Accelerated Partial Breast Irradiation (APBI)

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Clinical Presentation

• 70 year old female underwent annual bilateral screening mammogram
  – Abnormality was noted in the right breast
• Patient was otherwise asymptomatic with no associated skin changes or nipple discharge
Patient History

• Past Medical History
  – Hodgkin lymphoma s/p Mantle Field radiation of unknown dose/duration in 1988, Bone marrow transplant

• Past Surgical History
  – Umbilical Hernia Repair in 2021

• Medications
  – None

• No known drug allergies
Patient History (con’t)

• Gynecologic History
  – G2P2, 25 years old at first pregnancy
  – Menarche at age 13, menopause at age 39
  – She has not used oral contraceptives or hormone replacement therapy previously

• Social History
  – Caring for relative
  – Widow
  – Retired from work
  – No alcohol or tobacco use

• Family History
  – Mother: breast cancer at age 68
  – Father and paternal uncle: colon cancer
Physical Exam

• Vitals: BP 131/56, HR 75, RR 16, BMI 35.5
• General: Well developed, well nourished, in no acute distress.
• Lymphatics: No palpable bilateral cervical, axillary, or supraclavicular adenopathy
• CV: Regular rate, extremities well-perfused.
• Resp: Normal respiratory effort.
• Breast: In supine position; biopsy site in lateral right breast well healed; no palpable masses.
• Neurologic: CN II-XII grossly intact. No focal neurologic deficits appreciated.
Diagnostic Workup

• Diagnostic right mammogram
  – 0.5 cm focal asymmetry without associated calcifications

• Targeted US of right breast
  – On diagnostic mammogram and ultrasound 8:00 4 cm from the nipple there was a nodular asymmetry with partially well circumscribed and partially indistinct margins, that was hypoechoic with internal vascularity seen

• US-guided core needle biopsy
  – Invasive mucinous carcinoma
  – ER100, PR>90, HER2 1+, H2n- by IHC
  – Intermediate grade
Multidisciplinary Care

- Patient was seen in multidisciplinary clinic pre-operatively, she was interested in oncoplastic reduction
- Discussed options for local treatment with surgeon. if oncoplastic reduction to occur, accurate visualization of tumor bed essential (clips and/or seroma) to be candidate for APBI
- Presented options for local treatment: lumpectomy with: omission, whole breast irradiation (WBI), or accelerated partial breast irradiation (APBI)
- The patient elected to undergo APBI with IMRT following lumpectomy
Introduction to APBI

• Whole breast irradiation (WBI)
  – Standard of care after breast conservation surgery for early stage breast cancer.

• APBI introduced with possible advantages over WBI while providing equivalent LC in low risk patients
  – Shortened treatment course
    • Typically 2-5 days vs 3-5 weeks
  – Decreased radiation dose/toxicity
    • Reduced exposure to heart, lung, ribs.
Which patients should be considered for APBI?

• Must be candidates for breast-conserving therapy
  – No prior radiotherapy
  – No history of collagen vascular diseases
  – Not pregnant

• Consensus guidelines from ASTRO in 2017 put patients into 3 classes
  – Suitable
  – Cautionary
  – Unsuitable
### ASTRO consensus statement for APBI

<table>
<thead>
<tr>
<th></th>
<th>Suitable (Pt meets all criteria)</th>
<th>Cautionary (Pt meets all criteria)</th>
<th>Unsuitable (Pt meets any criteria)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>≥ 50</td>
<td>40-49</td>
<td>&lt; 40</td>
</tr>
<tr>
<td><strong>Tumor Size, T stage</strong></td>
<td>≤ 2 cm, Tis or T1</td>
<td>2.1 – 3 cm, T0 or T2</td>
<td>&gt; 3 cm, T3-T4</td>
</tr>
<tr>
<td><strong>N stage, surgery</strong></td>
<td>pN0 (SNBx or ALND)</td>
<td></td>
<td>pN1-3 or no nodal surgery</td>
</tr>
<tr>
<td><strong>Margins</strong></td>
<td>Negative (≤ 2 mm)</td>
<td>Close (&lt; 2 mm)</td>
<td>Positive</td>
</tr>
<tr>
<td><strong>LVI$^*$</strong></td>
<td>No</td>
<td>Limited/focal</td>
<td>Extensive</td>
</tr>
<tr>
<td><strong>ER status</strong></td>
<td>Positive</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td><strong>Centricity</strong></td>
<td>Unicentric</td>
<td>Microscopic multicentricity</td>
<td>Present</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td>Invasive ductal or favorable histology</td>
<td>Invasive lobular</td>
<td></td>
</tr>
<tr>
<td><strong>EIC or Pure DCIS</strong></td>
<td>If screen detected, low to intermediate grade, size ≤2.5 cm, resected with margins negative at &gt;3mm</td>
<td>≤ 3 cm and does not meet criteria for suitable</td>
<td>&gt; 3 cm</td>
</tr>
<tr>
<td><strong>Associated LCIS</strong></td>
<td>Allowed</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Neoadjuvant Tx</strong></td>
<td>Not allowed</td>
<td></td>
<td>Received</td>
</tr>
</tbody>
</table>

