Brachytherapy is better than external beam therapy for partial breast irradiation

For the proposition: Dorin Todor
Virginia Commonwealth University, Richmond, VA

AAPM 55th Annual Meeting, Indianapolis, IN, Aug 2013

Thank you Colin, Sonja and Stewart

"The laws of nature are but the mathematical thoughts of God." - Euclid

"There are two ways of establishing a proposition. One is by trying to demonstrate it upon reason, and the other is, to show that great men in former times have thought so and so, and thus to pass it by the weight of pure authority."

Speech of Hon. Abraham Lincoln at Columbus, Ohio, Sept 1859.
Political debates between Lincoln and Douglas

Politics

- The politics and the ethics of breast cancer, Beryl McCormick, *Brachytherapy*, 1 (2002) 179-180.

"The major networks and lay press carried the story …The politics of breast cancer was now involved"

Rebuttal

- Inconsistency, perspective, double talk and false virtue, Frank Vicini, Douglas Arthur, David Wazer, *Brachytherapy*, 1 (2002) 181-183.

APBI History

- **Interstitial multi-catheter implant represents the technique with the longest follow up to date**, with multiple series reporting outcomes with longer than 10-12 years follow-up. (1991-first patient treated by Dr. Kuske)
- **Balloon based APBI emerged in 2002** with the introduction of MammoSite balloon applicator. Multi-lumen balloons, Contura and Mammosite ML, followed shortly.
- **External beam RT** has also been developed as a method to deliver APBI, **initially described in 2003**.
- **Strut-based applicator was introduced in 2007** as a 'hybrid' technology combining single-entry benefit of the balloon-devices with the features of interstitial brachytherapy.

Metrics to compare APBI modalities

- Dosimetric parameters/constraints
- Radiobiology
- Radiotherapy treatment planning
- Radiation delivery
- Operator proficiency
- Availability, Cost

- **Clinical Outcomes**

Target volume

- Brachy traditionally **started with a 2cm margin** (in the 2D era) **from LC** for interstitial implants. **After 3D CT based, margins become 1.5cm. MammoSite – 1.0cm, SAVI - 1.0cm.**

- EBRT: Supine CTV=LC+1.5cm. PTV=CTV+(0.5+0.5)
  Prone CTV=LC+1.0cm. PTV=CTV
- As discussed in the original paper "***the appropriate CTV for partial-breast RT is subject to considerable debate***", and Baglan and co-authors *suggest the CTV be the lumpectomy cavity +1.5 cm uniformly expanded around the lumpectomy cavity but limited to 5 mm from the skin surface* and 5 mm from the lung–chest wall interface. Based on *studies of respiratory mobility the PTV is defined as CTV +0.5 cm to account for breathing motion* ***and*** *+0.5 cm to accommodate for expected variation in patient setup.*

- Vicini et al. [ref1] based on pathological analysis of 607 consecutive cases of Stage I and II breast cancer, concluded that "***A margin of 10 mm around the tumor bed should be adequate in covering disease remaining in the breast after lumpectomy in >90% of patients treated with PBI.***"

Smaller target volume in brachytherapy

- In "A dosimetric comparative study of 3D-CRT, IMRT and MammoSite partial breast", Khan *et al* founded that the PTV size in brachytherapy was 94.3±18.5cm^3 versus 184.3±54.6cm^3 .
- Does it matter?!
- In a dosimetric comparison of APBI techniques including multicatheter interstitial brachytherapy, 3D-CRT and supine vs. prone helical tomotherapy, Patel *et al* reported significant differences between techniques in the volume of breast tissue receiving 100%PD and 50%PD: **V100 was significantly lower for IB 12% vs. 15% for PT, 18% for ST and 26% for 3D-CRT**) and so **was V50 (24%-IB vs. 43%, 47% and 52% for PT, ST and 3D-CRT)**
- The authors concluded that the coverage of PTV for all techniques was excellent, and the dose to the heart was low in every case, however, the **interstitial brachytherapy and treatment of the patient in prone position resulted in greater normal tissue sparing** (especially ipsilateral breast and lung) as compared to supine position for 3D CRT.

Smaller integral dose Lower normal tissue toxicity

- In *"Comparison of three accelerated partial breast irradiation techniques: treatment effectiveness based upon biological models"*, Bovi et al found that "… **the integral dose to the non-target part of the breast is higher with 3D-CRT compared to interstitial and MammoSite brachytherapy** ."

- In "*Relationship between irradiated breast volume and late normal tissue complications: A systematic review*" Mukesh and coleagues reviewing the EORTC "boost versus no boost" trial, showed that "**the boost volume was associated with an increased risk of moderate and severe fibrosis**", with a cutoff value of 200cm^3. They also point out, citing a study by Borger et al. that "**there is a 4-fold increase of risk of fibrosis for every 100 cm^3 increase in boost volume**".

- The EORTC boost trials also provided quantitative information on the volumetric effect where **increasing the tumour bed margin from 1.5 cm to 3 cm doubles the rates of moderate/severe fibrosis from 15% to 30%.** However, it is possible that the increase in NTC is secondary to a combination of larger boost volume *and* a steeper dose–response curve as total dose increased …"

Other target problems

- Uncertainty in defining LC (w or w/o surgical clips)
- Dynamic variation of the tumor bed. Based on a study of 36 consecutive patients, Prendergast et al. in "*The Dynamic Tumor Bed: volumetric changes in the lumpectomy cavity during breast-conserving therapy*" conclude that "**the average post-lumpectomy cavity undergoes dramatic volumetric change after surgery and continues the change during RT**" and they quantify this change to an **average 2.1% per post-op day**. For a typical 7-10 days between a planning CT and a first day treatment, the change in LC volume could be around 15-20%.
- What is the likelihood that the planned dose distribution is actually delivered?
- Hasan et al. based on 16 patients treated with EB APBI who underwent CBCT before each fraction and daily helical CT, found a mean setup error per CBCT registration of 9±5mm. They concluded that "**The current CTV-to-PTV margin of 10 mm appears sufficient for ~92% of patients treated with EB APBI. Although expansion of the population PTV margin to 14 mm would provide ~97% confidence level for CTV coverage, online image guidance should be considered**."

Increase EBRT toxicity with increased total dose

- In 2012, Bourgier et al. reported in "Higher toxicity with 42 Gy in 10 fractions as a total dose for 3D-conformal accelerated partial breast irradiation: results from a dose escalation phase II trial" that "**Early toxicities were more severe and higher rates of late toxicities were observed after 42 Gy/10 fractions/5 days when compared to 40 Gy/10 fractions/5 days. This data suggest that 40 Gy/10 fractions/ 5 days could potentially be the maximum tolerance for PBI although longer follow-up is warranted to better assess late toxicities**."

