Accelerated Partial Breast Irradiation in brachytherapy: is shorter better?

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Disclosures:

- None
Learning Objectives:

- to review and understand the evolution and development of APBI using brachytherapy methods
- to understand the basis and limitations of radio-biological 'equivalence' between fractionation schedules
- to review commonly used and proposed fractionation schedules
**Iridium 192**

- Ir-192 ($T_{1/2} = 73.8$ days, $E_{\gamma, \text{mean}} = 380$ keV ) is the most common source for Remote Afterloaders.

- **Disadvantage**: relative short half-life (at least when compared with Co-60 ($T_{1/2} = 5.27$ yr, $E_{\gamma, \text{mean}} = 1253$ keV ) or Cs-137 ($T_{1/2} = 30.17$ yr, $E_{\gamma, \text{mean}} = 662$ keV ).

- **Advantage**: low average energy (~0.38 Mev, with a range from 0.136 to 1.062 MeV) so it is easily shielded requiring just 0.3 cm Pb as a half value layer.

- **Advantage**: high specific activity (450 Ci/g) allows the construction of high activity sources (10 Ci) of small diameter (0.6-1.1 mm).
Electronic brachytherapy

Axxent
Electronic Brachytherapy System

<table>
<thead>
<tr>
<th>Axxent HDR X-ray Source 2.2 Specifications</th>
<th>Part Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axxent HDR X-ray Source</td>
<td>7500</td>
</tr>
<tr>
<td>X-ray Tube Diameter</td>
<td>2.25 mm</td>
</tr>
<tr>
<td>Assembly Length</td>
<td>250 mm</td>
</tr>
<tr>
<td>Assembly Diameter</td>
<td>5.4 mm</td>
</tr>
<tr>
<td>X-ray Source Power</td>
<td>15 watts</td>
</tr>
<tr>
<td>Typical Treatment Time</td>
<td>10 min</td>
</tr>
<tr>
<td>Maximum Number of Treatments per X-ray Source</td>
<td>10</td>
</tr>
</tbody>
</table>

Source Includes:
- Integral water cooling sheath
- Low-force high-voltage connector
- Flexible high-voltage cable

Nominal Dose Rate: 0.6 Gy/min @ 3 cm in water
Important points

- eBx plans have dosimetric and biological features different from Ir-192 plans

- Tissue heterogeneities and patient boundary effects decrease dose to target and skin but increase dose to bones

- Enhancement of relative biological effectiveness (RBE). It is reported to be very similar to I-125 (1.4-1.5)

- eBx devices do not fall under existent regulatory scrutiny of radioactive sources. ASTRO Emerging Technology Committee issued a report on electronic brachytherapy (Int J Radiat Oncol Biol Phys, 2010 Mar 15; 76(4); 963-72)

Available methods for APBI

- Interstitial brachytherapy (LDR and HDR)
- Intra-cavitary brachytherapy (HDR)
  - Balloon catheter (single lumen/multi-lumen)
  - Hybrid techniques (SAVI)
- AccuBoost (HDR)
- Electronic balloon brachytherapy (Xoft Axxent)
- Permanent breast seed implants (LDR)
- Intra-operative brachytherapy (HDR, TARGIT 50kV X-rays)
- 3D conformal EBRT
Interstitial multi-catheter implants
Intra-cavitary devices

- Balloon based devices:
  - MammoSite
  - Contura

- Strut-based devices:
  - SAVI (Strut Adjusted Volume Implant)
  - Clear-Path
Balloon Catheter

‘MammoSite’

- MammoSite device (Proxima, Cytyc, Hologic)
- Inflatable Balloon Placed In Lumpectomy Cavity
- HDR brachytherapy 34 Gy in 10 fractions
- FDA clearance May 2002
- Since 2002, > 45,000 cases treated

Strut devices

ClearPath™ Breast Brachytherapy

Hybrid Device: “Best of Both Worlds”

Patel ASTRO 2006

In development with North American Scientific, Inc 2006

Novel Best Double Balloon Breast Applicator with Superior Dosimetry for Accelerated Partial Breast Irradiation, Abraham Mathews, Manny Subramanian, Michael Cutrer, Rupak Das and Krishnan Suthanthiran, Best Medical International, Inc., Springfield, VA, USA and University of Wisconsin, Madison, WI, USA -
SAVI Breast Brachytherapy

