Dedicated Breast CT as a Diagnostic Imaging Tool: Physics and Clinical Feasibility

Andrew Karellas, PhD, FAAPM, FACR

Department of Radiology
University of Massachusetts Medical School
Worcester, MA

Andrew.Karellas@umassmed.edu

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Disclosure

Scientific research collaboration with Koning Corporation, West Henrietta, NY

Disclaimer

- Mention of company or product names does not constitute as endorsement.
- Some of the techniques mentioned are not U.S. FDA approved for clinical use.

Collaborators

UMass Medical School
- Srinivasan Vedantham, PhD
- Suman Shrestha, MS
- Gopal Vijayaraghavan, MD
- Robert Quinlan, MD
- Ashraf Khan, MD

University of Rochester
- Avice M. O'Connell, MD

Georgia Institute of Technology
- Lei Zhu, PhD
- Linxi Shi, MS

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Objectives

1. Understand what differentiates dedicated breast CT (bCT) from Digital Mammography (DM) and Digital Breast Tomosynthesis (DBT)
2. Appreciate the main technological challenges in the deployment of bCT in clinical practice
3. Understand why bCT was introduced as a diagnostic breast imaging tool rather than as a screening modality

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Digital Mammography

- Improved diagnostic accuracy (dense breasts)
- Improved contrast
- Reduced dose

but .....

It is still limited by superposition of tissues, particularly in the dense breast.

How can this limitation be overcome?

Develop tomographic capability

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Digital Breast Tomosynthesis: State of the Art[1]

Srinivasan Vedantham, PhD
Andrew Karellas, PhD
Gopal R. Vijayaraghavan, MD, MPH
Daniel B. Kopans, MD

[1] From the Department of Radiology, University of Massachusetts Medical School, 55 Lake Ave North, Worcester, MA 01655 (S.V., A.K., G.R.V.); and Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, Mass (D.B.K.). Received June 13, 2014; revision requested July 18; revision received December 19; final version accepted December 30.

Radiology: Volume 277: Number 3—December 2015 ▪ *radiology.rsna.org*

Retrospective multireader multicase studies show either noninferiority or superiority of DBT compared with mammography

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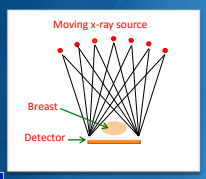
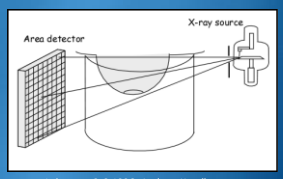
Tomosynthesis vs. Dedicated Breast CT

Tomosynthesis



Dedicated breast CT



Lab notes 3-6-1996; Andrew Karellas

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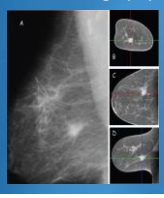
Dedicated Breast CT

- Overcomes the tissue superposition problem
- Eliminates breast compression
- Currently intended as adjunct or substitute for diagnostic mammography views

Mammography



Breast CT

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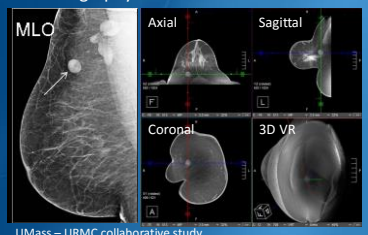
Dedicated Breast CT – Viewing options

Mammography Breast CT



- Breast can be viewed in any orientation without repeat acquisition
- Facilitates multi-planar reformats (MPR)

UMass – URMC collaborative study

Quantitative Imaging - Fibroglandular fraction

- Facilitates quantitative imaging (e.g., volumetric estimation of fibroglandular fraction)

Study	Mean
Vedantham et al[1]	15.8 ± 13%
Yaffe et al[2]	14.3 ± 10%
Nelson et al[3]	17.1 ± 15%

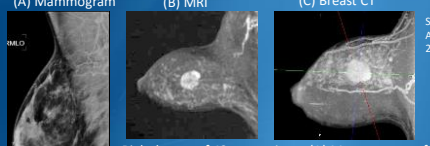

Dedicated breast CT: Fibroglandular volume measurements in a diagnostic population

Med Phys 2012; 39:7317-7328

[1] Vedantham et al., *Med Phys* 2012; 39:7317-7328
[2] Yaffe et al., *Med Phys* 2009; 36:5437-5443
[3] Nelson et al., *Med Phys* 2008; 35:1078-1086

Dedicated Breast CT – Contrast enhancement

(A) Mammogram (B) MRI (C) Breast CT



Source: O'Connell, A, Karellas A, Vedantham S. Breast J 2014; 20(6): 592-605.

