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Miami Beach, FL USA

Results of APBI Clinical Trials Using Intracavitary Single- and Multi-Channel Breast Brachytherapy Applicators

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Disclosure

Frank A. Vicini, MD, FACR, does not have any financial relationships or products or devices with any commercial interest related to the content of this activity of any amount during the past 12 months.

Outline

- Review the latest APBI data
- Update status of APBI (brachytherapy) as an option to deliver adjuvant radiation after lumpectomy using balloon-based brachytherapy
Latest APBI Data —
Outcome versus Technique

• Catheter-based brachytherapy
• MammoSite/Contura (balloon devices)
• SAVI

Published APBI Results —
Catheter-Based Brachytherapy (>10 years)

<table>
<thead>
<tr>
<th>Institution</th>
<th># Patients</th>
<th>Follow-Up (Months)</th>
<th>% Local Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIO-Hungary (phase II)</td>
<td>45</td>
<td>136</td>
<td>9.3*</td>
</tr>
<tr>
<td>RTOG 95-17</td>
<td>99</td>
<td>146</td>
<td>6.2</td>
</tr>
<tr>
<td>Hungary Phase III</td>
<td>129</td>
<td>144</td>
<td>6</td>
</tr>
<tr>
<td>WBH</td>
<td>199</td>
<td>113</td>
<td>5*</td>
</tr>
<tr>
<td>Orebro University</td>
<td>50</td>
<td>86</td>
<td>4+</td>
</tr>
<tr>
<td>MGH</td>
<td>48</td>
<td>84</td>
<td>2</td>
</tr>
<tr>
<td>Tufts/Brown University</td>
<td>33</td>
<td>84</td>
<td>9</td>
</tr>
<tr>
<td>NIO-Hungary (phase III)</td>
<td>128</td>
<td>81</td>
<td>4.7</td>
</tr>
<tr>
<td>Oschner Clinic</td>
<td>51</td>
<td>75</td>
<td>2.0</td>
</tr>
<tr>
<td>RTOG 95-17</td>
<td>99</td>
<td>74</td>
<td>4.0</td>
</tr>
<tr>
<td>Joe Arrington Cancer Center</td>
<td>214</td>
<td>72</td>
<td>4.2</td>
</tr>
<tr>
<td>German-Austrian MC Trial</td>
<td>173</td>
<td>71</td>
<td>--</td>
</tr>
<tr>
<td>University of Wisconsin***</td>
<td>136</td>
<td>60</td>
<td>4.8</td>
</tr>
<tr>
<td>Tufts-Brown University</td>
<td>33</td>
<td>58</td>
<td>6</td>
</tr>
<tr>
<td>Washington University</td>
<td>192</td>
<td>55</td>
<td>2.1</td>
</tr>
<tr>
<td>VCU</td>
<td>59</td>
<td>50</td>
<td>5.1</td>
</tr>
<tr>
<td>University of Wisconsin</td>
<td>247</td>
<td>48</td>
<td>3**</td>
</tr>
<tr>
<td>Joe Arrington Cancer Center</td>
<td>136</td>
<td>48</td>
<td>3.7</td>
</tr>
<tr>
<td>German-Austrian MC Trial</td>
<td>274</td>
<td>38</td>
<td>0.4</td>
</tr>
<tr>
<td>University Kansas</td>
<td>24</td>
<td>37</td>
<td>0</td>
</tr>
<tr>
<td>University of Perugia, Italy</td>
<td>80</td>
<td>30</td>
<td>0</td>
</tr>
<tr>
<td>Florence Italy</td>
<td>90</td>
<td>27</td>
<td>4.4</td>
</tr>
<tr>
<td>Totals</td>
<td>2309</td>
<td>27-136</td>
<td>0-9%</td>
</tr>
</tbody>
</table>

*12-year rate, = 7-year rate; ** High-risk patients; ***ASTRO Cautionary Group.
### Published APBI Results — Balloon/Device-Based Brachytherapy (<10 years)

