OVERVIEW OF RADIOTHERAPY IN BREAST CONSERVATION

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RT in Breast Cancer

- Combined Modality is the mainstay of treatment
- The adjuvant treatment after surgery should address
  - Local recurrence (RT)
  - Systemic disease (chemo, hormone)
Breast Conservation Therapy

Removal of only the tumor with a safe margin with axillary lymphadenectomy instead of mastectomy followed by radiotherapy to the breast
BCT History

THE PLACE OF RADIUM IN THE TREATMENT OF CANCER OF THE BREAST

- 325 patients with local removal of the breast tumor and radium implantation at the site of local incision as well as in the axilla.
- In 250 patients, the 5-year survival rate:
  71.4% for group 1 (disease confined to the breast),
  29.3% for group 2 (confined to breast and axilla),
  23.6% for group 3 (advanced or inoperable).
- Results comparable with radical mastectomy.

Prospective Randomized Trials Comparing Conservative Surgery and Radiation with Mastectomy for Early-Stage Breast Cancer

<table>
<thead>
<tr>
<th></th>
<th>Institut Gustave-Roussy</th>
<th>Milan</th>
<th>NSABP B-06</th>
<th>NCI</th>
<th>EORTC</th>
<th>Danish</th>
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</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>179</td>
<td>701</td>
<td>1,219</td>
<td>237</td>
<td>874</td>
<td>904</td>
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<table>
<thead>
<tr>
<th></th>
<th>Surgery</th>
<th>Follow-up (y)</th>
<th>Overall survival</th>
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<tbody>
<tr>
<td></td>
<td>2-cm gross margin</td>
<td>15</td>
<td>CS+RT (%)</td>
</tr>
<tr>
<td></td>
<td>Quadrantectomy</td>
<td>20</td>
<td>42</td>
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<tr>
<td></td>
<td>Lumpectomy</td>
<td>20</td>
<td>46</td>
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<td></td>
<td>Gross excision</td>
<td>18</td>
<td>59</td>
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<tr>
<td></td>
<td>1-cm gross margin</td>
<td>10</td>
<td>65</td>
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<tr>
<td></td>
<td>Wide excision</td>
<td>6</td>
<td>79</td>
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<table>
<thead>
<tr>
<th></th>
<th>Local recurrence</th>
<th></th>
<th>Mastectomy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CS+RT (%)</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Mastectomy (%)</td>
<td>14</td>
<td>14</td>
</tr>
</tbody>
</table>

BCS followed by RT equivalent to mastectomy for appropriately selected patients with EBC
Early Stage Breast Cancer

NIH Consensus Development Conference Statement (1990)

“Breast conservation treatment is an appropriate method of primary therapy for the majority of women with Stage I and II breast cancer and is preferable because it provides survival equivalent to total mastectomy and axillary dissection while preserving the breast”

“The recommended technique for breast conservation includes:
- local excision of primary tumor with clear margins
- Level I-II axillary node dissection
- breast irradiation to 4,500-5,000 cGy with or without a boost”
Rationale of BCT

- Breast cancer is a systemic disease with hematogenous spread early in the disease process.
- Surgery and Radiation as a combined modality:
  - Surgery alone- More failure at margins
  - Radiotherapy alone- More failure at the epicenter
- Using surgery to remove grossly visible tumor with a small margin and moderate-dose radiotherapy to treat the larger volume of tissue that may harbor residual disease.
Criteria for BCT

**Indications**
- Motivated Pts
- R T facilities
- Mammography
- Tumor < 5 cms
- Node N0/N1
- Good tumor breast ratio

**Contraindications:**

ABSOLUTE
- High probability of recurrence
  - Multicentric disease
  - Positive surgical margins
- High probability of complications from irradiation
  - CVD
  - Prior irradiation
  - Early pregnancy
Contraindications to BCT

RELATIVE:

- High probability of subsequent breast cancers

- Poor cosmetic results
  - Unfavorable tumor-breast ratio
  - Oncologically necessary removal of nipple-areola complex
  - Large medial lesions