Right breast of 43 y.o. patient. (A) Mammogram of extremely dense right breast showing a palpable, partially obscured mass. (B) Contrast enhanced MRI of the same breast showing the mass. (C) Contrast enhanced breast CT showing mass with better detail and clearly showing extensive nodular enhancement. CT suggests entire upper quadrant of the breast is involved with tumor.

Quantitative Imaging – Monitoring Neoadjuvant Treatment

ORIGINAL ARTICLE

Dedicated Breast CT: Feasibility for Monitoring Neoadjuvant Chemotherapy Treatment

Srinivasan Vedantham, Avice M O'Connell[1], Linxi Shi, Andrew Karellas, Alissa J Huston[2], Kristin A Shinner[3]

Department of Radiology, University of Massachusetts Medical School, Worcester, Massachusetts, [1]Departments of Imaging Sciences and [2]Medicine, Divisions of Hematology/Oncology and [3]Surgery, University of Rochester Medical Center, Rochester, New York, USA

Journal of Clinical Imaging Science | Vol. 4 | Issue 4 | Oct-Dec 2014

Collaboration between Avice O'Connell, MD, and UMass Medical School team.

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Quantitative Imaging – Monitoring Neoadjuvant Treatment

Non-contrast study

- Pre-treatment **bCT1**
- Adriamycin (Doxorubicin) Cytoxan (Cyclophosphamide) — 4 cy
- Mid-treatment **bCT2**
- Taxol (Paclitaxel) +/- Herceptin (Trastuzumab) — 4/12 cy
- Post-treatment **bCT3**

48 y.o. woman with IDC

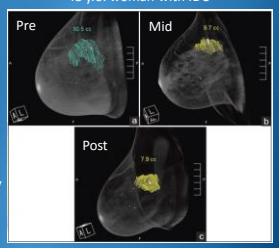

Image source: Vedantham et al J Clin Imaging Sci. 2014;4:64

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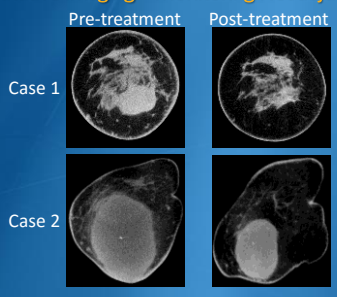
Quantitative Imaging – Monitoring Neoadjuvant Treatment



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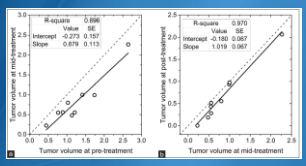
Quantitative Imaging – Monitoring Neoadjuvant Treatment



- Segmented tumor volumes were log-transformed (normality)
- 47% decrease in tumor volume from pre to mid-treatment
- 34% decrease in tumor volume from mid to post-treatment
- All patients were pathologically-assessed responders

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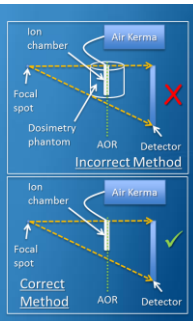
Dedicated Breast CT – Radiation Dose

- Metric: Mean Glandular Dose (MGD)
- Facilitates direct comparison with mammography
- Method:
  - Measure air kerma (mGy) at axis of rotation (AOR) without object (e.g., dosimetry phantom) over entire scan
  - Multiply by conversion factor ($D_g N^{CT}$) in units of (mGy/mGy)



