New Technologies in Radiation Oncology

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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 nodal radiation
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
>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 cavity at the time of surgery over 20-30 minutes
• INTRABEAM Radiotherapy System is a radiation treatment platform that has been adapted, studied and is cleared in the U.S. for intracavitary radiation to the tumor bed

• Generates and delivers a high dose of low energy (50KeV) x-rays in a precise, spherical distribution pattern
INTRABEAM System

INTRABEAM provides a treatment approach physicians can use with surgery alone or in conjunction with standard whole breast radiotherapy
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 (100 uses each)
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
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 Massarut, 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 Massarut, 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
Patient Characteristics

- The groups were evenly balanced
- Median age was 63 years (designed for women >45 y.o)
- 86% patients had tumors <=2cm,
- 85% of the tumors were grade 1-2
- 83% of the patients were node negative
- 90% of patients had negative margins
- Even distribution of ER/PR positive, HER2, LVI
Updated up to 5 years
Local Recurrence

Total Local Recurrences

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

- **Regional recurrence**
  - Log-rank p = 0.609

- **Death**
  - Log-rank p = 0.099
# TARGIT Trial
## Short-term Complications

<table>
<thead>
<tr>
<th>Complication</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>
Subset Analysis

- Increased recurrence in patients who
  - had their IORT after their initial lumpectomy as a second surgery suggesting a tumor microenvironment
  - PR negative patients
Ideal candidates

- Women age ≥ 50 years old
- Unifocal invasive ductal carcinoma
- Size ≤ 3 cm
- ER+/PR+
- Clinically node negative
- Negative surgical margins
- No LVI or EIC
Risk Adapted Approach

If patients are found to have the following 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
- 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

Arm 1
Photon RT

Arm 2
Proton RT
Eligibility – Patient characteristics

- Localized invasive breast cancer requiring breast/chest wall RT and comprehensive nodal RT including IMN treatment
  - Includes all stage I-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

• Aim 1: Assess the effectiveness of proton vs. photon therapy in reducing major cardiovascular events (MCE).
  □ Primary Hypothesis: For patients with locally advanced breast cancer, proton therapy will reduce the 10-year MCE rate after radiation from 6.3% to 3.8%.
  □ N=1,750 patients
• Aim 2: Assess the non-inferiority of proton vs. photon therapy in reducing breast cancer local-regional recurrence and in reducing any recurrence.
• Aim 3: Assess the effectiveness of proton vs. photon therapy in improving patient-reported body image and function and other measures of HRQOL.
• Aim 4: Develop predictive models to examine the association of radiation dose distribution (to heart and other normal tissues) and MCE and HRQOL.
Trial Update

- IRB approved at Penn and at NMCPC
- 40 patients accrued since March 2016
Questions?