- Personal preference of the patient
BCT: Technical aspects

- Pre-op evaluation of tumor by Radiation Oncologist
- Minimum margin 1 cm all around
- Separate incisions preferred for primary and axilla
- Pectoralis minor may be divided or preserved
- Surgical clips are left if brachytherapy not planned
Standard approach in BCT

- **BCS**
  - WLE + ALND

- **Whole breast RT**
  - 45-50 Gy/25#/5 weeks
  - Tangential fields – medial and lateral (Co-60 or 6 MV photons)
  - Newer techniques- IMRT, proton beam etc

- **Regional RT- only when indicated by post-op HPR**

- **Boost to tumor bed**
  - 10-16 Gy
  - Photon/ Electron/ Brachytherapy
Factors affecting cosmesis after BCS

- Removal of large volume of breast tissue
- Removal of Nipple-areola complex
- Location of tumor (Medial vs lateral)
- Post radiation fibrosis
Risk Factors for Local Relapse

- Young age increase risk
- Positive margins increase risk
- Systemic therapy lowers risk
- Higher RT doses lowers risk
- Extensive intra-ductal component increase risk
- LCIS increase risk
- Lobular histology - higher risk
- BRCA1-2 - higher relapse
- Larger tumors - higher local relapses
- Node-positive - higher local relapse
- ER/PR negative- higher local relapse
- Her 2+ tumors
RT in BCT

- Volume of irradiation
  Whole breast ----→ boost to the tumor site
  Axilla and SCF if necessary
- 45-50 Gy to whole breast by Ext RT
- 10-16 Gy boost by electron/photon/brachy
Limitations with conventional radiotherapy

- Dose inhomogenity
  - Due to continuous change of contour of breast.
  - 15-20 % dose inhomogenity may result in superior and inferior plane of breast.
  - Medial and lateral aspect of breast may get higher dose of radiation.

- Radiation accompaniments (lung, heart)
  aim of newer techniques is to further minimize the accompaniments.
RATIONALE FOR NEWER TECHNIQUES

- Improving dose homogeneity within the tumor
- Avoidance of radiation to normal structures
- Reduction of treatment related toxicities.
- Reduction of treatment time.
- Improvement in local control and survival.
NEWER EB-RADIOThERAPY TECHNIQUES IN EBC

- 3D CRT
- IMRT
- CT scan based planning
- Use of Tissue Compensators
- Gated Radiotherapy
- Partial Breast Irradiation
IMRT

- IMRT is an approach to conformal therapy that not only conforms high dose to tumor tissue but also conforms low dose to surrounding normal tissue.

- Dose intensity is varied in the tumor volume. A higher dose can be delivered to tumor tissue. Minimal dose is delivered to surrounding normal tissues.

Higher tumor control probability
Minimal side effects of radiotherapy
GATED RADIOTHERAPY

- Tumor motion taken into account while radiation treatment is being delivered.

- Techniques of Gating
  
  A. Breath hold technique
  - Active- airway of patient is temporarily blocked by a valve
  - Passive- the patient temporarily holds the breath

  B. Synchronized Gating
  - external devices are used to predict the phase of respiratory cycle while patient breathes freely
USE OF TISSUE COMPENSATORS

- Compensator- is a device which compensates for missing tissues.
- Use of tissue compensators improve dosimetry and reduce complications.
- Various types of tissue compensators are used
  - Tissue equivalent materials
  - MLC
Boost in BCT

METHODS

- Electron beam
- Photon beam - 3DCRT/IMRT
- Interstitial Brachytherapy
- IORT
- Mammosite
INTERSTITIAL BRACHYTHERAPY

- Main advantage lies in ability to tightly conform dose to a specified volume.
- Used as a boost following BCT along with EBRT

- Clinical situations where brachytherapy may be more useful than EBRT include – Large breasts
  - Deep seated tumors
  - Extensive intra-ductal comp.
  - Uncertain margins.