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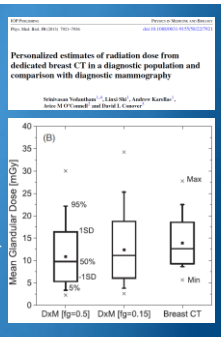
Dedicated Breast CT Diagnostic Imaging MGD

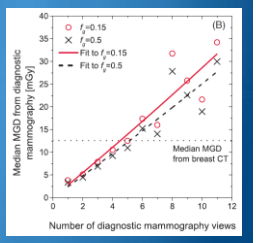
- MGD from breast CT is based on f_g of that breast
- MGD for diagnostic mammography (DxM) assumes either $f_g = 0.5$ or $f_g = 0.15$ (study median) for all breasts
- MGD from diagnostic breast CT is similar to, and within the range of DxM


Personalized estimates of radiation dose from dedicated breast CT in a diagnostic population and comparison with diagnostic mammography

Dedicated Breast CT - Diagnostic Imaging MGD

	DxM [fg=0.15]	Breast CT
Median MGD	11.1 mGy	12.6 mGy
Mean MGD	12.4 mGy	13.9 mGy
Range	2.6 – 34.2 mGy	5.7 – 27.8 mGy

- Median MGD from breast CT is equivalent to 4-5 diagnostic mammography views
- Mean and median number of diagnostic mammography views were 4.53 and 4, respectively



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Dedicated Breast CT – ROC study

From RSNA 2015

Clinical Performance of Dedicated Breast Computed Tomography in Comparison to Diagnostic Digital Mammography

Elodia B. Cole, MS | Amy S. Campbell, MD | Srinivasan Vedantham, PhD | Etta D. Pisano, MD | Andrew Karellas, PhD

Sunday 12:05-12:15 PM | SSA01-09 | Arie Crown Theater

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Dedicated Breast CT – ROC study

- Multi-reader multi-case fully-balanced retrospective reader study
- 235 cases – all with either biopsy-verification or 1-year follow-up [52 negative, 104 benign, 79 cancers; 93/183 (51%) calcifications]
- 18 readers interpreted in following modes (modalities):
  1. Standard 2-view DM (screening) + Breast CT (non-contrast)
  2. Standard 2-view DM + mammography supplemental views
- Interpretation using BIRADS scale (4 weeks washout period)
- Sensitivity improved with breast CT (88% vs. 84%, p=0.008)
- Specificity and AUC were not significantly different (p>0.075)

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Dedicated Breast CT – Regulatory approvals

- In the United States, one vendor has received US FDA approval for diagnostic use with:
  - Non-contrast imaging, and
  - Interpretation with standard 2-view mammogram
- The system has also received regulatory approvals from EU (CE-mark), Health Canada, Australia, and China FDA.

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Dedicated Breast CT (FDA/EU approved version)

Parameter	Value
X-ray tube†	RAD-71 SP (0.3 mm focus)
Target/Filter	W/Al
Tube voltage	49 kV
Tube current	50-200 mA (16 mA scout)
Pulse width	8 ms
Number of projections	300 over 360°
Scan time	10 s
Geometric magnification	1.42

Parameter	Value
Detector†	PaxScan 4030CB
Pixel pitch	0.194 mm
Pixel binning	2 x 2 (0.388 mm)
Dead-space	35.4 mm

Reference: O'Connell, et al. AJR:195, 2010

† Varian Medical Systems

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Dedicated Breast CT – Posterior coverage


Dedicated breast CT: Fibroglandular volume measurements in a diagnostic population

Srinivasan Vedantham, Linxi Shi, and Andrew Karellas

Med Phys 2012; 39:7317-7328

- Pectoralis muscle visualized in 107/137 (78%) breasts
- Need to improve posterior coverage


Dedicated breast CT: geometric design considerations to maximize posterior breast coverage

Srinivasan Vedantham, Andrew Karellas, Margaret M Emmons, Lawrence J Moss, Sarwat Hussain and Stephen P Baker

- Design goal: Posterior coverage similar to mammography in 95% of subjects
- Provided equation relating system geometry, focal spot position, and detector dead-space for table-top design

