Accelerated Partial Breast Irradiation in brachytherapy: is shorter better?

VIRGINIA COMMONWEALTH UNIVERSITY

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AAPM Annual Meeting Anaheim, CA – July 2015

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

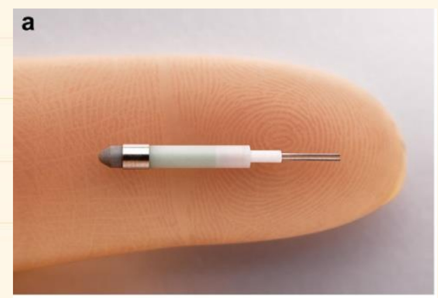
- Ir-192 ($T_{1/2}$ = 73.8 days, $E_{\gamma,\ mean}$ = 380 keV) is the most common source for Remote Afterloaders

- Disadvantage: relative short half-life (at least when compared with Co-60 ($T_{1/2}$ = 5.27 yr, $E_{\gamma,\ mean}$ = 1253 keV) or Cs-137 ($T_{1/2}$ = 30.17 yr, $E_{\gamma,\ mean}$ = 662 keV).
- Advantage: low average energy (~.38 Mev, with a range from 0.136 to 1.062MeV) so it is easily shielded requiring just 0.3cm Pb as a half value layer.
- Advantage: high specific activity (450Ci/g) allows the construction of high activity sources (10Ci) of small diameter (0.6-1.1 mm)

Electronic brachytherapy

Axxent®
Electronic Brachytherapy System

Axxent HDR X-ray Source 2.2 Specifications		Part Number
Axxent HDR X-ray Source		S7500
X-ray Tube Diameter	2.25 mm	
Assembly Length	250 mm	
Assembly Diameter	5.4 mm	
X-ray Source Power	15 watts	
Typical Treatment Time	10 min	
Maximum Number of Treatments per X-ray Source	10	
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

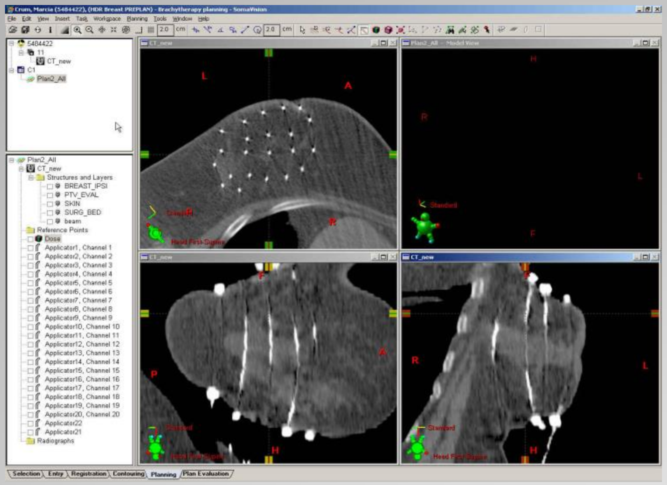
- eBx plans have dosimetric and biological features <u>different</u> from Ir-192 plans
- Tissue heterogeneities and patient boundary effects decrease dose to target and skin but increase dose to bones
- Enhancement of relative biological effectiveness (RBE). It is reported to be very similar to I-125 (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)

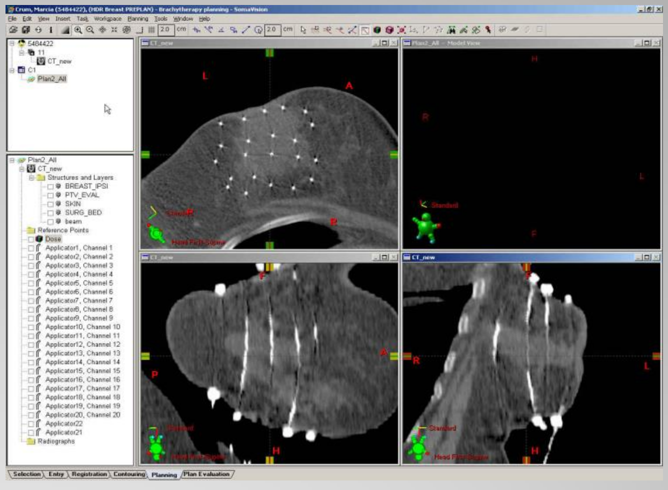
A comparison of the relative biological effectiveness of low energy brachytherapy source in breast tissue: A Monte Carlo study. Shane A. White, Thomas Rusch, Evelyn de Jong, Brigitte Reniers, 8th International ISIORT Conference, Cologne Sept 25-27, 2014

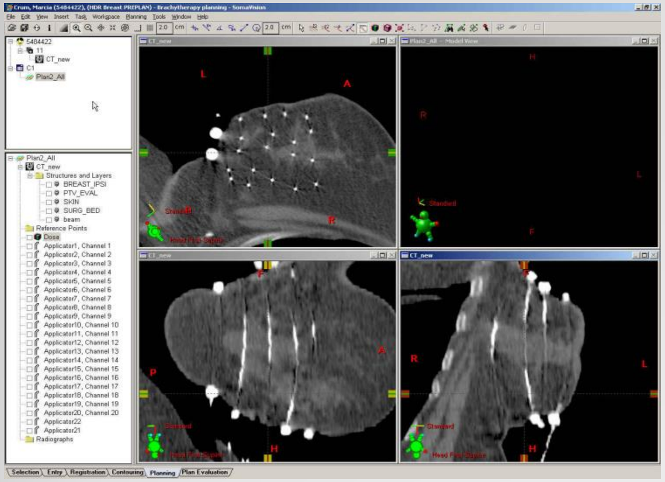
Available methods for APBI

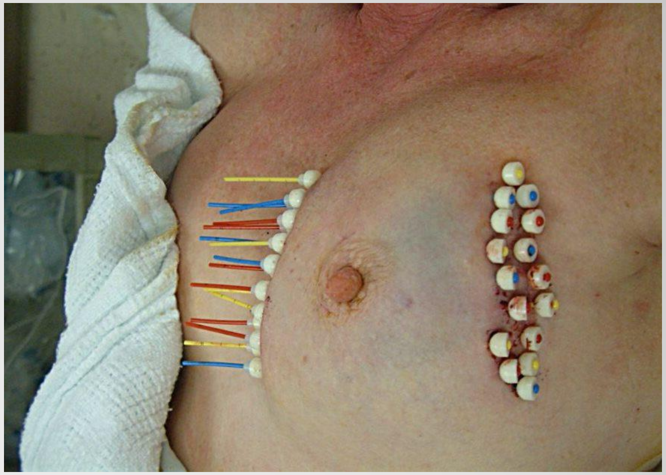
- Interstitial brachytherapy (LDR and HDR)
- Intra-cavitary brachytherapy (HDR)
  - Balloon catheter (single lumen/multi-lumen)
  - Hybrid techniques (SAVI)
- AccuBoost (HDR)
- Electronic balloon brachytherapy (Xoft Axxent)
- Permanent breast seed implants (LDR)
- Intra-operative brachytherapy (HDR,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

