

Clinical Experience with Non-Invasive Image-guided Breast Brachytherapy (NIBB)

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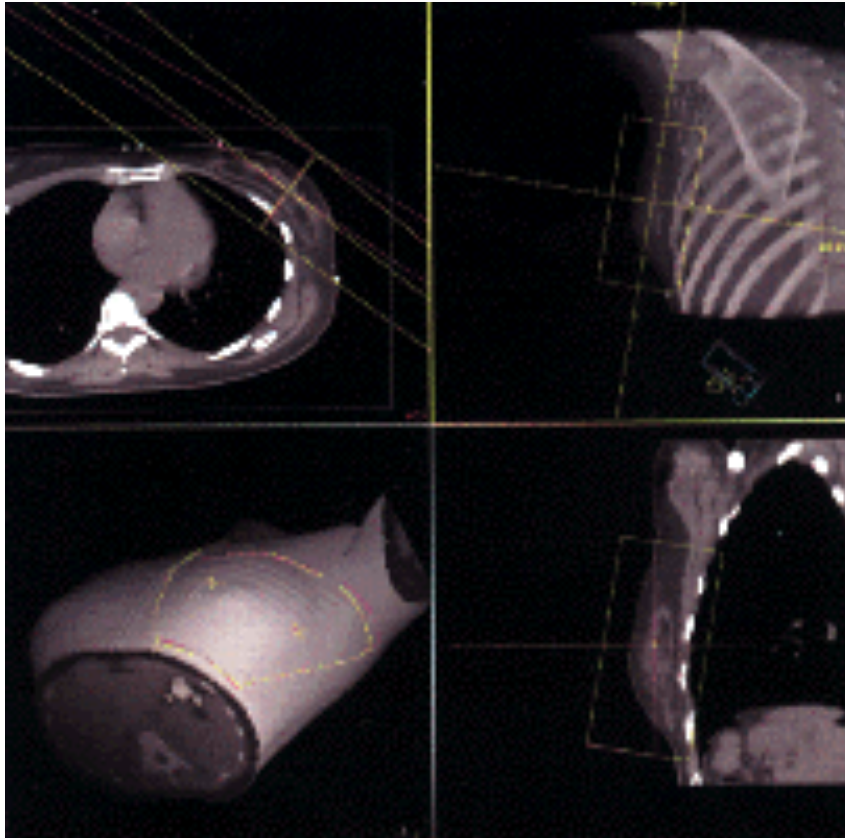
Disclosures

I have no conflicts of interest

Outline

- Background
- NIBB Clinical Implementation
- NIBB Vs. Electron boost
- NIBB for APBI
- Physics
- Conclusions

3D conformal Breast Irradiation



- Performed on a standard linear accelerator; non-invasive.
- Requires time for delineation and planning
- Concern for dose to heart, lung, and contralateral breast
- More issues with breathing motion and setup uncertainties.

Breast Boost: Are We Missing the Target?

A Dosimetric Comparison of Two Boost Techniques

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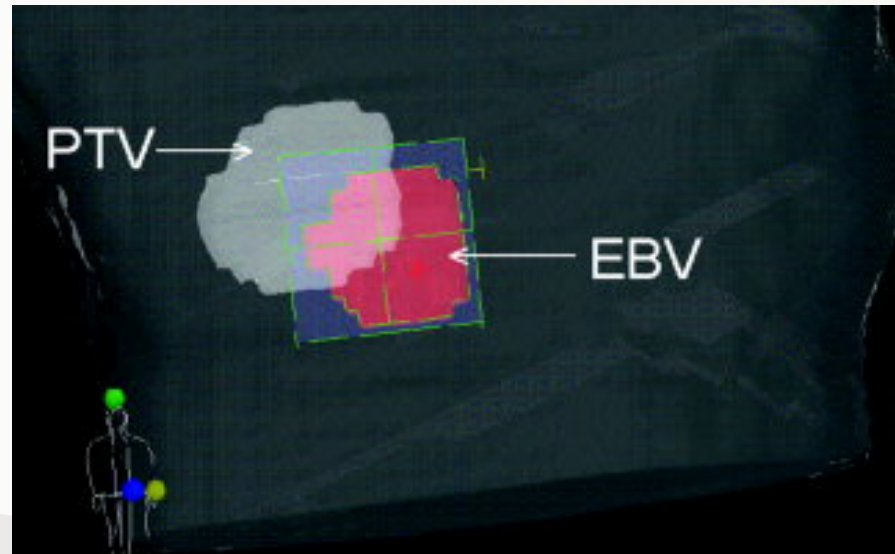
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BACKGROUND. Randomized trials have shown improved local control with the use of a breast boost for patients given breast-conserving treatment for breast carcinoma. Although the use of a breast boost is routine practice, no standard technique has been established. The authors compared the commonly used clinical technique with a technique based on computed tomography (CT) imaging of surgical clips in the tumor bed.

METHODS. Thirty patients underwent CT simulation for postoperative radiation treatment planning as part of breast conservation therapy. During simulation, a CT-compatible wire was placed on the patient's skin, outlining the intended electron boost field; an electron boost volume (EBV) was generated by contouring the tissue underlying the wire. Also contoured was a CT-based clinical target volume (CTV) using surgical clips and postsurgical changes in the tumor bed as a guide. A planning target volume (PTV) was generated using a 1 cm margin around the CTV. An electron beam treatment plan was generated for each technique using the FOCUS three-dimensional treatment planning system. Dose-volume histograms (DVH) were generated to determine the fraction of the PTV receiving 90% of the prescribed dose if treatment was delivered using the EBV. In addition, DVH analysis was done to determine the volume of normal tissue unnecessarily irradiated when using the EBV.

Minimal overlap of the two volumes was noted in the plans based on this patient, resulting in significant under dosing of the tumor bed and unnecessary irradiation of the breast tissue.



Breast Brachytherapy

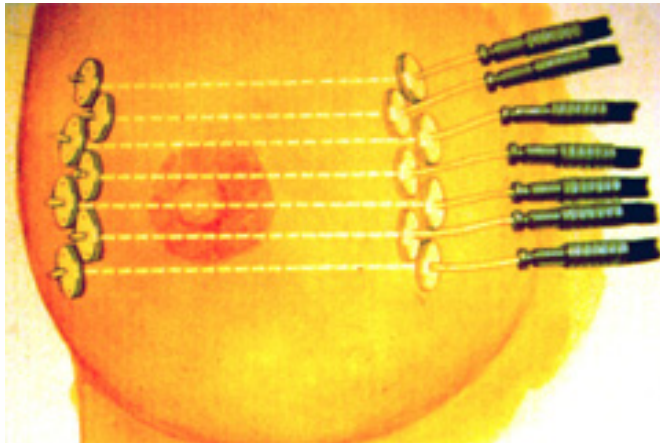
Interstitial Multi-catheter Brachytherapy:

Pros:

- Flexibility in conforming to complex geometry
- Long-term follow up data

Limitations:

- Invasive
- Risk of catheter related infection
- Not acceptable to many women



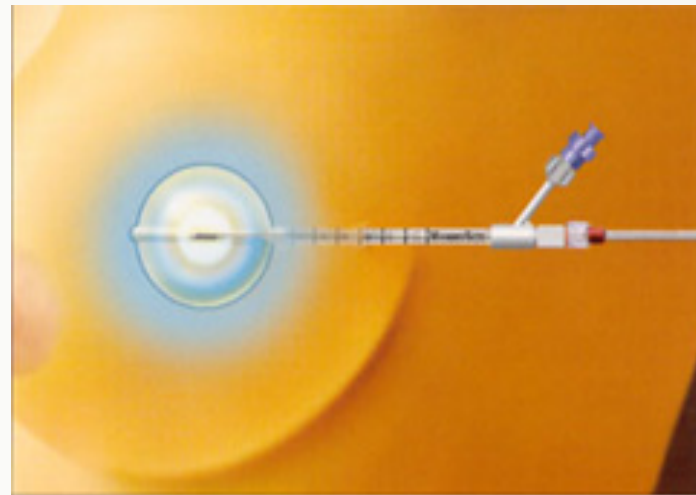
Intra-Cavitary Balloon Brachytherapy (MammoSite)

Pros:

- Simplified single entry technique
- Simplified dosimetric geometry

Limitation:

- Seroma cavity can mimic balloon shape



Concerns with current Breast Irradiation Techniques

- Cosmetic outcomes.
- Skin sparing.
- Invasive procedures.
- Post treatment complications (infection).
- Tumor targeting (are we missing the Target?).
- Radiation doses to the heart and lungs.