<table>
<thead>
<tr>
<th>Institution</th>
<th># Cases</th>
<th>Follow-Up (Months)</th>
<th>% Local Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDA Trial</td>
<td>43</td>
<td>66</td>
<td>0%</td>
</tr>
<tr>
<td>ASBS Registry</td>
<td>400</td>
<td>60</td>
<td>3.2%</td>
</tr>
<tr>
<td>NY Hospital/Cornell (DCIS)</td>
<td>48</td>
<td>60</td>
<td>6.3%</td>
</tr>
<tr>
<td>University of Wisconsin</td>
<td>26</td>
<td>48.5</td>
<td>3%*</td>
</tr>
<tr>
<td>ASBS Registry Trial</td>
<td>1449</td>
<td>51</td>
<td>2.6%</td>
</tr>
<tr>
<td>MUSC</td>
<td>99</td>
<td>46</td>
<td>3.1%</td>
</tr>
<tr>
<td>Texas Cancer Center</td>
<td>573</td>
<td>31</td>
<td>1.0%</td>
</tr>
<tr>
<td>Rush</td>
<td>70</td>
<td>26</td>
<td>6%</td>
</tr>
<tr>
<td>WBH</td>
<td>80</td>
<td>24</td>
<td>2.9%</td>
</tr>
<tr>
<td>VCU</td>
<td>483</td>
<td>24</td>
<td>1.2%</td>
</tr>
<tr>
<td>Tufts/VCU/NEMC</td>
<td>28</td>
<td>19</td>
<td>0%</td>
</tr>
<tr>
<td>Single Institution Experiences</td>
<td>1000</td>
<td>2-12</td>
<td>0-3%</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td><strong>3899</strong></td>
<td><strong>2-66</strong></td>
<td><strong>0-6.3%</strong></td>
</tr>
</tbody>
</table>

*High-risk patients

### Applicator APBI

- **ASBS MammoSite Registry Trial**
  - 1449 patients prospectively entered
  - 2002-2004
  - Single-lumen catheter (no longer utilized)
  - Final analysis (Shah et al, Ann Surg Onc 2013)
    - Median follow-up: 63 months
    - 5-year local recurrence: 3.8%
    - 5-year local recurrence DCIS: 4.1%
    - 5-year local recurrence IDC: 3.7%
    - 91% excellent/good cosmesis
## Applicator APBI

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Invasive Cases</th>
<th>DCIS Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=1449</td>
<td>N=1255</td>
<td>N=194</td>
</tr>
<tr>
<td></td>
<td>5-Yr Actuarial Rate</td>
<td>5-Yr Actuarial Rate</td>
<td>5-Yr Actuarial Rate</td>
</tr>
<tr>
<td>N (%)</td>
<td>3.8%</td>
<td>3.7%</td>
<td>4.1%</td>
</tr>
<tr>
<td></td>
<td>5-Yr Actuarial Rate</td>
<td>5-Yr Actuarial Rate</td>
<td>5-Yr Actuarial Rate</td>
</tr>
<tr>
<td>Ipsilateral breast tumor recurrence</td>
<td>41 (2.6)</td>
<td>34 (2.7)</td>
<td>7 (3.6)</td>
</tr>
<tr>
<td>TR/MM failure</td>
<td>12 (0.8)</td>
<td>8 (0.6)</td>
<td>4 (2.1)</td>
</tr>
<tr>
<td>Elsewhere failure</td>
<td>29 (2.0)</td>
<td>26 (2.1)</td>
<td>3 (1.5)</td>
</tr>
<tr>
<td>Axillary failures</td>
<td>9 (0.6)</td>
<td>8 (0.6)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Distant metastases</td>
<td>26 (1.8)</td>
<td>25 (2.0)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Disease-free survival</td>
<td>---</td>
<td>86.1%</td>
<td>---</td>
</tr>
<tr>
<td>Cause-specific survival</td>
<td>---</td>
<td>98.7%</td>
<td>---</td>
</tr>
<tr>
<td>Overall survival</td>
<td>---</td>
<td>92.4%</td>
<td>---</td>
</tr>
<tr>
<td>Contralateral failure</td>
<td>22 (1.5)</td>
<td>20 (1.6)</td>
<td>2 (1.0)</td>
</tr>
</tbody>
</table>