Interstitial multi-catheter implants







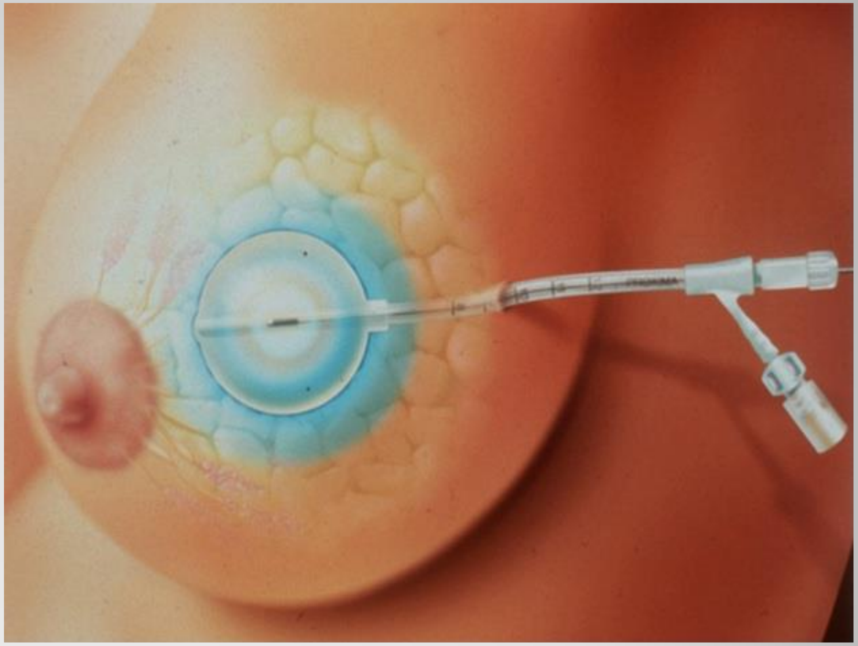


Intra-cavitary devices

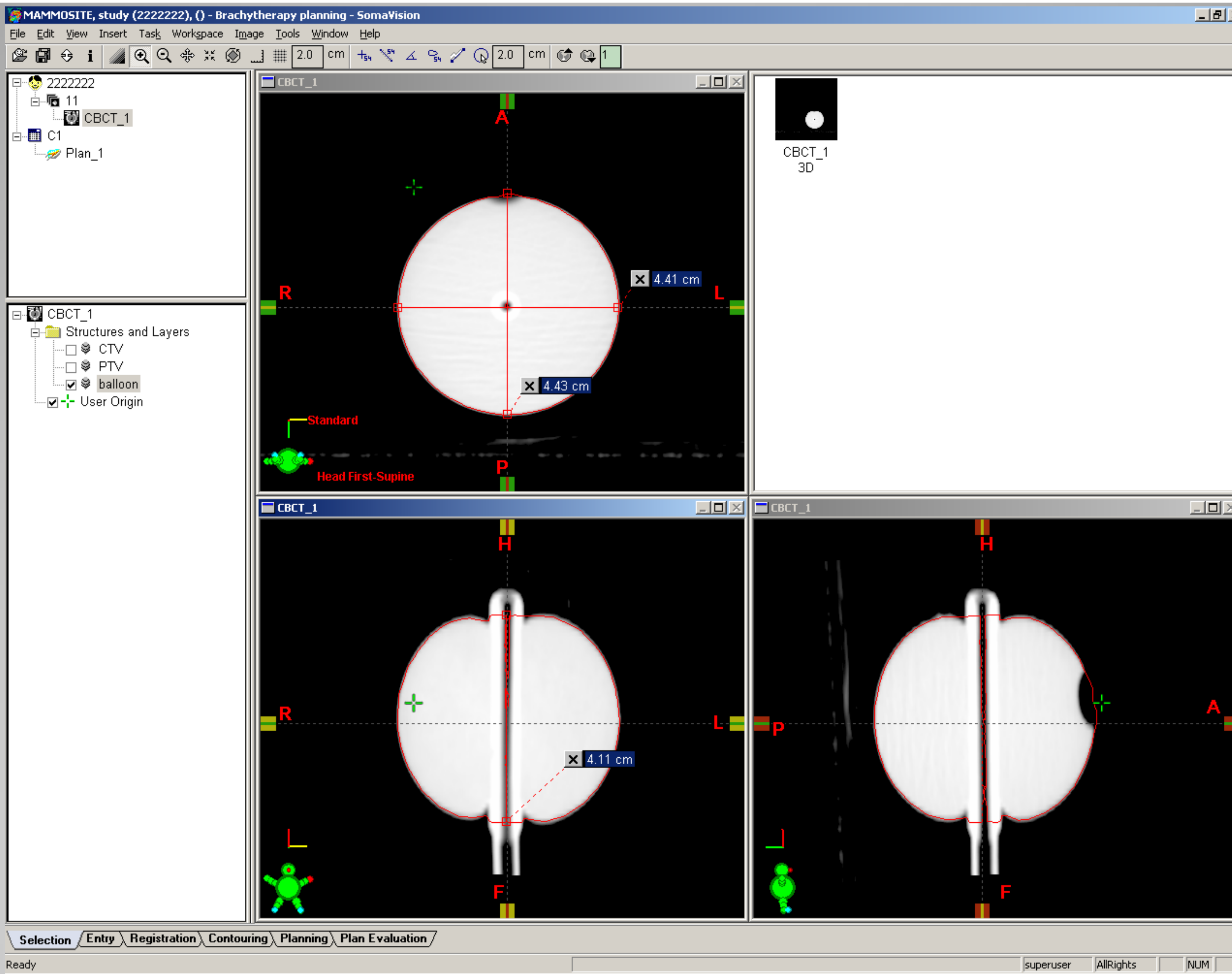
- Balloon based devices:
  - MammoSite
  - Contura
- Strut-based devices:
  - SAVI (Strut Adjusted Volume Implant)
  - Clear-Path

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*



Edmundson GK, Vicini FA, Chen PY, Mitchell C, Martinez AA, Dosimetric characteristics of the MammoSite RTS, a new breast brachytherapy applicator., Int J Radiat Oncol Biol Phys. 2002 Mar 15;52(4):1132-9.



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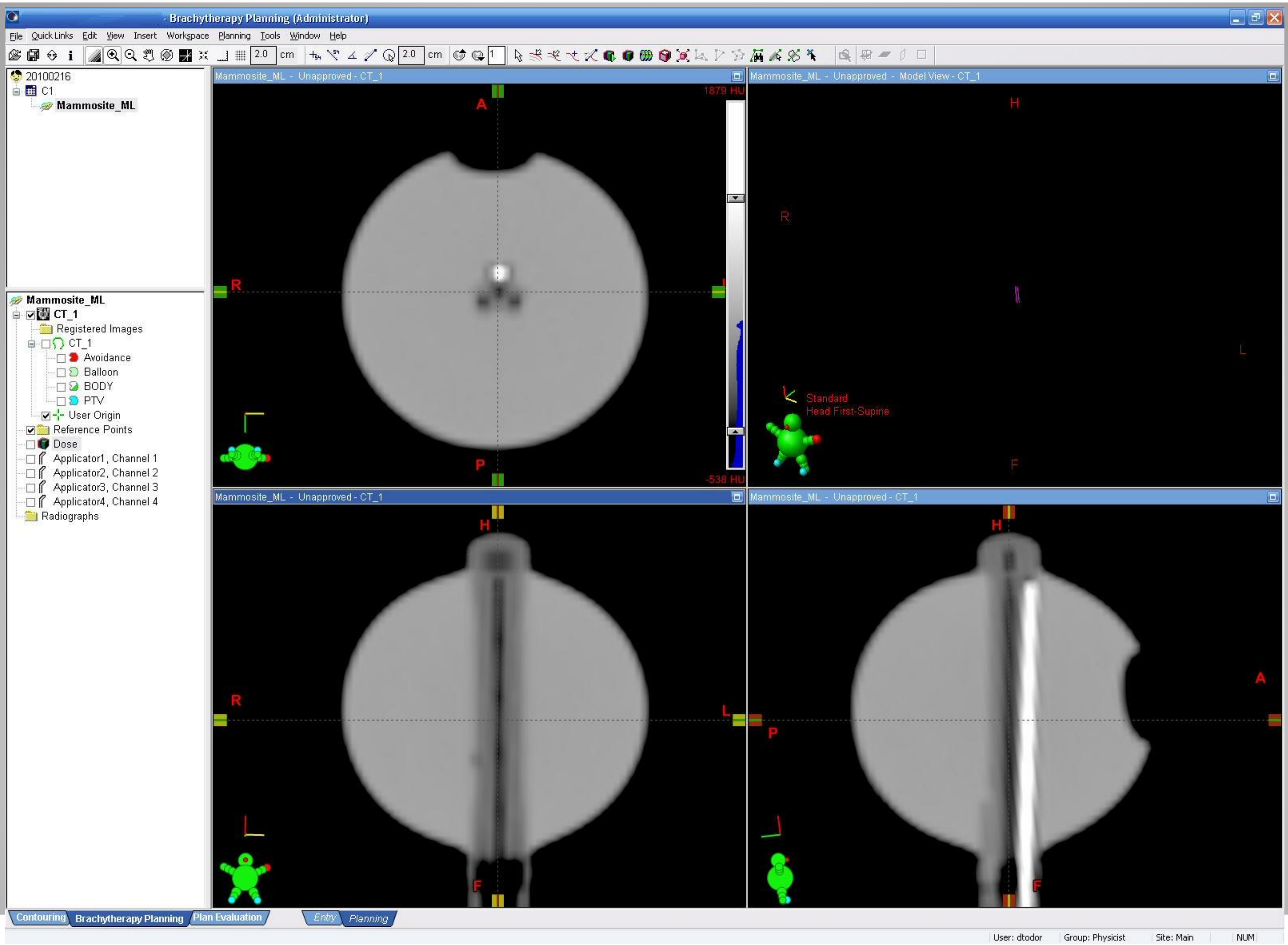

- Brachytherapy Planning (Administrator)
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Applicator2, Channel 2
Applicator3, Channel 3
Applicator4, Channel 4
Radiographs
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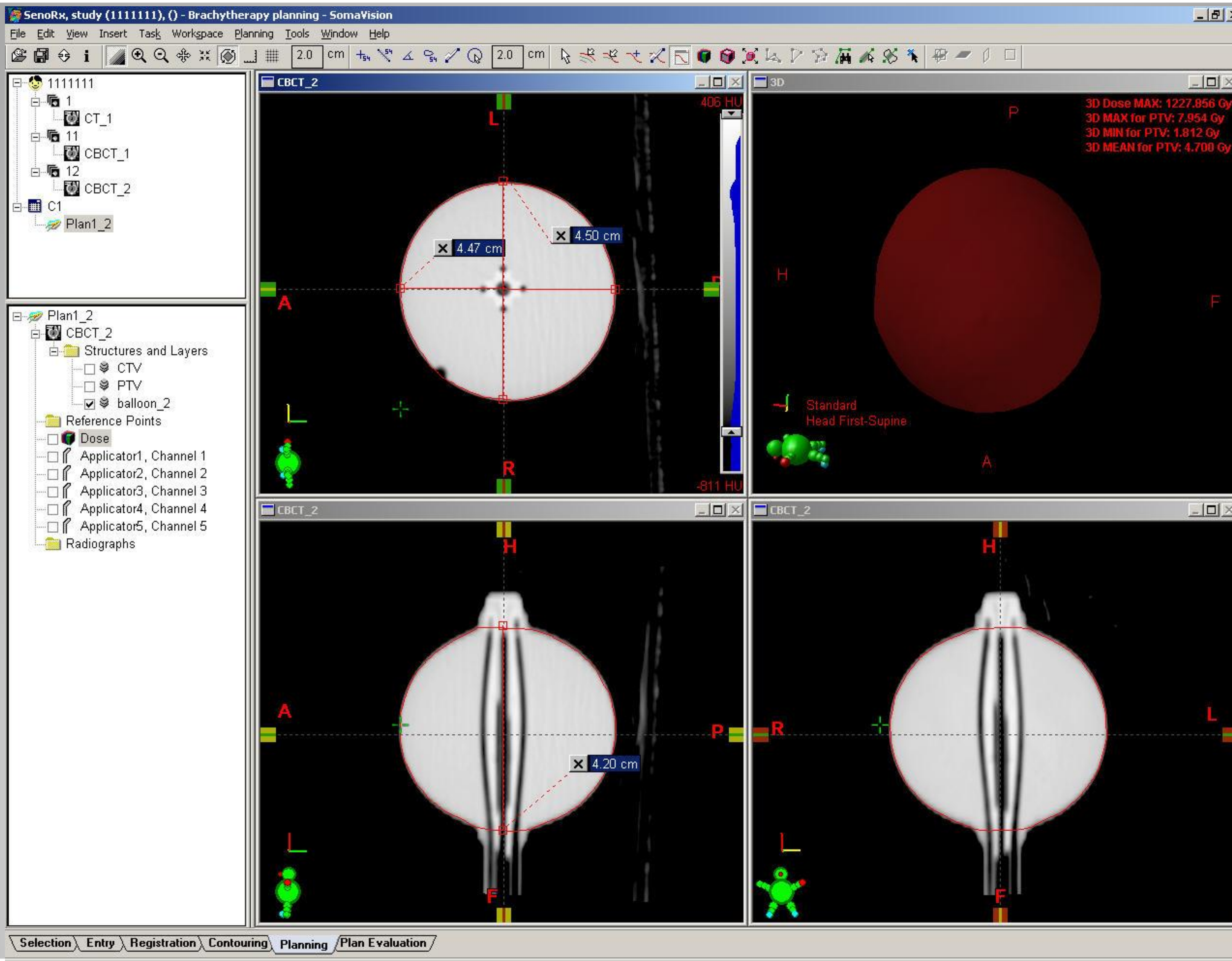
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Structures and Layers
CTV
PTV
balloon_2
Reference Points
Dose
Applicator1, Channel 1
Applicator2, Channel 2
Applicator3, Channel 3
Applicator4, Channel 4
Applicator5, Channel 5
Radiographs
CBCT_2
4.47 cm
4.50 cm
3D
3D Dose MAX: 1227.856 Gy
3D MAX for PTV: 7.954 Gy
3D MIN for PTV: 1.812 Gy
3D MEAN for PTV: 4.700 Gy
Standard
Head First-Supine
4.20 cm
Selection
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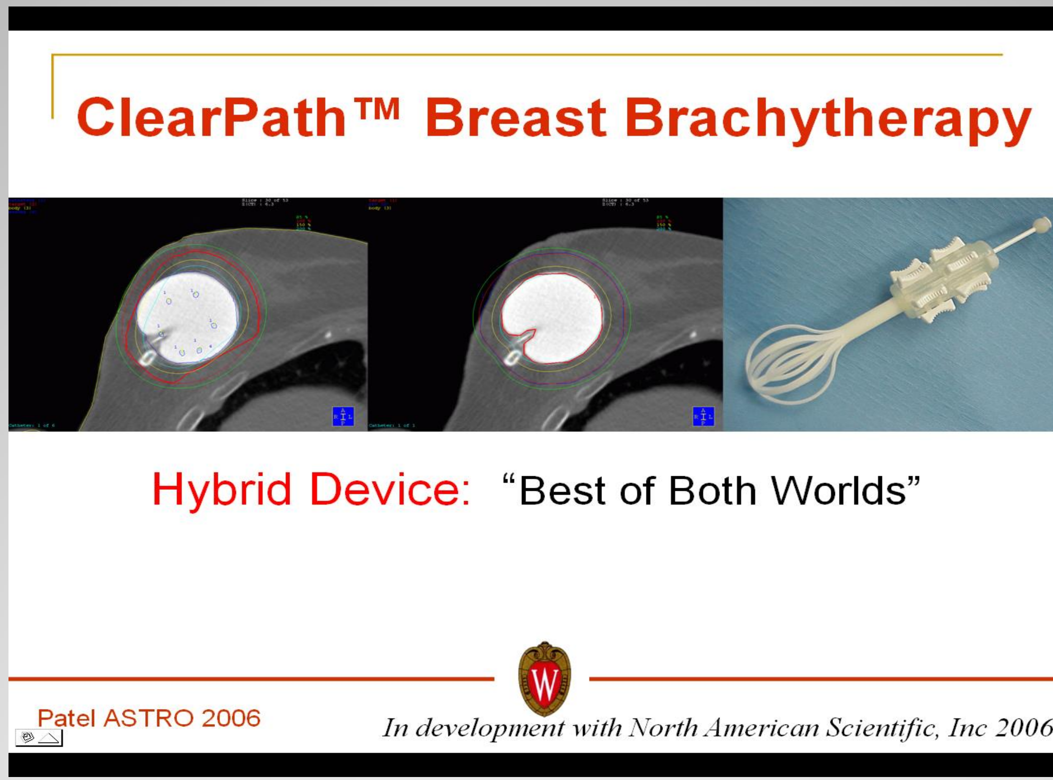
Contouring
Planning
Plan Evaluation

