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

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Acknowledgments

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.
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

- 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
Digital Breast Tomosynthesis: State of the Art

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

Tomosynthesis vs. Dedicated Breast CT

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

Dedicated Breast CT
Dedicated Breast CT – Viewing options

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

Quantitative Imaging - Fibro glandular fraction

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vedantham et al¹</td>
<td>15.8 ± 13%</td>
</tr>
<tr>
<td>Yaffe et al²</td>
<td>14.3 ± 10%</td>
</tr>
<tr>
<td>Nelson et al³</td>
<td>17.1 ± 15%</td>
</tr>
</tbody>
</table>

¹ Vedantham et al., Med Phys 2012; 39:7317-7328
² Yaffe et al., Med Phys 2009; 36:5437-5443


Dedicated Breast CT – Contrast enhancement

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.
Case 1

Case 2

Quantitative Imaging – Monitoring Neoadjuvant Treatment

Non-contrast study

Pre-treatment

Adriamycin (Doxorubicin)
Cytoxan (Cyclophosphamide)

Mid-treatment

Taxol (Paclitaxel) +/- Herceptin (Trastuzumab)

Post-treatment

Pre-treatment

Post-treatment

48 y.o. woman with IDC


4/12 cy

4 cy

Quantitative Imaging – Monitoring Neoadjuvant Treatment

Collaboration between Aice O’Connell, MD, and UMass Medical School team.

Quantitative Imaging – Monitoring Neoadjuvant Treatment

Dedicated Breast CT: Feasibility for Monitoring Neoadjuvant Chemotherapy Treatment

Srinivasan Vedantham, Avise M O’Connell, Linae Shi, Andrew Kouloulias, Alissa K Boston

Kerstin A Moller

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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

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 \(D_{NCT}\) in units of \((\text{mGy/mGy})\)

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
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

<table>
<thead>
<tr>
<th></th>
<th>DmM [k=0.15]</th>
<th>Breast CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median MGD</td>
<td>11.1 mGy</td>
<td>12.6 mGy</td>
</tr>
<tr>
<td>Mean MGD</td>
<td>12.4 mGy</td>
<td>13.9 mGy</td>
</tr>
<tr>
<td>Range</td>
<td>2.6 – 34.2 mGy</td>
<td>5.7 – 27.8 mGy</td>
</tr>
</tbody>
</table>

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

- 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 BI-RADS 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)
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.

Dedicated Breast CT (FDA/EU approved version)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-ray tube†</td>
<td>RAD-71 5P (0.3 mm focus)</td>
</tr>
<tr>
<td>Target/Filter</td>
<td>W/Al</td>
</tr>
<tr>
<td>Tube voltage</td>
<td>49 kV</td>
</tr>
<tr>
<td>Tube current</td>
<td>50-200 mA (16 mA scout)</td>
</tr>
<tr>
<td>Pulse width</td>
<td>8 ms</td>
</tr>
<tr>
<td>Number of projections</td>
<td>300 over 360°</td>
</tr>
<tr>
<td>Scan time</td>
<td>10 s</td>
</tr>
<tr>
<td>Geometric magnification</td>
<td>1.42</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detector†</td>
<td>PaxScan 4030CB</td>
</tr>
<tr>
<td>Pixel pitch</td>
<td>0.194 mm</td>
</tr>
<tr>
<td>Pixel binning</td>
<td>2 x 2 (0.388 mm)</td>
</tr>
<tr>
<td>Dead-space</td>
<td>35.4 mm</td>
</tr>
</tbody>
</table>

Parameter

† Varian Medical Systems

Dedicated Breast CT – Posterior coverage

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

Med Phys 2012, 39:7317-7338

• 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

Med Phys 2012, 39:7317-7338

References


† Varian Medical Systems
Not FDA-approved; used only under IRB-approved human subjects research protocols

- 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

**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

**Dedicated Breast CT (UMass prototype - Detector)**

- FDA system – PaxScan 4030CB
- UMass – PaxScan 4030MCT
- Chest-wall dead-space reduced by 15.6 mm
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?

Contrast-enhanced breast CT: Disease extent

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

- 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\(_2\)O\(_3\) 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

<table>
<thead>
<tr>
<th></th>
<th>PaxScan(^1)</th>
<th>Dexela(^\dagger)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generation</td>
<td>UMass</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Native pixel size (mm)</td>
<td>0.194</td>
<td>0.075</td>
</tr>
<tr>
<td>Frame rate (2x2 binning)</td>
<td>30</td>
<td>70</td>
</tr>
<tr>
<td>System noise (e-)</td>
<td>5948</td>
<td>360</td>
</tr>
<tr>
<td>Dead-space at chest-wall</td>
<td>18.6 mm 3 mm</td>
<td></td>
</tr>
<tr>
<td>Field of view (cm)</td>
<td>40 x 30</td>
<td>29 x 23</td>
</tr>
</tbody>
</table>

\(^{1}\) Varian Medical Systems; \(^\dagger\) 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

- 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

Drawn to scale

Single projection view of the largest breast imaged till-date:
- 20.5 cm diameter at chest-wall
- 15 cm chest-wall to nipple length
Halving of SPR, compared to current system

Dose reduction by ~25%

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

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...

Thank you

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

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 CBCT (left). Right panel shows the absolute difference.

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

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


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

- 10% MTF at 3.46 cm/mm, matches ~3.5 cm/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 CaCO₃ cluster

Quantitative Imaging – Monitoring Neoadjuvant Treatment

Case 1
Pre-treatment
Post-treatment
Registration/Segmentation
Preprocessing: Bilateral filter
Registration: 3-D slicer
Segmentation: KFCM

Case 2
Pectoralis
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.

Digital mammography  Tomosynthesis

Invasive ductal carcinoma
DBT improved the confidence of diagnosis

*Our vision for future concepts in breast CT

*Andrew Karellas and Srinivasan Vedantham plans