NIBB Unit

X-ray Tube

Compression
Plates

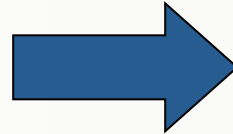
Imaging Cassette



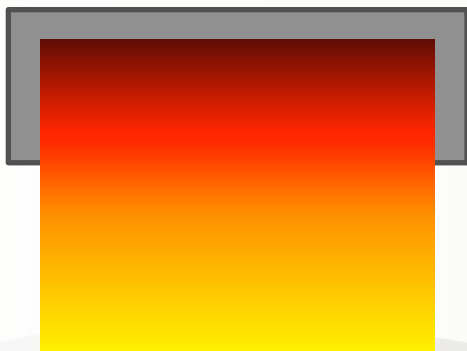
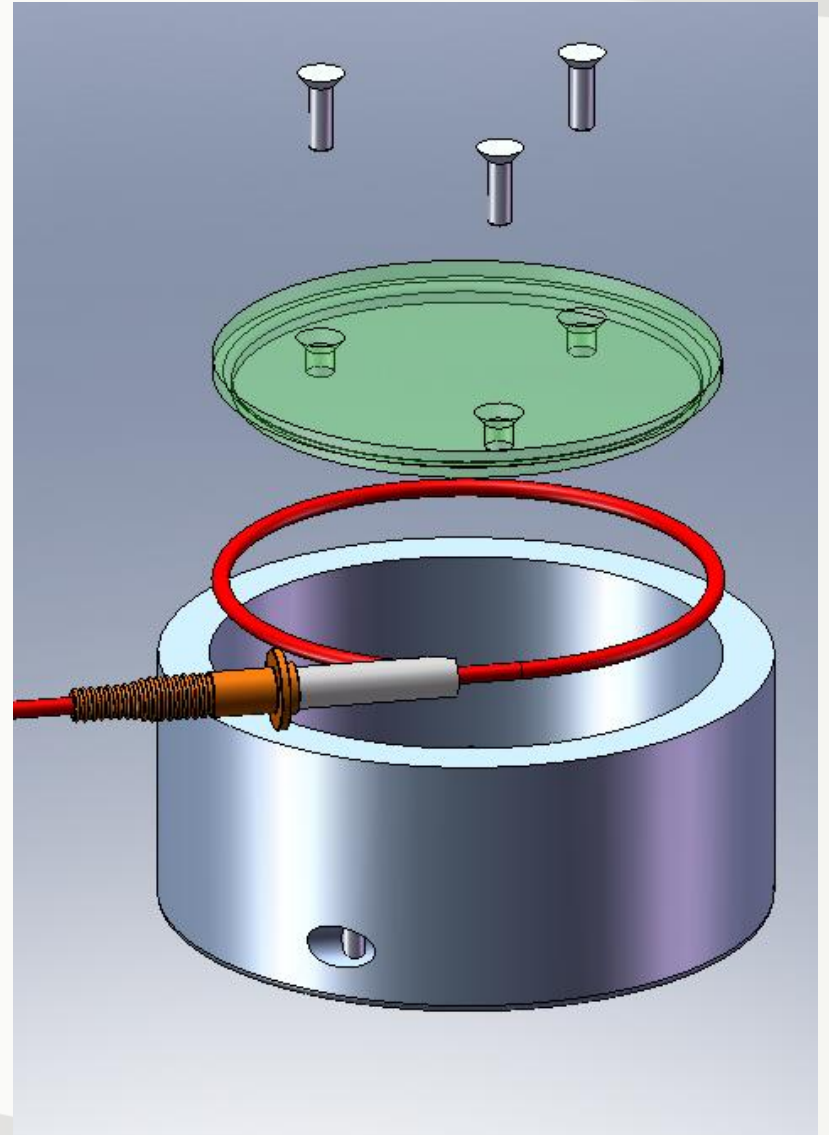
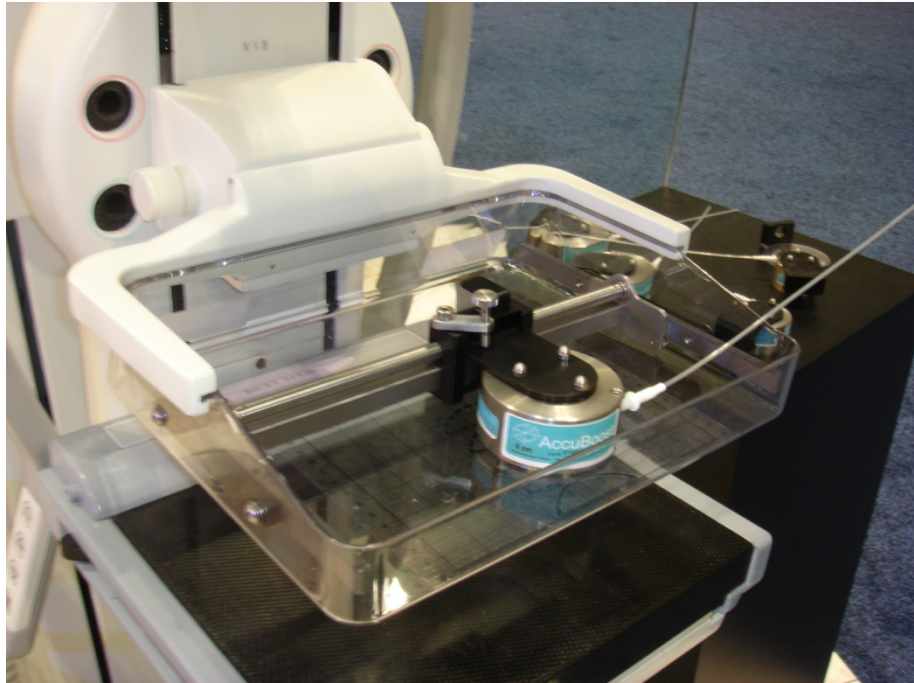
Process is repeated in an orthogonal axis



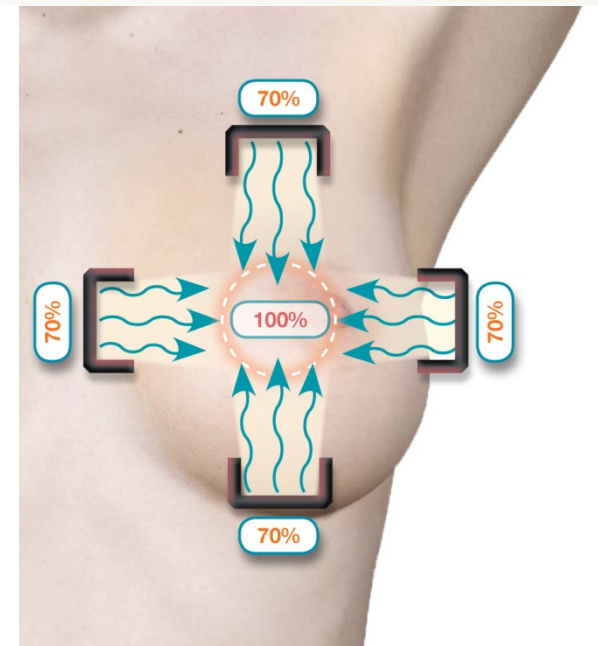
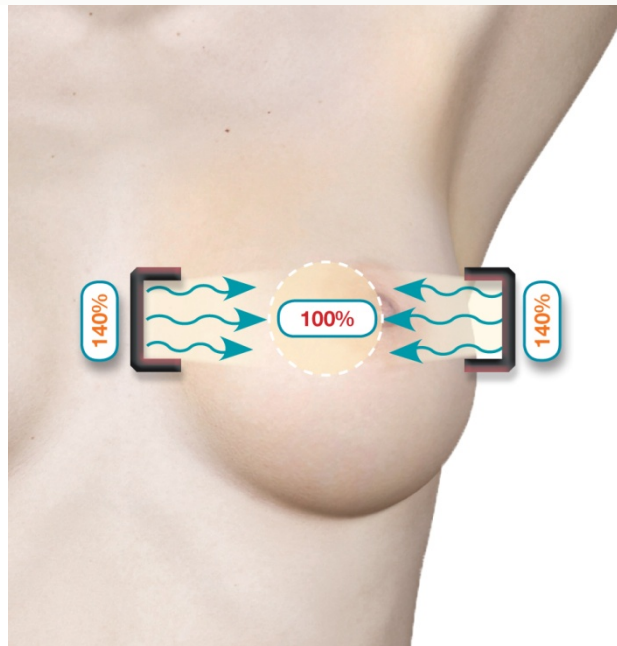
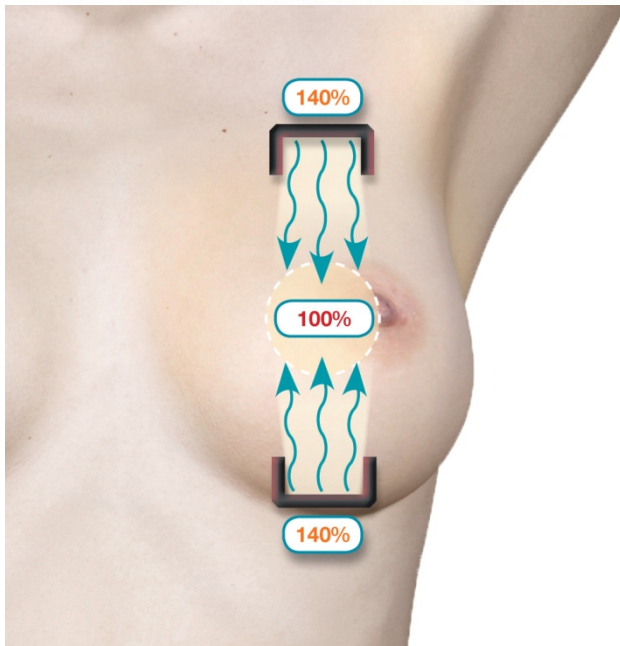
Breast
Compression