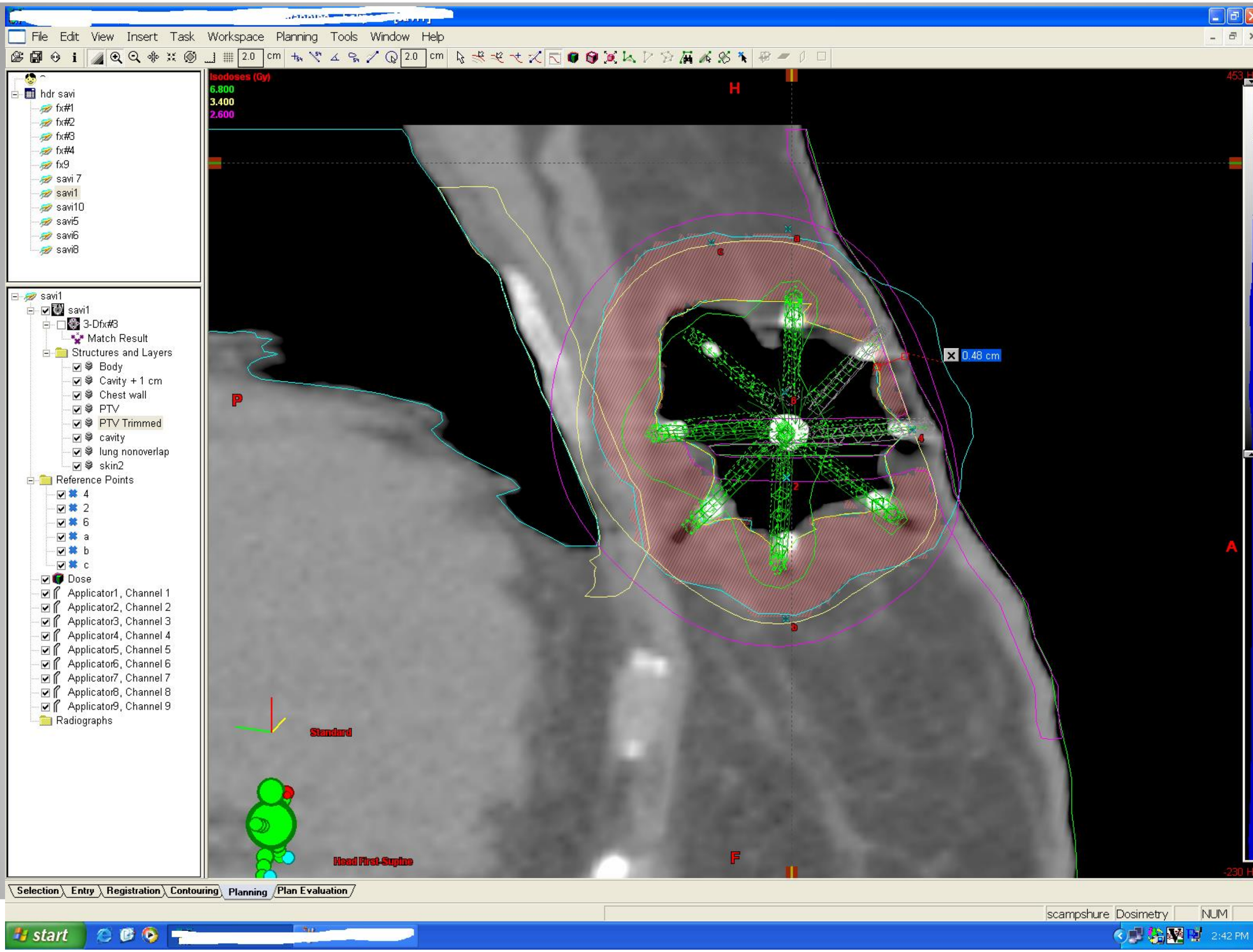
Strut devices



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 -

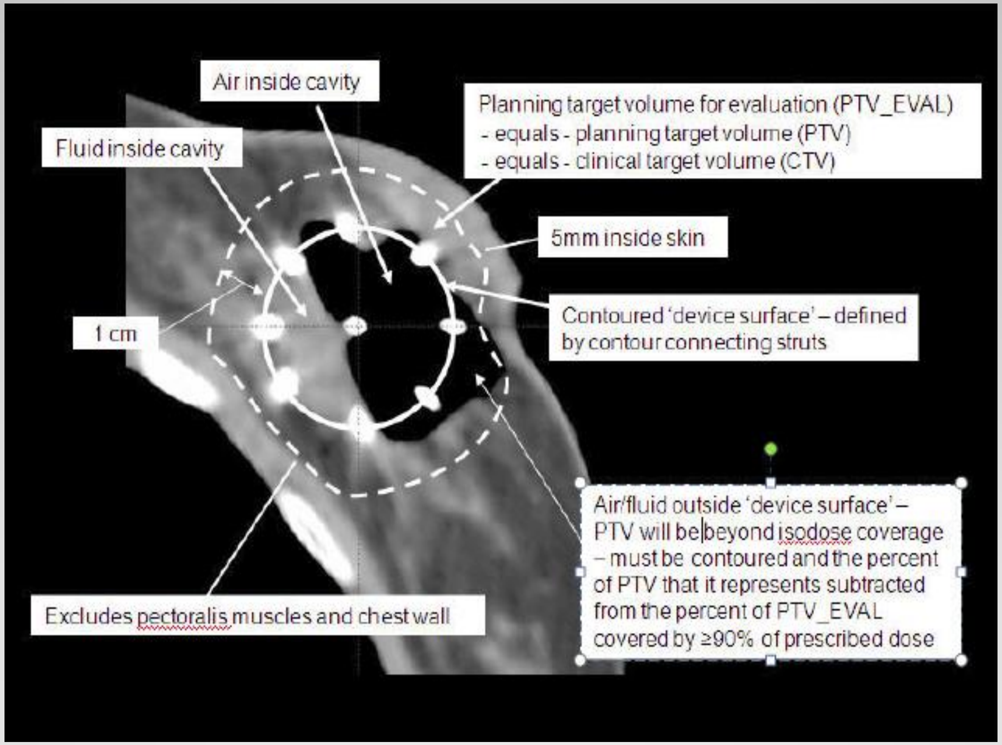
SAVI Breast Brachytherapy

6-1 Mini, 6-1, 8-1, 10-1 applicators



courtesy of Rebecca Kitchen M.S.,DABR, Radiation Oncology, Aurora BayCare Medical Center, Green Bay, WI

Comparing targets in various modalities: apples to apples or apples to oranges?