### ASBS MammoSite Registry Trial

- **Final toxicity analysis** (Shah et al, Brachytherapy 2013)
- Rate of any complication:
  - 24% at 1 year
  - 39% at any time
  - Similar to WBI
- Noninfectious
  - 15% at 1 year
  - 29% at any time
- Symptomatic seroma: 13.4% at any time
- Fat necrosis: 2.5%
- Infection: 9.6%
- Telangiectasia: 13.0%
### Published Results: Contoura MLB

<table>
<thead>
<tr>
<th>Author/Institution/Title</th>
<th># of Patients</th>
<th>Publication Status</th>
<th>Journal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cuttinno, et al./VCU – Massey Cancer Ctr</td>
<td>171</td>
<td>Published – November 2010</td>
<td>IJROBP (Red Journal)</td>
</tr>
<tr>
<td>Vici, Arthur, Todor, Julian, Lyden</td>
<td>33</td>
<td>Published – June 2010</td>
<td>Contemporary Journal of Brachytherapy</td>
</tr>
<tr>
<td>Israel, et al./The Breast Center – Marietta, GA</td>
<td>46</td>
<td>Published – November 2009</td>
<td>The American Surgeon</td>
</tr>
<tr>
<td>Brown, et al./WellStar Kennestone</td>
<td>204</td>
<td>Accepted – October 2009</td>
<td>Brachytherapy</td>
</tr>
<tr>
<td>Wilder, et al./Irvine, CA</td>
<td>52</td>
<td>Accepted – October 2009</td>
<td>The Breast Journal</td>
</tr>
<tr>
<td>Wooster, et al./WellStar Kennestone</td>
<td>204</td>
<td>Accepted – October 2009</td>
<td>Brachytherapy</td>
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<tr>
<td>Weller, et al./Irvine, CA</td>
<td>31</td>
<td>Published – September 2010</td>
<td>Brachytherapy</td>
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<td>Weller, et al./Irvine, CA</td>
<td>144</td>
<td>Published – April 2010</td>
<td>IJROBP (Red Journal)</td>
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<td>Weller, et al./Irvine, CA</td>
<td>52</td>
<td>Published – April 2009</td>
<td>Brachytherapy</td>
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<tr>
<td>Weller, et al./Irvine, CA</td>
<td>45</td>
<td>Published – October 2009</td>
<td>Brachytherapy</td>
</tr>
</tbody>
</table>

### Table 2: Cosmetic outcomes

<table>
<thead>
<tr>
<th>Visit (mo)</th>
<th>N</th>
<th>Excellent/good</th>
<th>First 400 cases—excellent/good</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>1018</td>
<td>963 (94.6)</td>
<td>277</td>
</tr>
<tr>
<td>24</td>
<td>859</td>
<td>806 (93.8)</td>
<td>234</td>
</tr>
<tr>
<td>36</td>
<td>768</td>
<td>716 (93.2)</td>
<td>211</td>
</tr>
<tr>
<td>48</td>
<td>681</td>
<td>620 (91.0)</td>
<td>182</td>
</tr>
<tr>
<td>60</td>
<td>484</td>
<td>442 (91.3)</td>
<td>155</td>
</tr>
<tr>
<td>72</td>
<td>357</td>
<td>323 (90.5)</td>
<td>108</td>
</tr>
<tr>
<td>84</td>
<td>331</td>
<td>300 (90.6)</td>
<td>96</td>
</tr>
</tbody>
</table>

| Last visit ≥ 72 months | N | Excellent/good | First 400 cases—excellent/good |
### SAVI 4.5 Year Comparison