6-1 Mini, 6-1, 8-1, 10-1 applicators
Comparing targets in various modalities: apples to apples or apples to oranges?
DOSIMETRIC CHARACTERISTICS OF THE MAMMOSITE RTS, A NEW BREAST BRACHYTHERAPY APPLICATOR


Department of Radiation Oncology, William Beaumont Hospital, Royal Oak, MI

The volume was about 7–8 cm³. Based on considerations of volume alone, this procedure yields an effective thickness of nearly 20 mm for both these patients (i.e., under ideal circumstances, this procedure yields a treatment volume very similar to that specified in RTOG 95-17, even though prescription is only to 1.0 cm.). Figure 7
Differences in Effective Target Volume Between Various Techniques of Accelerated Partial Breast Irradiation


Department of Radiation Oncology, William Beaumont Hospital, Royal Oak, MI

Purpose: Different cavity expansions are used to define the clinical target volume (CTV) for accelerated partial breast irradiation (APBI) delivered via balloon brachytherapy (1 cm) vs. three-dimensional conformal radiotherapy (3D-CRT) (1.5 cm). Previous studies have argued that the CTVs generated by these different margins are effectively equivalent. In this study, we use deformable registration to assess the effective CTV treated by balloon brachytherapy on clinically representative 3D-CRT planning images.

Methods and Materials: Ten patients previously treated with the MammoSite were studied. Each patient had two computed tomography (CT) scans, one acquired before and one after balloon implantation. In-house deformable registration software was used to deform the MammoSite CTV onto the balloonless CT set. The deformed CTV was validated using anatomical landmarks common to both CT scans.

Results: The effective CTV treated by the MammoSite was on average 7% ± 10% larger and 38% ± 4% smaller than 3D–CRT CTVs created using uniform expansions of 1 and 1.5 cm, respectively. The average effective CTV margin was 1.0 cm, the same as the actual MammoSite CTV margin. However, the effective CTV margin was non-uniform and could range from 5 to 15 mm in any given direction. Effective margins <1 cm were attributable to poor cavity–balloon conformance. Balloon size relative to the cavity did not significantly correlate with the effective margin.

Conclusion: In this study, the 1.0-cm MammoSite CTV margin treated an effective volume that was significantly smaller than the 3D-CRT CTV based on a 1.5-cm margin. © 2010 Elsevier Inc.
<table>
<thead>
<tr>
<th>APBI technique</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMB</td>
<td>• Mature clinical experience</td>
<td>• Invasive—catheters in place for 1 wk</td>
</tr>
<tr>
<td></td>
<td>• Flexible to conform to complex tumor bed geometry</td>
<td>• Multiple percutaneous catheters not acceptable to some patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Placement of catheters is technically demanding and requires specialized expertise</td>
</tr>
<tr>
<td>Single-lumen IBB</td>
<td>• Simple insertion technique</td>
<td>• Invasive—catheter in place for 1 wk</td>
</tr>
<tr>
<td></td>
<td>• Simple spherical dosimetric geometry</td>
<td>• Fixed dosimetric geometry, not flexibility to shape dose especially when skin or chest wall close to balloon</td>
</tr>
<tr>
<td></td>
<td>• Large clinical experience, just beginning to mature</td>
<td>• Improved flexibility to shape dose but limited</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Limited clinical experience</td>
</tr>
<tr>
<td>Multilumen IBB</td>
<td>• Simple insertion technique</td>
<td>• Invasive—catheter in place for 1 wk</td>
</tr>
<tr>
<td></td>
<td>• Simple spherical dosimetric geometry</td>
<td>• Multiple hotspots at catheter-tissue interface (unclear clinical significance)</td>
</tr>
<tr>
<td></td>
<td>• Improved flexibility to shape dose but limited</td>
<td>• Limited clinical experience</td>
</tr>
<tr>
<td>Multilumen cage-like intracavitary brachytherapy</td>
<td>• Simple insertion technique</td>
<td>• Invasive—catheter in place for 1 wk</td>
</tr>
<tr>
<td></td>
<td>• Flexibility to shape dose</td>
<td>• Multiple hotspots at catheter-tissue interface (unclear clinical significance)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Limited clinical experience</td>
</tr>
<tr>
<td>EBB</td>
<td>• Simple insertion technique</td>
<td>• Invasive—catheter in place for 1 wk</td>
</tr>
<tr>
<td></td>
<td>• Simple spherical dosimetric geometry</td>
<td>• Fixed dosimetric geometry</td>
</tr>
<tr>
<td></td>
<td>• No vault shielding required</td>
<td>• Increase surface dose (unclear clinical significance)</td>
</tr>
<tr>
<td></td>
<td>• Reduced heart, lung and nontarget breast dose</td>
<td>• Higher RBE (unclear clinical significance)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Limited clinical experience</td>
</tr>
<tr>
<td>PBSI</td>
<td>• Single 1-day procedure</td>
<td>• Invasive—single procedure without indwelling catheters</td>
</tr>
<tr>
<td></td>
<td>• Increased convenience</td>
<td>• Permanent seeds may not be acceptable to some patients</td>
</tr>
<tr>
<td></td>
<td>• Increased access in remote areas</td>
<td>• Not appropriate for large CTV volumes</td>
</tr>
<tr>
<td></td>
<td>• Flexible to conform to complex tumor bed geometry</td>
<td>• Not appropriate for large seroma cavities</td>
</tr>
<tr>
<td></td>
<td>• LDR may improve therapeutic ratio</td>
<td>• Limited clinical experience</td>
</tr>
<tr>
<td>NIBB</td>
<td>• Noninvasive</td>
<td>• Skin dose may be increased if there is significant skin overlap between orthogonal axes (exclusion criteria)</td>
</tr>
<tr>
<td></td>
<td>• Breast immobilization and image guidance</td>
<td>• Limited clinical experience</td>
</tr>
<tr>
<td></td>
<td>• Sparing of nontarget breast tissue compared with external beam techniques</td>
<td></td>
</tr>
</tbody>
</table>