Int. J. Radiation Oncology Biol. Phys., Vol. 52, No. 4, pp. 1132–1139, 2002

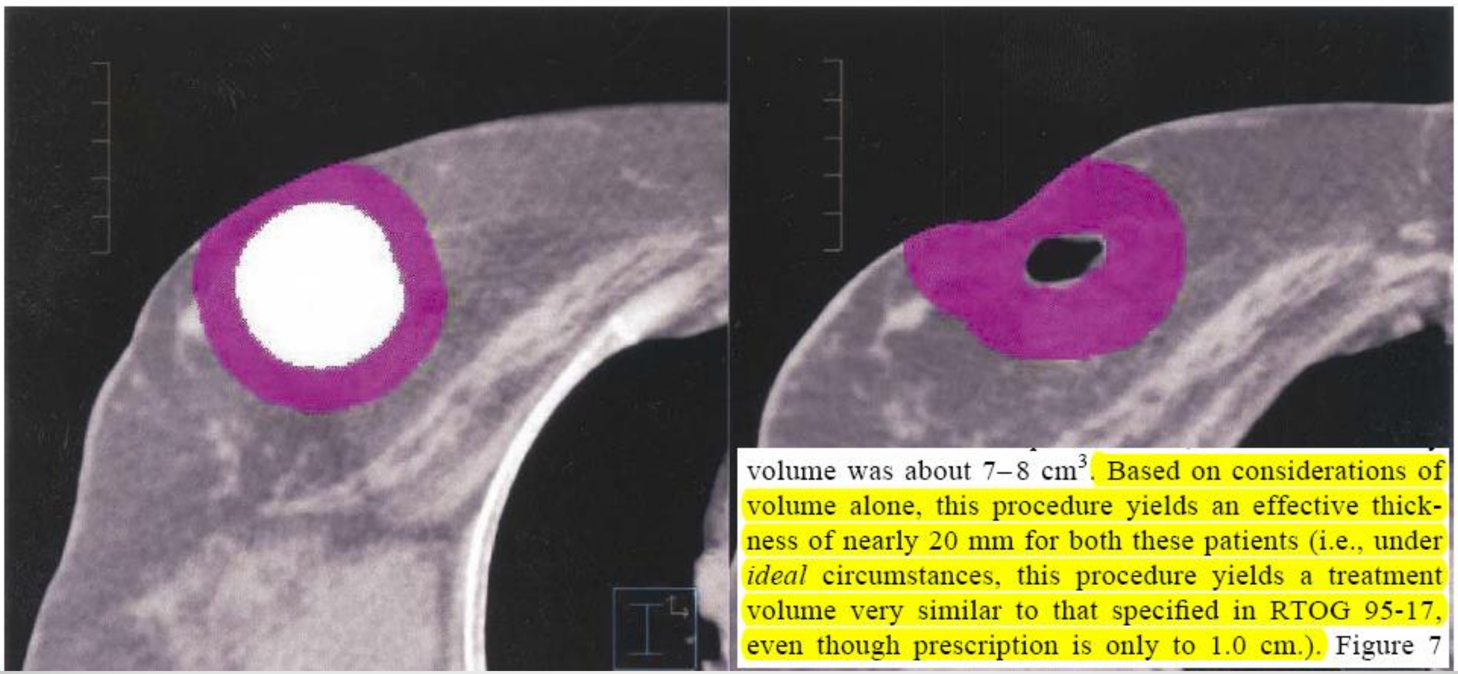
0360-3016/02/$–see front matter

PHYSICS CONTRIBUTION

DOSIMETRIC CHARACTERISTICS OF THE MAMMOSITE RTS, A NEW BREAST BRACHYTHERAPY APPLICATOR

Gregory K. Edmundson, M.Sc., Frank A. Vicini, M.D., Peter Y. Chen, M.D., Christina Mitchell, R.N., and Alvaro A. Martinez, M.D., F.A.C.R.

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



volume was about 7–8 cm^3. 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

Simona F. Shaitelman, M.D., Ed.M., Frank A. Vicini, M.D., Inga S. Grills, M.D., Alvaro A. Martinez, M.D., Di Yan, Sc. D., and Leonard H. Kim, M.S., A.Mus.D.

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.

Int. J. Radiation Oncology Biol. Phys., 2012 Jan 1; 82(1): 30-36

Comparison of APBI brachytherapy techniques

APBI technique	Advantages	Disadvantages
IMB	• Mature clinical experience • Flexible to conform to complex tumor bed geometry	• Invasive—catheters in place for 1 wk • Multiple percutaneous catheters not acceptable to some patients • Placement of catheters is technically demanding and requires specialized expertise
Single-lumen IBB	• Simple insertion technique • Simple spherical dosimetric geometry • Large clinical experience, just beginning to mature	• Invasive—catheter in place for 1 wk • Fixed dosimetric geometry, not flexibility to shape dose especially when skin or chest wall close to balloon
Multilumen IBB	• Simple insertion technique • Simple spherical dosimetric geometry • Improved flexibility to shape dose but limited	• Invasive—catheter in place for 1 wk • Improved flexibility to shape dose but limited • Limited clinical experience
Multilumen cage-like intracavitary brachytherapy	• Simple insertion technique • Flexibility to shape dose	• Invasive—catheter in place for 1 wk • Multiple hotspots at catheter-tissue interface (unclear clinical significance) • Limited clinical experience
EBB	• Simple insertion technique • Simple spherical dosimetric geometry • No vault shielding required • Reduced heart, lung and nontarget breast dose	• Invasive—catheter in place for 1 wk • Fixed dosimetric geometry • Increase surface dose (unclear clinical significance) • Higher RBE (unclear clinical significance) • Limited clinical experience
PBSI	• Single 1-day procedure • Increased convenience • Increased access in remote areas • Flexible to conform to complex tumor bed geometry • LDR may improve therapeutic ratio	• Invasive—single procedure without indwelling catheters • Permanent seeds may not be acceptable to some patients • Not appropriate for large CTV volumes • Not appropriate for large seroma cavities • Limited clinical experience
NIBB	• Noninvasive • Breast immobilization and image guidance • Sparing of nontarget breast tissue compared with external beam techniques	• Skin dose may be increased if there is significant skin overlap between orthogonal axes (exclusion criteria) • Limited clinical experience

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

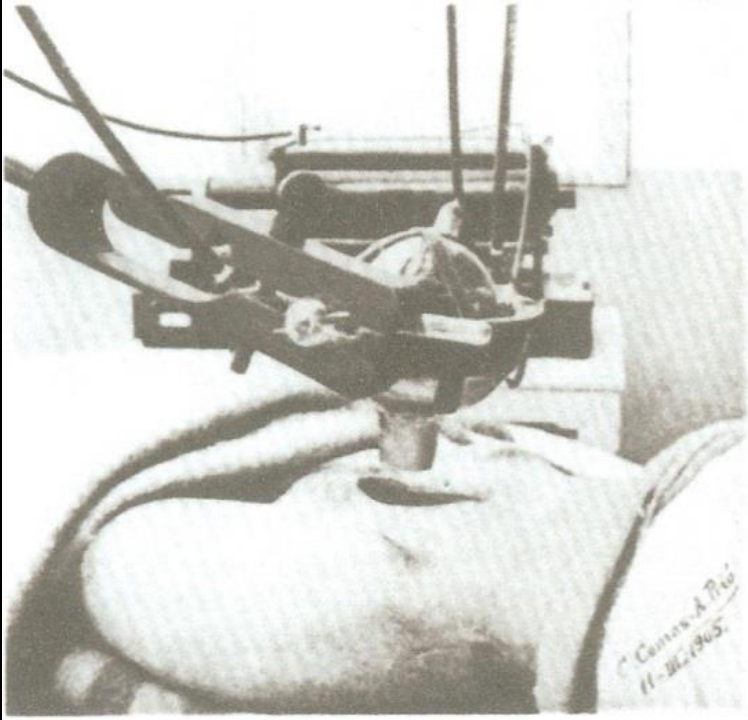


Fig. 1. Photographic document of the case report during roentgen treatment. Notice in the right-lower corner of the figure the note with the picture date: 11th March, 1905.

World Journal of Surgical Oncology

BioMed Central

Technical innovations

Open Access

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

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World Journal of Surgical Oncology 2009, 7:24 doi:10.1186/1477-7819-7-24

This article is available from: http://www.wjso.com/content/7/1/24

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

TRUE or FALSE ?

	Source	Dose at Surface	Dose at 1-cm Depth	Applicator Type	Treatment Time
IB	50 kV x-rays	20 Gy	5 Gy	Solid Spherical	20 – 45 minutes*
XB	50 kV x-rays	20 Gy	9–10 Gy	Balloon Catheter	17–26 minutes*

IB = Intrabeam™, XB = Xoft™, kV = kilovoltage, Gy = Gray.
* – Treatment time is dependant on applicator diameter used

IOERT

Surgical incision

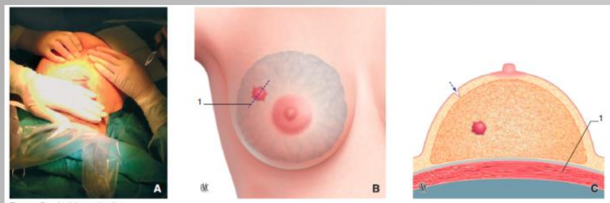


Figure 3. Incision cutanée.
A. Vue opératoire.
B. De face. 1. Incision cutanée.
C. De profil. 1. Muscle pectoral.

Lumpectomy

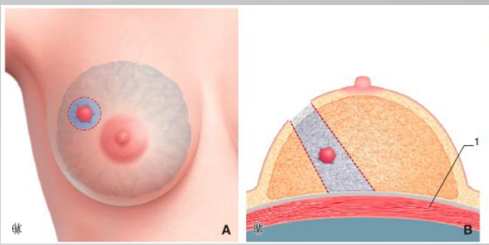


Figure 6. Tumorectomie.
A. De face.
B. De profil. 1. Muscle pectoral.

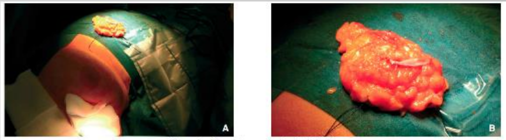


Figure 5. Pièce de tumorectomie orientée (A, B).

Tumour resection till the muscle

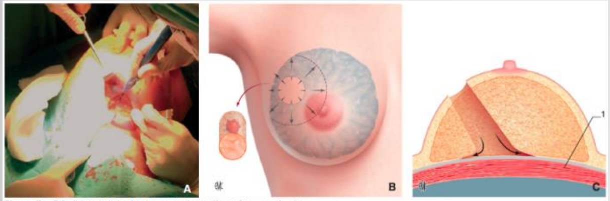


Figure 7. Décollement de la glande mammaire sur l'aponévrose pectorale.
A. Vue opératoire.
B. De face.
C. De profil. 1. Muscle pectoral.

Detachment of the gland

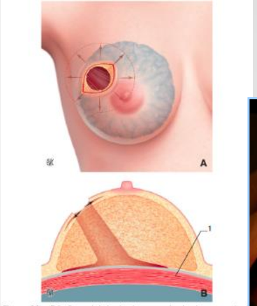


Figure 11. Décollement de la glande mammaire du plan sous-cutané
A. De face.
B. De profil. 1. Muscle pectoral.

Philippson C, Nogaret JM, EMC-Gynécologie, 2012; 7(4): 1-8

IOERT

Shield positioning on the muscle

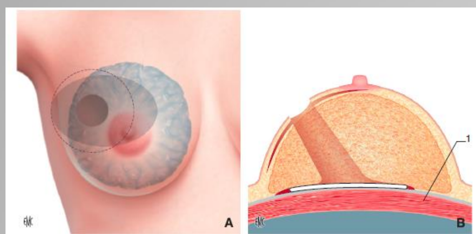


Figure 14. Mise en place de la plaque de protection.
A. De face.
B. De profil. 1. Muscle pectoral.

