Non-Invasive Image-guided Breast Brachytherapy (NIBB)

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AAPM Annual Meeting

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Disclosures

- Travel expenses subsidized by ART Corporation

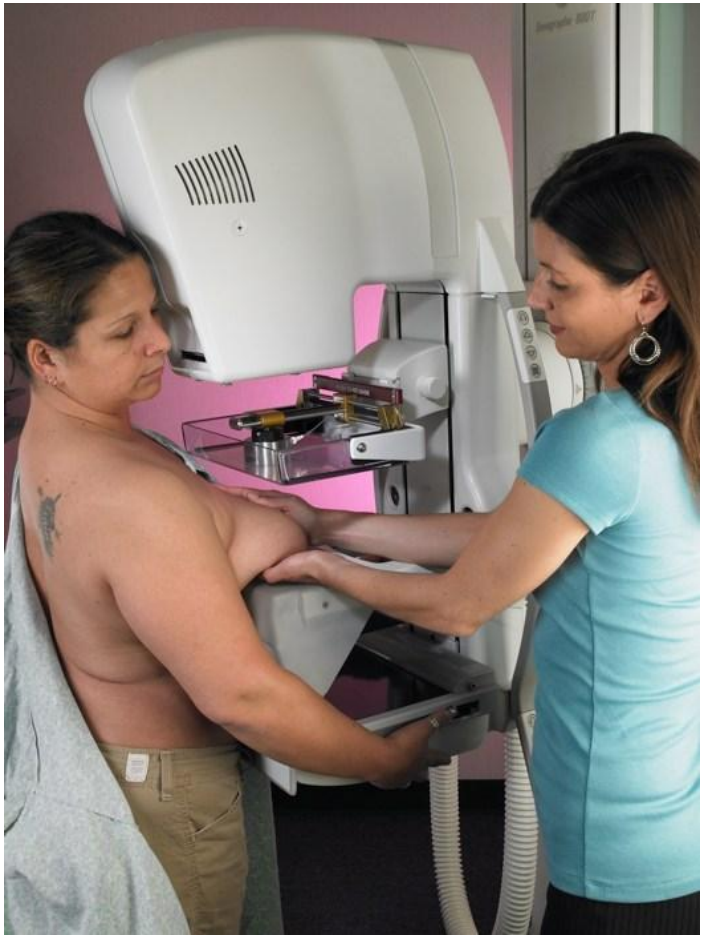
Learning Objectives

- Discuss the NIBB method
- Discuss updated clinical results of NIBB for APBI
- Discuss acute toxicity and toxicity avoidance for NIBB
- Future direction for APBI using NIBB

Non-invasive Image-guided Breast Brachytherapy (AccuBoost)