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$^*$Note: LVI stands for Lymph Vasculary Invasion.

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**Note:** The statement above is based on the ASTRO consensus on the use of APBI for early-stage breast cancer. The suitability for APBI is determined based on a combination of tumor and patient characteristics. Patients are categorized into suitable, cautionary, or unsuitable groups based on meeting or not meeting the specified criteria. The table above outlines the criteria for suitability, caution, and unsuitability for APBI, including age, tumor size and stage, nodal status, margins, LVI, estrogen receptor (ER) status, centricity, histology, and EIC or Pure DCIS. Associated LCIS is allowed, and neoadjuvant treatment is not allowed.
### ASTRO vs. ABS vs. ASBS

Comparison of criteria for approved group

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>≥ 50</td>
<td>≥ 50</td>
<td>≥ 45 (IDCA), ≥ 50 (DCIS)</td>
</tr>
<tr>
<td><strong>Tumor Size, T stage</strong></td>
<td>≤ 2 cm, Tis or T1</td>
<td>≤ 3 cm</td>
<td>≤ 3 cm</td>
</tr>
<tr>
<td><strong>N stage, surgery</strong></td>
<td>pN0 (SNBx or ALND)</td>
<td>pN0 (SNBx or ALN level I/II)</td>
<td>pN0 (SNBx)</td>
</tr>
<tr>
<td><strong>Margins</strong></td>
<td>Negative (≤ 2 mm)</td>
<td>Negative microscopic</td>
<td>Negative microscopic</td>
</tr>
<tr>
<td><strong>Centricity</strong></td>
<td>Unicentric, clinically unifocal</td>
<td>Unifocal</td>
<td></td>
</tr>
<tr>
<td><strong>LVSI</strong></td>
<td>Not present</td>
<td>Not present</td>
<td>Not present</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td>Invasive ductal or favorable histo</td>
<td>Any invasive</td>
<td>Any Invasive or DCIS</td>
</tr>
</tbody>
</table>

LIMES (LVSI, ILC, Margins Close, ER-, and Size > 2cm)
APBI Methodology

• Multiple methods available
  – Brachytherapy
    • Multi-catheter interstitial (High, Low, or Pulsed dose rates)
    • SAVI
    • Balloon catheterization (Mammosite, Contura)
  – External beam (EBRT)
    • Electrons
    • 3D-CRT/IMRT
    • Protons
  – Single-dose intraoperative radiotherapy (IORT)
• Multi-catheter interstitial brachytherapy has longest history, but currently data lacking to determine optimal method of delivering APBI.
GEC-ESTRO: Phase III trial
(Strnad et al. 2016)

- Interstitial multi-catheter brachytherapy to partial breast after breast conserving surgery
- 1184 patients treated prospectively with either WBI or APBI
  - Eligibility: Age > 40, negative margins, Tumor ≤3cm or DCIS with Van Nuys ≤ 8, pN0 or pNmi

<table>
<thead>
<tr>
<th>Modality</th>
<th>N</th>
<th>Median f/u</th>
<th>5-year local recurrence</th>
<th>5-year Cumulative Incidence</th>
<th>5-year DFS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Regional</td>
<td>Distant</td>
</tr>
<tr>
<td>WBI (50Gy / 25fx + 10Gy boost)</td>
<td>551</td>
<td>6.6 yrs</td>
<td>0.92%</td>
<td>0.18%</td>
<td>94.45% (95% CI 92.5-96.4)</td>
</tr>
<tr>
<td>APBI (32Gy / 8fx or 30.3Gy / 7fx BID)</td>
<td>633</td>
<td>6.6 yrs</td>
<td>1.44%</td>
<td>0.48%</td>
<td>95.03% (95% CI 93.3-96.7)</td>
</tr>
</tbody>
</table>
GEC-ESTRO: cont’d