- **Most of APBI clinical trials or prospective studies used an external beam irradiation (3D-conformal or intensity-modulated radiotherapy) with a total dose of 38.5 Gy.**

- According to the **National Surgical Adjuvant Breast and Bowel Project B-39/ Radiation Therapy Oncology Group 0413 protocol (NSABP-B39/ RTOG 0413**) treatment planning guidelines hot spots of up to 120%PD (46.2Gy) are allowed but no specific volume is specified.

- 40Gy is only 3.9% higher than 38.5Gy, 42Gy is 9% higher.

Operator dependency ?!

EDITORIAL

REPORTS OF UNEXPECTED LATE SIDE EFFECTS OF ACCELERATED PARTIAL BREAST IRRADIATION—RADIOBIOLOGICAL CONSIDERATIONS

SØREN M. BENTZEN, PH.D., D.SC.,* AND JOHN R. YARNOLD, M.D., FRCR.†

*Department of Human Oncology, University of Wisconsin School of Medicine and Public Health, Madison, WI and †Section of Radiotherapy, Institute of Cancer Research and Royal Marsden Hospital, Sutton, United Kingdom

1. Chen PY, Wallace M, Mitchell C, et al. Four-year efficacy, cosmesis, and toxicity using three-dimensional conformal external beam radiation therapy to deliver accelerated partial breast irradiation. Int J Radiat Oncol Biol Phys 2010, 76(4), 991-7

2. Hepel JT, Tokita M, Macausland SG, et al. Toxicity of three dimensional conformal radiotherapy for accelerated partial breast irradiation. Int J Radiat Oncol Biol Phys 2009;75: 1290–1296.

3. Jagsi R, Ben-David MA, Moran JM, et al. Unacceptable cosmesis in a protocol investigating intensity-modulated radiotherapy with active breathing control for accelerated partial-breast irradiation. Int J Radiat Oncol Biol Phys 2010;76:71–78.

Total dose, Fraction size, recovery kinetics… *"All in all, the APBI dose delivered by external beam radiotherapy appears unnecessarily high for a population of low-risk patients."*


"COMPLICATED"


"SIMPLE"

Availability
Operator dependency/proficiency

EBRT:

- Wide-spread availability “Every clinic has a linac but not every clinic has an HDR unit”

- Outcome depends less on the experience and operative skills

- Less expensive

Too ‘operator’ dependent and not widely available ?

This is much less ‘operator’ dependent and it is widely available

Economics

- In 2005, Suh et al. "*A cost comparison analysis of partial versus whole-breast irradiation after breast-conserving surgery for early-stage breast cancer.*" analyzed eight different breast RT techniques and concluded that:

- "Not all efforts to reduce overall treatment time result in total cost savings. **The least expensive partial breast-based RT approaches were the external beam techniques** (APBI-3D-CRT, APBI-IMRT). **Any reduced cost to patients for the HDR brachytherapy-based APBI regimens were overshadowed by substantial increases in cost to payers,** resulting in higher total societal costs; the cost of HDR treatment delivery was primarily responsible for the increased direct medical cost."

- In 2013, Shah et al. included in their cost analysis "*Cost-efficacy of acceleration partial-breast irradiation compared with whole-breast irradiation*." a cost minimization analysis, **incremental cost- effectiveness ratio** (ICER) analysis, and **cost per quality adjusted life year** (QALY) analysis. They concluded that " **When compared to WBI 3D-CRT, external beam APBI techniques represent a more cost-effective approach based on cost minimization with brachytherapy representing a cost-effective approach based on cost per QALY**"

Longer follow-up
Better dosimetric guidelines

- The Hungarian National Institute of Oncology PBI trial showed, after a median follow up of 66 months that while the **local recurrence rates were not different in the two trial arms** (WBI and PBI) the **cosmetic results were favorable for PBI**, with the rate of good and excellent cosmesis of 77.6% for the PBI group and 62.9% for the WBI.

- Wazer et al. "*Accelerated partial breast irradiation: an analysis of variables associated with late toxicity and long-term cosmetic outcome after high-dose-rate interstitial brachytherapy*." reported on the **variables associated with late toxicity and long term cosmetic outcome after PBI breast brachytherapy** using pooled data from Tufts Univ., Brown Univ. and VCU.

Longer follow-up Better dosimetric guidelines

- Case matched studies:
- Polgar – PBI Ir-192 7fx, 4 days, 30.6-36.4Gy vs WBI, 7 years follow up**. Excellent/good cosmesis 84.4%-PBI vs 68.3% in the WBI arm.**
- William Beaumont group matched 174 patients treated with Ir-192 (32Gy in 8Fx) with 174 patients treated with WBI (60Gy to tumor bed). **Excellent/good cosmesis 90%-PBI vs 83%-WBI** (45Gy in 25fx + boost 15Gy e^- or 10Gy HDR). At a median follow up of 43 months, **excellent/good cosmesis was 88.9% vs. 56%).**
- King et al. matched 51 patients treated with PBI (LDR Ir-192 45Gy in 4d or HDR Ir-192 32Gy in 8fx over 4 days) with 94 patients treated WBI at a median dose of 59Gy. At 20 months, 75% in the PBI group and 84% WBI had excellent/good cosmesis (p-not significant)

Longer follow-up Better dosimetric guidelines

- In "*Brachytherapy-based partial breast irradiation is associated with low rates complications and excellent cosmesis*", Brachytherapy 12 (2013) 278-284, Shah et al. reports on the The **ASBS breast brachytherapy registry is a prospective non-blinded multi-institutional registry trial**. A total of 1665 patients were enrolled and **1449 treated between 2002 and 2004 with a median followup of 63 months**. All patients were **treated with the MammoSite** (Hologic, Inc.) single-lumen device to deliver adjuvant APBI (34 Gy in 3.4 Gy fractions).