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

AccuBoost

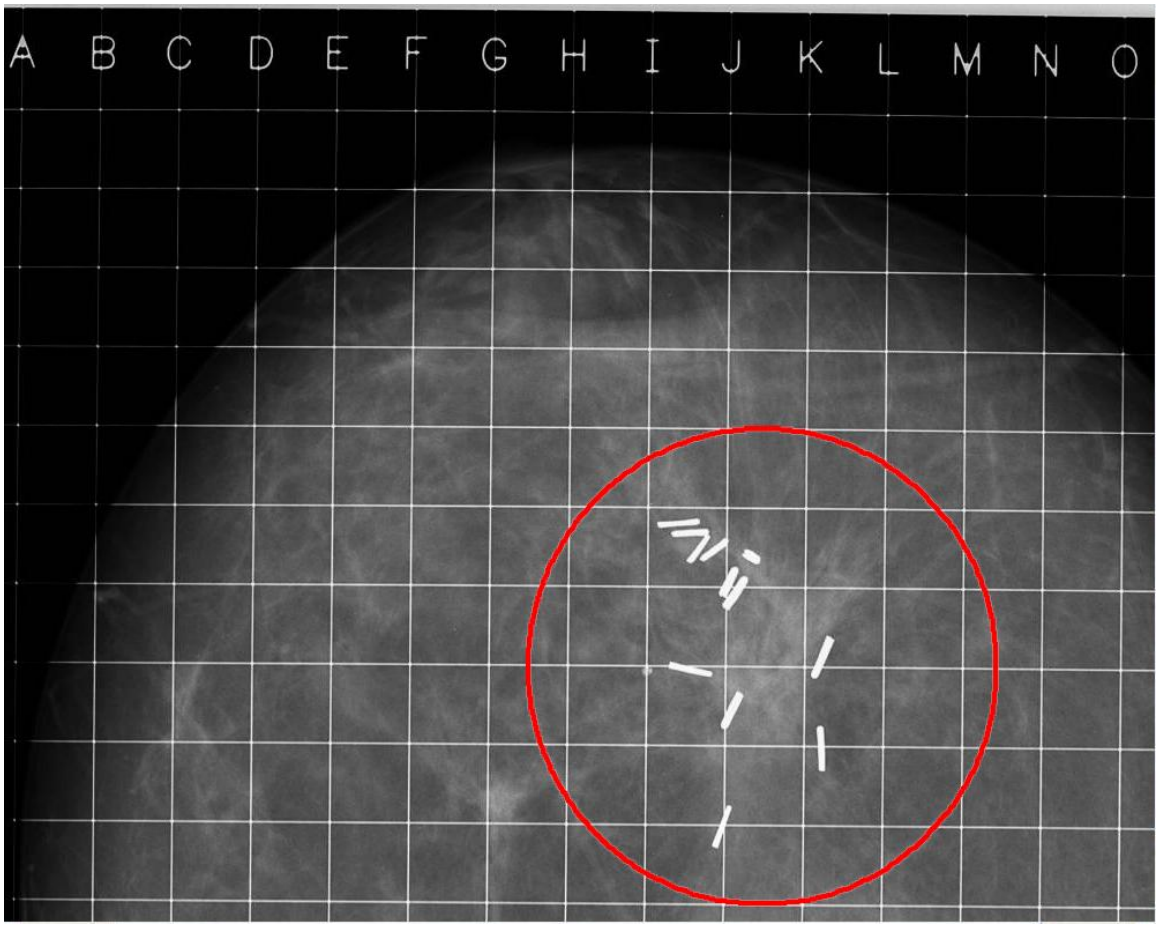


Breast Compression

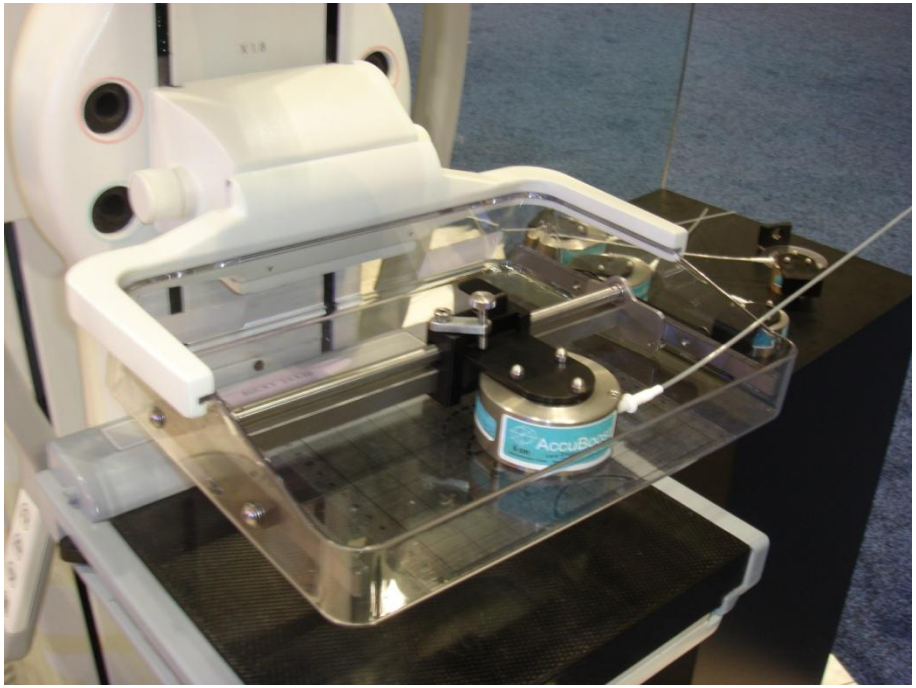
kV imaging
in immobilized position

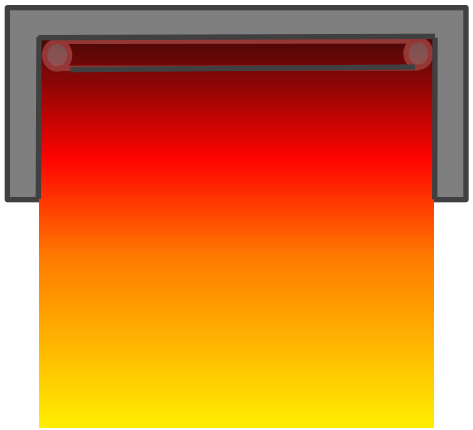