<table>
<thead>
<tr>
<th></th>
<th>SAVI 4.5 yr ASTRO 2013(^i)</th>
<th>ASBS MammoSite Registry 5 yr Ann Surg Oncol 2013(^ii)</th>
</tr>
</thead>
<tbody>
<tr>
<td># of Pts/Follow-up</td>
<td>101 pts/54 mo</td>
<td>1449 pts/63 mo</td>
</tr>
<tr>
<td>Telangiectasia</td>
<td>2.0%</td>
<td>Not reported</td>
</tr>
<tr>
<td>Seroma</td>
<td>2.0%</td>
<td>13.4%</td>
</tr>
<tr>
<td>Fat necrosis</td>
<td>0.0%</td>
<td>2.5%</td>
</tr>
<tr>
<td>Recurrence</td>
<td>2.0%</td>
<td>2.8%</td>
</tr>
</tbody>
</table>


### SAVI: Favorable Toxicity Rates at 4.5 Years

<table>
<thead>
<tr>
<th></th>
<th>Yashar, et al ASTRO 2013(^i)</th>
<th>Hong, et al ASTRO 2013(^ii)</th>
<th>Yashar, et al IJROBP 2010(^iii)</th>
</tr>
</thead>
<tbody>
<tr>
<td># of Pts/Follow-up</td>
<td>101 pts/54 mo</td>
<td>576 pts/36 mo</td>
<td>102 pts/22 mo</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>0%</td>
<td>0.2%</td>
<td>-</td>
</tr>
<tr>
<td>Telangiectasia</td>
<td>2%</td>
<td>1%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Symptomatic seroma</td>
<td>2%</td>
<td>3.1%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Fat necrosis</td>
<td>0%</td>
<td>0.7%</td>
<td>1.9%</td>
</tr>
</tbody>
</table>

Toxicity rates defined by CTCAE v.3


Brachytherapy:

**Arm 1:**
- LDR 45 Gy/3.5–6 days

**Arm 2:**
- HDR 34 Gy/10 fractions/5–7 days (3.4 Gy twice daily separated by 6 hours)
Patients

- Total patients entered: 100
- Ineligible: 2
- Analyzed: 98
- Median follow-up: 12.1 years

RTOG 95-17: Efficacy

<table>
<thead>
<tr>
<th>ISOLATED in-breast recurrence</th>
<th>5 year</th>
<th>10 year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td># (%)</td>
<td># at risk</td>
</tr>
<tr>
<td>In-breast recurrence at risk</td>
<td>4 3.1</td>
<td>84</td>
</tr>
<tr>
<td>In field</td>
<td>3 2.1</td>
<td>85</td>
</tr>
<tr>
<td>Out of field</td>
<td>1 1.0</td>
<td>85</td>
</tr>
<tr>
<td>In-breast &amp; regional recurrence</td>
<td>2 1.0</td>
<td>84</td>
</tr>
<tr>
<td>ALL In-breast recurrences</td>
<td>6 4.1</td>
<td>86</td>
</tr>
<tr>
<td>ISOLATED regional recurrence</td>
<td>3 3.1</td>
<td>84</td>
</tr>
<tr>
<td>ALL regional recurrences</td>
<td>5 4.1</td>
<td>87</td>
</tr>
<tr>
<td>ANY local-regional recurrence</td>
<td>9 7.2</td>
<td>84</td>
</tr>
<tr>
<td>Contralateral breast cancer</td>
<td>5 3.1</td>
<td>88</td>
</tr>
</tbody>
</table>
10-Year Published Data
WBI vs. APBI With Interstitial

- Matched Pair Analysis – Beaumont/F. Vicini
  - 199 patient clinical match
  - Tumor size, nodal status, age, margins, ER status, Tam
  - Comparing WBRT to APBI (interstitial)
- Results
  - Local control rates: WBI = 4%, APBI = 5%


APBI — Phase III Trials

- Ten Phase III trials
- Four PBI techniques:
  - Brachytherapy RT (Interstitial/MammoSite)
    - NSABP B-39/RTOG 0413
    - GEC-ESTRO Working Group
    - National Institute of Hungary
  - Single-Fraction Intra-Operative RT
    - European Institute of Oncology
    - University College of London
  - Fractionated External Beam RT
    - NSABP B-39/RTOG 0413
    - National Institute of Hungary
    - Canadian Phase III trial
    - Medical Research Council-UK
    - Barcelona
    - Florence
    - Spain
National Institute of Oncology  
- Budapest, Hungary -