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Dedicated Breast CT (UMass prototype)

- System fully paid-for by UMass
- Built to UMass specifications
- Redesign targets posterior coverage improvement
- New x-ray tube (M-1583)
- Prompted change of generator
- New detector (PaxScan 4030MCT)
- New table-top design

Not FDA-approved; used only under IRB approved human subjects research protocols

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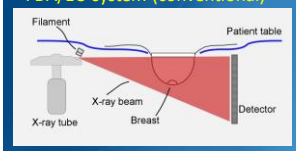
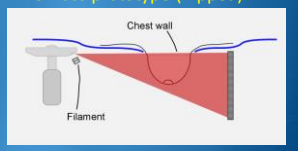
X-ray tube (UMass)

FDA/EU system (conventional)



- RAD 71 SP (0.3 mm focus)
- 200 mA max
- 49 kV max
- 0.35 MHU

UMass prototype (flipped)



- M-1583 (0.3 mm focus)
- 250 mA max
- 70 kV max
- 1.5 MHU (4.3 x more)
- Focal spot closer to chest-wall by 18.4 mm

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Dedicated Breast CT (UMass prototype - Detector)

FDA system – PaxScan 4030CB

UMass – PaxScan 4030MCT

Chest-wall dead-space reduced by 15.6 mm

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Contrast-enhanced breast CT: Disease extent

- Women diagnosed with invasive lobular carcinoma (ILC)
- ILCs more often than ductal cancers
  - Occur as multifocal, multicentric and bilateral disease
  - Have higher initial mastectomy, re-excision, and final mastectomy rates
- Current standard-of-care: Breast MRI (high sensitivity, but tumor size concordant with pathology in less than 70% of cases)
- Primary aim: With pathology size as reference standard, compare tumor size from breast CT and breast MRI
- Secondary aim: Is CE-BCT as sensitive/specific as breast MRI?

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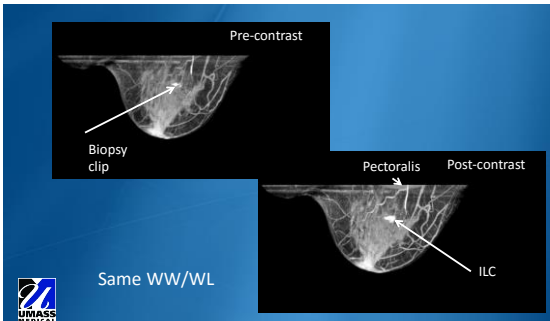

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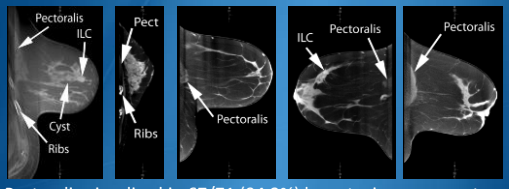
UMass prototype – Posterior coverage in ILC study (sagittal)



- Pectoralis visualized in 67/71 (94.3%) breasts; improvement from 78%
- Further improvement possible by using a detector with dead-space similar to mammography

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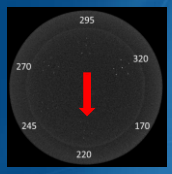
UMass prototype QC with calcification phantom



$CaCO_3$ specks in microns

- 13 cm diameter phantom
- Fibroglandular composition ($f_g = 0.15$)
- Ramp filtered FBP
- Voxel size: 0.155 mm
- MGD: matched to diagnostic mammography[1] (4.5 views, 12 mGy)
- $CaCO_3$ specks

Note: ACR mammography accreditation phantom uses Al_2O_3 specks. For CT, this phantom may not represent the best choice for image quality evaluation.