Pictures courtesy of Advanced Radiation Therapy, LLC

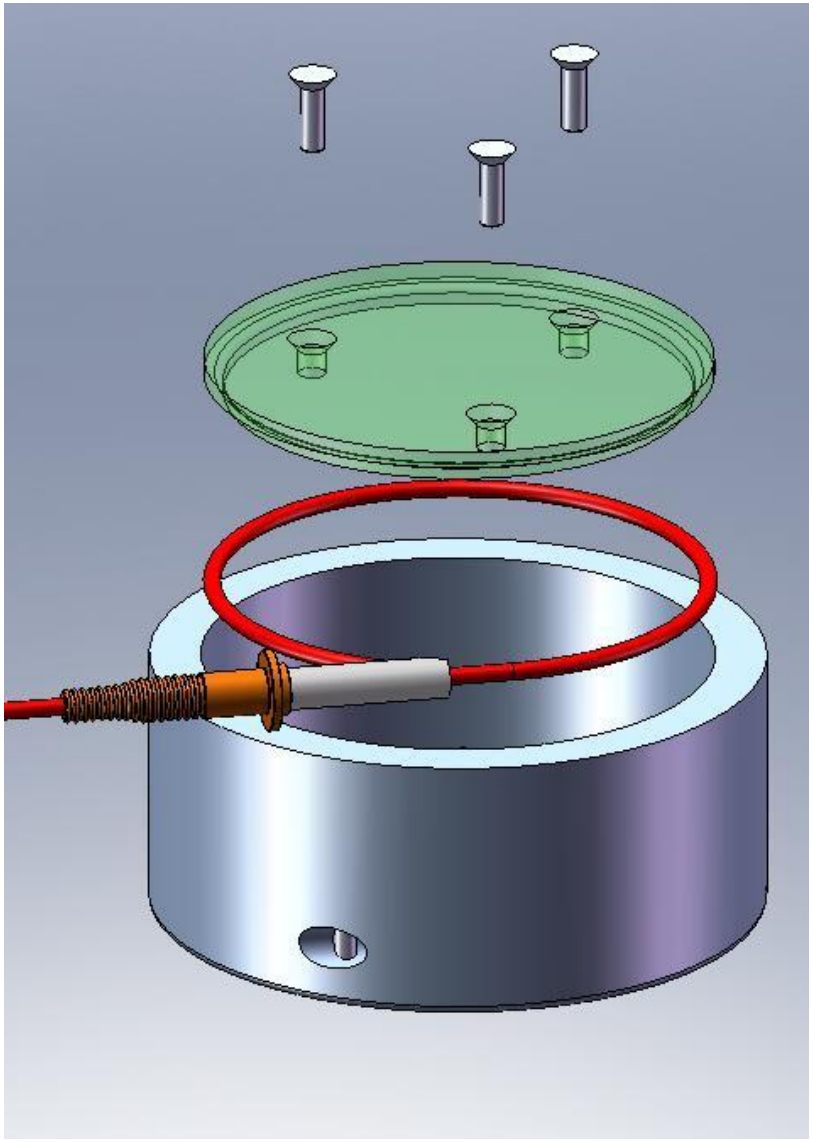
Applicator Selection



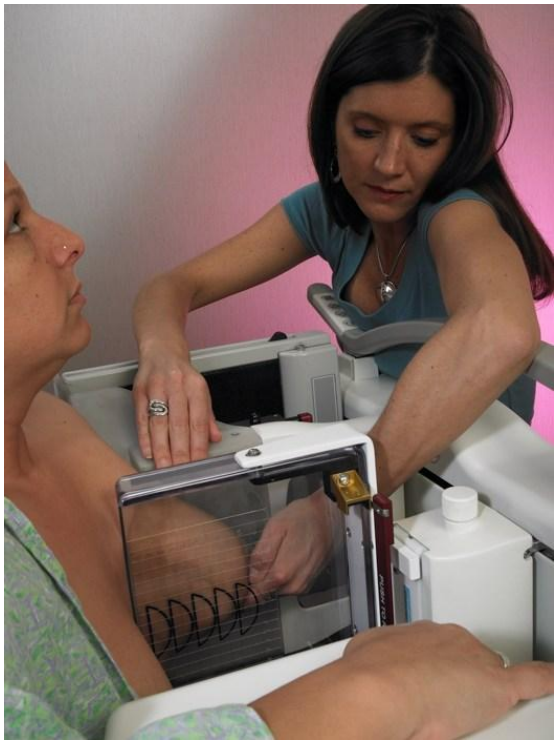
Tumor bed with 1 cm margin
6 cm Round Applicator