APBI = accelerated partial breast irradiation; IMB = interstitial multicatheter brachytherapy; IBB = intracavitary balloon brachytherapy; EBB = electronic balloon brachytherapy; PBSI = permanent breast seed implant; NIBB = noninvasive image-guided breast brachytherapy; LDR = low-dose rate; RBE = radiobiologic effect; CTV = clinical tumor volume.
Intra-operative brachytherapy

Fig. 1. Photographic document of the case report during roentgen treatment. Notice in the right-lower corner of the figure the note with the picture date: 11th March, 1905.
**Technical innovations**

**Intraoperative radiation therapy in the treatment of early-stage breast cancer utilizing xoft axxent electronic brachytherapy**

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**Table 1: A comparison of IB and XB methods of IORT**

<table>
<thead>
<tr>
<th>Source</th>
<th>Dose at Surface</th>
<th>Dose at 1-cm Depth</th>
<th>Applicator Type</th>
<th>Treatment Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>IB</td>
<td>50 kV x-rays</td>
<td>20 Gy</td>
<td>5 Gy</td>
<td>Solid Spherical</td>
</tr>
<tr>
<td>XB</td>
<td>50 kV x-rays</td>
<td>20 Gy</td>
<td>9–10 Gy</td>
<td>Balloon Catheter</td>
</tr>
</tbody>
</table>

IB = Intrabeam™, XB = Xoft™, kV = kilovoltage, Gy = Gray.

* – Treatment time is dependant on applicator diameter used
IOERT

Surgical incision

Lumpectomy

Tumour resection till the muscle

Detachment of the gland

Shield positioning on the muscle

Suture of the tumour bed

Applicator positioning

Shield extraction, oncoplastic surgery

Soft docking

Permanent seed implants

First report of a permanent breast 103Pd seed implant as adjuvant radiation treatment for early-stage breast cancer.

Fignon JP, Keller B, Rakovitch E, Sarkescica R, Easton H, Que W
Department of Radiation Oncology, Sunnybrook and Women’s Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada. Jean-Philippe.Fignon@sw.ca

Tolerance and acceptance results of a palladium-103 permanent breast seed implant Phase III study.

Fignon JP, Rakovitch E, Keller EM, Sarkescica R, Chartier C.
Department of Radiation Oncology, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada. Jean-Philippe.Fignon@sunnybrook.ca


**FIG. 1.** Contributions of primary and scattered photons to total absorbed dose at the photon energies investigated in this work. (a) 28.4 keV, (b) 100 keV, (c) 350 keV, and (d) 662 keV. The calculations are for point sources inside cubic phantoms with side lengths of 20 cm at 28.4 keV and 40 cm at the higher energies. The dose distributions are derived by an extended version of EGS4 and multiplied by the distance squared and normalized to the primary photon energy.
Ratios of (a) mass energy absorption coefficients, (b) mass attenuation coefficients, and (c) unrestricted mass collision stopping powers of the bulk tissues relative to water, illustrating the range of radiological parameters for cancerous and normal soft tissues.
TABLE I. Sensitivity of commonly treated anatomic sites to dosimetric limitations of the current brachytherapy dose calculation formalism. Items flagged as “Y” indicate the authors opinion that significant differences between administered and delivered dose are possible due to the highlighted dosimetric limitation.