[1] Vedantham et al., *Phys Med Biol* 2013; 58:7921-7936

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UMass prototype – Ongoing research

	PaxScan† 4030MCT	Dexela‡ 2923CL
Generation	UMass	Ongoing
Native pixel size (mm)	0.194	0.075
Frame rate (2x2 binning)	30	70
System noise (e-)	5948	360
Dead-space at chest-wall	18.6 mm	3 mm
Field of view (cm)	40 x 30	29 x 23

† Varian Medical Systems; ‡ Perkin-Elmer

- Smaller pixel pitch and lower noise may improve microcalcification visibility
- 3 mm dead-space can improve posterior coverage
- However, smaller field of view (29 x 23 cm)

Hence, investigating laterally shifted detector geometry to extend the field of view

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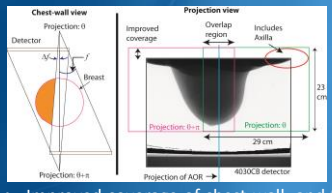
UMass – Ongoing research with laterally-shifted detector



Drawn to scale

Single projection view of the largest breast imaged till-date: 20.5 cm diameter at chest-wall and 15 cm chest-wall to nipple length

- Improved coverage of chest-wall, and the potential to image the axilla and lower lymph nodes
- With the extended FOV, width-truncation unlikely for off-centered breast

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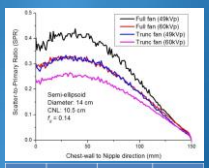
UMass – Ongoing research with laterally-shifted detector Monte Carlo simulations

Partial irradiation of the breast in each projection and using 60 kV lead to:

- Halving of SPR, compared to current system
- Dose reduction by ~25%



Δf	$d = 10$	$d = 14$	$d = 18$
0.25°	46%	47%	48%
1.5°	27%	34%	37%
2.7°	10%	21%	27%

Data source: Konate S, Vedantham S, Shi L, Karellas A. [abstract]. 2013 AAPM Annual Meeting Program, Med Phys. 2013; 40(6):124.

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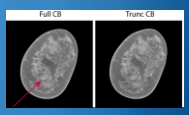
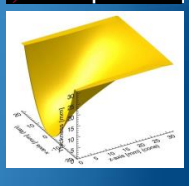
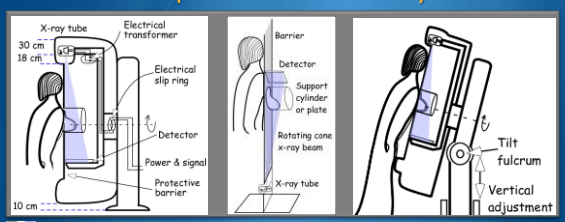
UMass – Ongoing research

- Laterally-shifted detector geometry: image reconstruction and quantitative evaluation
  [Vedantham S, Konate S, Shrestha S, Vijayaraghavan GR, Karellas A. Proceedings 2016 CT Meeting, Bamberg, Germany, 291-294.]
- Cascaded linear systems modeling
  [Vedantham S, Shrestha S, Shi L, Vijayaraghavan GR, Karellas A. 2016 AAPM Annual Meeting Program. Med Phys 2016; 43(6): 3346]
- 3-D beam-shaping filter
  [Vedantham S, Shi L, Karellas A. 2015 AAPM Annual Meeting Program. Med Phys 2015; 42(6): 3574-5]





Our vision for breast CT Concepts from our laboratory



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Conclusions on Breast CT

- ✓ Full isotropic spatial resolution
- ✓ True multi-planar and 3D imaging
- ✓ Major improvements have been made on chest wall coverage
- ✓ Work on improved visualization of subtle microcalcifications is now in progress.
- ✓ Dose reduction research now in progress
- ✓ Targeted applications: Diagnostic work-up, monitoring of the effectiveness of treatment, planning for radiation therapy …
- ✓ Screening ? More challenging...

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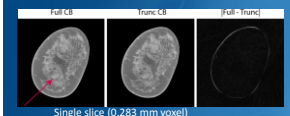
Thank you

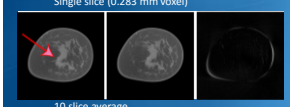
UMASS MEDICAL SCHOOL

UMass – Ongoing research with laterally-shifted detector
Quantitative evaluation of artifacts



Single slice (0.283 mm voxel)

Soft tissue lesion (arrow) is discernible in truncated cone-beam reconstruction (middle) that emulates the laterally-shifted detector geometry and appears visually similar to full CBBCT (left). Right panel shows the absolute difference.