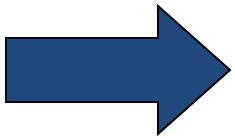


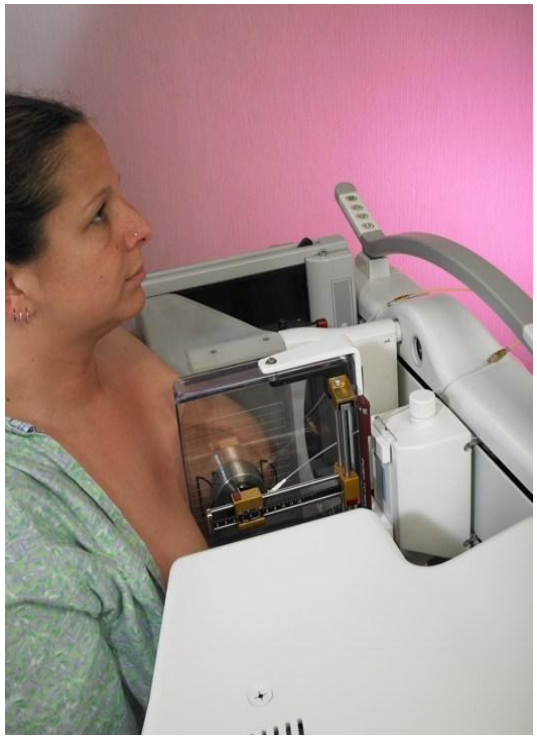




Process is repeated in an orthogonal axis





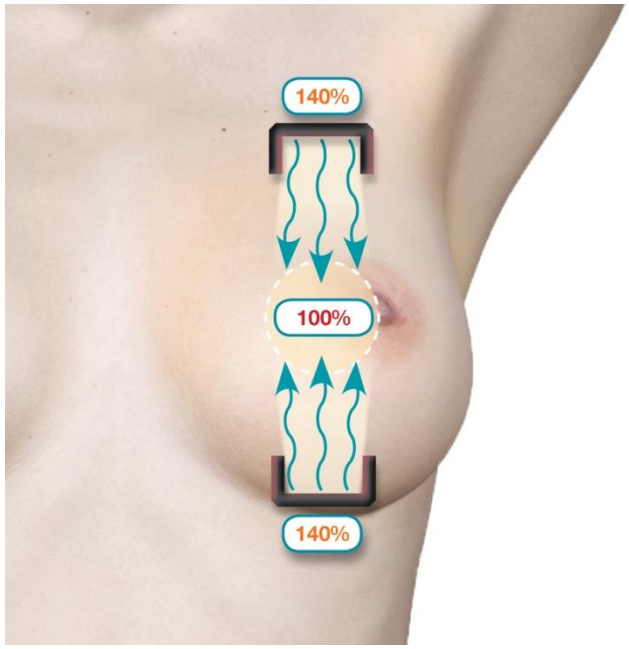


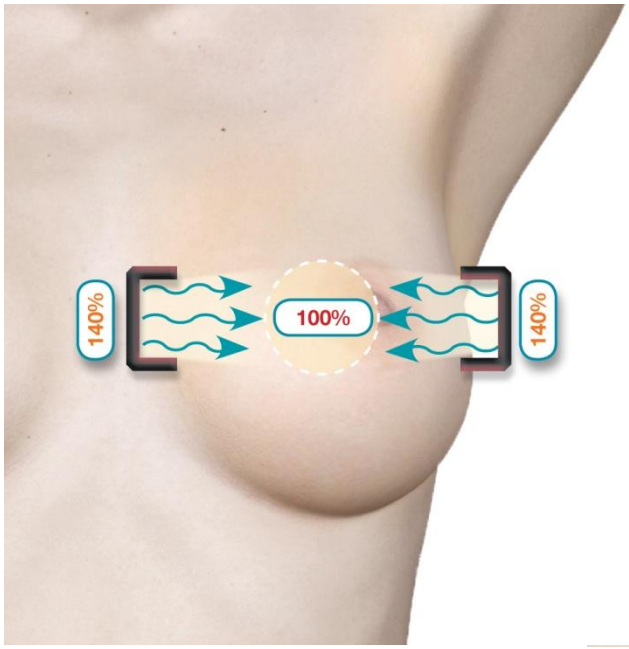
Breast Compression

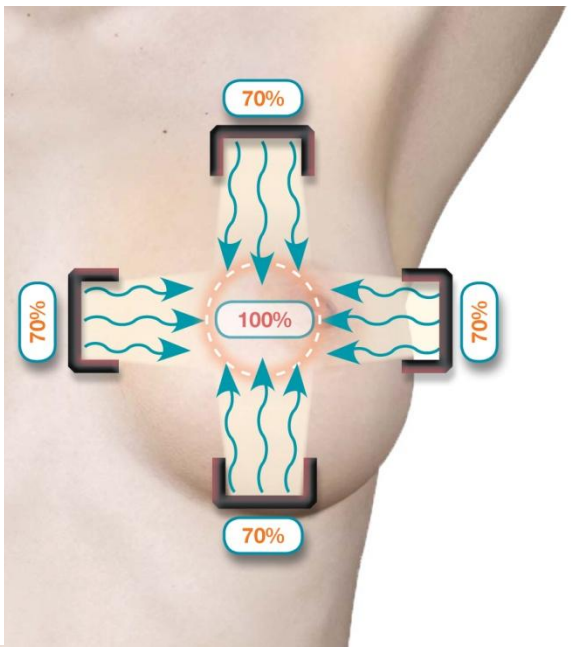
kV imaging in immobilized position

Pictures courtesy of Advanced Radiation Therapy, LLC

Two Orthogonal Treatment Axes





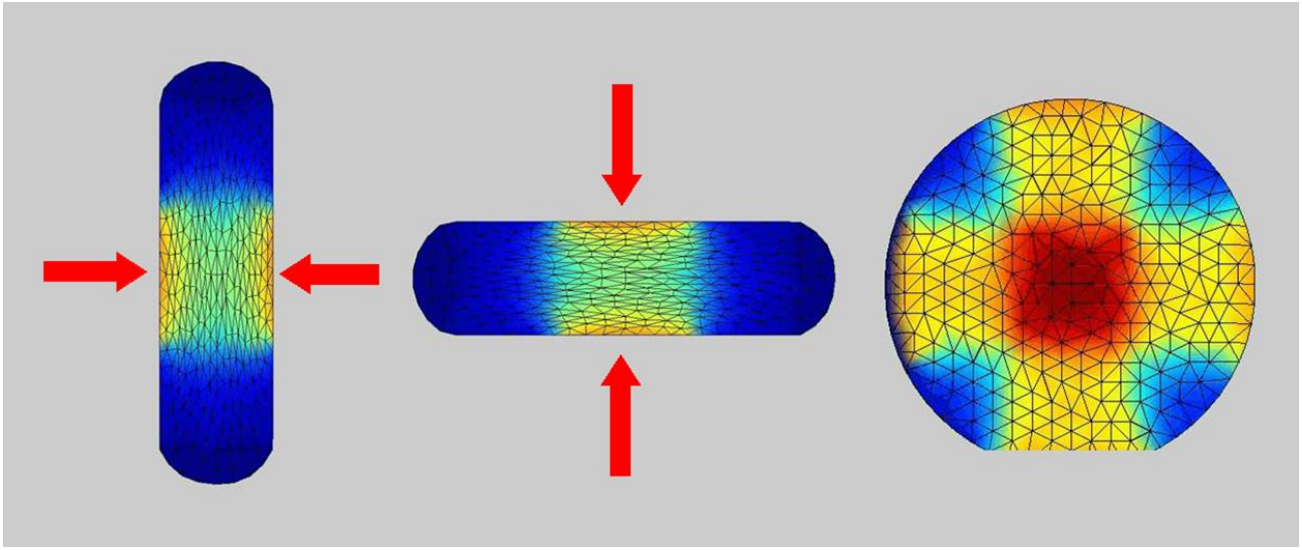


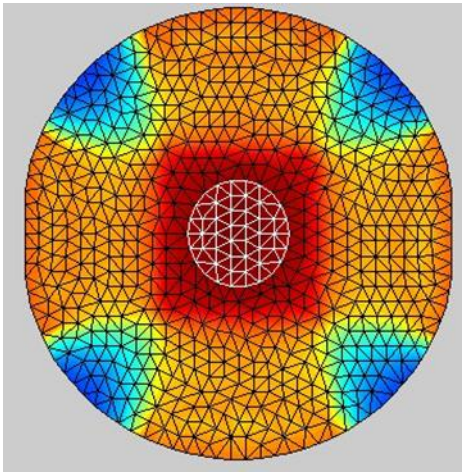
Reduced Skin dose

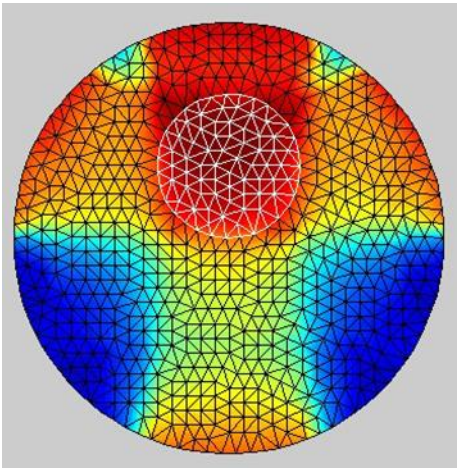
Benefits of Breast Compression

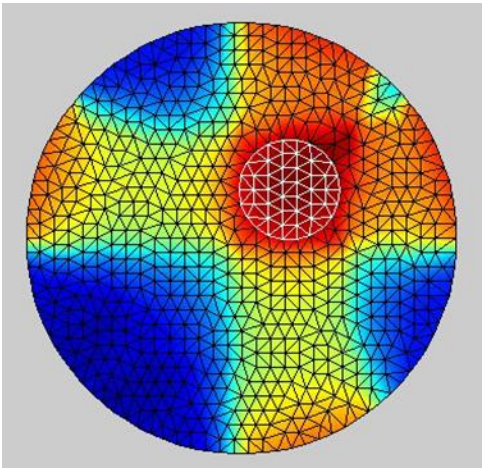
- Breast compression achieve 3 very important functions:
  - Breast immobilization.
  - Decrease separation reduced skin dose.
  - Displaces non-target breast tissue out of the radiation field.