Figure 12. Plaque de protection (plomb-aluminium).

Suture of the tumour bed

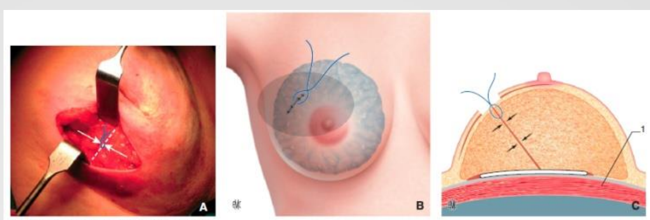


Figure 15. Fermeture de la glande mammaire.
A. Vue opératoire (flèches).
B. De face.
C. De profil. 1. Muscle pectoral.

Philippson C, Nogaret JM, EMC-Gynécologie, 2012; 7(4): 1-8

IOERT

Applicator positioning

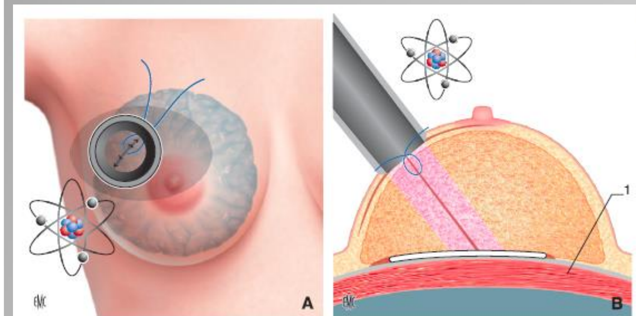
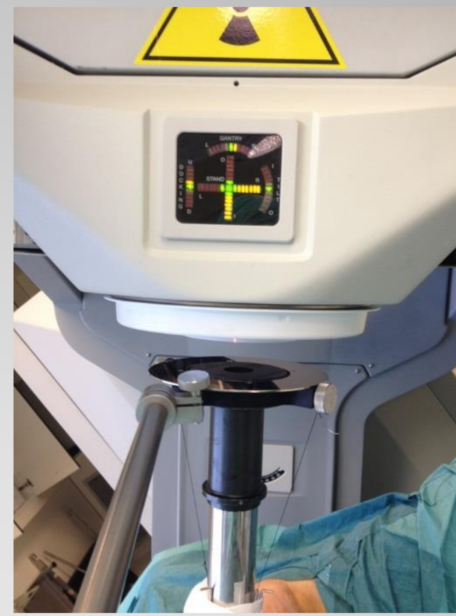


Figure 19. Mise en place du cône.
A. De face.
B. De profil. 1. Muscle pectoral.

Soft docking



Shield extraction, oncoplastic surgery

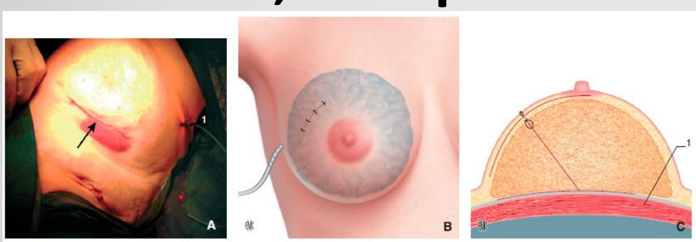
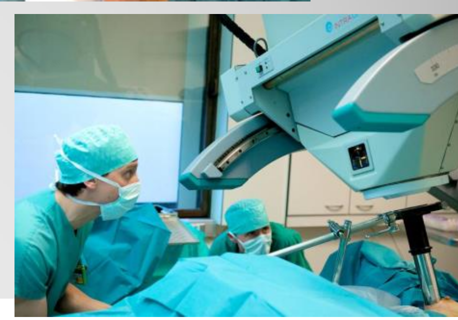
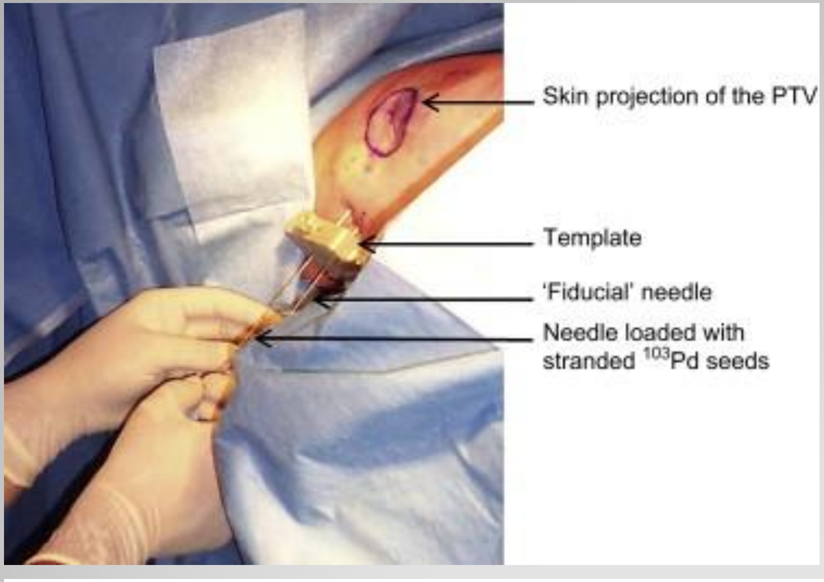


Figure 21. Fermeture.
A. Vue opératoire (flèche). 1. Drain de Redon.
B. De face.
C. De profil. 1. Muscle pectoral.



Philippson C, Nogaret JM, EMC-Gynécologie, 2012; 7(4): 1-8

Permanent seed implants



Int J Radiat Oncol Biol Phys. 2006 Jan 1;64(1):176-81. Epub 2005 Sep 22.

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

Pignol JP, Keller B, Rakovitch E, Sankreacha R, Easton H, Que W.

Department of Radiation Oncology, Sunnybrook and Women's Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada. Jean-Philippe.Pignol@sw.ca

Int J Radiat Oncol Biol Phys. 2009 Apr 1;73(5):1482-8. doi: 10.1016/j.ijrobp.2008.06.1945. Epub 2008 Oct 18.

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

Pignol JP, Rakovitch E, Keller BM, Sankreacha R, Chartier C.

Department of Radiation Oncology, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada. Jean-Philippe.Pignol@sunnybrook.ca

Basics

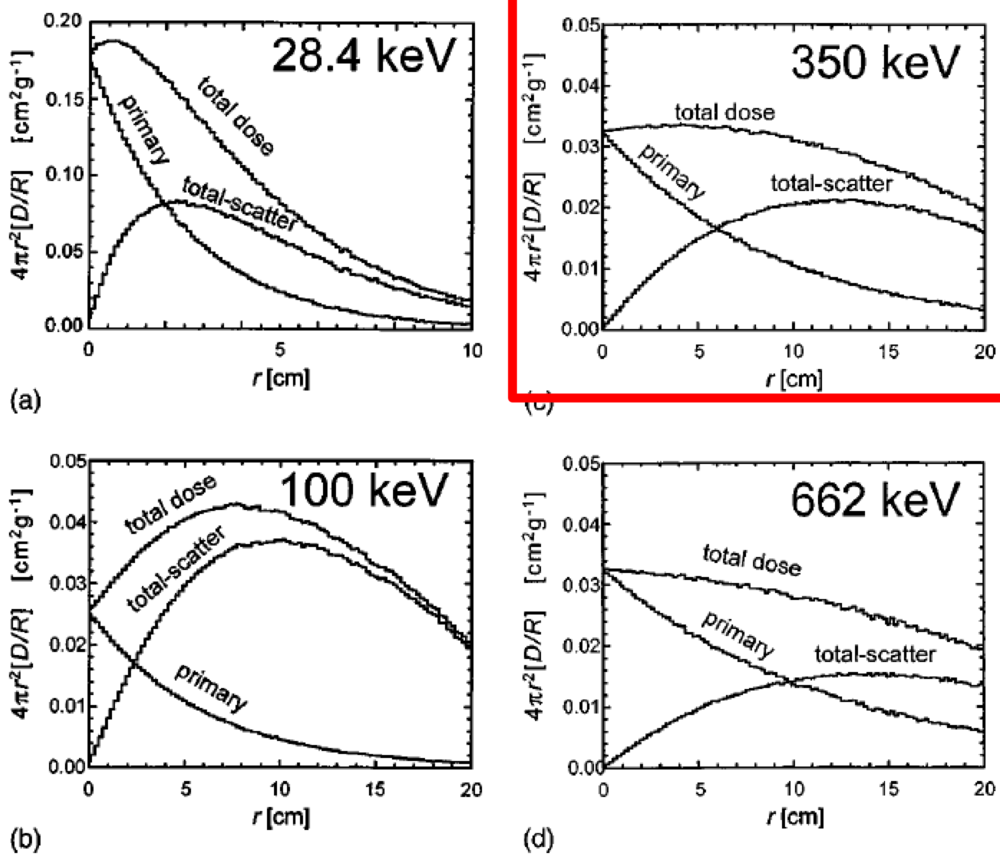
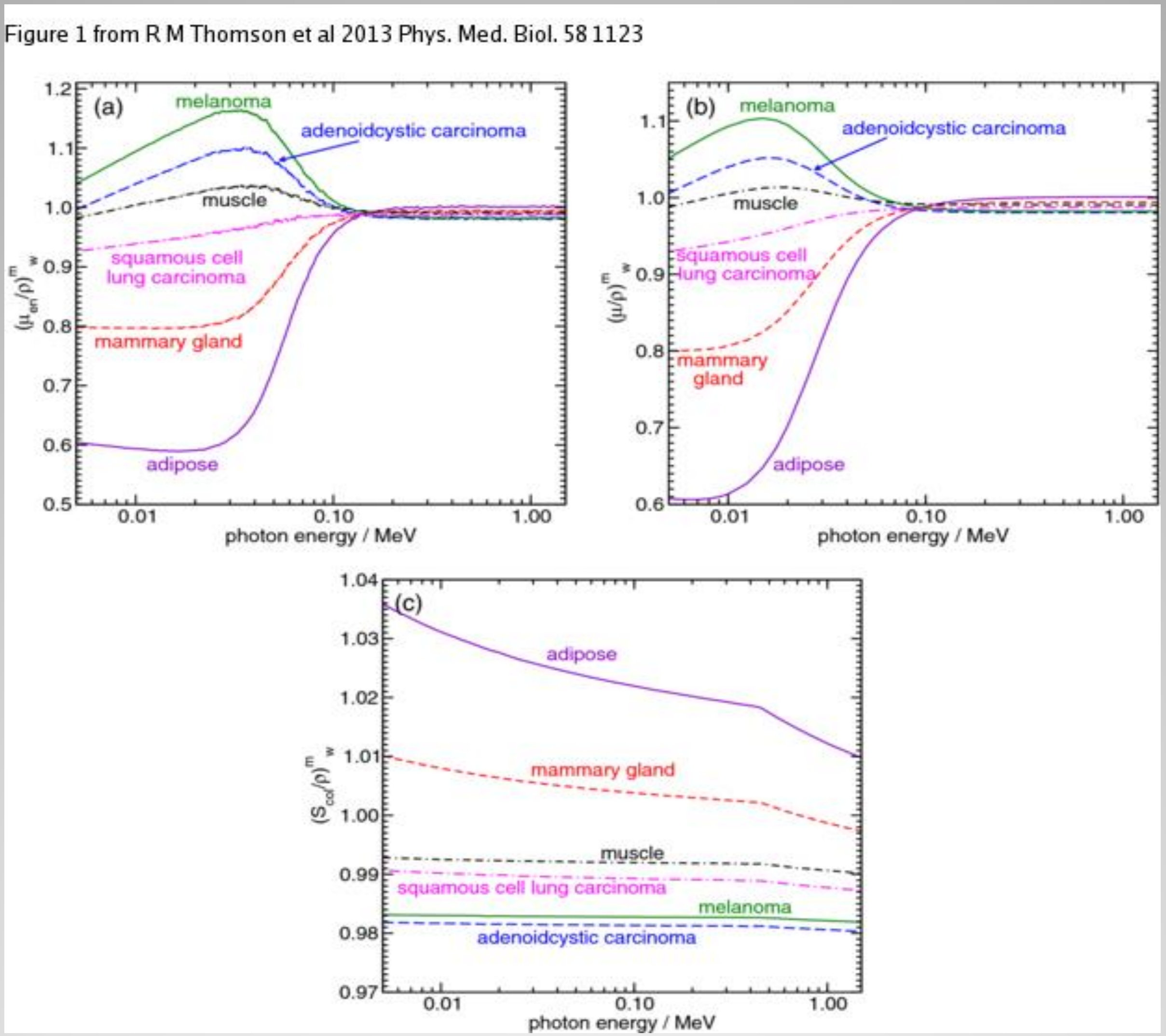