kV imaging
in immobilized
position



Two Orthogonal Treatment Axes

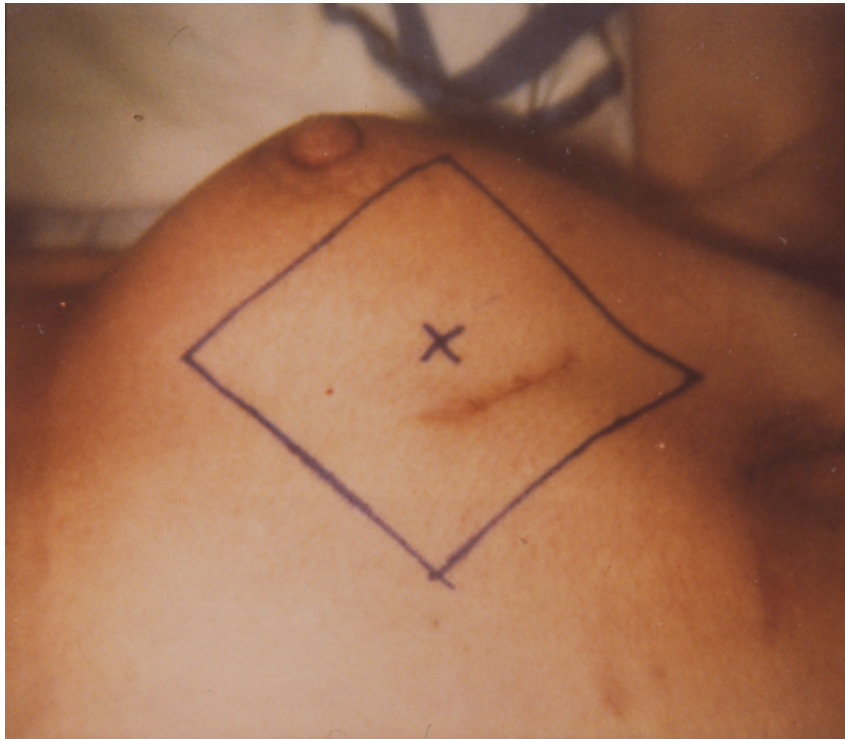


Cranial–Caudal (CC)

Medial–Lateral (ML)

Electrons vs NIBB

Electron Boost Targeting

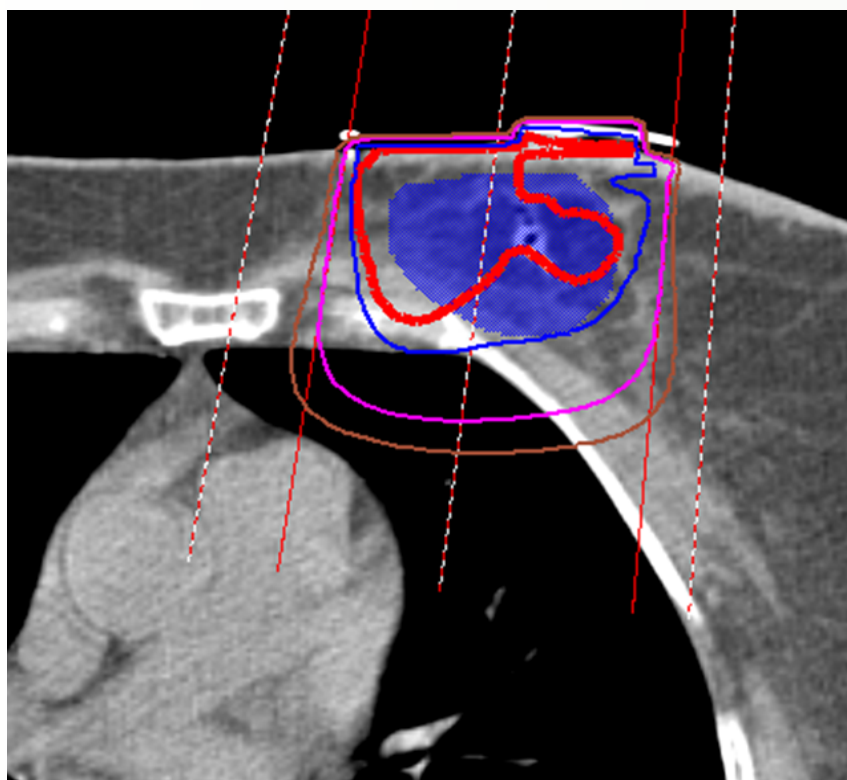


NIBB Targeting

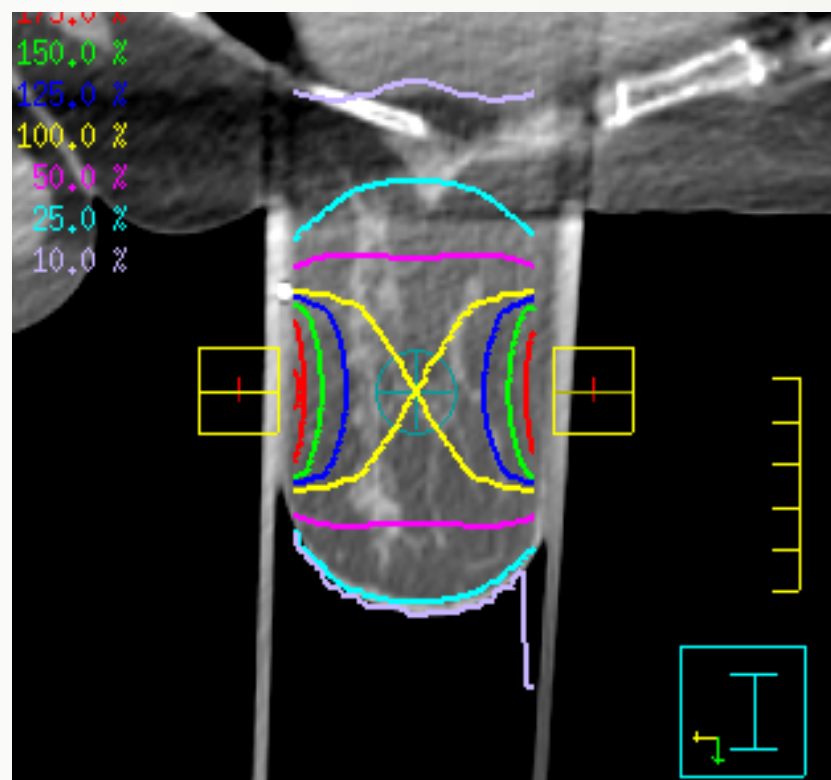


NIBB Vs Electron Boost Dosimetry

Conventional Electron Boost – 90% isodose line grazes the lung & 50% isodose line penetrates deeply into the chest cavity