- Shorter treatment times
INTR AOPERATIVE RADIOTHERAPY (IORT)

- IORT is a radiotherapeutic technique which delivers a single dose of radiation to tumor bed or to exposed tumor during surgery.

- It is used mainly as a boost to be followed by EBRT.

- Rationale: 85% of relapses in BCT after RT occur in the operated area.

Techniques:
- IOHDR
- IOERT
MAMMOSITE

- Can be used for primary radiation or as a boost
- HDR with Iridium –192 source is used.
- Places the radiation source inside the lumpectomy cavity.
- Cosmetic results are good to excellent in 88% of cases.
- Dose prescribed at 1cm from applicator surface
- Treatment usually completed in 5 days
- A minimum skin to balloon surface distance of 5mm required
- The principal dose limiting factor is the dose to overlying skin
Accompaniments:
- Due to device placement-
  Mild erythema, pain, drain leakage, ecchymosis.
- Due to radiation therapy-
  Erythema, dry desquamation

Factors limiting use of mammosite
Balloon - cavity conformance
Skin – balloon cavity surface distance
Better Local Control with RT Boost

### Dose fractionations used in various prospective randomized studies of boost versus no boost.

<table>
<thead>
<tr>
<th>Trial</th>
<th>Number of patients</th>
<th>EBRT (dose/fraction)</th>
<th>Boost (dose/fraction)</th>
<th>LR (%)</th>
<th>Median Follow-up (year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bartelink et al. 11</td>
<td>2657</td>
<td>50 Gy/25 fr</td>
<td>-</td>
<td>10.2</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>2661</td>
<td>50 Gy/25 fr</td>
<td>16 Gy/8 fr</td>
<td>6.2</td>
<td></td>
</tr>
<tr>
<td>Romestaing et al. 24</td>
<td>503</td>
<td>47-50 Gy/20 fr</td>
<td>-10 Gy/4 fr</td>
<td>4.5</td>
<td>3.3</td>
</tr>
<tr>
<td></td>
<td>521</td>
<td>50 Gy/20 fr</td>
<td>-</td>
<td>3.6</td>
<td></td>
</tr>
<tr>
<td>Teissier et al. 25</td>
<td>327</td>
<td>48-50 Gy/25 fr</td>
<td>-</td>
<td>6.8</td>
<td>6.1</td>
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<tr>
<td></td>
<td>337</td>
<td>50 Gy/25 fr</td>
<td>10 Gy/5 fr</td>
<td>4.3</td>
<td></td>
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<tr>
<td>Polgar et al. 26, 27</td>
<td>103</td>
<td>49-50 Gy/25 fr</td>
<td>-</td>
<td>15.5</td>
<td>5.3</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>50 Gy/25 fr</td>
<td>12-16 Gy/3-8 fr</td>
<td>6.7</td>
<td></td>
</tr>
<tr>
<td>Graham et al. 28*</td>
<td>674</td>
<td>50 Gy/25 fr</td>
<td>-</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
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<td>674</td>
<td>45 Gy/25 fr</td>
<td>-</td>
<td>NR</td>
<td></td>
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<tr>
<td>Nagykalnai et al. 29</td>
<td>55</td>
<td>50 Gy/25 fr</td>
<td>-</td>
<td>10.7</td>
<td>3.8</td>
</tr>
<tr>
<td></td>
<td>56</td>
<td>50 Gy/25 fr</td>
<td>10 Gy HDR/20 Gy LDR</td>
<td>5.4</td>
<td></td>
</tr>
</tbody>
</table>
Delineation of Tumor Bed for Boost

- Clinical-history and patients' recollection of tumor position, clinical photographs, tattoos, surgical scar
- Mammography
- Surgical clips
- Ultrasonography
- Computerized tomography (CT) scan
- Magnetic resonance imaging (MRI)
- *Peroperative placement of catheters*
### Selected Randomized Trials of Breast-conserving Surgery with or without Radiation