FIG. 1. Contributions of primary and scattered photons to total absorbed dose at the photon energies investigated in this work. (a) 28.4 keV, (b) 100 keV, (c) 350 keV, and (d) 662 keV. The calculations are for point sources inside cubic phantoms with side lengths of 20 cm at 28.4 keV and 40 cm at the 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.

The collapsed cone superposition algorithm applied to scatter dose calculations in brachytherapy.
Carlsson AK, Ahnesjö A. Med Phys. 2000 Oct;27(10):2320-32.



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.

Anatomic site	Source energy	Absorbed dose	Attenuation	Shielding	Scattering	Beta/kerma dose
Prostate	High	N	N	N	N	N
	Low	Y	Y	Y	N	N
Breast	High	N	N	N	Y	N
	Low	Y	Y	Y	N	N
GYN	High	N	N	Y	N	N
	Low	Y	Y	N	N	N
Skin	High	N	N	Y	Y	N
	Low	Y	N	Y	Y	N
Lung	High	N	N	N	Y	Y
	Low	Y	Y	N	Y	N
Penis	High	N	N	N	Y	N
	Low	Y	N	N	Y	N
Eye	High	N	N	Y	Y	Y
	Low	Y	Y	Y	Y	N

The evolution of brachytherapy treatment planning. Rivard MJ, Venselaar JL, Beaulieu L. Med Phys. 2009 Jun;36(6):2136-53.

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 3.0cm^3 maximum difference in V100, V150 and V200.

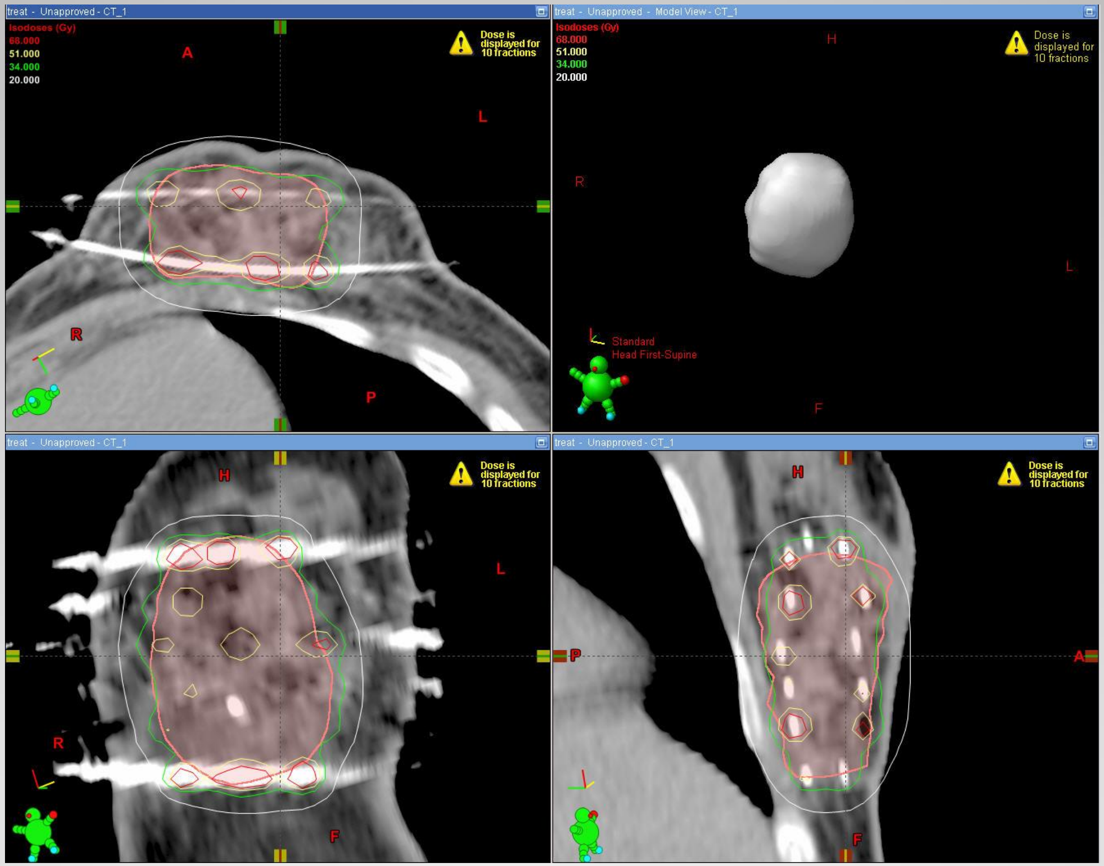
- However, differences of potential clinical significance were discovered in balloon based treatment techniques: an average difference of 8% for maximum skin dose (with maximum values >10% when single dwell position was used in a large balloon) and an average difference of 7% for maximum rib dose.

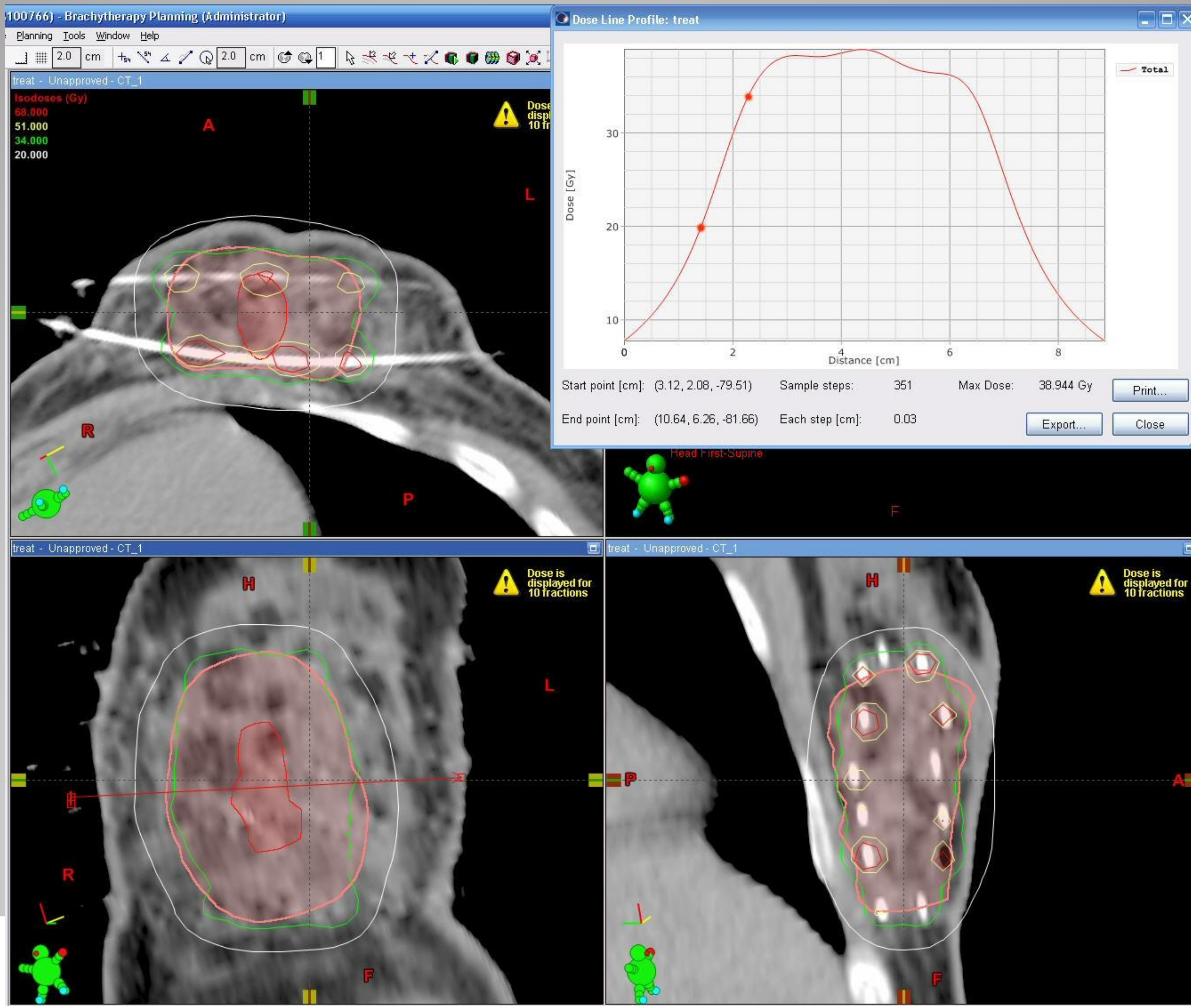
- The Acuros based computation suggests that target coverage may be less than previously expected (by TG43) by up to 5.5% (D95 and D90). Consequently, computation with Acuros suggests actual delivered dose to all breast tissue is less than previously represented by TG43 based calculations. The maximum difference was observed in conjunction with a large balloon (>5.5cm diameter) with a decrease in V100 of 16.9 cm^3 and an average decrease for all cases of 8.9cm^3; differences in V150 and V200 were in the range of 2.5 to 5.7cm^3 and 0.2 to 2.2cm^3, respectively.