- **The rate of excellent/good cosmesis was 90.6% at 84 months.** The rate of a complication (symptomatic seroma, infection, fat necrosis, telangiectasias) at 1 year/any time point was 24.2%/38.5%, whereas the rate of noninfectious complications at 1 year/any time point was 14.8%/28.9%. **The rate of symptomatic seroma, fat necrosis, infection, and telangiectasia at any time was 13.4%, 2.5%, 9.6%, and 13.0%, respectively.**

Interim Cosmetic and Toxicity Results From RAPID: A Randomized Trial of Accelerated Partial Breast Irradiation Using Three-Dimensional Conformal External Beam Radiation Therapy

Ivo A. Olivotto, Timothy J. Whelan, Sameer Parpia, Do-Hoon Kim, Tanya Berrang, Pauline T. Truong, Iwa Kong, Brandy Cochrane, Alan Nichol, Isabelle Roy, Isabelle Germain, Mohamed Akra, Melanie Reed, Anthony Fyles, Theresa Trotter, Francisco Perera, Wayne Beckham, Mark N. Levine, and Jim A. Julian

Processed as a Rapid Communication manuscript

Author affiliations appear at the end of this article.

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0732-183X/13/3199-1/$20.00

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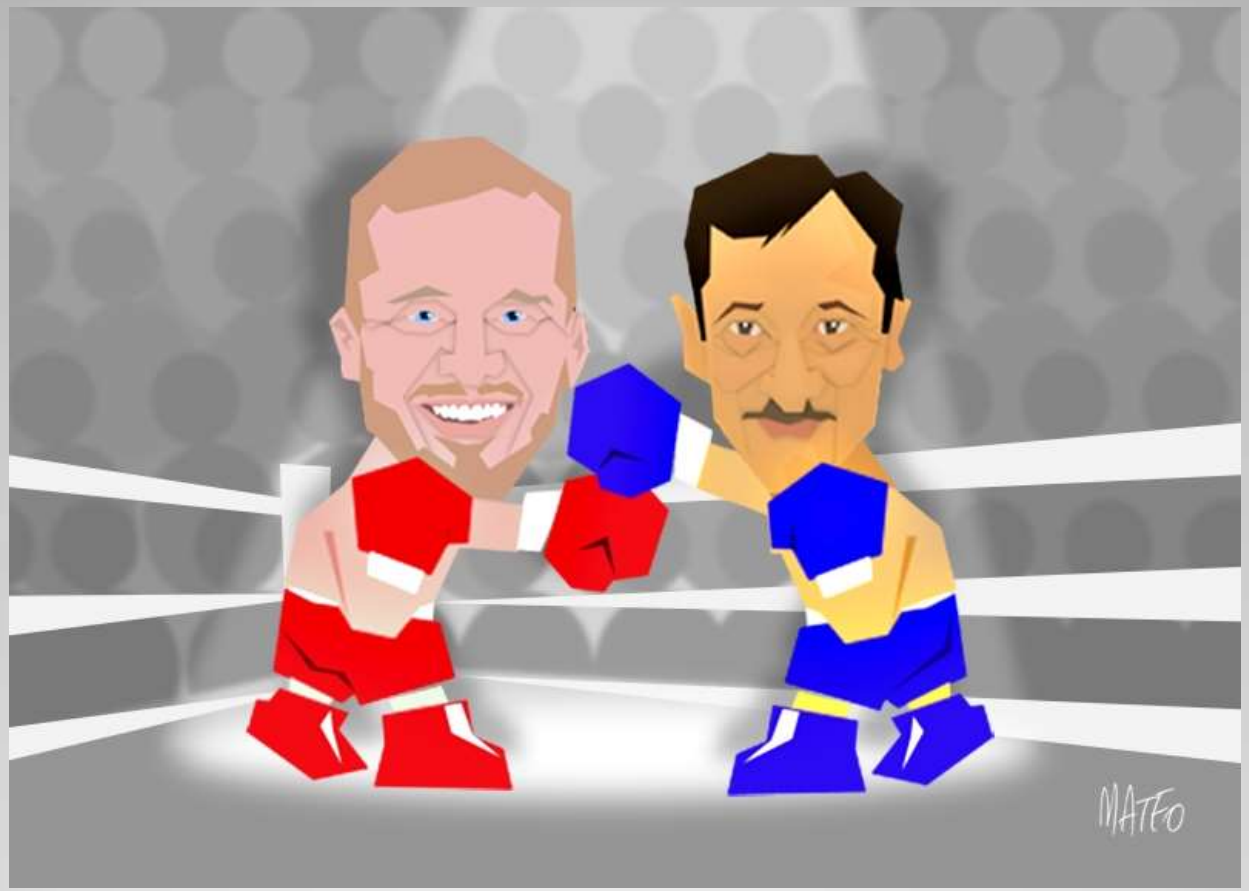
ABSTRACT

Purpose
To report interim cosmetic and toxicity results of a multicenter randomized trial comparing accelerated partial-breast irradiation (APBI) using three-dimensional conformal external beam radiation therapy (3D-CRT) with whole-breast irradiation (WBI).

Patients and Methods
Women age > 40 years with invasive or in situ breast cancer ≤ 3 cm were randomly assigned after breast-conserving surgery to 3D-CRT APBI (38.5 Gy in 10 fractions twice daily) or WBI (42.5 Gy in 16 or 50 Gy in 25 daily fractions ± boost irradiation). The primary outcome was ipsilateral breast tumor recurrence (IBTR). Secondary outcomes were cosmesis and toxicity. Adverse cosmesis was defined as a fair or poor global cosmetic score. After a planned interim cosmetic analysis, the data, safety, and monitoring committee recommended release of results. There have been too few IBTR events to trigger an efficacy analysis.

Results
Between 2006 and 2011, 2,135 women were randomly assigned to 3D-CRT APBI or WBI. Median follow-up was 36 months. Adverse cosmesis at 3 years was increased among those treated with APBI compared with WBI as assessed by trained nurses (29% *v* 17%; $P < .001$), by patients (26% *v* 18%; $P = .0022$), and by physicians reviewing digital photographs (35% *v* 17%; $P < .001$). Grade 3 toxicities were rare in both treatment arms (1.4% *v* 0%), but grade 1 and 2 toxicities were increased among those who received APBI compared with WBI ($P < .001$).

Conclusion
3D-CRT APBI increased rates of adverse cosmesis and late radiation toxicity compared with standard WBI. Clinicians and patients are cautioned against the use of 3D-CRT APBI outside the context of a controlled trial.