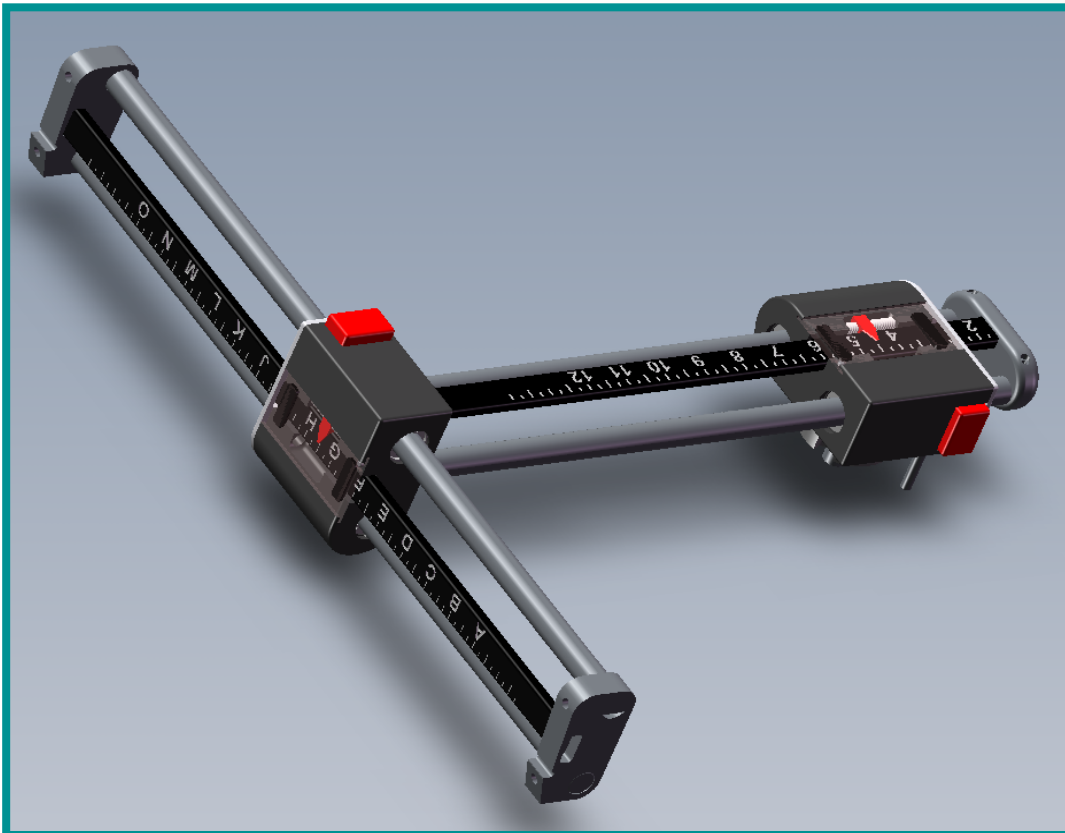
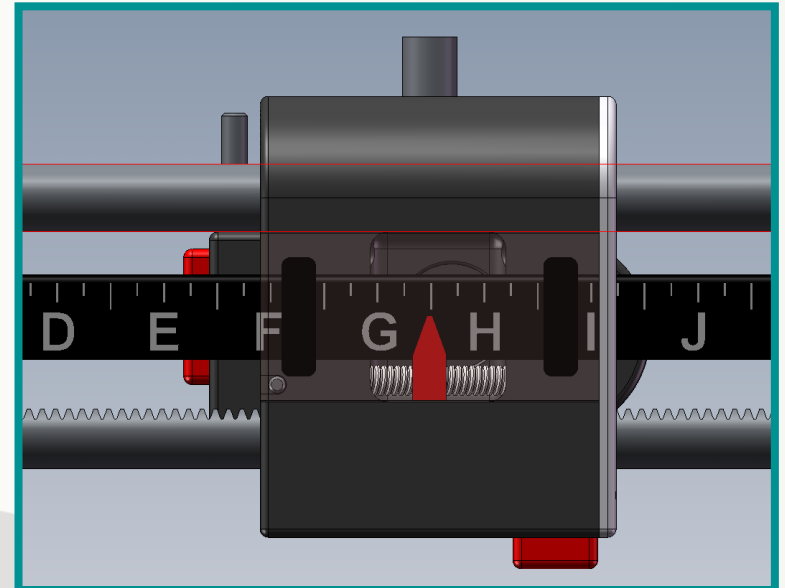
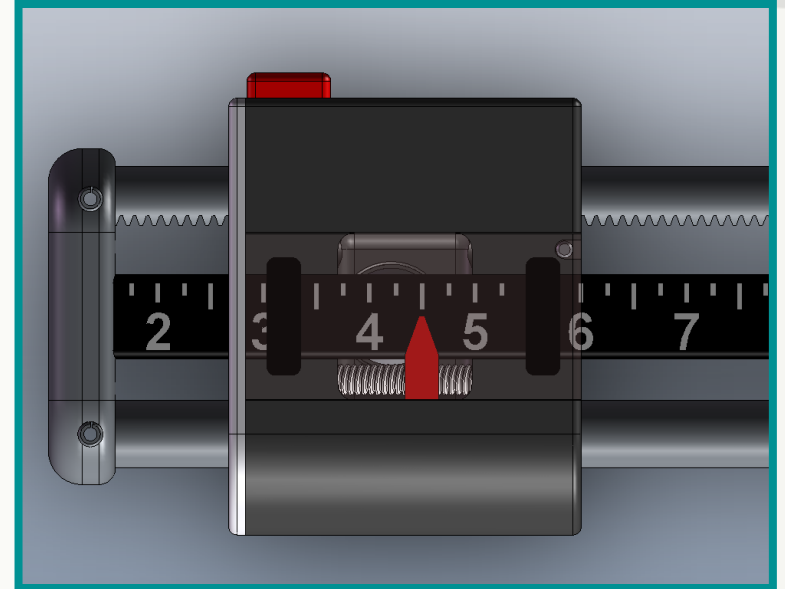


AccuBoost – The 10% isodose line barely penetrates the chest cavity



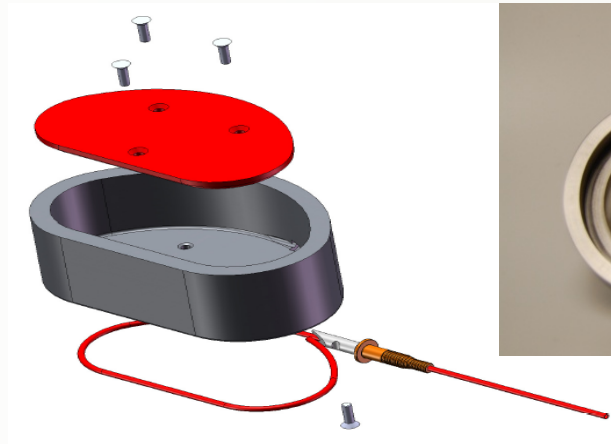
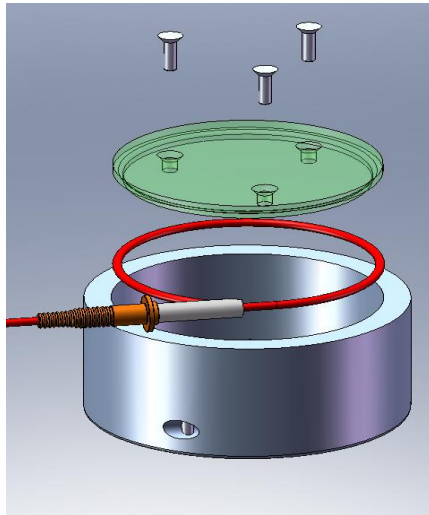
Position Adjustment

The positioning accessories for the pair of applicators are set to the alphanumeric coordinates of the isodose center.



