Management of Postmenopausal Women with T1 ER+ Tumors: Options and Tradeoffs

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Case Study

- 59 yo woman with new palpable mass
- Diagnostic imaging reveals 1.4cm mass
- Undergoes core bx
- ER+,PR+,Her2-, Ki-67 10% Grade 2 IDC
- Clinically node negative
- No other risk factors

Surgery

- Lumpectomy +/- radiation
- Mastectomy w/immediate reconstruction
- Sentinel lymph node biopsy

Lumpectomy and Radiation

- Early Breast Cancer Trialists’ Collaborative Group
- Are there patients that might do well with less?
  - Hypofractionation
  - IORT
  - No radiation

Lancet 2011
Shared Decision Making

- Preference
- Risk assessment
- Convenience
- Tradeoff

Hypofractionation
3-week course

- Standard whole breast radiation
  - 50 Gy total over 25 fractions (5 weeks)
- Hypofractionation (3 week schedule)
  - 40 Gy total of 15 fractions (START B)
  - 42.5 Gy total 16 fractions (Canadian Trial)

START B

- Median age 57
- 64% had tumors <2cm
- 23% Node positive
- 75% Grade I or II
- 43% received a tumor-bed boost

Cumulative risk of local-regional tumor relapse
Treatment effect was not different irrespective of age, axillary node status, grade chemotherapy use or tumor bed boost.

Canadian Trial
- 75% over the age of 50
- 80% had tumors <2cm
- All node negative
- 80% Grade I or II
- No tumor-bed boost

Patient is >50 years old at diagnosis
- Pathologic stage T1-2 N0 and treatment was BCS
- Patient has not been treated with systemic chemotherapy*
- Dose requirements at central axis (min 93%, max 107%)
Partial Breast Irradiation

Site of LR after BCS

<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>% in index q.</th>
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<tbody>
<tr>
<td>Clark RM, 1982</td>
<td>680</td>
<td>96%</td>
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<tr>
<td>Schnidt SJ, 1984</td>
<td>231</td>
<td>83%</td>
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<tr>
<td>Boyages J, 1990</td>
<td>783</td>
<td>81%</td>
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<tr>
<td>Kurtz, JM, 1990</td>
<td>1593</td>
<td>86%</td>
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<tr>
<td>Fisher B, 1992</td>
<td>1843</td>
<td>100%</td>
</tr>
<tr>
<td>Veronesi U, 1993</td>
<td>570</td>
<td>90%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>5770</td>
<td>91%</td>
</tr>
</tbody>
</table>

Methods for Partial Breast Irradiation

- 3D Conformal
- Multicatheter Interstitial
- Balloon Catheter (Mammosite, SAVI)
- Intraoperative Radiation

3D Conformal Radiation

- Linear accelerator
- More “normal” breast tissue irradiated
- Identifying target can be difficult
- Concern for toxicity with high dose
Interstitial Radiation

- CT simulation
- Lumpectomy cavity identified
- Insertion of needles followed by catheters

Balloon Catheter

- Await final pathology following lumpectomy
- Balloon placed in office setting

Intraoperative Radiation

- Given at time of lumpectomy or at second surgery
- Can also be used as boost

ASTRO Guidelines
ASTRO “Suitable Group”

Factor | ALL of the following must be present
--- | ---
Age | \[\geq 60\] years
Tumour size | \[\leq 2\] cm
Margins | Negative by at least 2mm
ER status | Positive
Multicentricity | Single tumor
Histology | Invasive Ductal/favorable subtype
Extensive Intraductal Component (>25% DCIS) | Absent
Lymphovascular invasion | Absent
Lymph nodes | Node Negative

ASTRO “Cautionary Group”

Factor | All patients who do not fall into Suitable or Unsuitable groups
--- | ---
Age | 50-59 years
Tumour size | 2.1 – 3cm
Margins | Close \(< 2\) mm
ER status | Negative
Multicentricity | Clinically Unifocal
Histology | Invasive Lobular
Extensive Intraductal Component (>25% DCIS) | Absent
Lymphovascular invasion | Limited or Focal
Lymph nodes | 

ASTRO “Unsuitable Group”