Other issues worth talking about

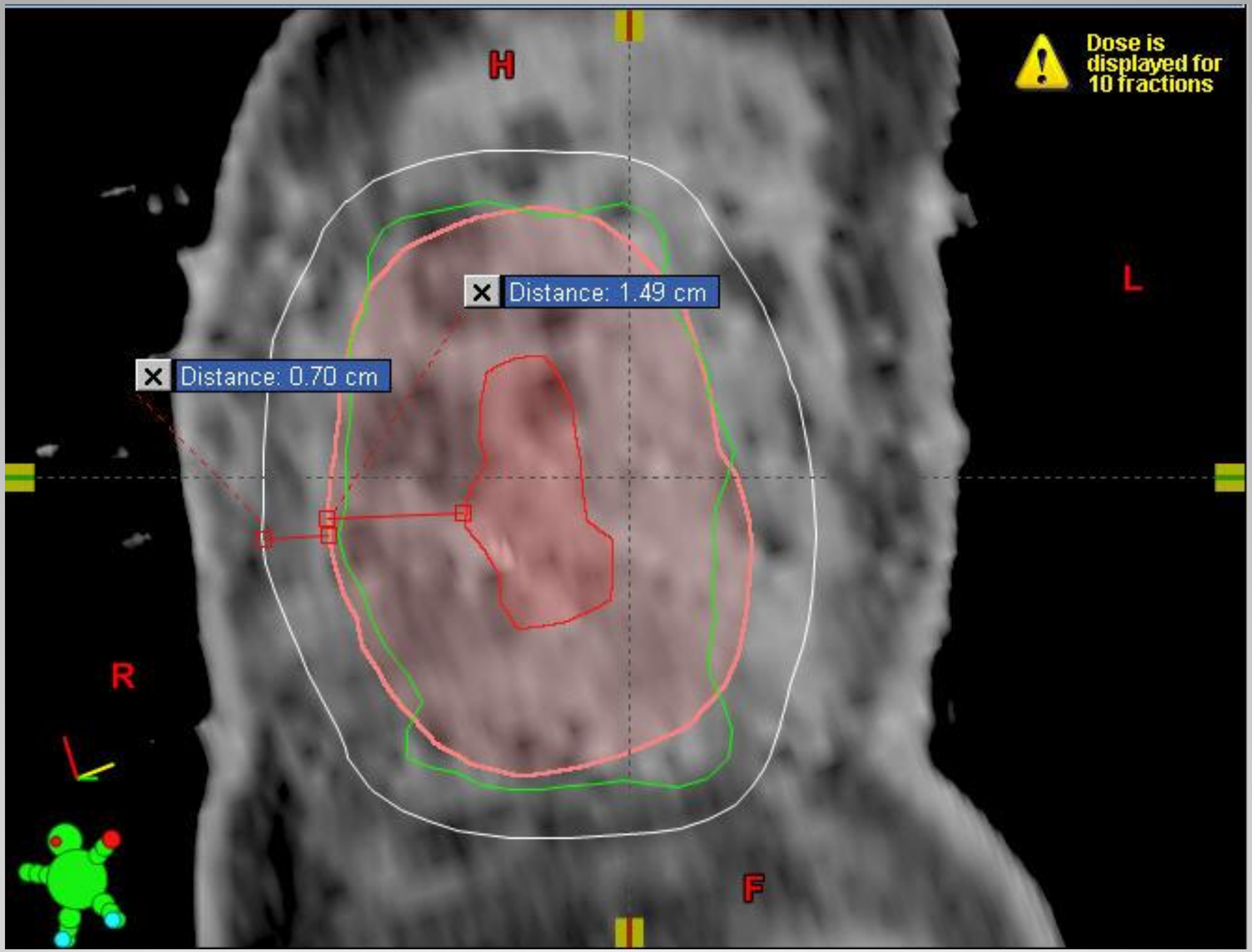
- The issue of margins: margins should be seen/used in the context of the dose distribution created by a certain treatment.
- Better understanding and modeling of both tumor control and normal tissue complications. Cellular damage response and the fate of a cell and the maintenance of tissue functions (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

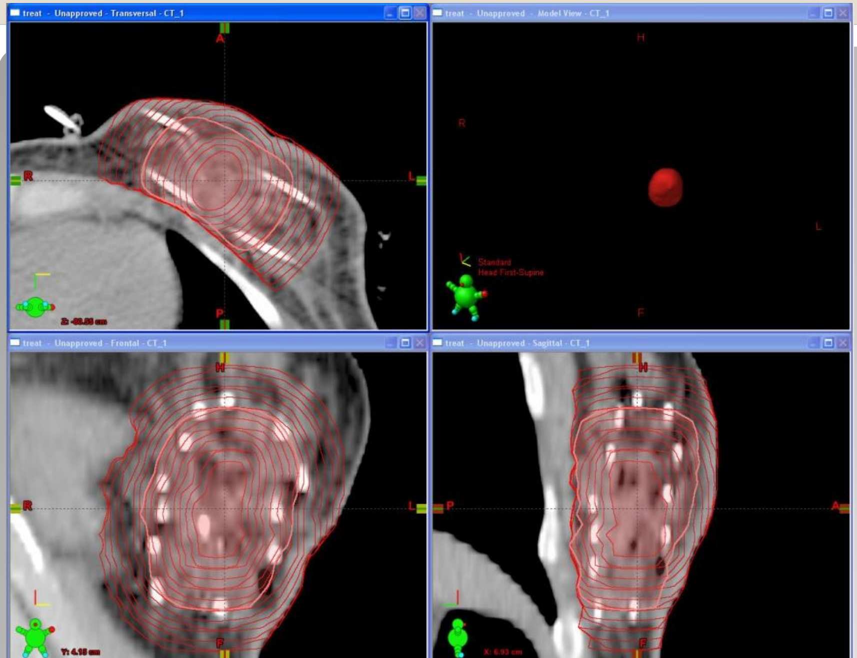




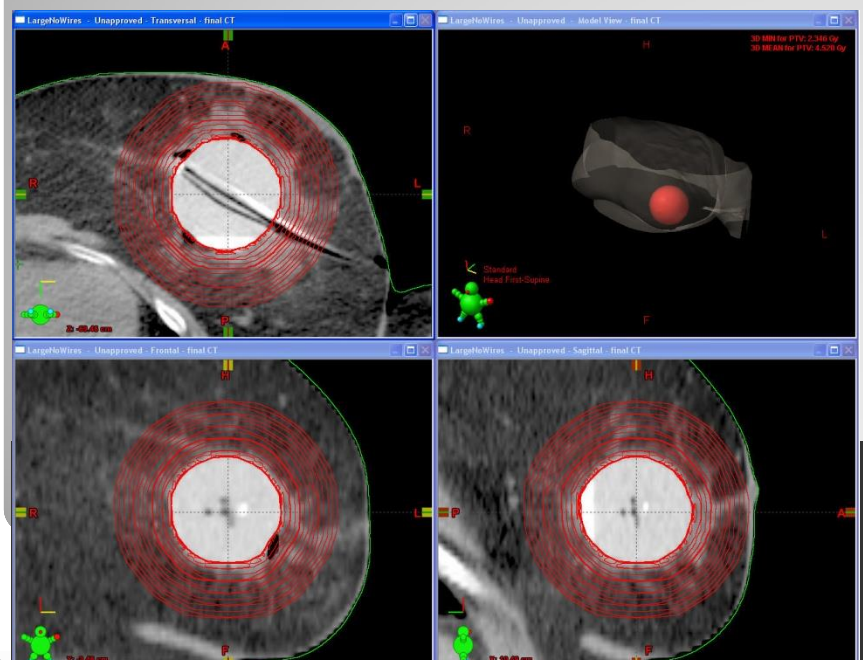
100766) - Brachytherapy Planning (Administrator)
Planning Tools Window Help
treat - Unapproved - CT_1
Isodoses (Gy)
68.000
51.000
34.000
20.000
Dose Line Profile: treat
Dose [Gy]
Distance [cm]
Total
Start point [cm]: (3.12, 2.08, -79.51)
End point [cm]: (10.64, 6.26, -81.66)
Sample steps: 351
Each step [cm]: 0.03
Max Dose: 38.944 Gy
Print...
Export...
Close
Head First-Supine
Dose is displayed for 10 fractions

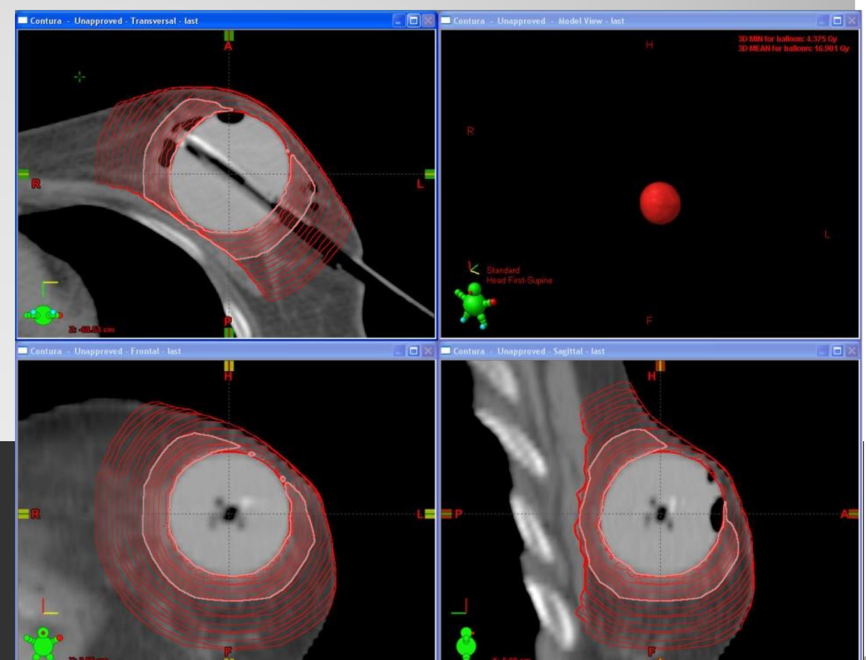


H
Dose is displayed for 10 fractions
L
Distance: 1.49 cm
Distance: 0.70 cm
R
F



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.