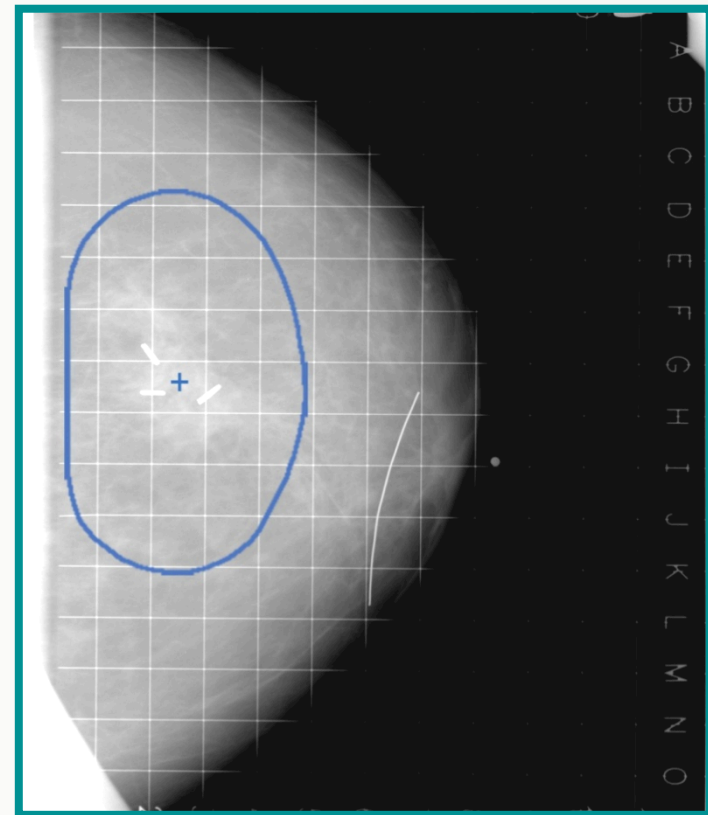
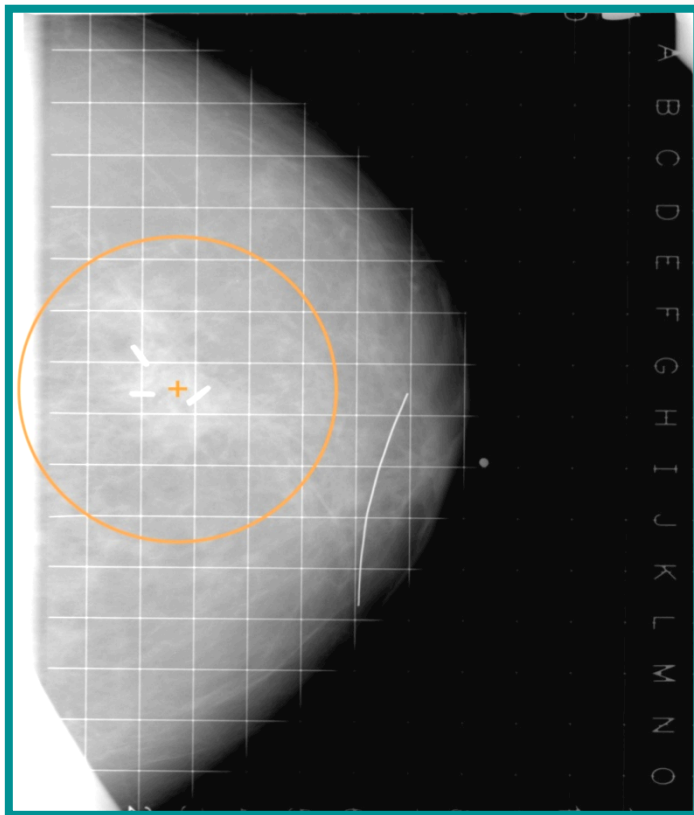
Applicators

- 1st Generation Round Applicators
- D-Applicators
- 2nd Generation Round Applicators (skin-dose optimized SDO) and (dose-rate optimized DRO) applicators

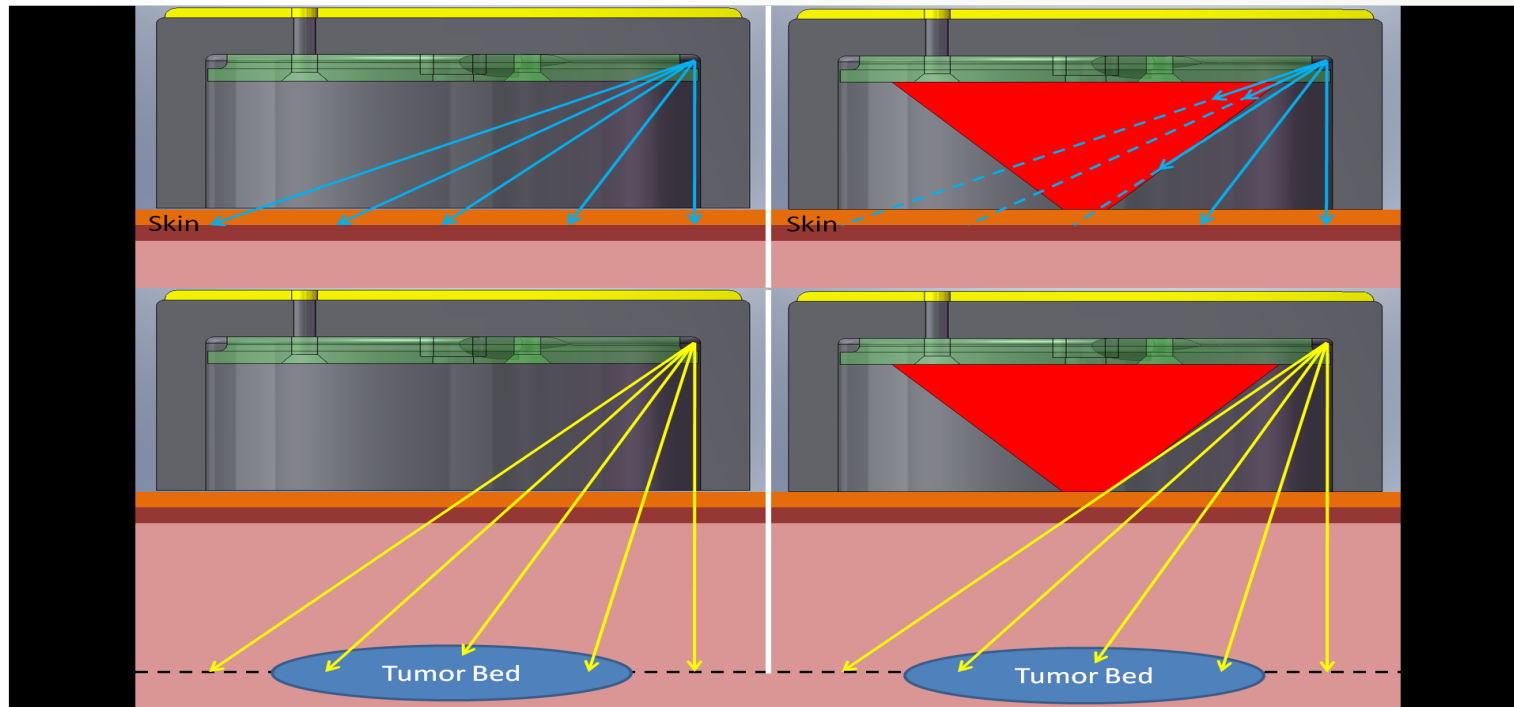


D-Applicator

The D-Shaped Applicators avoid interference with the chest wall for deep seated lumpectomies.



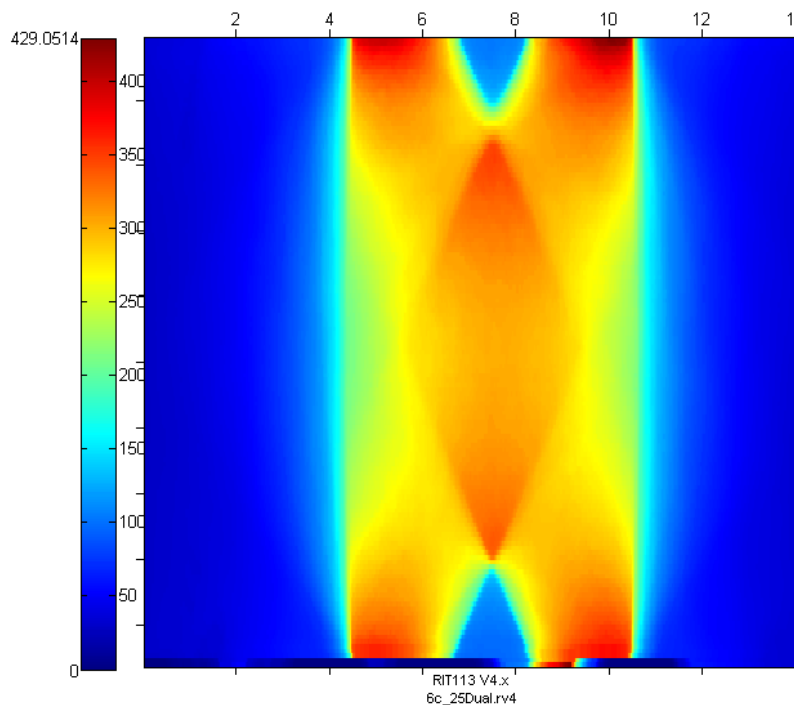
Schematic Comparison of 1st and 2nd Generation Applicators