Factor | Any of the following must be present
--- | ---
Age | \(<50\) years
Tumour size | \(> 3\) cm
Margins | Positive
ER status | Negative
Multicentricity | More than 1 tumour
Histology | Invasive Lobular
Extensive Intraductal Component (>25% DCIS) | Present
Lymphovascular invasion | Extensive
Lymph nodes | Positive

Shared Decision Making

_workflow: Are patients willing to accept additional risk for convenience or quality of life_
Patient Preference
for choosing intra-operative or external-beam radiotherapy following breast conservation


Options A & B

Option A
The standard method of receiving radiation therapy

Option B
A new way of receiving radiation developed in the last few years.

The next few slides will show you some information comparing:

Option A or Option B?

The following slides will ask you to choose between Options A & B based on what you have learned so far and also based on different rates of local recurrence 10 years after diagnosis.

Preference

Additional Accepted Risk of Local Recurrence to Receive Intraoperative Radiation

Additional 10-year local recurrence risk (%)

# of Subjects

90% choose IORT
66% accept additional risk
Median risk accepted 2.5%
Partial Breast Data

Mammosite Registry 5yr

- Median Age 65
- Median T =1cm
- N0 = 83%
- 5% chemo

IORT TARGIT 5yr Data

- 80% >50yo
- 80% T1
- 90% Grade I,II

ELIOT IORT 5yr Data

- Higher Risk
- 21% N1
- 23% Grade 3
- 41% Ki67 >20%
Lumpectomy Alone

636 Patients Randomized

<table>
<thead>
<tr>
<th>Total treated</th>
<th>RT + Tam n=317</th>
<th>Tam alone n=319</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;75</td>
<td>176 56%</td>
<td>172 54%</td>
</tr>
<tr>
<td>ER+</td>
<td>308 97%</td>
<td>310 97%</td>
</tr>
<tr>
<td>Size &lt; 2cm</td>
<td>295 93%</td>
<td>296 93%</td>
</tr>
<tr>
<td>No ax dissect</td>
<td>200 63%</td>
<td>203 64%</td>
</tr>
</tbody>
</table>

- Median follow-up 12.6 yrs
- Local recurrence 9% vs. 2%
- No survival difference
**Outcome after recurrence**

- **BCS XRT** → IBTR 6 → **Salvage mastectomy**
- **BCS alone** → IBTR 27 → **Re-BCS XRT**

Hughes et al., 2013

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**Results**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Tam + RT</th>
<th>Tam alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast rec</td>
<td>6 (2%)</td>
<td>27 (9%)</td>
</tr>
<tr>
<td>Ultimate mastectomy</td>
<td>4 (2%)</td>
<td>10 (4%)</td>
</tr>
<tr>
<td>Second primary</td>
<td>36 (12%)</td>
<td>33 (9%)</td>
</tr>
<tr>
<td>Distant Met</td>
<td>21 (5%)</td>
<td>15 (5%)</td>
</tr>
<tr>
<td>Death</td>
<td>157 (33%)</td>
<td>166 (33%)</td>
</tr>
<tr>
<td>Death other causes</td>
<td>145</td>
<td>148</td>
</tr>
<tr>
<td>Death breast cancer</td>
<td>12</td>
<td>8</td>
</tr>
</tbody>
</table>

No statistical difference for any outcome

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**Post-menopausal women with luminal A subtype might not require breast radiotherapy**

- 304 tumors were subtyped (total in study 769)
- Lum A, Lum B, Her2, Basal-like
- Median follow-up 10yrs
- LR for radiation group 5%, no radiation 13.8%
- Lum A (n=133)
  - Tam alone LR = 8%
  - Tam + XRT LR = 4.6%

Wei et al., ASCO Presentation 2012
Axillary surgery

ACOSOG Z0011

Randomized trial of axillary node dissection in women with clinical T1-2 N0 M0 breast cancer who have a positive SN

165 investigators, 177 institutions, patients accrued from 5/99-12/04

ACOSOG Z0011 Inclusion Criteria

Eligibility

- Clinical T1 T2 N0 breast cancer, age >18
- H&E-detected metastases in SN (AJCC 5th edition)
- Lumpectomy with whole breast irradiation
- Adjuvant systemic therapy by choice