• **Toxicity and cosmesis** (Polgár et al. 2017)
  
  – Skin toxicity at 5 years (% of pts):
    • APBI: Grade 2-3 (12%), 0% G4+
    • WBI: Grade 2-3 (9.7%), 0% G4+
  
  – Breast pain at 5 years (% of pts):
    • APBI: Grade 2-3 (8.4%), 0% G4+
    • WBI: Grade 2-3 (11.9%), 0% G4+

• Interstitial multi-catheter brachytherapy-based APBI is noninferior to WBRT with regards to outcome and cosmetic outcome
UK IMPORT LOW: Phase III trial
(Coles et al. 2017)

- Comparing APBI to WBI or reduced-dose WBI + simultaneous boost (SIB) IMRT after breast conserving therapy
- 2018 patients treated prospectively, randomized to three groups
  - Eligibility: Age ≥ 50, unifocal IDC, grade 1-3, margins ≥ 2mm, Tumor ≤3cm, 0-3 nodes

<table>
<thead>
<tr>
<th>Modality</th>
<th>N</th>
<th>Median f/u</th>
<th>5-year Cumulative Incidence</th>
<th>5-year Any Breast Cancer Event</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Local</td>
<td>Regional</td>
</tr>
<tr>
<td>WBI (40Gy / 15fx)</td>
<td>674</td>
<td>72.2 mos</td>
<td>1.1% (95% CI 0.5-2.3)</td>
<td>1.1% (95% CI 0.5-2.3)</td>
</tr>
<tr>
<td>WBI + SIB (36Gy + 40Gy / 15fx)</td>
<td>673</td>
<td>72.2 mos</td>
<td>0.2% (95% CI 0.02-1.2)</td>
<td>0.2% (95% CI 0.02-1.2)</td>
</tr>
<tr>
<td>PBI (40Gy / 15fx)</td>
<td>669</td>
<td>72.2 mos</td>
<td>0.5% (95% CI 0.2-1.4)</td>
<td>0.8% (95% CI 0.3-1.8)</td>
</tr>
</tbody>
</table>
UK IMPORT LOW: cont’d

• **Change in breast appearance** (Coles et al. 2017)
  
  – Patients reported at 5 years (% of pts):
    
    • WBI: 47.7 % (95% CI 41.1-54.8)
    
    • Reduced WBI + SIB: 36.7: (95% CI 30.6-43.6) p<0.05
    
    • PBI: 35.1% (95% CI 28.7-43.5) p <0.001
  
  – Physician reported at 5 years (% of pts):
    
    • WBI: 27.6 % (95% CI 22.5-33.6)
    
    • Reduced WBI + SIB: 21.1: (95% CI 17.2-25.7) p=0.47
    
    • PBI: 20 % (95% CI 15.6-25.4) p=0.10

• EBRT APBI outcomes noninferior to WBI when using IMRT. Low overall adverse events with worse patient-reported cosmesis with APBI
NSABP B39/RTOG 04-13: Phase III trial  
(Vicini et al, 2019)

- APBI after breast-conserving surgery for early stage breast cancer
- 4216 patients treated prospectively with WBI or APBI
  - Eligibility: Stage I/II, unifocal, invasive non-lobular, negative margins, Tumor ≤3cm, Level I/II ALND with 0-3 positive nodes without ECE.
  - APBI was either brachytherapy (Mammosite, interstitial) or EBRT

<table>
<thead>
<tr>
<th>Modality</th>
<th>N</th>
<th>Median f/u</th>
<th>10-year failure</th>
<th>Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ipsilateral breast</td>
<td>Overall</td>
</tr>
<tr>
<td>WBI (50Gy / 25 fx in 5 weeks)</td>
<td>2109</td>
<td>10.2 yrs</td>
<td>3.90%</td>
<td>91.30%</td>
</tr>
<tr>
<td>APBI (34Gy / 10fx brachy BID or 38.5Gy / 10fx EBRT BID in 5 days)</td>
<td>2107</td>
<td>10.2 yrs</td>
<td>4.60%</td>
<td>90.60%</td>
</tr>
</tbody>
</table>
RTOG 04-13: Phase III trial (cont’d)