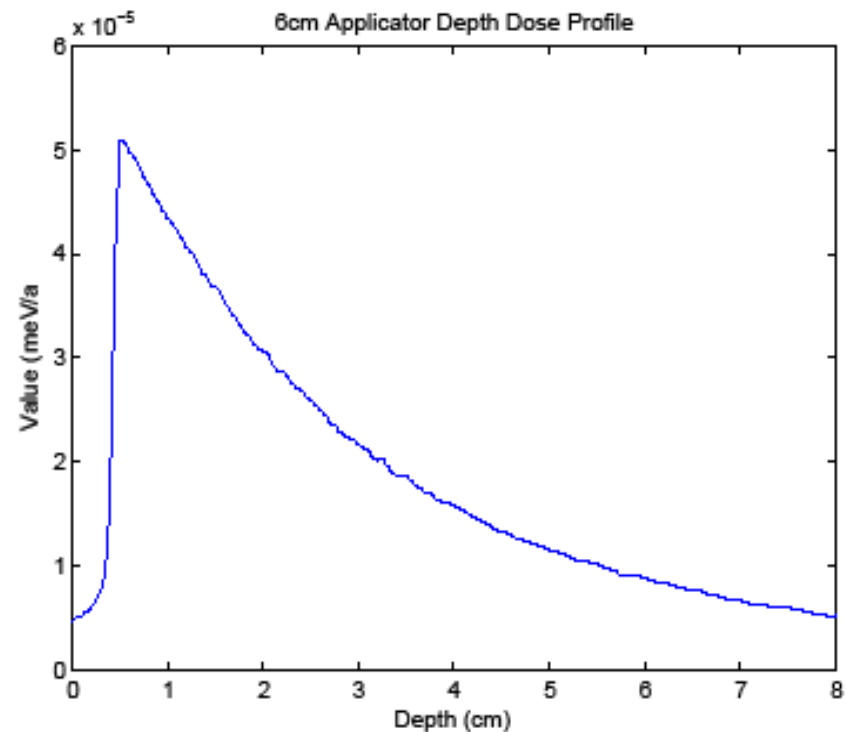
Second generation applicators: different height
(25mm, 19 mm), coned field

2nd Generation Round Applicators

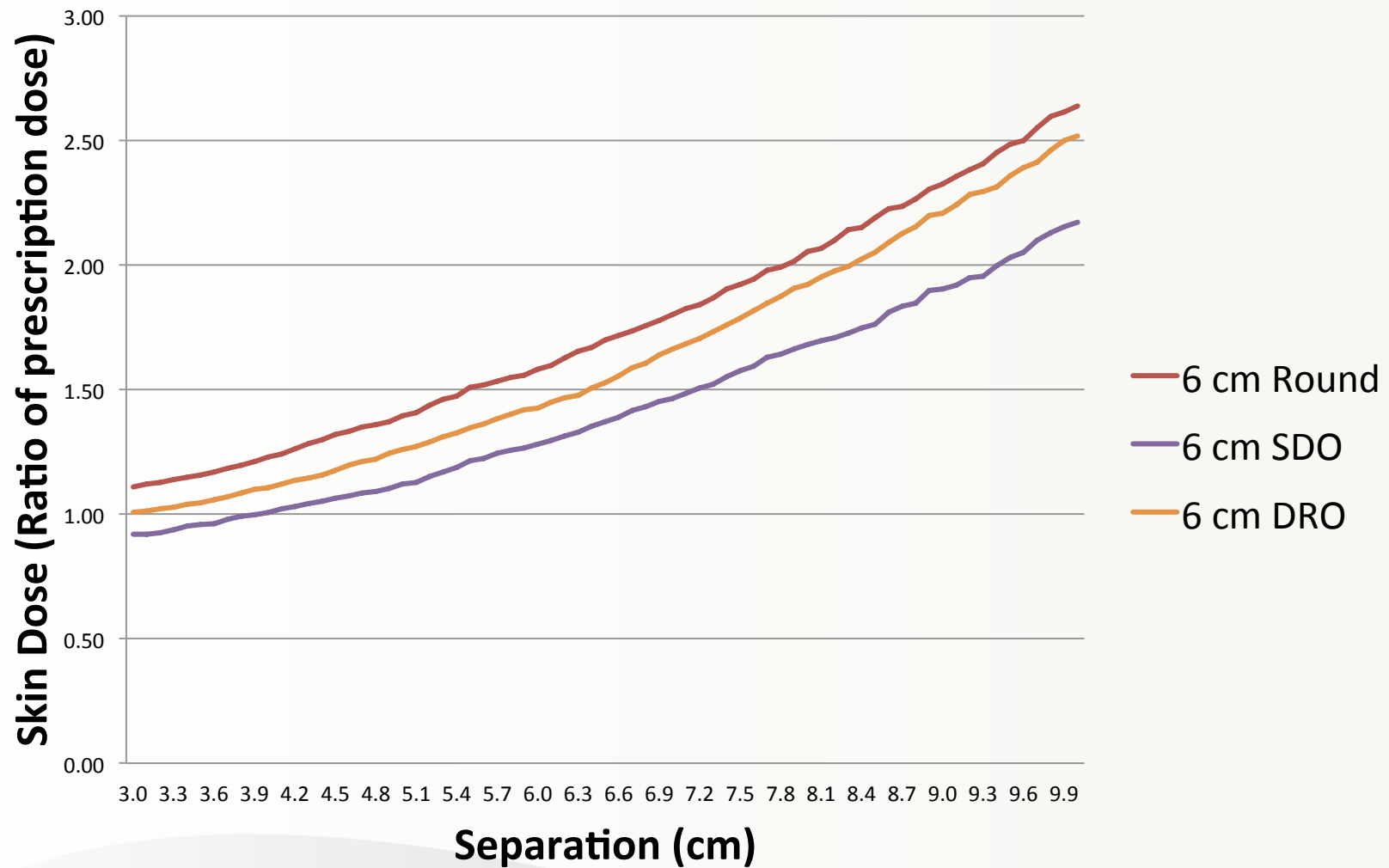
Gafchromic film



Depth Dose profile



Average Skin Dose by Applicator Type



Toxicity for NIBB Vs EB in WBI

Breast Boost Using Noninvasive Image-Guided Breast Brachytherapy vs. External Beam: A 2:1 Matched-Pair Analysis

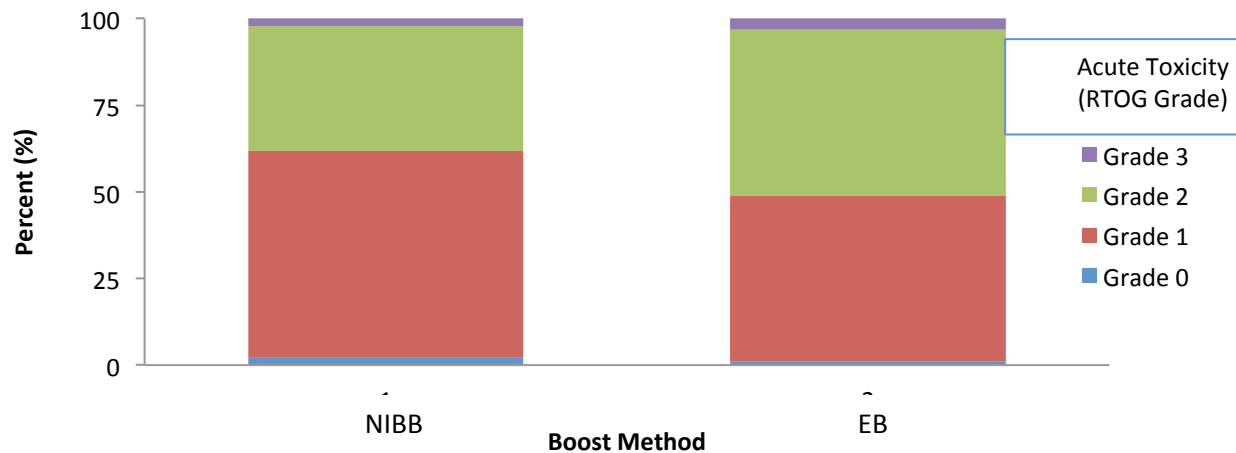
Kara Lynne Leonard,^{1,2} Jaroslaw T. Hepel,^{1,2} John R. Styczynski,²
Jessica R. Hiatt,² Thomas A. DiPetrillo,^{1,2} David E. Wazer^{1,2}

Abstract

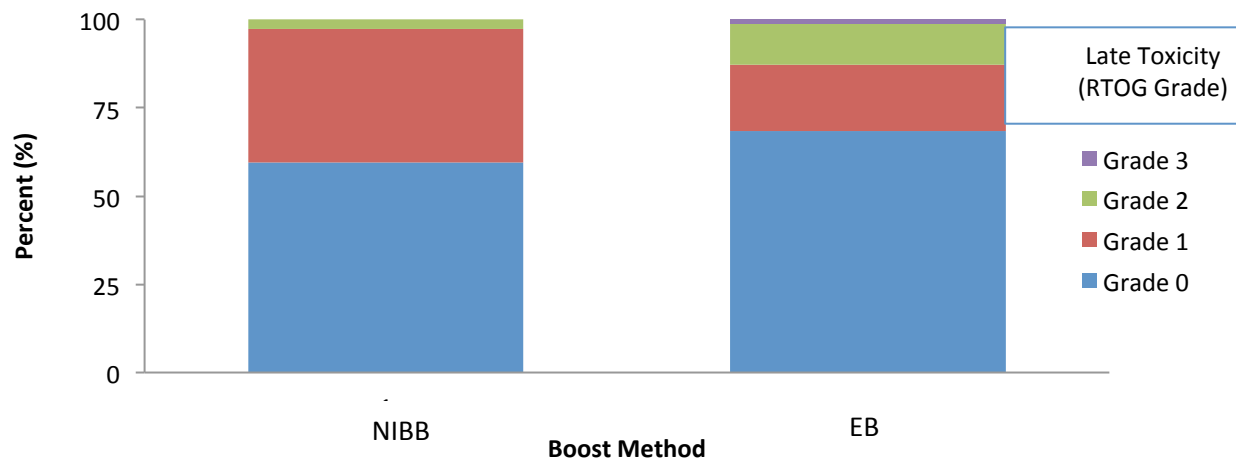
Outcomes were compared for 47 women with breast cancer undergoing breast-conserving therapy with whole breast irradiation (WBI) and noninvasive breast brachytherapy (NIBB) boost and 94 matched control subjects treated with WBI and electron beam (EB) boost. Acute desquamation occurred in 39% and 52% of patients, respectively. There was less skin/subcutaneous toxicity in those treated with NIBB than in those treated with EB ($P = .046$). NIBB compares favorably with EB.