10 slice average

Microcalcification cluster (arrow) is discernible in truncated cone-beam reconstruction (middle) and appears visually similar to full CBBCT (left). Right panel shows the absolute difference.

Data source: Vedantham S, Konate S, Shrestha S, Vijayaraghavan GR, Karellas A. Proceedings 2016 CT Meeting, Bamberg, Germany, 291-294.

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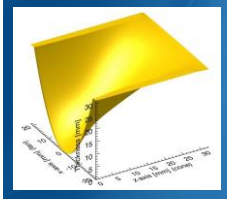
UMass – Ongoing research: 3D Beam-shaping filter



- Highest radiation dose at breast periphery
- Modulate the x-ray beam to reduce the dose to the periphery (3D beam-shaping filter)
- 3-D beam-shaping filter designed from a total of 132 breast volumes × 180 projection angles = 23,760 realizations

Data source: Vedantham S, Shi L, Karellas A. [abstract]. 2015 AAPM Annual Meeting Program. Med Phys 2015; 42(6): 3574-5

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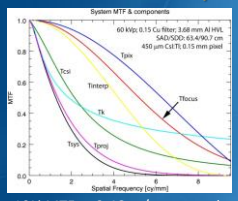
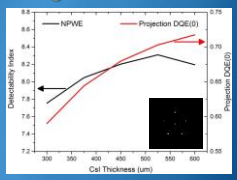
UMass – Ongoing research with laterally-shifted detector Cascaded linear systems modeling – CMOS detector



10% MTF at 3.46 cy/mm, matches ~3.5 cy/mm from Gazi et al., Med Phys. 2015;42(4):1973.



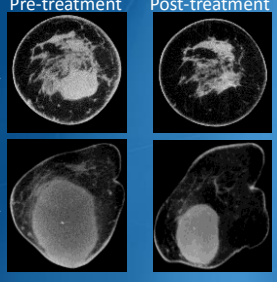
Although projection $DQE(0)$ increases with CsI:Tl thickness, detectability index is maximized with 525 μm CsI:Tl for detecting 220 μm $CaCO_3$ cluster

Quantitative Imaging – Monitoring Neoadjuvant Treatment

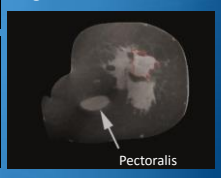
Pre-treatment | Post-treatment

Case 1

Case 2



Registration/Segmentation
Preprocessing: Bilateral filter
Registration: 3-D slicer
Segmentation: KFCM



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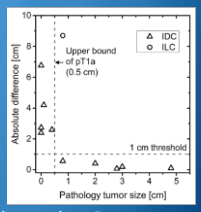
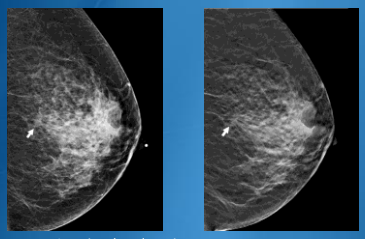
Quantitative Imaging – Monitoring Neoadjuvant Treatment

- Truth: Pathology reported tumor size following surgery
- The largest tumor dimension (size) in post-treatment bCT was estimated over all sagittal planes that correspond to the manner in which the surgical specimen was sectioned by pathology



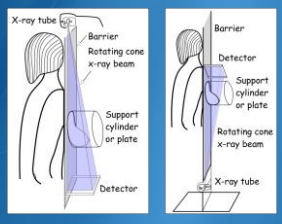
For invasive ductal carcinoma and tumors larger than 5 mm (biopsy clip size is 3 mm), tumor size from automated segmentation was concordant with pathology at 1 cm threshold. 43

Digital mammography Tomosynthesis



Invasive ductal carcinoma
DBT improved the confidence of diagnosis 4 4

*Our vision for future concepts in breast CT



*Andrew Karellas and Srinivasan Vedantham plans 45