MATEO

IN SUMMARY

1. Brachytherapy is more conformal. Smaller treatment volumes, lower integral dose, lower normal tissue toxicity
2. Brachytherapy is the modality with the longest follow-up
3. Variables associated with late toxicity and long term cosmetic outcome are well understood and refined in brachytherapy
4. Brachytherapy is a cost effective modality
5. Dose inhomogeneity and dose gradient outside of the 'Target' offers a distinct advantage for tumor control.
6. Brachytherapy offers a lower toxicity profile than EBRT

INSTEAD of REBUTTAL

- In their proposal for **RTOG 0319** A PHASE I/II TRIAL TO EVALUATE THREE DIMENSIONAL CONFORMAL RADIATION THERAPY (3D-CRT) CONFINED TO THE REGION OF THE LUMPECTOMY CAVITY FOR STAGE I AND II BREAST CARCINOMA (9/30/03), the authors included these potential advantages:
  - The potential elimination of an additional invasive procedure.
  - The elimination of variability in operator experience (no surgical experience is required as with brachytherapy).
  - The more precise 3-dimensional (3-D) delineation of the tumor bed volume using computerized tomography (CT).
  - The more precise delivery of irradiation using 3-D radiation techniques.
  - A significantly reduced amount of time to plan the radiation treatment.
  - Immediate implementation of this technique in most radiation facilities (with 3D treatment capabilities) across the country, if proven successful.
  - A larger proportion of potential candidates for the technique due to greater patient preference for a non-invasive procedure.

Insert catheters/single entry device or:

- Setup and verification (CBCT)
- Breathing motion or active breathing control
- Lumpectomy cavity variation. Surgical clips motion.

Double, Triple trouble

- "Double trouble" was the term coined by Withers regarding the significance of a hot spot in a dose plan that receives not only a ***higher total dose*** but also *a* ***higher dose per fraction*****.**
- Typically considered **safe if hot spots are limited in volume** (?!) and dose gradients are restricted between 95-107%PD.
- Leonard *et al*. (2013, IJROBP, Vol 85, No 3, pp623-629) points out to "**3D-CRT target volumes typically 2- to 3-fold larger than brachytherapy volumes**". In order to compensate for the differences due to dose homogeneity, a prescribed dose of 38.5Gy was established for 3D-CRT, this exposing a larger volume to a larger dose with a larger dose/fx.

- Increased late toxicity due to small increases in fractional dose (from 3.0Gy to 3.3Gy) and a cumulative dose of 4 Gy (39 vs 42.9Gy) was previously reported (Yarnold, 2005, Radiother. Oncol. 75-9-17) in a phase 3 trial conducted at Royal Marsden Hospital, which randomized patients to received 42.9Gy in 13 fx, 39Gy in 13fx or 50Gy in 25fx to the whole breast.

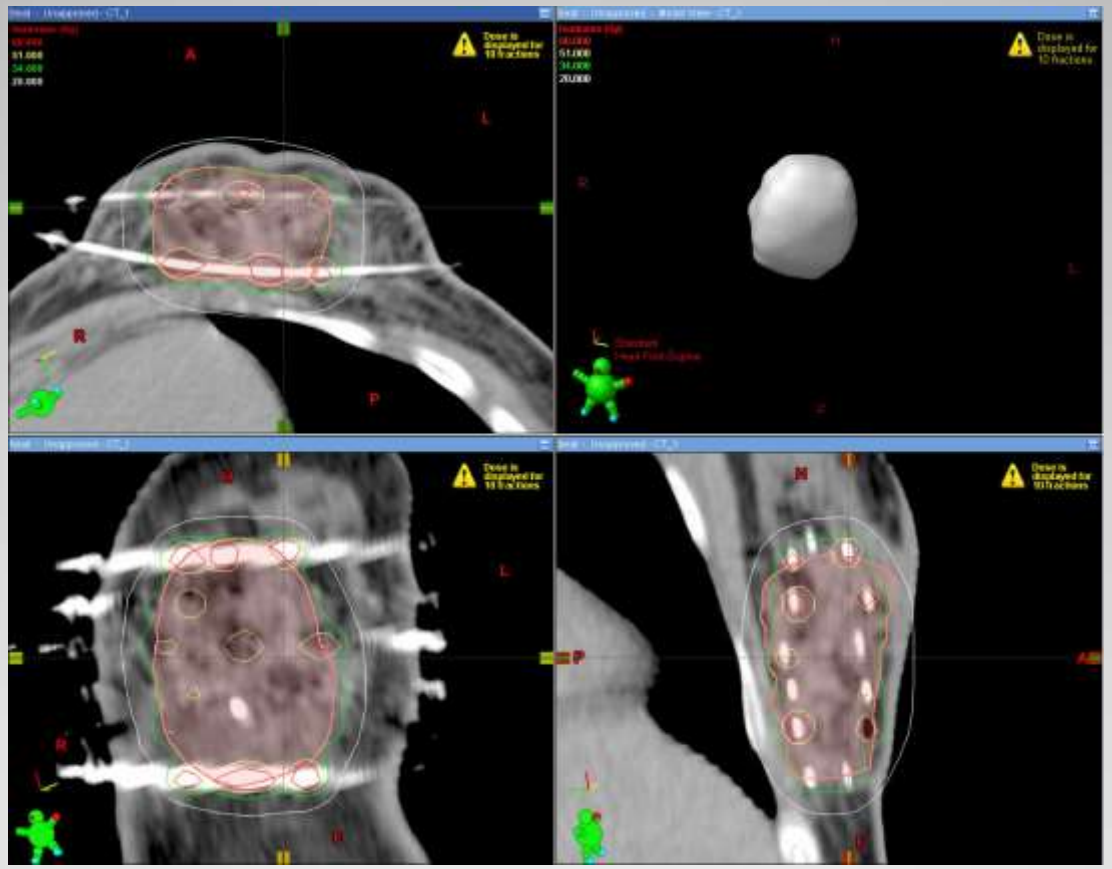
- Hepel et al (2009) found that **the size of 3D-CRT target volume in proportion to the overall breast volume** (PTV_EVAL/WBV) correlated with poor cosmesis and grade 2-4 subcutaneous fibrosis.