Background: To compare clinical outcomes and toxicity in patients treated with NIBB boost with those in patients treated with external beam (EB) boost. **Patients and Methods:** Women with early stage breast cancer treated with WBI and NIBB boost were identified. Control subjects treated with EB boost identified as the best possible match with respect to age, stage, chemotherapy use, and fractionation were chosen for a 2:1 comparison. Acute toxicity, late toxicity, and oncologic outcomes were reviewed. The McNemar nonparametric test was used to evaluate marginal homogeneity between matched pairs. **Results:** One hundred forty-one patients were included in the analysis: 47 patients treated with NIBB boost and 94 matched control subjects treated with EB boost (electron, $n = 93$) or 3-D conformal radiation ($n = 1$). Grade 2+ desquamation developed in 18 patients (39%) treated with NIBB boost and in 49 patients (52%) treated with EB boost ($P = .07$). Breast size, electron energy, and fractionation predicted for acute desquamation ($P < .0001$, $P < .001$, and $P = .006$). Median follow-up was 13.6 months. One patient (2%) who received NIBB had Grade 2+ skin/subcutaneous fibrosis 15 months after completion of treatment. Among those treated with EB, 9 patients (9.5%) developed Grade 2+ subcutaneous fibrosis, and 1 patient had recurrent cellulitis. There was statistically significantly less combined skin/subcutaneous toxicity in those treated with NIBB than in those treated with EB ($P = .046$). **Conclusion:** NIBB boost is associated with favorable short-term clinical outcomes compared with EB.

Acute Toxicity



Late Skin/Subcutaneous Toxicity



Partial Breast Irradiation

- Convenience
 - Treatment in 1 week or less rather than 4-7 weeks.
- Sparing of non-target tissues
 - Decreased acute skin reaction
 - Potential for decreased late effects and improved cosmetic outcomes
 - Sparing of lung and heart

Dosimetric Comparison of APBI using 3D-CRT and NIBB

Three-Dimensional Dose Modeling of the AccuBoost Mammography-Based Image-Guided Non-Invasive Breast Brachytherapy System for Partial Breast Irradiation



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¹*Department of Radiation Oncology, Tufts Medical Center, Tufts University School of Medicine, Boston, MA*

²*Department of Radiation Oncology, Rhode Island Hospital, Brown University School of Medicine, Providence, RI*

Results: PTV Dose Comparison

APBI	PTV Vol (cc)	PTV D _{max} (Gy)	PTV D _{min} (Gy)	PTV D _{mean} (Gy)
Median AccuBoost [p25-p75]	77.9 [58.2, 118.7]	45.5 [42.7, 48.6]	33.9 [29.3, 35.5]	39.5 [37.1, 40]
Median 3D-CRT [p-25-p75]	221.6 [202, 360.2]	40 [39.7, 40.6]	31.4 28.6, 32.7]	38.6 [38, 38.6]
p-value	0.01	0.06	0.25	0.64



No difference in
target Coverage

Results: PTV Dose Comparison

APBI	PTV Vol (cc)	PTV D _{max} (Gy)	PTV D _{min} (Gy)	PTV D _{mean} (Gy)
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p-value	0.01	0.06	0.25	0.64



NIBB more heterogeneous
like other brachytherapy
techniques

Results: PTV Dose Comparison

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p-value	0.01	0.06	0.25	0.64



Target volume
decrease → 1/3!!

Normal Tissue D_{max} Comparison

APBI	CW Max (cGy)	Lung Max (cGy)	Skin Max (cGy)
Median AccuBoost [p25-p75]	32.4 [27.4, 88.4]	18.7 [17.6, 25.4]	94.8 [76.5, 101]
Median 3D-CRT [p-25-p75]	99.9 [95.1, 100.5]	91.9 [88.4, 98]	104 [103.5, 106]
p-value	0.01	0.02	0.04

Normal Tissue D_{max} Comparison

APBI	CW Max (cGy)	Lung Max (cGy)	Skin Max (cGy)
Median AccuBoost [p25-p75]	32.4 [27.4, 88.4]	18.7 [17.6, 25.4]	94.8 [76.5, 101]
Median 3D-CRT [p-25-p75]	99.9 [95.1, 100.5] x3	91.9 [88.4, 98] x4.5	104 [103.5, 106] x1.1
p-value	0.01	0.02	0.04

Non-invasive Image-guided Breast Brachytherapy

- Novel technique for partial breast irradiation
 - Non-invasive
 - Precision Targeting
 - Breast immobilization
 - No need for large PTV margins
 - Image-guidance
 - Collimated photon emissions using Tungsten alloy applicators
 - Utilizes HDR ^{192}Ir source

Physics

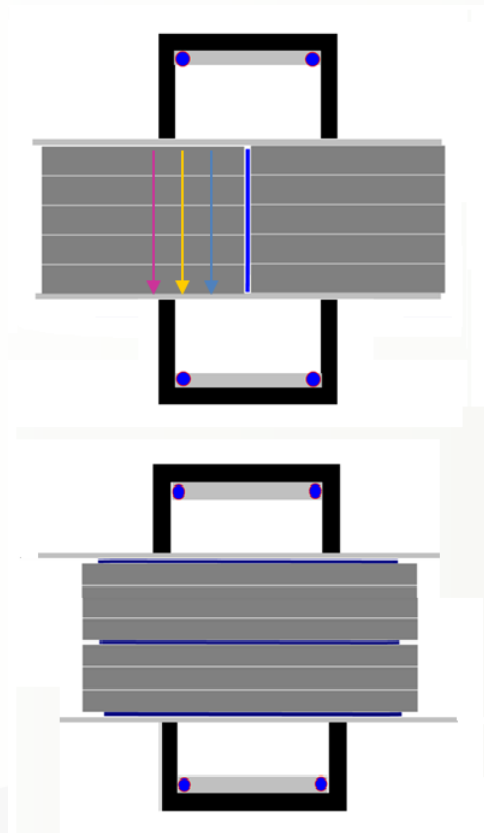
Verification Studies

Dose Delivery

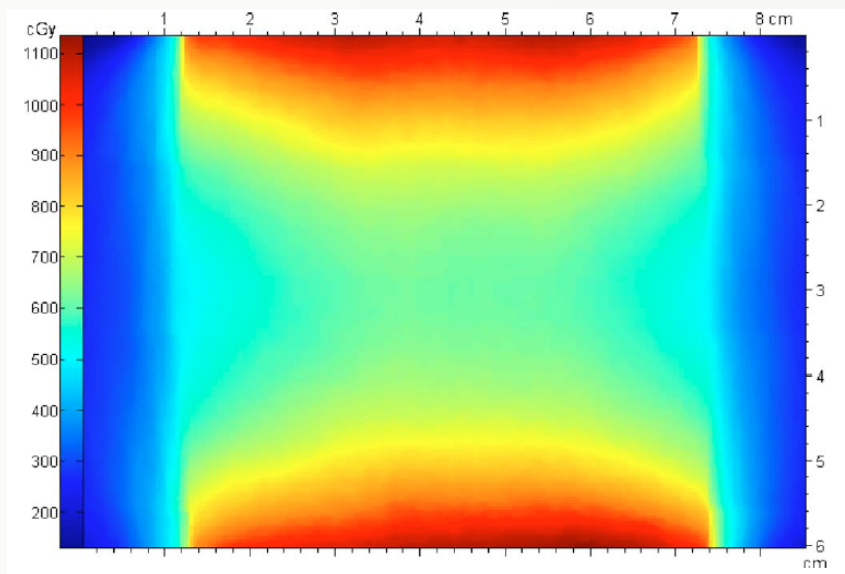
- QA phantom based verification of dose delivered to simulated breast center
- Methods
 - Ionization Chamber
 - Gafchromic Film