• **Toxicity and cosmesis** (Vicini et al. 2019)
  – Skin toxicity at 10 years (% of pts):
    - APBI: Grade 1 (40%), Grade 2 (44%), Grade 3 (10%), <1% G4+
    - WBI: Grade 1 (31%), Grade 2 (59%), Grade 3 (7%), <1% G4+

• APBI did not meet criteria for equivalence to WBI in controlling for IBTR, but with an absolute difference of 0.7%, study concluded that APBI may be an acceptable alternative for some women
RAPID: Phase III trial
(Whelan et al. 2019)

• EBRT APBI after breast-conserving surgery for early stage breast cancer
• 2135 patients treated prospectively with WBI (hypofrac and conventional) or APBI
  – Eligibility: Age > 40, Tumor ≤ 3cm, IDC or DCIS

<table>
<thead>
<tr>
<th>Modality</th>
<th>N</th>
<th>Median f/u</th>
<th>8-year ipsilateral breast recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WBI</strong></td>
<td>1065</td>
<td>8.6 yrs</td>
<td>2.8% (95% CI 1.8-3.9)</td>
</tr>
<tr>
<td>(50Gy / 25fx or 42.5Gy / 16fx)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>APBI</strong></td>
<td>1070</td>
<td>8.6 yrs</td>
<td>3.0% (95% CI 1.9-4.0%)</td>
</tr>
<tr>
<td>(38.5Gy / 10fx BID in 5-8 days)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
RAPID: Phase III trial (cont’d)

- **Toxicity and cosmesis** *(Whelan et al. 2019)*
  - Induration or telangiectasia at 8 years (% of pts)
    - WBI: Grade 2+ (13%)
    - APBI: Grade 2+ (32%), p < 0.0001
  - Absolute difference in adverse cosmesis (fair or poor) at 7 years 18% lower (95% CI 12.9-22.3) in APBI group

- APBI is noninferior to WBI in terms of local disease control

- Late skin toxicity and cosmesis worse with APBI using this dosing regimen
Florence Trial - Phase III trial

- Accelerated Partial-Breast Irradiation Compared With Whole-Breast Irradiation for Early Breast Cancer
- 520 patients treated prospectively with WBI or APBI
  - Eligibility: Age > 40, early BC, multifocal, intraductal carcinoma, <5mm surgical margins, tumor ≤2.5cm

<table>
<thead>
<tr>
<th>Modality</th>
<th>N</th>
<th>Median f/u</th>
<th>10-year failure rates</th>
<th>Survival rates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ipsilat. br</td>
<td>Contralat. br</td>
</tr>
<tr>
<td>WBI (50Gy / 25fx)</td>
<td>260</td>
<td>10.7 yrs</td>
<td>2.50%</td>
<td>3.20%</td>
</tr>
<tr>
<td>APBI (30Gy / 5fx) IMRT</td>
<td>260</td>
<td>10.7 yrs</td>
<td>3.70%</td>
<td>0.80%</td>
</tr>
</tbody>
</table>

ASSOCIATION OF RESIDENTS IN RADIATION ONCOLOGY  

ARRO
Florence Trial- Phase III trial (cont’d)

- **Toxicity and cosmesis** (Meattini et al. 2020)
  - Toxicity within 6 months of treatment (% of pts):
    - APBI: Grade 1 (19.1%), Grade 2 (2%), No Grade 3
    - WBI: Grade 1 (28.8%), Grade 2 (31.2%), Grade 3 (6.5%)
  - Physician rated cosmesis at 10 years (% of pts):
    - APBI: Excellent (94.7%), Good (5.3%), Fair (0%), Poor (0%)
    - WBI: Excellent (72.7%), Good (25.4%), Fair (1.9%), Poor (0%)

- IBRT incidence was not significantly different between APBI and WBI

- Treatment related toxicity and cosmesis outcomes significant favor APBI for low-risk early breast cancer
Intraoperative Radiotherapy (IORT)

• TARGIT-A: randomized phase III (Vaidya et al. 2020)
  – 2298 patients: PBI IORT (20Gy/ 1fx) or WBI (45-56Gy)
    • Immediate IORT 5-year local recurrence: 2.11% vs. 0.95% (not inferior)
    • Delayed IORT 5-year local recurrence: 3.96% vs. 1.05% (inferior)
    • 20% of IORT patients needed WBI due to adverse pathology

• ELIOT: randomized phase III (Veronesi et al. 2013)
  – 1305 patients: PBI IORT (21Gy/ 1fx) or WBI (50Gy / 25fx + 10Gy)
    • 15-year Ipsilateral Breast Tumor Recurrence – 13% vs. 2.4% (inferior)
    • 40% of recurrences within radiation field
    • Not all of patients would satisfy ASTRO APBI appropriateness

