New Technologies in Radiation Oncology

Catherine Park, MD, MPH
Advocate Good Shepherd Hospital
Breast Radiation

- Early Stage Breast Cancer
  - Whole Breast Radiation
    - Delivered to the whole breast
    - Boost to the lumpectomy cavity
  - Partial Breast Radiation
    - Treats part of the breast in less than one week
- Locally Advanced Breast Cancer
  - Whole breast or chest wall radiation plus regional lymph nodes
Whole Breast Radiation

- Treat whole breast followed by a boost to the lumpectomy cavity over 4-7 weeks of daily radiation
- Necessary for some cancers
- Inconvenient, may not be necessary
- The further away you live from a RT facility the more likely patients are to have a mastectomy or have a lumpectomy and not get the necessary RT
Partial Breast Irradiation

Rationale

>90% of local breast recurrences after breast conserving surgery occur in the tumor bed region.

Major effect of post-lumpectomy RT is to decrease the risk of recurrence in the tumor bed region.

Whole breast RT may not be needed in appropriately selected patients.
Accelerated Partial Breast Irradiation (APBI)

- Reduced
  - Burden and Inconvenience
  - Side Effects
  - Cost

- By
  - Lower Dose
  - Fewer Visits
  - Shorter Treatment times
  - Target Index Quadrant
How Do We Deliver Partial Breast Radiation

10 treatments over 5 Days
The Next Step in Partial Breast Radiation
INTRABEAM
INTRABEAM System

- radiotherapy delivered directly into the tumor bed at the time of surgery over 20-30 minutes
- Delivers a high dose of radiation using low dose X-rays right where you need it
Radiation Dose Delivery

The INTRABEAM X-ray source generates and emits a uniform spherical distribution of low energy X-rays which are released at the probe tip.

High dose radiation is delivered at the surface of the tumor bed.

Low energy X-rays are rapidly absorbed over a depth of a 1-2 cm margin around the applicator, sparing surrounding healthy tissue.

2.5-5 cm Diameter
Intrabeam System

- Surgeon performs lumpectomy
- Surgeon sizes the cavity for the appropriate applicator
- The Intrabeam system is draped and applicator is affixed to the X-ray source
- Surgeon places the applicator inside the surgical cavity

Dose Calculation

- Radiation for 20-30 mins
- Approximately 15-20% need more radiation due to adverse features
Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): an international, prospective, randomised, non-inferiority phase 3 trial

Jayant S Vaidya, David J Joseph, Jeffrey S Tobias, Max Bulsara, Frederik Wenz, Christobel Saunders, Michael Alvarado, Henrik L Flyger, Samuele Massarat, Wolfgang Eiermann, Mohammed Keshtgar, John Dewar, Uta Kraus-Tiefenbacher, Marc Sütterlin, Laura Esserman, Helle M R Holtveg, Mario Roncadin, Steffi Pigorsch, Marinos Metaxas, Mary Falzon, April Matthews, Tammy Corica, Norman R Williams, Michael Baum

Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial

Jayant S Vaidya, Frederik Wenz, Max Bulsara, Jeffrey S Tobias, David J Joseph, Mohammed Keshtgar, Henrik L Flyger, Samuele Massarat, Michael Alvarado, Christobel Saunders, Wolfgang Eiermann, Marinos Metaxas, Elena Sperk, Marc Sütterlin, Douglas Brown, Laura Esserman, Mario Roncadin, Alastair Thompson, John A Dewar, Helle M R Holtveg, Steffi Pigorsch, Mary Falzon, Eleanor Harris, April Matthews, Chris Brew-Groves, Ingrid Potyka, Tammy Corica, Norman R Williams, Michael Baum, on behalf of the TARGIT trialists' group
What is the Evidence for Intraoperative Radiation?