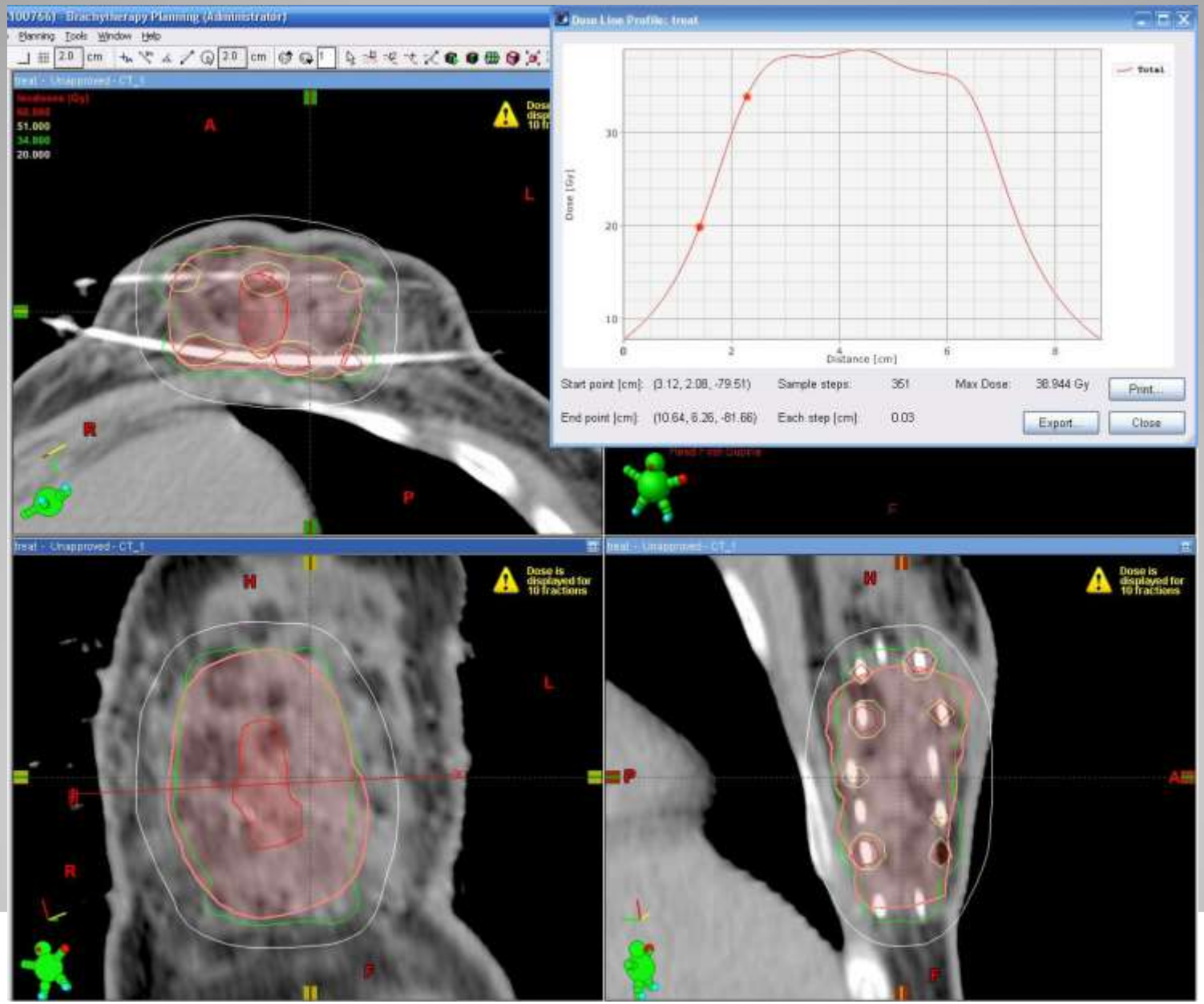
- In their analysis of three toxicity reports after 3D-CRT, Bentzen and Yarnold state: "These data are supportive of a **powerful volume effect**, even though brachytherapy data are not directly comparable to APBI data generated by external beam".

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 of the spatial organization of breast duct anatomy and the intraductal spread of primary invasive breast cancer.
- Customizing RT treatment to risk-groups based on genetic testing
- 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.
- **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.**