Fine Element Analysis (FEA) Deformable Model

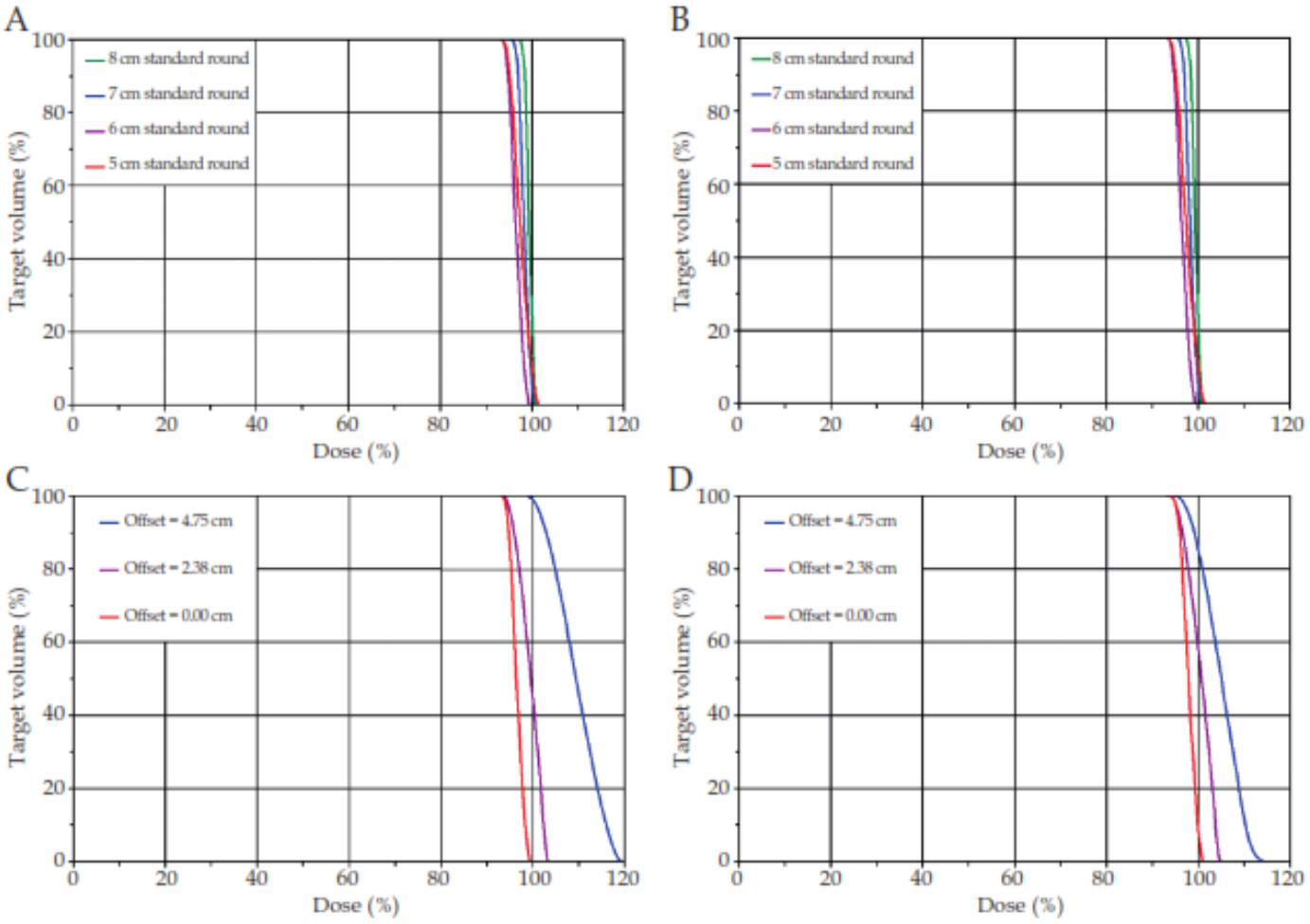






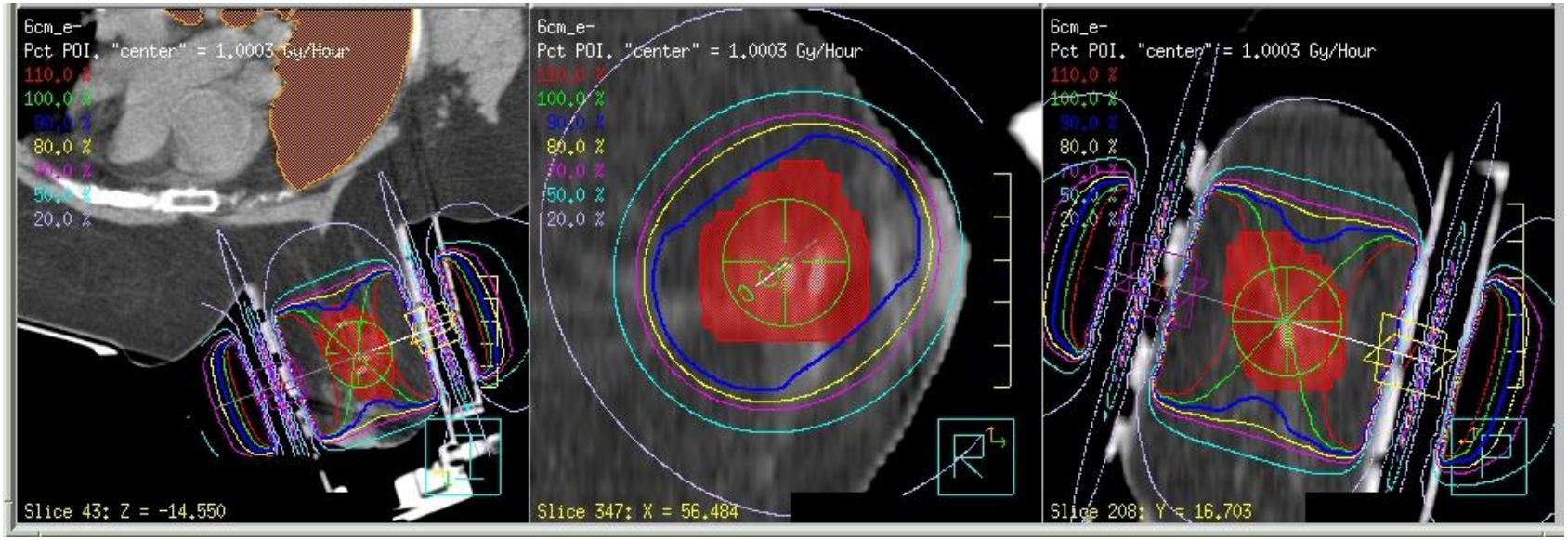


Fine Element Analysis (FEA) Deformable Model

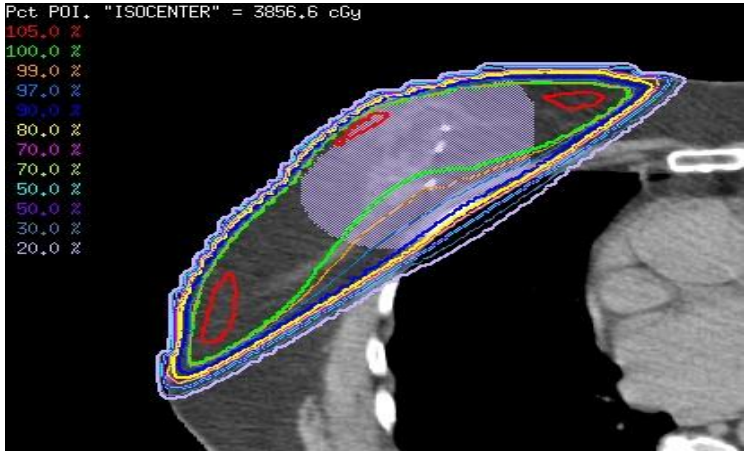


Rivard et al. JCB 2015

Dosimetric Comparison of APBI using 3D-CRT and NIBB



NIBB



3D-CRT

Sioshansi et al. IJROBP 2011

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

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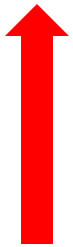

NIBB more heterogeneous like other brachytherapy techniques

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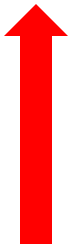