Ineligibility

- Third field (nodal irradiation)
- Metastases in SN detected by IHC
- Matted nodes
- 3 or more involved SN

ACOSOG Z0011 Patient and Tumor Characteristics

<table>
<thead>
<tr>
<th></th>
<th>ALND (n=420)</th>
<th>SLNB only (n=436)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>56 (24-92)</td>
<td>54 (25-90)</td>
</tr>
<tr>
<td>Clinical Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>68%</td>
<td>71%</td>
</tr>
<tr>
<td>T2</td>
<td>32%</td>
<td>29%</td>
</tr>
<tr>
<td>ER(+)</td>
<td>83%</td>
<td>83%</td>
</tr>
<tr>
<td>PR(+)</td>
<td>68%</td>
<td>70%</td>
</tr>
<tr>
<td>LVI(+)</td>
<td>41%</td>
<td>35%</td>
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</table>

Giuliano A et al, ASCO 2010; JAMA 2011
**ACOSOG Z0011**

- 58% of both groups had chemotherapy; 46% of both groups had hormonal therapy.
- 96% of ALND group and 97% of SLND group had at least one mode of systemic therapy.

**Summary**

- Axillary recurrence was low—2 in ALND group and 4 in SLND group.
- No significant difference between groups in OS and DFS between groups.
- Only age, ER and use of adjuvant systemic therapy were associated with OS and DFS.
- Type of operation was not associated with outcome.

**ACOSOG Z0011: Locoregional Recurrences**

<table>
<thead>
<tr>
<th>Recurrence Type</th>
<th>ALND (n=420)</th>
<th>SLND (n=436)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local</td>
<td>15 (3.6%)</td>
<td>8 (1.8%)</td>
</tr>
<tr>
<td>Regional</td>
<td>2 (0.5%)</td>
<td>4 (0.9%)</td>
</tr>
<tr>
<td>Total Locoregional</td>
<td>17 (4.1%)</td>
<td>12 (2.8%)</td>
</tr>
</tbody>
</table>

**Sufficient to Change Practice?**

- Caveats:
  - Most women (83%) had ER-positive cancers and would thus be expected to recur late, BUT....
  - Median follow up is 6.3 years.
  - Unknown whether patients in SLND group had extended radiation fields, as this data was not collected as part of the study.
Advocate Options

- Risk-adapted local therapy
- SLN biopsy alone – omit axillary dissection
- Radiation after lumpectomy?
- One size does NOT fit all
- Many options to choose from and we need to be their advocate

<table>
<thead>
<tr>
<th>TARGIT group</th>
<th>EBRT group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>&lt; 45 years</td>
<td>17</td>
</tr>
<tr>
<td>45 – 54 years</td>
<td>212</td>
</tr>
<tr>
<td>55 – 64 years</td>
<td>443</td>
</tr>
<tr>
<td>65 – 74 years</td>
<td>355</td>
</tr>
<tr>
<td>&gt; 74 years</td>
<td>86</td>
</tr>
<tr>
<td>Pathological tumour size</td>
<td></td>
</tr>
<tr>
<td>&lt;1cm</td>
<td>381</td>
</tr>
<tr>
<td>1-2 cm</td>
<td>531</td>
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<tr>
<td>&gt;2cm</td>
<td>144</td>
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<tr>
<td>Unknown</td>
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<td>Tumour grade</td>
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<tr>
<td>Grade I (n)</td>
<td>341</td>
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<tr>
<td>Grade II (n)</td>
<td>540</td>
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<tr>
<td>Grade III (n)</td>
<td>159</td>
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<tr>
<td>Unknown (n)</td>
<td>73</td>
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<tr>
<td>Number of Lymph node involved</td>
<td></td>
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<tr>
<td>0</td>
<td>866</td>
</tr>
<tr>
<td>1-3</td>
<td>155</td>
</tr>
<tr>
<td>&gt;3</td>
<td>38</td>
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<tr>
<td>Unknown</td>
<td>54</td>
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<tr>
<td>TOTAL</td>
<td>1113</td>
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