**TARGIT Trial**

*Targeted Intraoperative RadioTherapy*

An international prospective randomized trial run at 33 centers in 11 countries from 2000 to 2012

- n=3452 patients
- Compared standard whole breast radiation vs IORT
- If adverse features found, then additional whole breast radiation
Updated up to 5 years
Local Recurrence

Local Recurrence if IORT is performed at the time of initial lumpectomy
Regional Recurrence and Death

B. Regional recurrence

C. Death

Log-rank p=0.099

Number at risk
TARGIT 1679 1251 966 683 495 294
EBRT 1696 1243 957 676 481 297

Log-rank p=0.609

Number at risk
TARGIT 1721 1285 997 706 514 309
EBRT 1730 1272 978 693 496 302
# TARGIT Trial
## Short-term Complications

<table>
<thead>
<tr>
<th>Condition</th>
<th>IORT</th>
<th>Standard</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematoma</td>
<td>1.0%</td>
<td>0.6%</td>
<td>0.338</td>
</tr>
<tr>
<td>Seroma (&gt;3 aspirations)</td>
<td>2.1%</td>
<td>0.8%</td>
<td>0.012</td>
</tr>
<tr>
<td>Infection</td>
<td>1.8%</td>
<td>1.3%</td>
<td>0.292</td>
</tr>
<tr>
<td>Skin breakdown</td>
<td>2.8%</td>
<td>1.9%</td>
<td>0.155</td>
</tr>
<tr>
<td>RTOG Grade 3 or 4 (telangiectasia, fibrosis)</td>
<td>0.5%</td>
<td>2.1%</td>
<td>0.002</td>
</tr>
<tr>
<td>Major Toxicity (skin breakdown, delayed wound healing)</td>
<td>3.3%</td>
<td>3.9%</td>
<td>0.443</td>
</tr>
</tbody>
</table>
Ideal candidates

- Women age $\geq 50$ years old
- Unifocal invasive ductal carcinoma
- Size $\leq 3$ cm
- ER+/PR+
- Lymph node negative
- Negative surgical margins
- No LVI or EIC
Risk Adapted Approach

If patients are found to have adverse features they are offered External Beam Whole Breast Radiation

- Positive lymph nodes
- Positive margins
- Extensive Intraductal Component
- Invasive Lobular Carcinoma
- Lymphovascular Invasion
Benefits of IORT

- Initial data show low rates of recurrence
- Pt is done with local therapy at the time of lumpectomy
- Would significantly decrease mastectomy rates in areas far from Rad Onc centers
- Increased RT compliance for lumpectomy pts
- Decrease health care costs
- Could be done prior to oncoplastic surgery
Limitations of IORT

- Length of follow-up is limited
- Treatment is delivered pre-pathology
- Suboptimal for node positive patients or large tumors as stand alone therapy
- Rigid Applicators require larger incisions (also HDR systems)
- DCIS Data is limited
IORT at Good Shepherd

- First case March of 2012
- Over 160 patients
- No recurrences
- 1 wound complication
Locally Advanced Breast Patients

- Stage II and III patients
- Treat chest wall and regional lymph nodes
Comparison of techniques
Proton

- Dosimetric Advantages

- We don’t now has this translates clinically in terms of local control and long term toxicity
Locally Advanced Breast Cancer (Stage IIA-IIIC) Requiring breast/chest wall and regional nodal RT (including IMN)

RANDOMIZATION

<table>
<thead>
<tr>
<th>Arm 1</th>
<th>Arm 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Photon RT</td>
<td>Proton RT</td>
</tr>
</tbody>
</table>
Eligibility – Patient characteristics

• Localized invasive breast cancer requiring breast/chest wall RT and comprehensive nodal RT including IMN treatment
  □ Includes all stage II-III invasive breast cancer
    • Includes T1-T3/N0
    • Includes T4/inflammatory
  □ Includes loco-regional recurrence
    • No prior RT and no metastatic disease
  □ Left and right sided
PCORI – Study Aims

• N=1750 patients
• Does it decrease cardiac events?
• Is it as good as photons (xrays) in terms of recurrence
• Quality of life measures
Questions?