SBRT for Breast Cancer
– from Idea to Clinical Reality

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More than 1.5 Million New Cases Per Year

Stage Distribution Over Time

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<tbody>
<tr>
<td>Localized</td>
<td>48%</td>
<td>63%</td>
</tr>
<tr>
<td>Regional</td>
<td>41%</td>
<td>29%</td>
</tr>
<tr>
<td>Metastatic</td>
<td>7%</td>
<td>6%</td>
</tr>
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NIH Consensus Statement: Treatment of early-stage breast cancer; 1990 18–21
### Oxford Overview of Trials of BCS +/- RT

- NSABP B-06
- Milan 3
- Uppsala-Orebro
- St. George’s
- Ontario

- NSABP B-21
- West Midlands
- CRC UK
- Swedish
- Scottish

EBCTCG, Lancet 366, 2087-2005
Punglia RS et al, NEJM 356, 2399, 2007
EBCTCG, Lancet. 378: 1707–16, 2011 (17 trials, n=10,800)

### Summary of Trials of BCS +/- RT

<table>
<thead>
<tr>
<th>(At 15 years)</th>
<th>BCS Alone</th>
<th>BCS + RT</th>
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<tbody>
<tr>
<td>Local Recurrence</td>
<td>32.0%</td>
<td>10.3%</td>
</tr>
<tr>
<td>BC Mortality</td>
<td>35.9%</td>
<td>30.5%</td>
</tr>
<tr>
<td>Any Death</td>
<td>40.5%</td>
<td>35.2%</td>
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### Why RT improves LC & OS?

**Multi-focal, multi-centric nature**
- Gallanger and Martin, Cancer 24:1170-78, 1969 (N=113)

Most LR happens near the excision site.
A Reasonable Model

68% do not need RT 32% need RT

Role of RT: sterilize residual tumorlets or microextension left in the breast by surgeons

No Need to Treat the Entire Breast

Pioneered by Clinicians at W. Beaumont Hospital

LDR
1-125 implants

HDR
Breast HDR template

Mounting Clinical Evidence


NSABP B-39 (RTOG 0413) APBI trial

NSABP B-39/RTOG 0413: “a randomized Phase III study of conventional whole breast irradiation (WBI) versus partial breast irradiation (PBI) for women with Stage 0, I or II breast cancer,” activated March 21, 2005.

- Brachy: ~5% LR in 5 yrs, >80% with good cosmesis
  - Invasive, operator dependent
- MammoSite: ~1% LR in 3 yrs, (93% ER+, 6% node+)
  - Infection (9.3%), persistent seroma (32.6% at 5yr)
- 3DCRT or IMRT (~73%): 3.85Gy x 10 BID, ~2.3% LR @3yrs
  - 25% grade 2+ subcut fibrosis (Hepel et al), 29% adverse cosmesis compared to WBI (RAPID trial).
Is there a convenient, consistent, noninvasive, less toxic way?

Time to validate idea

Questions:
1) Can it compete with Brachy?
2) Can it do better than IMRT?

Method:
- Monte-Carlo simulation of a focal spot with 36 2.5cm diameter Co-60 beams, 36cm SAD
- Dynamic Dose Painting ignoring shot deformations

7-field IMRT vs GammaPod™
Brachy-like dose distribution

The SBIR Grant Proposal

Vacuum Cups and Imaging Couch
Beam Configuration

- 15 mm and 25 mm collimators
- 36 Co-60 sources continuously rotating
- Beams focus at the isocenter

Prototype in 2010

Close up of source geometry

GammaPod™ system does not yet have a certificate of conformity and is not presently available for commercial distribution in the U.S.
Dose Distribution Measurement
Dose Distribution for 25 mm Static Shot - xy plane (axial)

Dose Distribution Measurement
Dose Distribution for 25 mm Static Shot - xz plane (coronal)

Patient Plan Verification
New Design

Prone, external beam, partial breast irradiation

Patient standing on the treatment loader, with shielding doors closed.

Patient lying prone, above the treatment position, with shielding doors open.

Example Dose Distributions

45 cc target

215 cc target

SRS + APBI

3.5cm Tumor+3mm gets 18Gy
6.1 cm Tumor bed gets 10Gy

No need for surgery
No need for 5-7 weeks of radiation
1-3 irradiation is enough
Cardiac Toxicity of Radiotherapy

From Darby et al: Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer, NEJM 368(11), 2013

Heart and lung dose estimates (left breast target)

In this example:
- Heart: V5% = 6.5%
- Lung: V5% = 4.3%
- RTOG0413/NSABP B39 constraints:
  - Heart: V5% < 40%
  - Lung: V30% < 15%

Consortium

- University of Maryland
- KU Medical Center
- UT Southwestern Medical Center
- Allegheny Health Network
Currently Proposed Consortium Trials

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<tr>
<th></th>
<th>Pre-op</th>
<th>Post-op</th>
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<tbody>
<tr>
<td>Fractionated</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>Single-fraction</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>GammaPod</td>
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<td>•</td>
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<tr>
<td>WBI</td>
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Clinical feasibility study - boost

Summary

• An idea of a dedicated breast SBRT system conceived during clinical service
• Enabled by grant funding
• Clinical realization through a commercial venture

Acknowledgement

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Clinical Consortium Members
Xcision Employees