• Schema:
  – Arm I: External Beam Whole Breast RT  
    • 50 Gy in 25 fractions  
  – Arm II: Partial Breast Irradiation  
    • Brachytherapy: 5.2 Gy x 7  
    – 258 enrolled (Trial Closed)  
    – Trial closed to support GEC-ESTRO Phase III trial

National Institute of Oncology  
- Budapest, Hungary -

• Results/New Data:
  – Presented at ESTRO 2012  
  – 10-year update (median f/u: 120 months)  
  – No differences noted in local failure  
    • 5.9% vs. 5.1%  
  – 81% E/G cosmesis with APBI vs. 63% with WBI

Radiother Oncol 2013  
Jun 3  
S0167-8140(13)00220-X
GEC-ESTRO — Multicenter Phase III Trial

**BCS**
(n = 1170)

- 50 Gy whole breast EB I + 10 Gy E L E boost
- 7 x 4.3 Gy HDR-BT
- or 8 x 4 Gy HDR-BT
- or 50 Gy PDR-BT

**Status:**
- Activated May 2004

**Accrual:**
- 1195 enrolled, 2009 (closed)

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**Presented at ESTRO 2012**

- No differences in toxicity at 5 years!
- Outcome data not yet reported

**Results should be available on efficacy in 2014**
NSABP B-39/RTOG 0413
Phase III APBI Trial

Eligible Patients with Lumpectomy
RANDOMIZED

Whole Breast Irradiation after Adjuvant Chemotherapy
50 Gy (2.0 Gy/fraction) or 50.4 Gy (1.8 Gy/fraction) to whole breast, followed by optional boost to ≤60 Gy

Partial Breast Irradiation prior to Adjuvant Chemotherapy
For a total of 10 treatments given on 5 days over 5 to 10 days:
- 34 Gy in 3.4 Gy fractions
- Interstitial Brachytherapy or MammoSite Balloon Catheter
- 38.5 Gy in 3.85 Gy fractions
- 3D Conformal External Beam

NSABP B-39/RTOG 0413

- Open:
  - March 21, 2005
- Accrual:
  - Completed May 2013: 4216
- Participating Sites:
  - 78 – NSABP
  - 142 – RTOG/CTSU
- PBI Technique:
  - 71.0%: 3D Conformal
  - 23.3%: MammoSite
  - 5.7%: Interstitial
  - 0.2%: SAVI (5 cases)
  - 0.1%: Contura (3 cases)
### NSABP B-39/RTOG 0413

- **Open:**
  - March 21, 2005
- **Accrual:**
  - Completed May 2013: 4216
- **Participating Sites:**
  - 78 – NSABP
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- **PBI Technique:**
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  - 5.7%: Interstitial
  - 0.2%: SAVI (5 cases)
  - 0.1%: Contura (3 cases)

### NSABP B-39/RTOG 0413 - Current Status -

- **Toxicity:**
  - Adverse events, including toxicities, second primary cancers and deaths monitored continuously (q/month)
  - Progress reports presented to Data Monitoring Committee (DMC) at 6-month intervals (reviewed internally monthly)
  - To date, DMC has found no reason for concern
  - Majority of dermatologic toxicities, pain, fibrosis-cosmesis, infection, etc., have been Grade 1 and 2 (<2% grade III)

**Multicatheter Brachytherapy**

**Target Volume Definitions**

CTV = PTV = PTV_EVAL = 1.5-cm expansion of cavity

(5 mm within skin and bounded by posterior breast extent)

---

**Multicatheter Brachytherapy**

Dose: 3.4 Gy bid x 5 days – 34 Gy

**Normal tissue:** <60% of the whole breast reference volume should receive ≥50% of the prescribed dose

**Dose homogeneity:**

Volume of tissue receiving:

- 150% (V150) of the prescribed dose ≤70 cc
- 200% (V200) of the prescribed dose ≤20 cc