<table>
<thead>
<tr>
<th>Study</th>
<th>T, N</th>
<th>No. of Patients</th>
<th>Follow-Up (yrs)</th>
<th>LR</th>
<th></th>
<th></th>
<th></th>
<th>p Value</th>
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</thead>
<tbody>
<tr>
<td>Fisher et al.</td>
<td>&lt;4 cm node positive/negative</td>
<td>930</td>
<td>10</td>
<td>12.4</td>
<td>40.9</td>
<td>&lt;.001</td>
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<tr>
<td>Liljegren et al.</td>
<td>&lt;2 cm node negative</td>
<td>381</td>
<td>10</td>
<td>8.5</td>
<td>24.0</td>
<td>.0001</td>
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<tr>
<td>Veronesi et al.</td>
<td>&lt;2.5 cm</td>
<td>579</td>
<td>10</td>
<td>5.8</td>
<td>23.5</td>
<td>&lt;.001</td>
<td></td>
<td></td>
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<tr>
<td>Clark et al.</td>
<td>&lt;2 cm node negative</td>
<td>837</td>
<td>3</td>
<td>5.5</td>
<td>25.7</td>
<td>&lt;.001</td>
<td></td>
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</tr>
<tr>
<td>Fisher et al.</td>
<td>&lt;2 cm node negative</td>
<td>1,009</td>
<td>8</td>
<td>2.8</td>
<td>16.5</td>
<td>&lt;.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Winzer et al.</td>
<td>&lt;2 cm node negative</td>
<td>347</td>
<td>5.9</td>
<td>3.2</td>
<td>27.8</td>
<td>&lt;.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Isolated local recurrence (events/woman-years)

<table>
<thead>
<tr>
<th>Year started and study name</th>
<th>RT sites</th>
<th>Events/woman-years</th>
<th>BCS + RT events</th>
<th>Logrank Variance</th>
<th>Ratio of annual event rates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Allocated</td>
<td>Allocated</td>
<td>O-E</td>
<td>BCS + RT : BCS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BCS</td>
<td>BCS + RT</td>
<td>0-E</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Variance of 0-E</td>
<td></td>
</tr>
</tbody>
</table>

#### (a) Radiotherapy only to conserved breast: 14% node positive

- **1976 NSABP B-06**: BW*, 125/6862 285/4991 -93.3 84.8
- **1981 Uppsala-Örebro**: BW, 10/1636 43/1511 -17.7 12.7
- **1982 St George’s London**: BW*, 12/1202 31/1047 -11.5 9.6
- **1984 Ontario COG**: BW + S, 53/3543 155/2754 -58.2 48.2
- **1987 INT Milan 3**: BW + S*, 19/2478 60/2005 -25.1 18.2
- **1989 NSABP B-21**: BW + S*, 6/1810 40/1729 -17.3 11.2
- **1991 Swedish BCCG**: BW, 33/3718 92/3429 -30.8 30.5

**5-year risk**
- 7.2% 25.6%

**Subtotal**
- 258/4 706/1 -254.0 215.3

#### (b) Radiotherapy to conserved breast and other sites: 24% node positive

- **1982 St George’s London**: BW + AF*, 14/620 30/380 -10.9 9.7
- **1985 Scottish**: BW + S+(AF)+ IMC, 16/2598 83/2260 -33.0 22.5
- **1985 West Midlands, UK**: BW + S+ AF + IMC, 42/2398 104/1929 -36.8 34.2
- **1986 CRC, UK**: Various, 33/1604 77/1454 -24.3 25.7

**Subtotal**
- 105/7 294/2 -105.0 92.1

**5-year risk**
- 7.7% 26.7%

**Total (a+b)**
- 363/7 1000/7 -359.0 307.4

**5-year risk**
- 7.3% 25.9%

**Heterogeneity between 11 strata: \( \chi^2_{10} = 7.8; \ p = 0.6 \)**

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*Lancet 2005;366:2087–2106,*
# Meta-analysis of survival EBCTCG