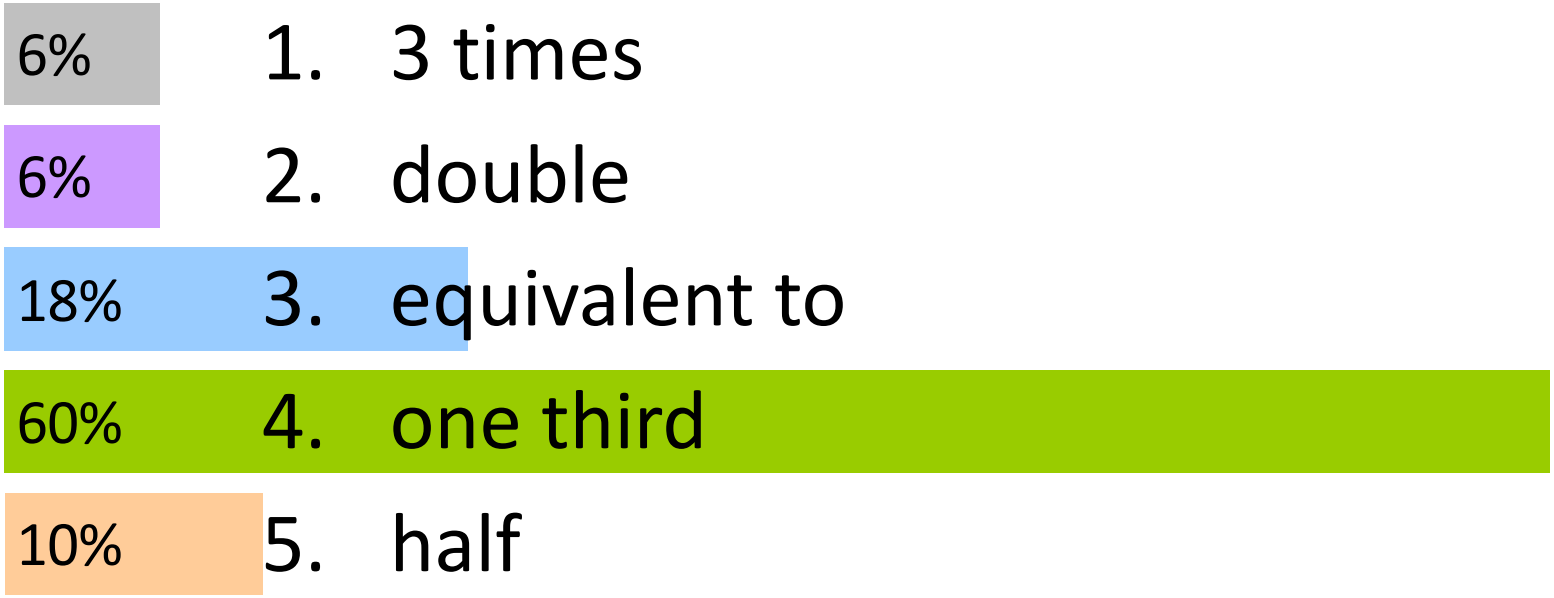
Target volume decrease → 1/3!!

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

x3 x4.5 x1.1

According to Sioshansi et al., the planning target volume defined for an NIBB APBI treatment is _____ the volume of a 3DCRT APBI treatment.



Correct answer: 4 – one third

Sioshansi S, Rivard MJ, Hiatt JR, Hurley AA, Lee Y, Wazer DE.

Dose modeling of noninvasive image-guided breast brachytherapy in comparison to electron beam boost and three-dimensional conformal accelerated partial breast irradiation.

Int J Radiat Oncol Biol Phys. 2011 Jun 1;80(2):410-6

NIBB to deliver APBI: Potential Advantages

- Non-invasive

  → More acceptable to many patients

- Oncoplastic reconstruction OK and no need for indwelling balloon catheter

  → No increased risk of persistent seroma

- Breast immobilization and image-guidance

  → No need for large PTV margins

  → Potential for decrease in fibrosis

- Potential for improved cosmetic outcomes over existing APBI techniques

NIBB to deliver APBI: Potential Disadvantages

- Long treatment times

  → Treatment of each axis could take up to 30 minutes depending on compression and source strength

- Resource intense

  → Physicist and MD at console for entire treatment (1hr+)

- Potential for error

  → Manual transfer of data from nomogram to console

Methods

- Prospective Phase II trial. IRB approved and monitored by the BrUOG data safety monitoring board. (BrUOG trial Br-251; NCT01463007)
- Enrolled patients received APBI using NIBB.
- 34Gy in 10 fractions using Ir-192 HDR source was delivered to the CTV/PTV which included the lumpectomy cavity with a 1 cm margin.
- 2 orthogonal axes were treated for each fraction and separation was limited to ≤ 8cm.
- Treatment was either daily or BID based on pt preference.
- Patients are followed clinically at regular intervals. Mammography is performed yearly. Photographs for cosmetic assessment are taken at baseline and at each f/u visit.
- Toxicity assessment is based on CTCAE v3.0. Cosmetic outcome is assessed based on the Harvard scale.

NIBB for APBI

- Prospective clinical trial completed accrual
- 40 patients completed protocol treatment

Table 1. Patient, Tumor, and Treatment Characteristics.

Age	
Mean	68 yrs
Range	50 - 92 yrs
Histology	n (%)
IDC	22 (55%)
Inv. Mucinous	2 (5%)
Inv. Tubular	1 (2.5%)
DCIS	15 (37.5%)
Tumor size	
Mean	1.1 cm
Range	0.3 – 3.0 cm
Lymph Node Status	
Positive	0 (0%)
Receptor status	
ER positive	39 (97.5%)
Her-2-Neu positive	0 (0%)
ASTRO Guidelines (ref)	
Suitable	19 (47.5%)
Cautionary	21 (52.5%)
Unsuitable	0 (0%)
Volumes (cc)	Mean (range)
Whole breast	1591 (365 - 3569)
Tumor bed	22.4 (1.1 – 69.6)
Breast compression	
Mean	6.5 cm
Range	3.4 – 9.4 cm
Applicator Type	
1st Generation	8 (20%)
Mixed	18 (45%)
2nd/3rd Generation	14 (35%)
Treatment schedule	
Daily	29 (72.5%)
BID	11 (27.5%)

Results – Treatment tolerability

- Treatment was well tolerated by all patients
- Treatment time
  - Average treatment time per axis: 14 min (range 5-20 min)
  - Average time from start of first axis to completion of orthogonal axis: 43 min (range 30-63 min)
- Discomfort during breast compression
  - Median score: 1 (range 0-7) (10 point pain scale)
- Treatment related fatigue
  - 95% No to mild fatigue (Grade 0-1)

Results – Acute Skin Reaction

- No skin reaction (Gr 0): 8pts (20%)
- Faint erythema (Gr 1): 21pts (53%)
- Moderate erythema (Gr 2): 11pts (28%)
- No pt developed Gr 3 skin reaction or moist desquamation.
- Maximum skin reaction typically seen after completion of treatment to 2 weeks.

First vs. Second Generation Applicators

- Second generation round applicators have conical center which reduces skin dose compared to first generation round and D-shaped applicators.
- Rate of Grade 2 acute skin reaction was associated with both applicator type and breast compression.