The issue of margins




Brachytherapy Planning (Administrator)
Planning Tools Window Help
Dose Line Profile: treat
Total
Dose [Gy]
Distance [cm]
Start point [cm]: (3.12, 2.08, -79.51)
Sample steps: 351
Max Dose: 38.944 Gy
End point [cm]: (10.64, 6.26, -81.66)
Each step [cm]: 0.03
Print...
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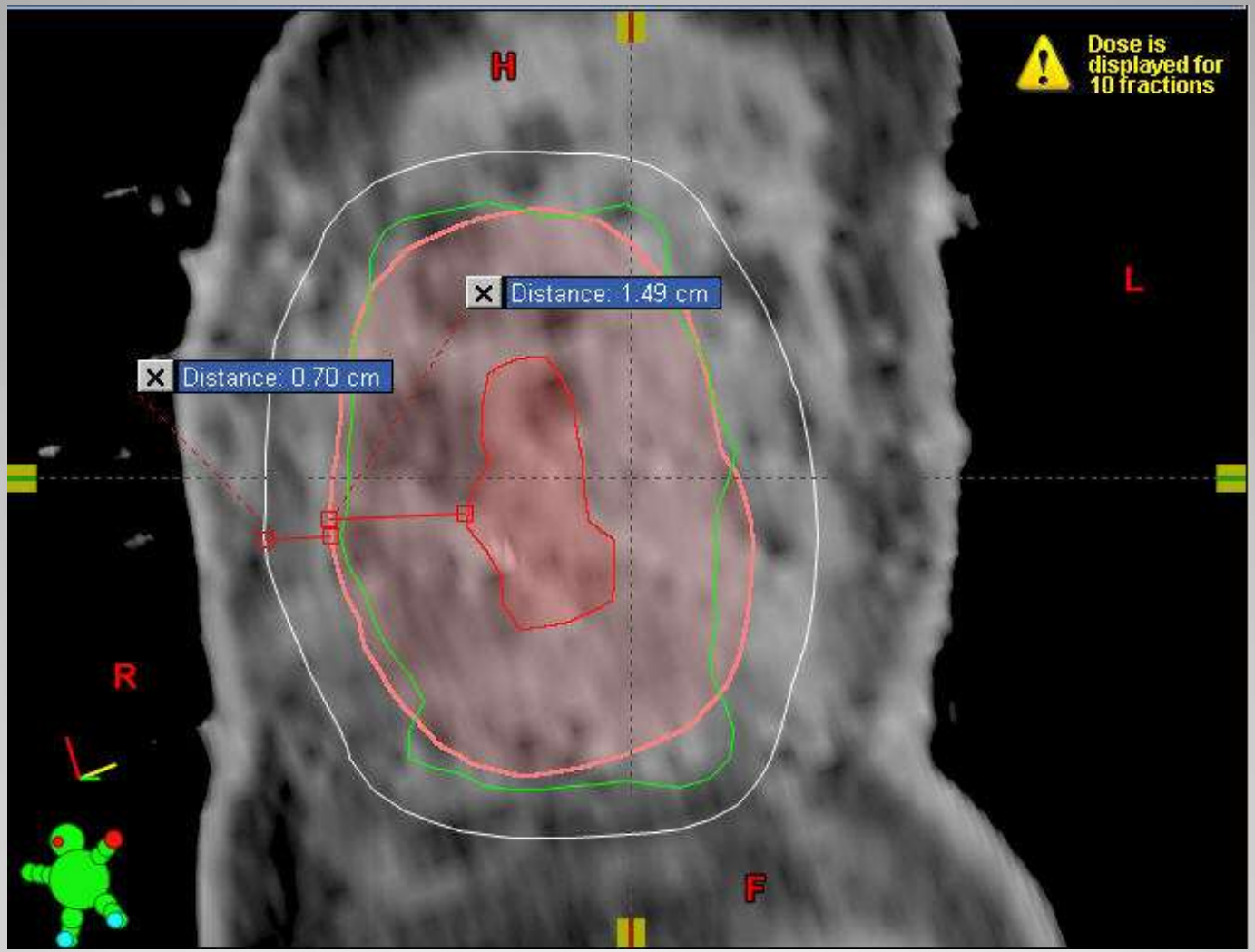
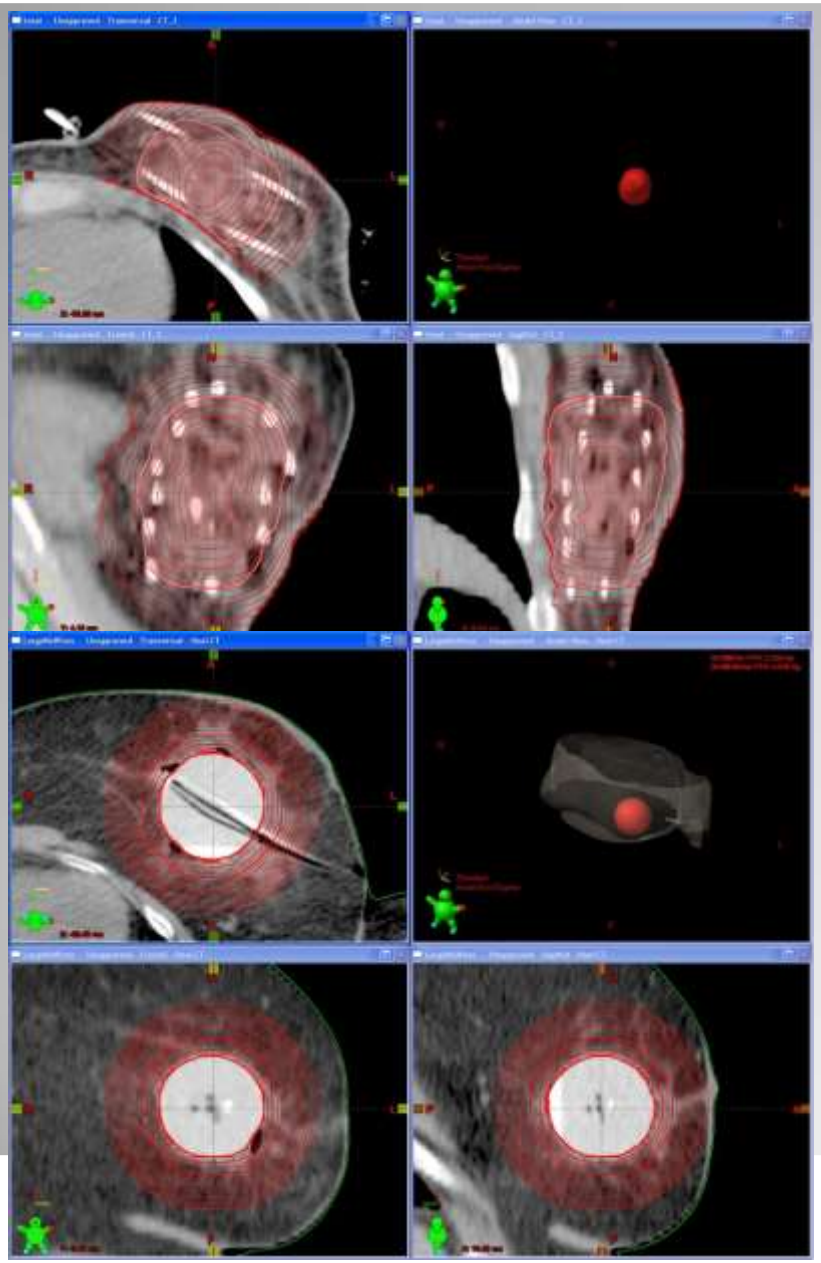
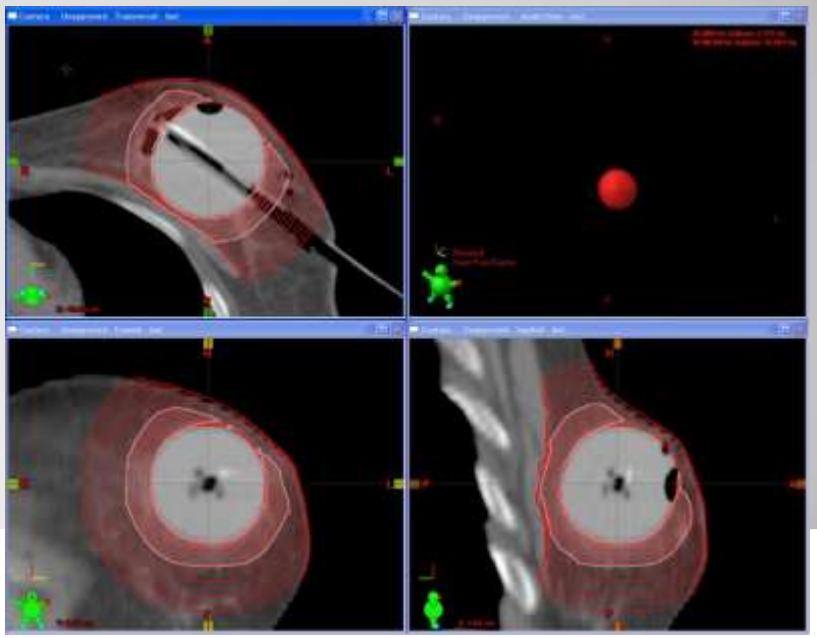
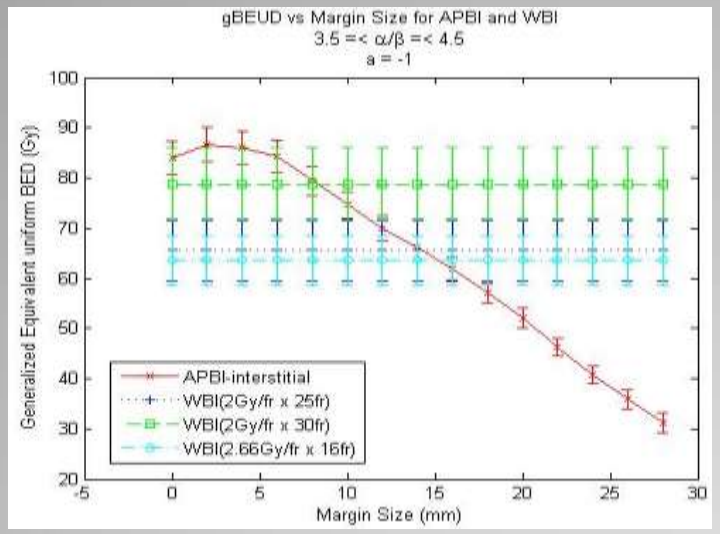
Close
Dose is displayed for 10 fractions