• IORT APBI remains controversial with faster treatment and lower costs, but concerns for patient selection and effectiveness
Accelerated Partial Breast Irradiation (APBI)

- Studies of APBI suggest that rates of local control in selected low-risk patients with early-stage breast cancer are comparable to those treated with standard WBRT. However, compared to standard WBRT, several studies document an inferior cosmetic outcome with external beam delivery methods of APBI. Follow-up is limited and studies are ongoing.
  - Patients are encouraged to participate in clinical trials.
  - The NCCN Panel accepts the updated 2016 version of the ASTRO APBI guideline consensus statement, which now defines patients age ≥50 years to be considered "suitable" for APBI if:
    - Invasive ductal carcinoma measuring ≤2 cm (pT1 disease) with negative margin widths of ≥2 mm, no LVI, ER-positive, and BRCA negative; or
    - Low/intermediate nuclear grade, screening-detected DCIS measuring size ≤2.5 cm with negative margin widths of ≥3 mm.

- RT dosing

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Method</th>
<th>Reference</th>
</tr>
</thead>
</table>
Treatment

- Our patient underwent lumpectomy
  - Invasive ductal carcinoma measuring 3mm
  - Associated DCIS
  - Surgical resection margins widely negative (>10mm for all margins)
  - ER100, PR>90, HER2 1+, H2n- by IHC
  - SLNBx reviewed intraoperatively 0/2 LNs positive for disease
Treatment Planning

• Clinical target volume was drawn with a uniform 1 cm 3-D margin around surgical clips
• Second uniform 3-D 1 cm margin was added to obtain planning target volume
• Six 6MV step and shoot IMRT coplanar fields were used
• Patient was positioned supine with wing board with a vacloc and arms up
• Radiation was aligned to surgical clips daily
• 30Gy in 5 fractions every other day
• Clips were reviewed for evidence of migration but none
• Per the Italian Trial protocol that CTV limited to 3mm from skin, PTV was allowed to extend 4 mm into ipsilateral lung and limited 3 mm from the skin
Treatment Planning
Treatment Planning

![Graph showing dose-volume histograms for different ROIs/POIs in treatment planning.]

<table>
<thead>
<tr>
<th>Dose</th>
<th>ROI/POI</th>
<th>Clinical goal</th>
<th>Value</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plan dose: Right breast...</td>
<td>BREAST_L contract</td>
<td>At most 100 cGy dose at 0.00 cm³ volume</td>
<td>78 cGy</td>
<td>✔️</td>
</tr>
<tr>
<td>Plan dose: Right breast...</td>
<td>BREAST_L contract</td>
<td>At most 200 cGy dose at 0.00 cm³ volume</td>
<td>78 cGy</td>
<td>✔️</td>
</tr>
<tr>
<td>Plan dose: Right breast...</td>
<td>CTV</td>
<td>At least 90.00 % volume at 3000 cGy dose</td>
<td>99.22 %</td>
<td>✔️</td>
</tr>
<tr>
<td>Plan dose: Right breast...</td>
<td>CTV</td>
<td>At least 95.00 % volume at 2850 cGy dose</td>
<td>100.00 %</td>
<td>✔️</td>
</tr>
<tr>
<td>Plan dose: Right breast...</td>
<td>Lung (Right)</td>
<td>At most 10.00 % volume at 1000 cGy dose</td>
<td>5.21 %</td>
<td>✔️</td>
</tr>
<tr>
<td>Plan dose: Right breast...</td>
<td>PTV</td>
<td>At least 3000 cGy dose at 95.00 % volume</td>
<td>3000 cGy</td>
<td>✔️</td>
</tr>
<tr>
<td>Plan dose: Right breast...</td>
<td>PTV</td>
<td>At most 2.00 % volume at 3237 cGy dose</td>
<td>1.33 %</td>
<td>✔️</td>
</tr>
<tr>
<td>Plan dose: Right breast...</td>
<td>Uninvolved Breast</td>
<td>At most 50.00 % volume at 1500 cGy dose</td>
<td>36.05 %</td>
<td>✔️</td>
</tr>
</tbody>
</table>
Treatment Set Up
with daily CBCT before each fraction
Portal View
References


Please provide feedback regarding this case or other ARRO cases to arrocase@gmail.com