## Breast cancer mortality (deaths/women)

<table>
<thead>
<tr>
<th>Year started and study name</th>
<th>RT sites</th>
<th>Deaths/women</th>
<th>Allocated BCS + RT</th>
<th>Allocated BCS</th>
<th>BCS + RT deaths</th>
<th>Ratio of annual death rates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Logrank O-E</td>
<td>Variance of O-E</td>
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<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td>-19.7</td>
<td>135.0</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-2.3</td>
<td>16.8</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-25</td>
<td>10.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-16.4</td>
<td>51.5</td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td>-6.2</td>
<td>21.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.5</td>
<td>3.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-3.9</td>
<td>18.0</td>
</tr>
</tbody>
</table>

(a) Radiotherapy only to conserved breast: 14% node positive

(b) Radiotherapy to conserved breast and other sites: 24% node positive

### (a) Subtotal

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>-45.8</th>
<th>257.4</th>
<th>0.84 (SE 0.06), 2p = 0.004</th>
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<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td>28.0%</td>
<td>33.2%</td>
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</table>

### (b) Subtotal

<table>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>-26.9</th>
<th>125.3</th>
<th>0.81 (SE 0.08), 2p = 0.02</th>
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<tbody>
<tr>
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<td></td>
<td></td>
<td>28.2%</td>
<td>35.1%</td>
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</tr>
</tbody>
</table>

### Total (a+b)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>-72.7</th>
<th>382.7</th>
<th>0.83 (SE 0.05), 2p = 0.0002</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>30.5%</td>
<td>35.9%</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity between 11 strata: $\chi^2_{10} = 3.8; p = 0.96$

*Lancet* 2005;366:2087–2106,
Effect of RT after BCS on local recurrence and on breast cancer mortality—15-year probabilities. EBCTCG Meta-analysis

Lancet 2005;366:2087–2106,
Attitudes and treatment outcome of breast conservation therapy for stage I & II breast cancer using peroperative iridium-192 implant boost to the tumour bed.

- Surgery with peroperative implantation of iridium-192 to deliver a boost.
- Whole breast irradiation was delivered 3-4 weeks after the boost.
- Cosmesis was assessed at the end of 6 months from completion of therapy.
- There were no locoregional failures at a median follow up of 42 months.
- One patient experienced a systemic relapse.
- Cosmesis was good to excellent in 80% of patients.
- Breast conservation therapy using peroperative iridium-192 implant provides excellent locoregional disease control and cosmesis.

Breast conservation therapy for breast cancer: Patient profile and treatment outcome at a tertiary care cancer centre


<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surgery</strong></td>
<td></td>
</tr>
<tr>
<td>Quadrantectomy</td>
<td>08</td>
</tr>
<tr>
<td>Wide Excision</td>
<td>64</td>
</tr>
<tr>
<td>Re-excision of tumor bed</td>
<td>30</td>
</tr>
<tr>
<td>ALND</td>
<td>102</td>
</tr>
<tr>
<td><strong>Radiotherapy</strong></td>
<td></td>
</tr>
<tr>
<td>Whole breast</td>
<td>102</td>
</tr>
<tr>
<td>Tumor bed boost</td>
<td>102</td>
</tr>
<tr>
<td>Brachytherapy</td>
<td>22</td>
</tr>
<tr>
<td>Electron</td>
<td>80</td>
</tr>
<tr>
<td>Axilla</td>
<td>28</td>
</tr>
</tbody>
</table>