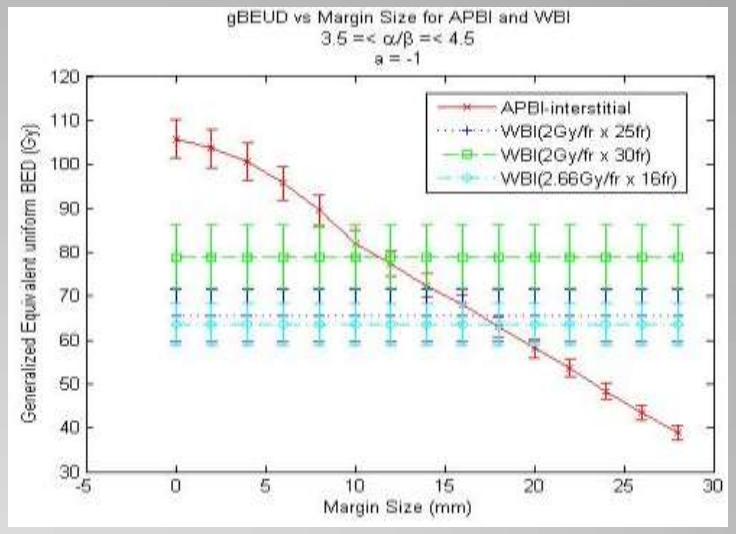

H
Dose is displayed for 10 fractions
Distance: 1.49 cm
L
Distance: 0.70 cm
R
F



While we accept these margins as a given and use them for treatment planning, we challenge the concept of ‘true’ target by creating a ‘variable’ or ‘continuous’ target, leading to an ‘onion’ model.




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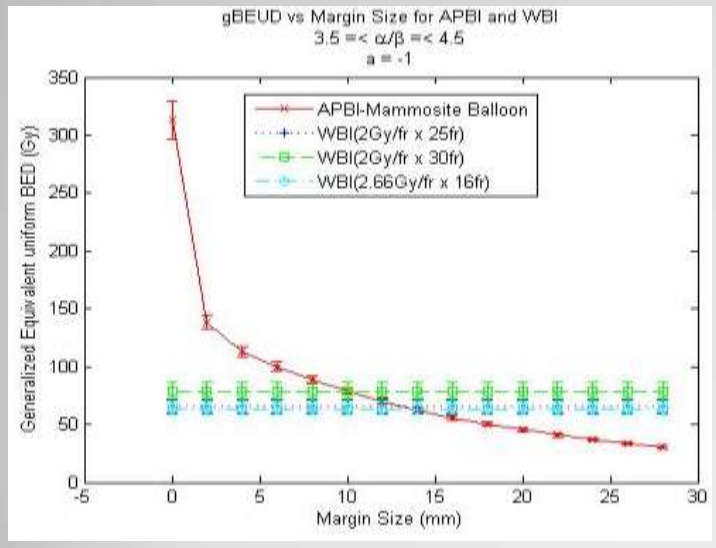
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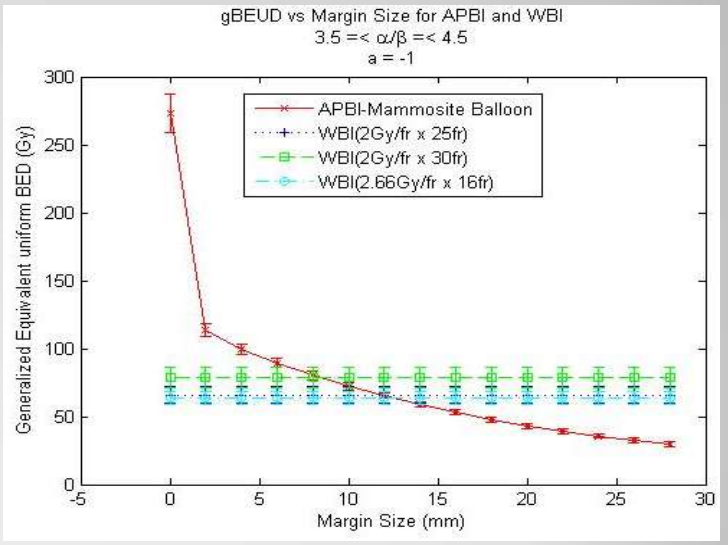
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APBI-Mammosite Balloon
WBI(2Gy/fr x 25fr)
WBI(2Gy/fr x 30fr)
WBI(2.66Gy/fr x 16fr)

In their work "Effect of breast-duct anatomy and wound-healing responses on local tumour recurrence after primary surgery for early breast cancer " Mannino and Yarnold state:

"*Despite the improvement in outcome for women with early breast cancer undergoing breast conservation surgery and radiotherapy, there are significant gaps in our understanding of local tumour relapse*."

Intraductal patterns of spread and interpatient variation in ductal anatomy are not taken into consideration by conventional surgical techniques, which consist mainly of removing a spheroidal volume.