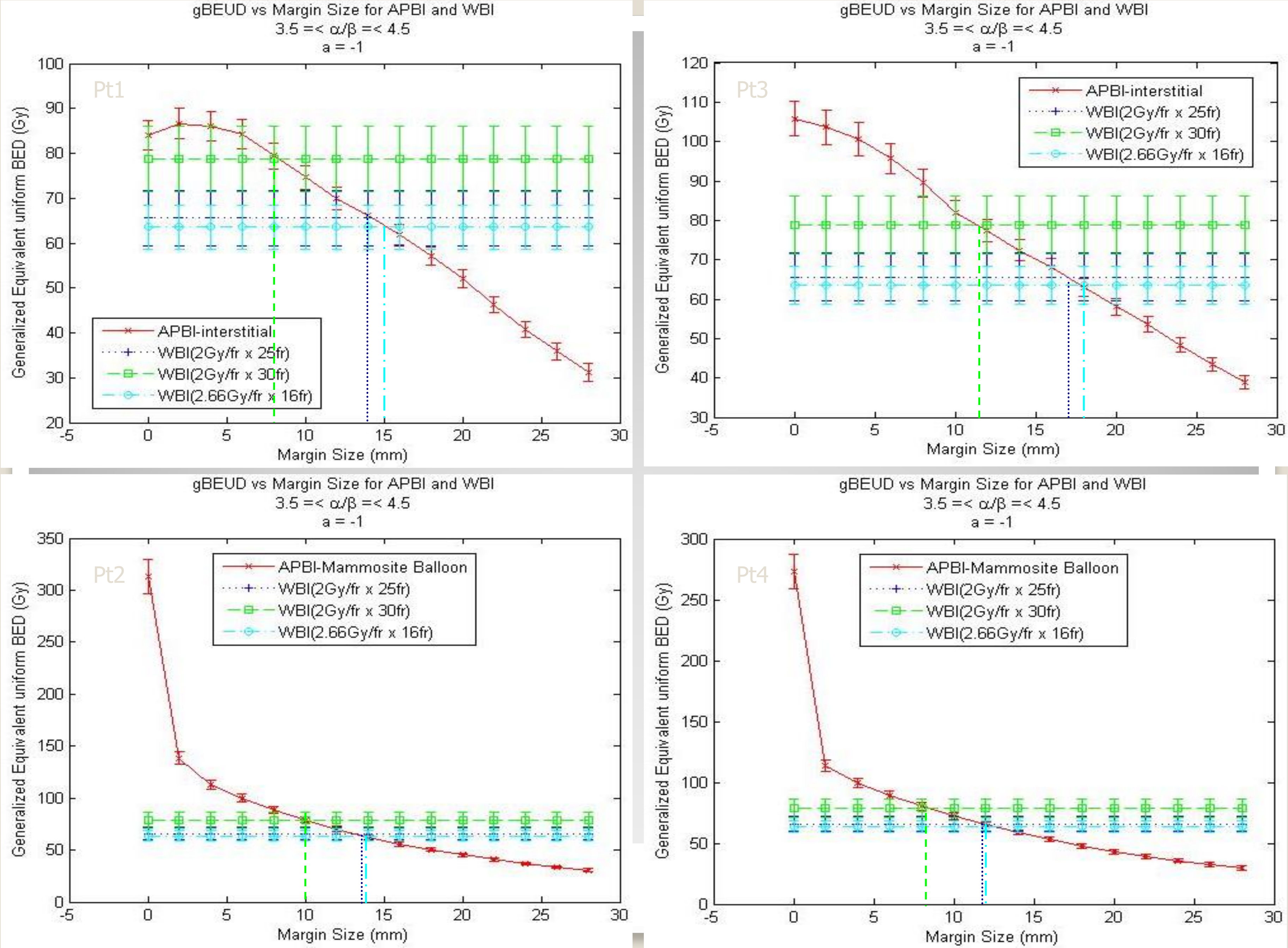
EUBED denotes the BED which, if uniformly delivered to the CTV, would give the same fraction of surviving cells as a given non-uniform BED distribution

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

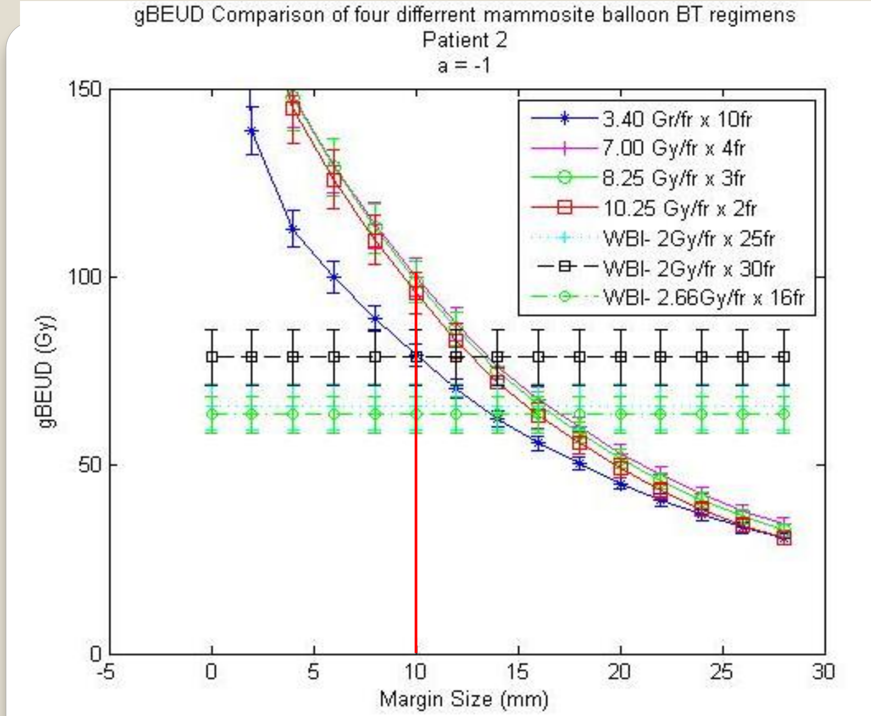
EUD contains an additional unit-less volume parameter "a" that is tissue and end point specific

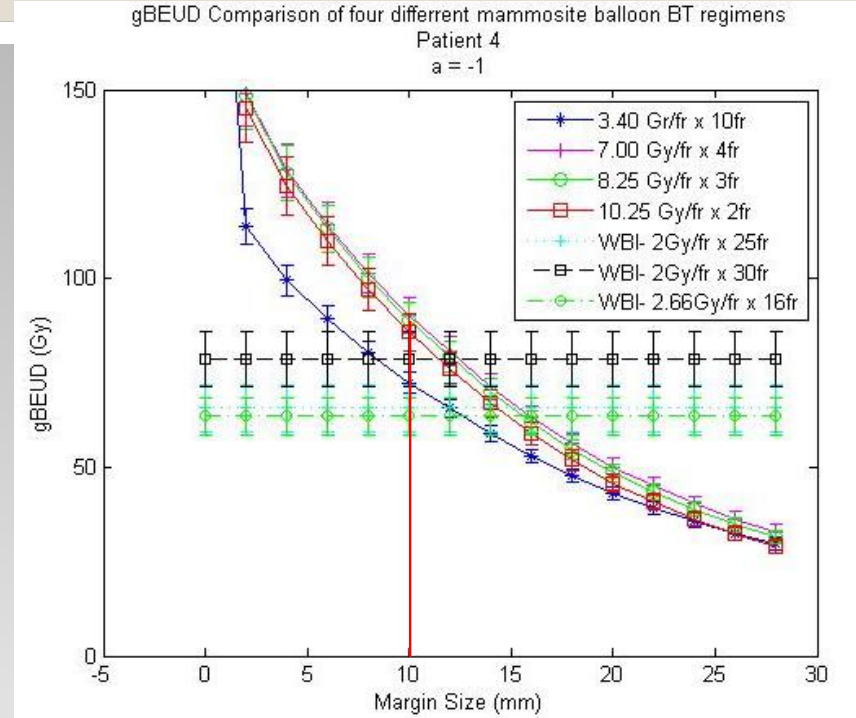
$$gBEUD = \left(\frac{1}{N}\sum_{i=1}^{N} BED(i)^{a}\right)^{1/a}$$

$$EUD = \left(\frac{1}{N}\sum_{i=1}^{N} d(i)^{a}\right)^{1/a}$$



gBEUD vs Margin Size for APBI and WBI
3.5 =< α/β =< 4.5
a = -1
Pt1
APBI-interstitial
WBI(2Gy/fr x 25fr)
WBI(2Gy/fr x 30fr)
WBI(2.66Gy/fr x 16fr)
Generalized Equivalent uniform BED (Gy)
Margin Size (mm)
gBEUD vs Margin Size for APBI and WBI
3.5 =< α/β =< 4.5
a = -1
Pt3
APBI-interstitial
WBI(2Gy/fr x 25fr)
WBI(2Gy/fr x 30fr)
WBI(2.66Gy/fr x 16fr)
Generalized Equivalent uniform BED (Gy)
Margin Size (mm)
gBEUD vs Margin Size for APBI and WBI
3.5 =< α/β =< 4.5
a = -1
Pt2
APBI-Mammosite Balloon
WBI(2Gy/fr x 25fr)
WBI(2Gy/fr x 30fr)
WBI(2.66Gy/fr x 16fr)
Generalized Equivalent uniform BED (Gy)
Margin Size (mm)
gBEUD vs Margin Size for APBI and WBI
3.5 =< α/β =< 4.5
a = -1
Pt4
APBI-Mammosite Balloon
WBI(2Gy/fr x 25fr)
WBI(2Gy/fr x 30fr)
WBI(2.66Gy/fr x 16fr)
Generalized Equivalent uniform BED (Gy)
Margin Size (mm)





Relative to current standard fractionation scheme (3.4 Gy x 10fx) we find that gBEUD

at GTV + 1.0 cm	7Gy x 4fx	8.25Gy x 3fx	10.25Gy x 2fx
Patient 2	26%	25%	21%
Patient 4	25%	23%	19%

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.