1st Generation Applicators


2nd Generation Applicators

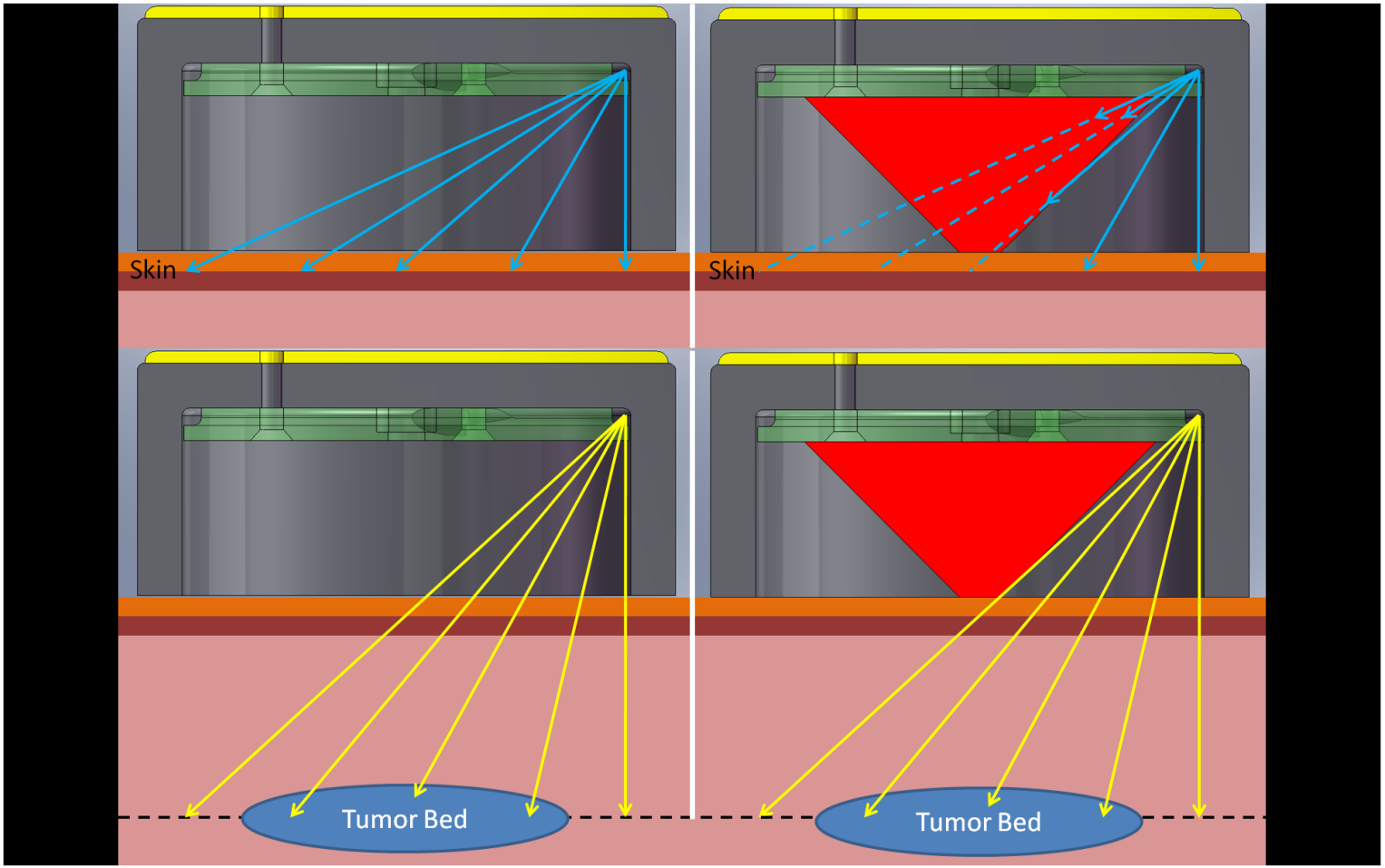
Acute Skin Reaction by Applicator Type

Table 3. Acute Skin Toxicity by Applicator Type

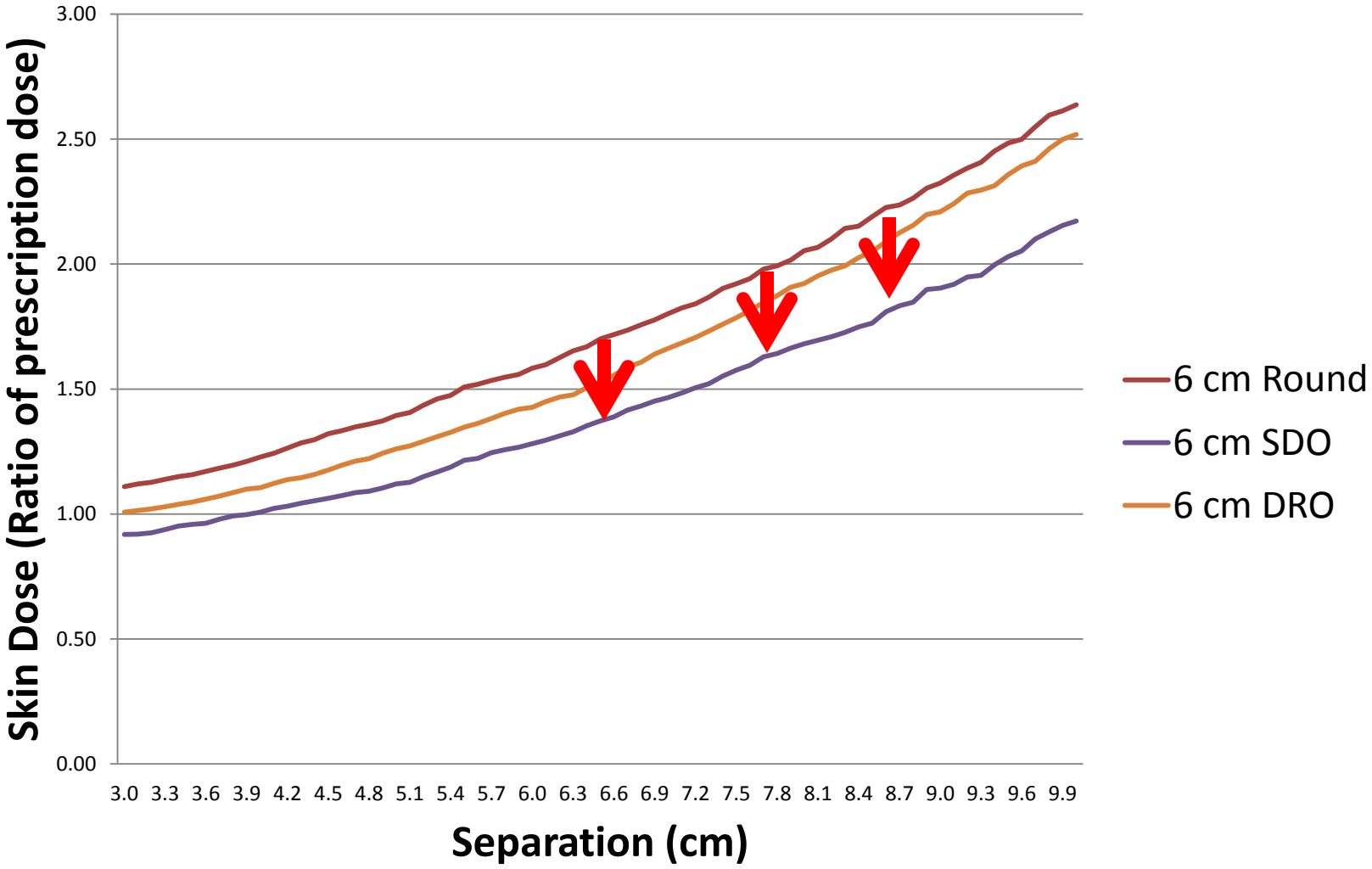
Applicator	**Grade 2 Toxicity % (n)**
1st Generation	62.5% (5/8)
Mixed	33.3% (6/18)
2nd/3rd Generation	0% (0/14)