Table 1. Profile of patients who had breast conservation therapy (n=102)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;35</td>
<td>20 (19.6)</td>
</tr>
<tr>
<td>35–50</td>
<td>57 (55.9)</td>
</tr>
<tr>
<td>&gt;50</td>
<td>25 (24.5)</td>
</tr>
<tr>
<td><strong>Menopausal status</strong></td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>53 (52)</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>49 (48)</td>
</tr>
<tr>
<td><strong>Parity</strong></td>
<td></td>
</tr>
<tr>
<td>Nulliparous</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Multiparous</td>
<td>98 (96)</td>
</tr>
<tr>
<td><strong>Tumour location (quadrant)</strong></td>
<td></td>
</tr>
<tr>
<td>Upper outer</td>
<td>61 (59.8)</td>
</tr>
<tr>
<td>Upper inner</td>
<td>19 (18.6)</td>
</tr>
<tr>
<td>Lower outer</td>
<td>14 (13.7)</td>
</tr>
<tr>
<td>Lower inner</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Central</td>
<td>5 (4.9)</td>
</tr>
<tr>
<td><strong>pTNM stage</strong></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>24 (23.5)</td>
</tr>
<tr>
<td>II A</td>
<td>40 (39.2)</td>
</tr>
<tr>
<td>II B</td>
<td>26 (25.4)</td>
</tr>
<tr>
<td>III A</td>
<td>9 (8.8)</td>
</tr>
<tr>
<td>III B</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
</tr>
</tbody>
</table>
Results

Only 19.6% of EBC underwent BCT
5YR Projected DFS 82% and OS- 88%

<table>
<thead>
<tr>
<th>Site</th>
<th>n</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local</td>
<td>1</td>
<td>(1)</td>
</tr>
<tr>
<td>Contralateral primary</td>
<td>2</td>
<td>(19)</td>
</tr>
<tr>
<td>Systemic</td>
<td>7</td>
<td>(6.8)</td>
</tr>
<tr>
<td>Liver</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Skeletal</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Liver and lung</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Lung and brain</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Skeletal and brain</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
Partial Breast Irradiation

Definition

Delivery of larger doses/fraction of radiation to the lumpectomy cavity (plus 1-2 cm margin) after breast conserving surgery in patients with early stage breast cancer.
PBI: Concept

Selected cases (low risk)

- Partial breast
  - Only the breast tissue adjacent to the tumor bed is irradiated
- Accelerated schedules
  - Dramatic reduction in duration of RT to 1-5 days

⇒ Accelerated Partial Breast Irradiation (APBI)
80% of breast recurrences after BCS occur at or near the tumor bed, implicating residual tumor foci from the original index tumor.

- Major effect of post-lumpectomy radiotherapy: reduce risk of recurrence in tumor bed region.
- Incidence of ‘elsewhere’ failures 3-5%.
- Some ‘elsewhere’ failures- new primaries, unaffected by whole breast irradiation.
- Whole breast radiation may not be needed in “appropriately” selected cases.
## Failures Outside of the Tumor Bed in Randomized Trials Comparing Lumpectomy with/without Postop RT

<table>
<thead>
<tr>
<th>Trial</th>
<th>Median f/u (mo)</th>
<th>Surgery alone</th>
<th>Surgery plus RT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>NSABP-B06</td>
<td>125</td>
<td>17 / 636</td>
<td>2.7</td>
</tr>
<tr>
<td>Milan</td>
<td>39</td>
<td>4 / 273</td>
<td>1.5</td>
</tr>
<tr>
<td>Uppsala-Orebro</td>
<td>64</td>
<td>7 / 197</td>
<td>3.5</td>
</tr>
<tr>
<td>Ontario</td>
<td>43</td>
<td>15 / 421</td>
<td>3.5</td>
</tr>
</tbody>
</table>

PBI: Potential advantages

- Reduces overall treatment time
  - Improves acceptability of BCT
  - Reduces waiting time for radiotherapy
  - Improves access to radiotherapy treatment machines
- Smaller treatment volumes
  - Large dose per fraction may be delivered without an increase in toxicity
  - Normal structures like heart, lungs, contralateral breast may be spared
- Better cosmetic results (lower skin & breast parenchyma integral dose)
- Eliminate scheduling problems with systemic chemotherapy
- Cost savings
  - Reduces hospital visits
  - Reduces absence from work and associated income losses
- Improves quality of life
Patient selection

