additional axillary, supraclavicular and internal mammary LN irradiation:**
- 4 positive lymph nodes.
- Invasive tumors that did not receive axillary dissection.
- *Internal mammary nodes*: controversial but in individual with medially located tumors > 5cm or in patients with 4 > nodes.
Who Receives Whole Breast Radiation

• **Contraindications to RT:**
  – Pregnancy (absolute contraindication).
  – Prior RT to breast.
    • Combined RT is an excessive dose to the chest wall, e.g., in Hodgkin disease with previous mantle radiation.
  – Connective Tissue disease:
    • Scleroderma
    • Lupus
    • RA
Advantages of Whole Breast Radiation

- **WBI decreases the risk of local recurrence:**
  - 2/3 reduction in LRR regardless of type of surgery.
  - WBI eradicates subclinical deposits of tumor not removed in BCT.
  - Decreasing LRR has a direct effect on survival benefits.
    - Older studies found no differences in survival w/ WBI vs. no RT.
    - Attributed to increased morbidity and mortality associated with WBI.
    - New WBI techniques are being used with increased survival rates.
  - NSABP B-06 trial showed 14% LRR in patients with BCT and RT vs. 39% in patients with BCT alone over 20 year period.
Advantages of Whole Breast Radiation

- WBI decreases the LRR con’t.: 

<table>
<thead>
<tr>
<th>Trials</th>
<th>Local Recurrence Risk</th>
<th></th>
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<th>Reduction in LRR w/ WBI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Population</td>
<td>No WBI</td>
<td>WBI</td>
<td></td>
</tr>
<tr>
<td>NSABP B-06</td>
<td>Lumpectomy</td>
<td>39%</td>
<td>14%</td>
<td>25%</td>
</tr>
<tr>
<td>EBCTCG 1995 Study</td>
<td>BCT w/ node pos.</td>
<td>20%</td>
<td>7%</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td>MRM w/ node pos.</td>
<td>26%</td>
<td>7%</td>
<td>19%</td>
</tr>
<tr>
<td>EBCTCG 2005 Study</td>
<td>BCT w/ node pos.</td>
<td>23%</td>
<td>6%</td>
<td>17%</td>
</tr>
<tr>
<td></td>
<td>MRM w/ node neg.</td>
<td>6%</td>
<td>2%</td>
<td>4%</td>
</tr>
</tbody>
</table>
Advantages of Whole Breast Radiation

- **Improves survival:**
  - Older studies found no difference in overall survival with WBI.
  - New studies have found improved overall survival.
  - Secondary to improved RT techniques.
  - Premenopausal DBCCGT showed:
    - N = 1708, Stage II or III.
    - Chemo = cyclophosphamide, methotrexate and fluorouracil (CMF).
    - WBI = irradiation to the chest wall, supra and infraclavicular, axillary and IM LNs.

<table>
<thead>
<tr>
<th>10 Year Follow-up Results</th>
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<tbody>
<tr>
<td><strong>TM w/ AND, chemo</strong></td>
</tr>
<tr>
<td>w/ WBI</td>
</tr>
<tr>
<td>w/o WBI</td>
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Advantages of Whole Breast Radiation

- **Improves survival con’t:**
  - New studies have found improved overall survival con’t.
  - Postmenopausal DBCCGT showed:
    - N = 1375, Stage II or III.
    - Tamoxifen without chemotherapy.
    - WBI = irradiation to the chest wall, supra and infraclavicular, axillary and IM LNs.

### 10 Year Follow-up Results

<table>
<thead>
<tr>
<th></th>
<th>LRR</th>
<th>DFS</th>
<th>OS</th>
</tr>
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<tbody>
<tr>
<td>TM w/ AND, tamoxifen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>w/ WBI</td>
<td>8%</td>
<td>36%</td>
<td>45%</td>
</tr>
<tr>
<td>w/o WBI</td>
<td>35%</td>
<td>24%</td>
<td>36%</td>
</tr>
</tbody>
</table>
Advantages of Whole Breast Radiation

• **Improves survival con’t:**
  – New studies have found improved overall survival con’t.
  • The British Columbia Trial showed:
    – N = 318, premenopausal, Stage I or II.
    – Chemo = CMF.
    – WBI = irradiation to the chest wall, supra and infraclavicular, axillary and IM LNs.
      » Total radiation dose = 37.5 Gy
    – At 15 years the OS was not effected by WBI but at 20 years OS was significantly effected.