p=0.001

Schematic Comparison of 1st and 2nd Generation Applicators



Average Skin Dose by Applicator Type



Results – Late Side Effects and Cosmetic Outcome

- Early results are very favorable
- Median f/u 1 year
- IBTR: 2.5%
- E/G Cosmesis: 97.5%
- SubQ Fibrosis Gr 2-3: 0%
- No Grade 2 or greater late toxicity.

Late Toxicity CTCAE v3.0
Hyperpigmentation
Telangiectasia
Skin Atrophy
Skin/Subcutaneous Tissue Induration/fibrosis
Fibrosis-cosmesis
Soft tissue necrosis
Seroma
Breast Pain
Deformity Nipple/areolar
Breast volume/hypoplasia
Fat Necrosis (Lovey et al, IJROBP 2007)

Future Directions: NIBB ABPI Fast trial

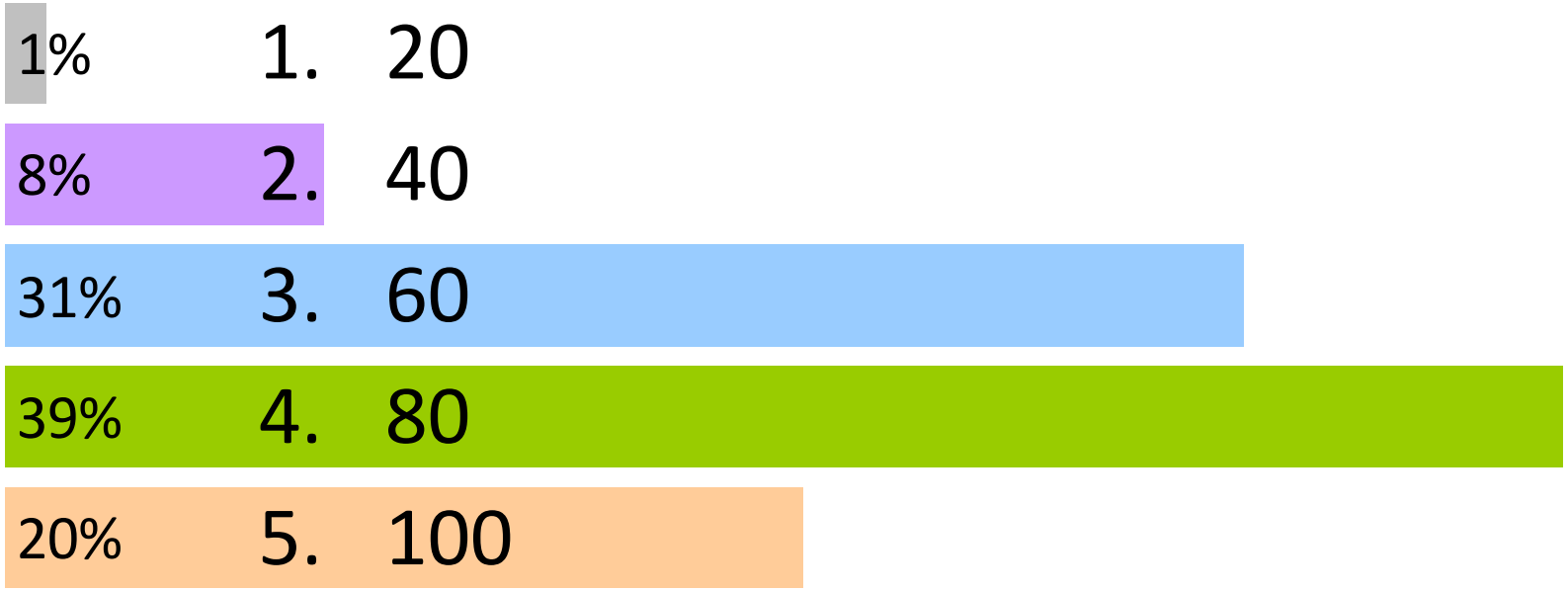
- Rationale:
  - ¾ of patients elected for once daily treatment
    → patients don't like BID.
  - However, this results in treatment delivered over 2 weeks
    → not ideal in regards to convenience.
- NIBB APBI Fast trial → 5 daily fractions
- Dose: 28.5Gy (5.7Gy per fraction)

Patient Selection/Eligibility

- NIBB feasible in most patients.
- Patients with larger breast size more likely to be good candidates.
- Posterior tumor beds can be challenging to reach.
- Surgical clips helpful in defining tumor bed and increase eligibility likelihood.

Hepel et al. Brachytherapy 2014

Hepel et al. found that nearly ___% of patients with surgical clips were able to be treated using the NIBB technique.



Correct answer: 4 – 80%

Hepel JT, Leonard KL, Hiatt JR, DiPetrillo TA, Wazer DE.

Factors influencing eligibility for breast boost using noninvasive image-guided **breast** brachytherapy.

Brachytherapy. 2014 Nov-Dec;13(6):579-83

Conclusions

- NIBB to deliver boost and APBI is feasible and well tolerated by patients.
- Acute skin reaction is mild and infrequent.
- Virtually no skin reaction is seen with $2^{nd}/3^{rd}$ generation applicators.
- Early results of late outcomes are encouraging.
  - no significant late toxicity, and good cosmetic outcomes.
  - Freedom from IBTR 97.5%.
- Additional patients and longer follow up is needed to confirm these late endpoints.