During the past 10–15 years, much research on **clinical radiation has focused on the tumour bed** as the sole target of the intervention (so-called partial-breast radiotherapy) or as the target of an additional booster dose after whole-breast radiotherapy. **The definition of the clinical target volume for both of these approaches is still purely geometrical**— i.e., a radial margin is added to the surgical cavity, in the same way that the surgeon currently widens resected margins. As for surgery, the **anatomical and pathological data suggest that there is clearly scope for investigating if a shift to an anatomical or functional definition of the clinical target volume would be beneficial in younger patients.**

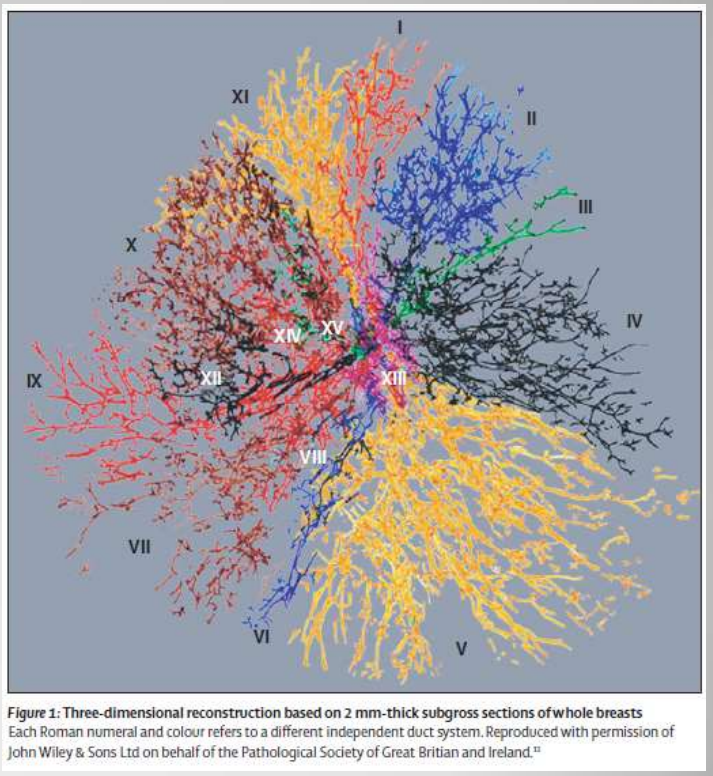

Figure 1: **Three-dimensional reconstruction based on 2 mm-thick subgross sections of whole breasts**
Each Roman numeral and colour refers to a different independent duct system. Reproduced with permission of John Wiley & Sons Ltd on behalf of the Pathological Society of Great Britian and Ireland.[11]

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The Breast

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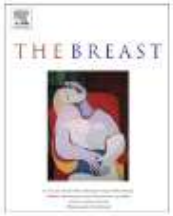

Review

"The Infinite Maze" of breast cancer, signaling pathways and radioresistance

Orit Kaidar-Person [a], Christine Lai [b], Abraham Kuten [a], Yazid Belkacemi [c,*], On behalf of AROME [d]

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[b] Massachusetts Institute of Technology, Boston, MA, USA
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ABSTRACT

The parallel growth in our understanding of tumor biology and genetics might be the key to understanding local recurrence after optimal treatment is applied. Data suggest that genetic alterations and breast cancer molecular subtypes have an effect on radiotherapy efficacy and that the HER2, EGFR/PI3K/Akt signaling pathways play a pivotal role in modulation of post-irradiation survival. These pathways have been found to be involved in radiosensitivity and/or radioresistance, tumor cell proliferation, and hypoxia. Therefore, affecting the functional activity of key players combined with radiotherapy might be the future of breast irradiation.

Example of reporting of toxicity after brachytherapy

- Garsa et al. in "*Analysis of fat necrosis after adjuvant high-dose-rate interstitial brachytherapy for early stage breast cancer*", Brachytherapy 12 (2013) 99-106, reports on 236 women treated with HDR "Median follow-up was 56 months. The crude rate of fat necrosis was 17.6%. The rate of symptomatic fat necrosis was 10.1%. **In univariate analysis,** acute breast infection and anthracycline-based chemotherapy, **number of catheters, volume encompassed by the prescription isodose, volume encompassed by the 150% isodose (V150), volume encompassed by the 200% isodose, and integrated reference air kerma were significantly associated with fat necrosis.**

- Dosimetric goals before November 2003 included >95% of the PTV receiving the prescribed dose and the prescription dose or mean central dose >0.7. Mean central dose was defined as the mean of the local minimum doses between each set of three adjacent source lines within the source pattern (11). **Since November 2003, the dosimetric goals were >95% of the PTV receiving the prescribed dose, V150<=50 cm^3, V200<=20 cm^3, and dose homogeneity index (DHI), defined as 1-(V150/V100)>=0.7 (12).**

Example of reporting of toxicity after brachytherapy

Of the brachytherapy-related factors that were significant in univariate analysis, **V150 was most predictive and used in the multivariate analysis.** In a multivariate analysis including V150, acute infection, and anthracycline-based chemotherapy, **only V150 was significantly associated with an increased risk of fat necrosis .**

The calculated optimal cutpoint for V150 was 65 cm^3. The rate of fat necrosis in patients with a V150 less than 65 cm^3 was 15.4% compared with a rate of 38.5% when the V150 was 65 cm^3 or greater (p=0.011).

Cavity volume (cm^3)	
Mean (SD)	23.1 (19)
Number of catheters	
Mean (range)	20 (7–37)
V_{100} (cm^3)	
Mean (SD)	239 (100)
V_{150} (cm^3)	
Mean (SD)	47.5 (21.9)
V_{200} (cm^3)	
Mean (SD)	16.6 (6.6)
DHI	
Mean (SD)	0.80 (0.06)
IRAK	
Mean (SD)	0.34 (0.08)

SD = standard deviation; V_{100} = volume encompassed by the prescription isodose; V_{150} = volume encompassed by the 150% isodose; V_{200} = volume encompassed by the 200% isodose; DHI = dose homogeneity index = $1 - (V_{150}/V_{100})$; IRAK = integrated reference air kerma.


MATEO

PROPOSAL

- Develop an APBI registry
- Revise and establish new quality indicators for APBI treatments
- Conduct comparative effectiveness studies that include clinical outcome, toxicity and other measures.
- Optimize patient selection and resource allocation

Economics

- In a "*Cost comparison of radiation treatment options after lumpectomy for breast cancer.*" Ann Surg Oncol. 2012 Oct;19(10), Greenup et al. modeled costs in a 1000-patient theoretical cohort, based on 2011 CPT codes. Estimated per-patient cost of radiation was **US$5,341.81 for APBI**, **US$9,121.98 for C-RT**, and **US$13,358.37** for WBRT.

- When patients received the least expensive radiation regimen for which they were eligible, 14 % received no-RT, 44 % received APBI, 7 % received C-RT, and 35 % defaulted to WBRT. Using a cost-minimization strategy, estimated RT costs were US$7.67 million, versus US$13.36 million had all patients received WBRT, representing cost savings of US$5.69 million per 1,000 patients treated.

- A cost-minimization strategy results in a 43 % reduction in estimated radiation costs among women undergoing breast conservation.