Dose Homogeneity Index will be ≥ .75

DHI = the volume ratio (1 – V150/V100)
Multicatheter Brachytherapy

**Acceptable:**
- Dose volume analysis of target will:
  - Confirm that $\geq 90\%$ of the prescribed dose is covering $\geq 90\%$ of the PTV_EVAL
- Dose homogeneity criteria met
- Critical normal tissue DVHs within 5%
- Dose delivered over 5–10 days

Multicatheter Brachytherapy

**Unacceptable:**
- Dose volume analysis of the target volume
  - $< 90\%$ of the prescribed dose and/or $< 90\%$ coverage of the PTV_EVAL
- Dose homogeneity criteria are not met
- Critical normal structure DVH exceeds 5%
- Dose delivered over a period of time extending $> 10$ days
MammoSite Brachytherapy
Target Volume Definitions

CTV = PTV = PTV_EVAL = 1.0-cm expansion of cavity
(5 mm within skin and bounded by posterior breast extent)

Dose: 3.4 Gy bid x 5 days – 34 Gy

Normal tissue:
<60% of the WBRV should receive ≥50% of the prescribed dose

Tissue-balloon conformance:
measure trapped air

Balloon symmetry:
physical geometry will not deviate >2 mm

Minimal balloon surface-skin distance:
ideally ≥7 mm,
if 5–7 mm, then confirm skin dose <145%

Dose homogeneity:
Volume of tissue receiving:
150% (V150) of the prescribed dose ≤50 cc
200% (V200) of the prescribed dose ≤10 cc
MammoSite Brachytherapy

**Acceptable:**

- All four parameters must be met
- Dose volume analysis of target will:
  - Confirm that $\geq 90\%$ of the prescribed dose is covering $\geq 90\%$ of the PTV_EVAL
  - The volume of trapped air/fluid will be accounted for:

$$\text{%PTV_EVAL coverage} = \left(\frac{\text{vol trapped air/ vol PTV_EVAL}}{\text{vol PTV_EVAL}}\right) \times 100 \geq 90\%$$

- Critical normal tissue DVHs within <5%
- Dose delivered over 5–10 days

MammoSite Brachytherapy

**Unacceptable:**

- Any of the parameters not met
- Dose volume analysis of the target volume
  - $<90\%$ of the prescribed dose and/or $<90\%$ coverage of the PTV_EVAL
  - The volume of tapped air/fluid will be accounted for as previous

- Critical normal structure DVH exceeds 5%
- If dose delivered over a period of time extending $>10$ days
IORT?

- Radiation delivered without final pathology
  - Re-excision required?
  - Nodal radiation required?
- Dedicated equipment in the O/R
- Scheduling surgeon and radiation oncologist
- Lack of dosimetric Q/A
  - Tissue to applicator conformance?
  - True margin/target coverage

Brachytherapy Alternative to Intra-op RT?
2-Day Device-based APBI (4 fractions)

- Post-pathology patient selection
- Image-guided treatment with recordable parameters of quality
- Familiar technique, no added cost to implement
- Established RTOG/NSABP sites active in breast brachytherapy
Four-Year Results Using Balloon-Based Brachytherapy to Deliver Accelerated Partial Breast Irradiation With a Two-Day Dose Fractionation Schedule

Ben Wilkinson, MD
Frank A. Vicini, MD, FACR

Methods

- Prospective, Phase II trial, 45 patients, activated Jan 2004
- APBI using MammoSite RTS (single-lumen)
- Incl: age >40 years, T <3 cm, N+ <3, negative margin, skin distance >7 mm
- Excl: >3 LN, ECE, prior BrCa, DM, EIC, Collagen Vasc Dz
- 2800 cGy in 4 fractions over 2 days, Rx to 1 cm from surface
- Dwell positions: single (n=35), three (n=9), five (n=1)
- Primary endpoints: OS and LR
- Secondary endpoints: acute/chronic toxicity, adverse events, RNF, DM, DFS, and CSS
Results