<table>
<thead>
<tr>
<th>Anatomic site</th>
<th>Source energy</th>
<th>Absorbed dose</th>
<th>Attenuation</th>
<th>Shielding</th>
<th>Scattering</th>
<th>Beta/kerma dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>High</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Breast</td>
<td>High</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>GYN</td>
<td>High</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Skin</td>
<td>High</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Lung</td>
<td>High</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Penis</td>
<td>High</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Eye</td>
<td>High</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
</tr>
</tbody>
</table>

Acuros vs. TG-43 study

- 100 dosimetric plans using (Mammosite, Contura, and multi-cath) were recalculated using Acuros.
- Dosimetric parameters extracted and compared:
  - Max skin dose, max rib dose, D90, D95, V100, V150, V200
- Geometric parameters recorded:
  - Balloon diameter, distance to skin, distance to rib
- All Contura patients have 3 plans (SLSD, SLMD, MLMD) and each was recomputed using Acuros.
Comparison of dosimetric plans for interstitial multi-catheter implants revealed minimal variance between TG43 based and Acuros computation methods: an average difference of 2.8% in the maximum skin dose, a less than 2% in target coverage and only a 3.0cm³ maximum difference in V100, V150 and V200.

However, differences of potential clinical significance were discovered in balloon based treatment techniques: an average difference of 8% for maximum skin dose (with maximum values >10% when single dwell position was used in a large balloon) and an average difference of 7% for maximum rib dose.

The Acuros based computation suggests that target coverage may be less than previously expected (by TG43) by up to 5.5% (D95 and D90). Consequently, computation with Acuros suggests actual delivered dose to all breast tissue is less than previously represented by TG43 based calculations. The maximum difference was observed in conjunction with a large balloon (>5.5cm diameter) with a decrease in V100 of 16.9 cm³ and an average decrease for all cases of 8.9cm³; differences in V150 and V200 were in the range of 2.5 to 5.7cm³ and 0.2 to 2.2cm³, respectively.
Other issues worth talking about

- The issue of **margins**: margins should be seen/used in the context of the dose distribution created by a certain treatment.

- Better understanding and modeling of both tumor control and normal tissue complications. Cellular damage response and the fate of a cell and the maintenance of tissue functions (homeostasis) and ‘supracellular’ (or tissue level) responses and mechanism are two fundamental things. Our models do not capture this hierarchic organization.

- Customizing RT treatment to risk-groups based on genetic testing
The issue of margins
While we accept these margins as a given and use them for treatment planning, we challenge the concept by creating a ‘true’ or ‘effective’ target by comparing its radiobiological effects with other existent treatments.
EUBED denotes the BED which, if uniformly delivered to the CTV, would give the same fraction of surviving cells as a given non-uniform BED distribution

\[ EUBED = -\frac{1}{\alpha} \ln\left(\frac{1}{N} \sum_{i=1}^{N} e^{-\alpha \text{BED}(i)}\right) \]

EUD contains an additional unit-less volume parameter “a” that is tissue and endpoint specific

\[ g\text{BEUD} = \left(\frac{1}{N} \sum_{i=1}^{N} \text{BED}(i)^{a}\right)^{\frac{1}{a}} \]

\[ EUD = \left(\frac{1}{N} \sum_{i=1}^{N} d(i)^{a}\right)^{\frac{1}{a}} \]
Relative to current standard fractionation scheme (3.4 Gy x 10fx) we find that gBEUD

<table>
<thead>
<tr>
<th></th>
<th>7Gy x 4fx</th>
<th>8.25Gy x 3fx</th>
<th>10.25Gy x 2fx</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient 2</strong></td>
<td>26%</td>
<td>25%</td>
<td>21%</td>
</tr>
<tr>
<td><strong>Patient 4</strong></td>
<td>25%</td>
<td>23%</td>
<td>19%</td>
</tr>
</tbody>
</table>
Instead of conclusions

- In most cases targets and prescription doses are just conventions. As we move from Ir-192 to other sources and modalities, one should re-examine the relationship between dose and its spatial extent.

- We should make good use of the fact that various APBI treatment modalities deliver fundamentally different dose distributions and try to integrate them in a model.