- Age: Postmenopausal
- T2 or less
- N0
- Low grade
- Negative surgical margins
- ER +

- Exclude
  - Young patients
  - Large tumors
  - N+
  - High grade
  - Multicentric
  - Invasive lobular histology
  - EIC
  - Positive surgical margins
# Patient Selection Criteria

<table>
<thead>
<tr>
<th></th>
<th>ABS (^1)</th>
<th>ASBS (^2)</th>
<th>William Beaumont Hospital (^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>(\geq 45)</td>
<td>(\geq 50)</td>
<td>(\geq 45)</td>
</tr>
<tr>
<td>Histology</td>
<td>Unifocal, IDC</td>
<td>IDC or DCIS</td>
<td>IDC</td>
</tr>
<tr>
<td>Tumor size</td>
<td>(\leq 3\text{cm})</td>
<td>(\leq 2\text{cm})</td>
<td>(\leq 2\text{cm})</td>
</tr>
<tr>
<td>Surgical margins</td>
<td>Negative</td>
<td>Negative (\geq 2\text{mm})</td>
<td>Negative</td>
</tr>
<tr>
<td>Nodal status (Axillary/sentinel)</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
</tr>
<tr>
<td>Cavity to skin distance</td>
<td>Not stated</td>
<td>Not stated</td>
<td>(&gt;5\text{mm})</td>
</tr>
</tbody>
</table>

\(^{2}\) ASBS Consensus statement for APBI. April 30, 2003.  
PBI: Techniques

- Brachytherapy
  - Interstitial Brachytherapy
  - Mammosite balloon brachytherapy

- Intraoperative radiotherapy
  - Intraoperative electrons (IOERT)
  - Targeted intraoperative radiotherapy (TARGIT)
  - Brachytherapy

- EBRT
  - Electrons
  - 3D-CRT
  - IMRT
  - Protons
Outside of multi-institutional studies and institutional protocols, patients should be carefully selected for APBI and properly informed of the benefits and risks of this type of radiation treatment.

The following selection criteria when considering patients for treatment with APBI:

- Age 45 years old or greater
- Invasive ductal carcinoma or ductal carcinoma in situ
- Total tumor size (invasive and DCIS) less than or equal to 3 cm in size
- Negative microscopic surgical margins of excision
- Axillary lymph nodes/sentinel lymph node negative
Surgeons, radiation oncologists and physicists who will be utilizing the various APBI techniques should be adequately trained to allow for optimum radiation therapy planning and treatment.

All patients should be monitored regularly to identify adverse events as well as local recurrences.

Continuous, long-term, outcomes-based monitoring of APBI is desirable.
## Comparison of selected APBI techniques

<table>
<thead>
<tr>
<th>Technique</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
</table>
| **Interstitial brachytherapy** | • Oldest method, so extensive FU data available  
• Most adaptable to oddly shaped surgical cavities  
• New image-guided methods for catheter placement available | • Learning curve required  
• Relies heavily on operator experience  
• Most invasive of the APBI techniques—often requires GA for catheter placement |
| **3-D Conformal EBRT**   | • Noninvasive  
• ↑ dose homogeneity  
• Potential for best cosmesis | • Newest technique, so experience relatively limited  
• Time-consuming planning process  
• Larger volume of breast treated |
| **MammoSite**           | • Easiest for patient and oncology team  
• Widely available | • Requires close communication between surgeon and radiation oncologist  
• Limited ability to adapt to less-than-ideal surgical cavity |
Conclusions

- Radiotherapy is an integral part of BCT
- RT improves local control and survival
- Evidence of better Local Control with RT Boost
- APBI may be an alternative to whole breast radiotherapy
  - Smaller treatment volume
  - Shorter treatment time
  - Dose intensity
  - Reduced toxicity
  - Increased acceptability (patient / physician)
- APBI Requires:
  - Optimal patient selection
  - Appropriate target delineation
  - Meticulous QA
THANK YOU