<table>
<thead>
<tr>
<th>20 Year Follow-up Results</th>
<th>LRR</th>
<th>DFS</th>
<th>OS</th>
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<tbody>
<tr>
<td>MRM w/ AND, chemo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>w/ WBI</td>
<td>7%</td>
<td>48%</td>
<td>47%</td>
</tr>
<tr>
<td>w/o WBI</td>
<td>18%</td>
<td>31%</td>
<td>37%</td>
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</tbody>
</table>
Advantages of Whole Breast Radiation

• **Improves survival con’t:**
  - New studies have found improved overall survival con’t.
  - EBCTCG 2005 study showed:
    - Meta-analyses of 78 randomized trials from 1995 to 2000.
      » 10 trials with N=7311 for BCT w/ and w/o RT to the conserved breast.
      » 25 trials with N=9933 for mastectomy w/ and w/o RT.
    - 70% reduction in local recurrence after BCT with WBI.
    - ¾ of local recurrence occurs during the first 5 years.
Advantages of Whole Breast Radiation

- **Improves survival con’t:**
  - New studies have found improved overall survival con’t.
  - EBCTCG 2005 study showed:

<table>
<thead>
<tr>
<th>Population</th>
<th>LRR</th>
<th>Mortality from BC</th>
<th>Reduction in Mortality w/ RT</th>
<th>Overall Mortality</th>
<th>Reduction in mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCT w/o WBI</td>
<td>26%</td>
<td>35.9%</td>
<td>NA</td>
<td>40.5%</td>
<td>NA</td>
</tr>
<tr>
<td>BCT w/ WBI</td>
<td>7%</td>
<td>30.5%</td>
<td>5.4%</td>
<td>35%</td>
<td>5.3%</td>
</tr>
<tr>
<td>MRM w/o WBI</td>
<td>23%</td>
<td>60.1%</td>
<td>NA</td>
<td>64.2%</td>
<td>NA</td>
</tr>
<tr>
<td>MRM w/ WBI</td>
<td>6%</td>
<td>54.7%</td>
<td>5.4%</td>
<td>59.8%</td>
<td>4.4%</td>
</tr>
</tbody>
</table>
Is Radiation Therapy Necessary?

- **Who is at low enough risk to eliminate RT?**
  - Populations with lower recurrence rates:
    - More extensive surgery.
    - Older women.
    - Lack of family history.
  - Multiple studies have attempted to identify a population who does not require RT however, there is a significant reduction in LRR with the use of RT in all populations.

- **Even with adjuvant systemic therapy, e.g. tamoxifen or chemotherapy, RT reduces the rate of recurrence.**

- **WBI therapy is recommended as the standard of care for women with BC.**
Side Effects of Whole Breast Irradiation

• Morbidity and Mortality associated with RT has decreased as the technology has improved.

• **Short-term Side Effects:**
  – Skin changes
  – Fatigue (most common during treatment)

• **Long-term Side Effects:**
  – Vascular injury
    • Causing cardiac morbidity and increased mortality in older studies.
    • The DBCCGT showed that there was no difference in cardiac mortality or morbidity in patients receiving WBI.
  – Rib Fractures (1.8%)
  – Arm lymphedema (most common)
Side Effects of Whole Breast Irradiation

• **Long-term Side Effects con’t:**
  – Brachial plexopathy (14%)
  – Radiation pneumonitis (1-5%)
  – Secondary malignancies – sarcomas (<1%), ANLL (1-3%)
  – Contralateral breast cancer
Whole Breast vs. Partial Breast Irradiation

• WBI is the *STANDARD OF CARE*!!
• No long term randomized trials using PBI as RT.
• Studies to date have used patients with small tumors, wide negative margins.
• Studies of PBI have shown 2/3 of recurrence outside the areas of PBI.
• Residual disease has been identified in 41% of mastectomy specimens > 2cm from the initial tumor.
  – WBI eradicates these subclinical deposits.
Summary

- WBI is administered for local BC control and decreases the risk of local recurrence.
- WBI has a strong effect on systemic disease with increased overall survival.
- Chemotherapy alone does not prevent local and systemic recurrences.
- The combination of surgical removal, chemotherapy and radiation therapy are required to give the best chance of survival for individuals with breast cancer.
The Future

- PBI needs further studies to prove the long term outcomes are comparable to the current WBI.
- PBI may decreased side effects from RT.
- PBI may be easier to administer over shorter periods of time and be associated with decreased cost.
References:

References:

- Pierce, L. Techniques and complication of breast and chest wall irradiation for early stage breast cancer. Up to Date. Latest update June 29, 2006.