Round applicator film measurements

QA setup



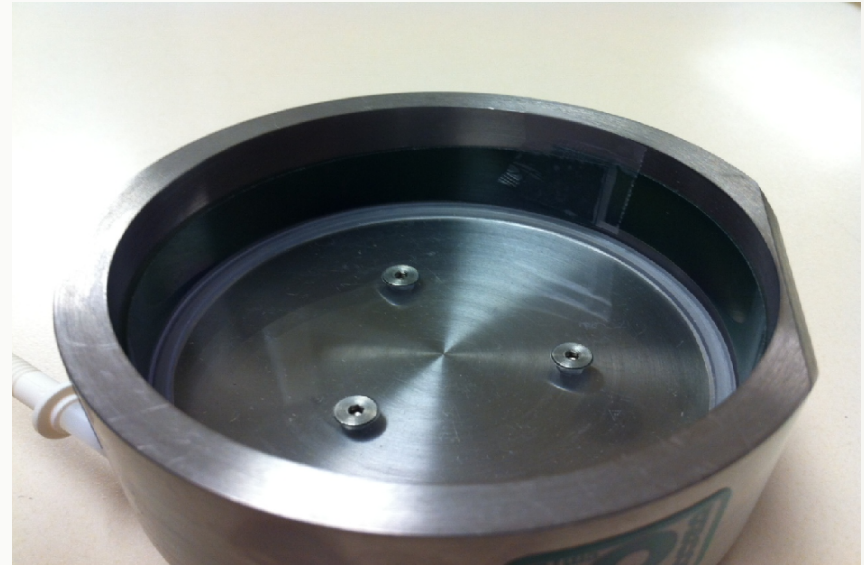
Gaph chromic film isodose distribution using two 6 cm diameter Round applicator



Verification Studies

Source Position Verification

- Gafchromic film
- Apply to film, tape into circle
- Run source to 500 mm beyond end of current transfer tube, verify no obstruction
- Expose film with all required dwell positions



Continuing QA

Key Considerations

- Plate Separation (compression thickness)
- Applicator Catheters (inspection and replacement)
- Transfer Tubes
- Alignment Verification
- Integration into overall x-ray QA
- Image Quality Verification

Second Check Options

- 2nd review all primary inputs
- Second Check tables
- Create independent analytical fit to measured data (dose-depth curves)

Round Applicator Treatment Nomogram

Patient name

RadOnc #

Treatment date	2/28/2009
Treatment fraction	2 of 5
Isocenter location	L5
Mammography unit gantry angle [degrees]	-90
Applicator size [mm]	50
Source strength [Ci]	10.00
Plate separation [30-80 mm]	40
Percent isodose line [70%-100%]	100%
Prescription breast dose [Gy] per fraction	1.00
Center dose rate [Gy/h]	17.06
Treatment time [minutes] for 2 catheters	3.52

Documentary Inputs

Calculation Inputs

Dose delivery nomogram

Catheter #	1	2
Dose from catheter [Gy]	0.50	0.50
Dose calculation medium	breast	breast
Dwells [#]	15	15
Total time [minutes]	1.76	1.76
Dwell positions	Dwell time (s)	Dwell time (s)
1	7.0	7.0
2	7.0	7.0
3	7.0	7.0
4	7.0	7.0
5	7.0	7.0
6	7.0	7.0
7	7.0	7.0
8	7.0	7.0
9	7.0	7.0
10	7.0	7.0
11	7.0	7.0
12	7.0	7.0
13	7.0	7.0
14	7.0	7.0
15	7.0	7.0
16		
17		
18		
19		
20		
21		
22		
23		
24		

Second Check Tables

Applicator = 7 cm Round

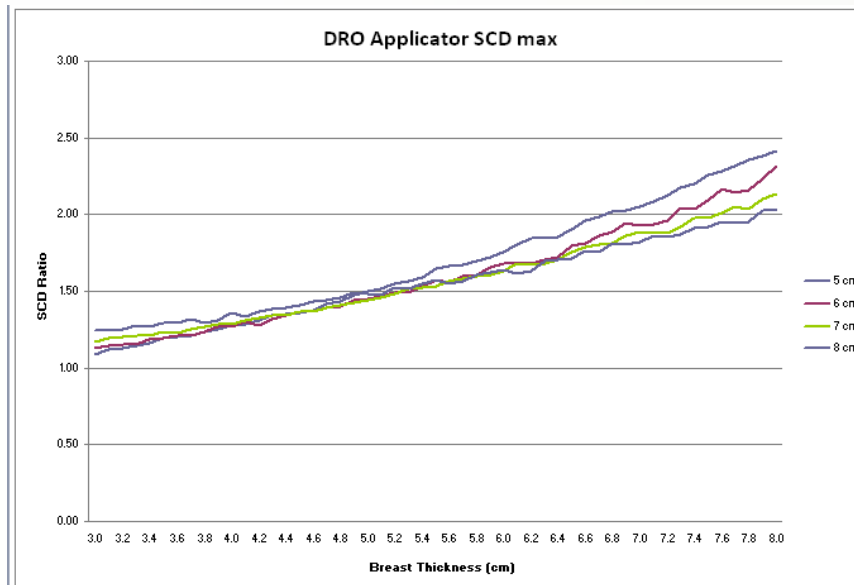
21 Dwell Positions per Catheter

Time per dwell in Seconds

		Compression thickness (mm)										
		30	35	40	45	50	55	60	65	70	75	80
Source Strength (Ci)	12.0	8.9	9.7	10.5	11.3	12.2	13.2	14.2	15.4	16.5	17.8	19.1
	11.5	9.3	10.1	10.9	11.8	12.8	13.8	14.9	16.0	17.3	18.6	20.0
	11.0	9.7	10.5	11.4	12.3	13.3	14.4	15.5	16.8	18.0	19.4	20.9
	10.5	10.2	11.0	11.9	12.9	14.0	15.1	16.3	17.6	18.9	20.3	21.9
	10.0	10.7	11.6	12.5	13.6	14.7	15.8	17.1	18.4	19.8	21.4	22.9
	9.5	11.3	12.2	13.2	14.3	15.4	16.7	18.0	19.4	20.9	22.5	24.2
	9.0	11.9	12.9	13.9	15.1	16.3	17.6	19.0	20.5	22.1	23.7	25.5
	8.5	12.6	13.6	14.8	16.0	17.3	18.6	20.1	21.7	23.4	25.1	27.0
	8.0	13.4	14.5	15.7	17.0	18.3	19.8	21.4	23.0	24.8	26.7	28.7
	7.5	14.3	15.4	16.7	18.1	19.6	21.1	22.8	24.6	26.5	28.5	30.6
	7.0	15.3	16.6	17.9	19.4	21.0	22.6	24.4	26.3	28.4	30.5	32.8
	6.5	16.4	17.8	19.3	20.9	22.6	24.4	26.3	28.4	30.5	32.8	35.3
	6.0	17.8	19.3	20.9	22.6	24.5	26.4	28.5	30.7	33.1	35.6	38.2
	5.5	19.4	21.1	22.8	24.7	26.7	28.8	31.1	33.5	36.1	38.8	41.7
	5.0	21.4	23.2	25.1	27.1	29.3	31.7	34.2	36.9	39.7	42.7	45.9
	4.5	23.8	25.7	27.9	30.2	32.6	35.2	38.0	41.0	44.1	47.4	51.0
	4.0	26.7	29.0	31.4	33.9	36.7	39.6	42.7	46.1	49.6	53.4	57.4

SCD Tables/Plots

- General Guidance for Applicator Selection
- Max Skin dose for a given applicator type and breast separation



Applicator Selection Table

SCD Ratio - Average					
Breast thickness (cm)	Applicator diameter				
	4	5	6	7	8
3	1.24	1.16	1.15	1.13	1.11
3.5		1.29	1.19	1.16	
4		1.37	1.28	1.22	
4.5		1.43	1.38	1.27	
5		1.53	1.45	1.35	
5.5		1.68	1.55	1.43	
6		1.83	1.71	1.55	
6.5		1.94	1.79	1.64	
7		2.09	1.84	1.73	
8	2.46	2.39	2.17	2.01	1.79

Limitations of NIBB

- No Interlock system (no record and verify)
- Online treatment planning and applicators selection
- Not an option for all patients
- Can be exhausting for some patients
- Requires long Physics and Physicians time

Conclusions

- NIBB represents an alternative non-invasive tumor bed boost and APBI modality.
 - Uniquely addresses sources of intra/interfraction motion with breast immobilization and pre-treatment kV mammography.
- Preliminary studies shown low normal tissue toxicity and favorable cosmetic outcomes.
- NIBB can achieve better cosmetic with delivery of NIBB boost for with WBI.
- Achieve lower doses to the CW, heart and lung

Questions?