- Median age 66 (range 48–83), size 0.6 cm (0.2–2.3 cm), 5% LN + (n=2), median f/u: 3.7 years (2.4–7.0 years)
- Toxicities (all chronic toxicities ≤ grade 2)
- Fat necrosis and seroma associated with incr. balloon fill vols ($P = 0.01$)
- Rib fx (n=3) not associated with $D_{\text{max}}$ rib ($P = 0.31$); 2 fx patients $D_{\text{max}} \geq 160\%$ Rx

<table>
<thead>
<tr>
<th>Erythema/ Hyperpigmentation</th>
<th>Induration (Fibrosis)</th>
<th>Fat Necrosis</th>
<th>Seroma</th>
<th>Rib Fx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr 1</td>
<td>Gr 2</td>
<td>Gr 1</td>
<td>Gr 2</td>
<td>Gr 1</td>
</tr>
<tr>
<td>Acute</td>
<td>53%</td>
<td>9%</td>
<td>4%</td>
<td>0%</td>
</tr>
<tr>
<td>3 yrs</td>
<td>27%</td>
<td>2%</td>
<td>32%</td>
<td>2%</td>
</tr>
<tr>
<td>4 yrs</td>
<td>18%</td>
<td>2%</td>
<td>44%</td>
<td>7%</td>
</tr>
</tbody>
</table>

Results

- Length of implant: 4.8 days (range 3–10 days) with current trial vs. 8.6 days (range 6–14 days) institutional average for typical 5-day fractionation pattern (79% reduction) ($P < 0.001$)
- Cosmesis: 65% good + 31% excellent = 96% overall good or excellent cosmetic result
- Clinical outcomes: (no local/regional failure, 2 patients with DM)

<table>
<thead>
<tr>
<th>IBTR</th>
<th>RNF</th>
<th>DM</th>
<th>DFS</th>
<th>CSS</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>0%</td>
<td>4%</td>
<td>96%</td>
<td>100%</td>
<td>93%</td>
</tr>
</tbody>
</table>
Limitations

• Small sample size, non-randomized
• Short follow-up

Conclusions

• Similar clinical outcomes vs. historical reports of APBI using 5-day fractionation
• Acceptable rates of chronic toxicity
• 7-year data recently analyzed: No change!!!!
Update on Phase II “Overnight” Study

PIs: Khan, Arthur, Vicini
Sponsor: CR Bard (Murray Hill, NJ)

- 3 cohorts of 30 patients (n=90) with predefined stopping criteria for toxicity
- 4 fractions (7 Gy x 4), 3 fractions (8.25 Gy x 3), 2 fractions (10.25 Gy x 2)
- Primary endpoint: Assuming true LRR is 3%, upper limit of a 95% confidence interval (calculated using the Wilson method) will exclude 10% rate with 90 patients
- 30 women on cohort 1, median f/u 28 months
- 30 women on cohort 2, >6 months f/u
- No > grade 2 toxicity events, no safety events

Contura Overnight Trial Study Design

- Acceptable rates of toxicities in each 30 patient cohort includes:
  - ≤10 in-breast complications > Grade II
    i.e.,
    Acute skin toxicity
    Severe fibrosis
    Telangiectasia
    Infection
    Symptomatic fat necrosis
    Breast pain requiring narcotics
    AND
  - ≤1 non-breast complication > Grade II
    i.e.,
    Rib fracture
    Acute pneumonitis
Study Endpoints

**Primary: Local control**
- Success if locoregional failure rate is ≤10% at 3 years

**Secondary:**
- Toxicity: acceptable rates (as previously stated)
- Cosmesis: good/excellent rates exceed 80% at 3 years

Dosimetric Criteria

- Target coverage: 95/95 (with 5% relaxation)
- V150: ≤40 cc
- V200: ≤10 cc
- Max skin dose: 100% PD
- Max rib dose: 100% PD
Future Goals

- Continue and complete accrual to Overnight trial
- Randomized phase II or III in NRG with toxicity/QOL endpoints?
- Readjust dose to reflect 50 Gy = 6.25 Gy x 4
- “Suitable” patients are eligible
- Conduct Registry Trial:
  - Any intracavitary device that meets dosimetric criteria!
  - ASTRO suitable patients only

Thank You!