Digital Breast Tomosynthesis: 
Update and Pearls for Implementation

Emily F. Conant, M.D.
Professor, Chief of Breast Imaging
Department of Radiology
Hospital of the University of Pennsylvania
Philadelphia, PA

Outline

• Digital Breast Tomosynthesis (DBT) – the new standard of care
• Breast cancer screening outcomes with DBT:
  • Population level
  • Patient level
    – Outcomes by age
    – Outcomes by density
  • Issues of xray dose – synthetic imaging
• Limitation of DBT

Tomosynthesis Dataset:
2D/3D (Hologic Combo Acquisition)

Arc of motion of x-ray tube, showing individual exposures

Tomosynthesis Acquisition

Arc of motion of x-ray tube, showing individual exposures
"3D" Dataset

Tomosynthesis Dataset: 2D/3D (Hologic Combo Acquisition)

Digital Breast Tomosynthesis

The new, better mammogram:
- Recall reduction (-15-37%)
- Increased invasive cancer detection (up to 50%)
- No increase in situ detection (no overdiagnosis)

DBT Screening Outcomes
Summary of DBT Screening Studies

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Volumes</th>
<th>DM versus DBT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skanne (2013)</td>
<td>12,000</td>
<td>Recall Rate (%)</td>
</tr>
<tr>
<td>Caste (2013)</td>
<td>2,100 CM from DBT</td>
<td></td>
</tr>
<tr>
<td>Lang (2015)</td>
<td>1,000</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Radiosensitive</th>
<th>Detection</th>
<th>Decrease in Recall of up to 33%</th>
<th>Increase in Cancer Detection up to 52%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Friedewald (2014)</td>
<td>7,292 DM</td>
<td>45%</td>
<td>15%</td>
</tr>
<tr>
<td>McCarthy (2014)</td>
<td>281,187</td>
<td>15%</td>
<td>15%</td>
</tr>
<tr>
<td>Greenberg (2014)</td>
<td>142,883</td>
<td>15%</td>
<td>15%</td>
</tr>
<tr>
<td>Conant (2014)</td>
<td>12,631</td>
<td>16%</td>
<td>16%</td>
</tr>
</tbody>
</table>

Sub-populations reported in Friedewald, et al.

Recall Reduction

DBT reduces false positive call-backs:
47yr-old presents for screening, focal asymmetry, left lateral on CC

Tomosynthesis imaging shows no abnormality. (Tissue superimposition present on 2D)

The improvement in outcomes achieved with DBT directly address the major concerns regarding screening for breast cancer with mammography:

- Too many false positives (low specificity)
- Too few cancers detected (low sensitivity)
- Over-diagnosis (high DCIS)
DBT reduces false positive call-backs:
43yr-old presents for baseline screening. Architectural distortion?

On sequential DBT slices, each component of "lesion" is a separate structure (note localizer positions).

No recall needed!

Improved Cancer Detection

46 year old woman presents for screening...
Cancer detected on DBT alone:
68-year-old woman presenting for screening
The 2D mammogram was interpreted as negative

Findings: Architectural distortion, irregular mass in UOQ, best on DBT. Work up was directly to US.

Pathology: Invasive lobular carcinoma

Teaching point: it’s not all about density...
Limitations of early trials

- Most studies “first, prevalent” round screening
- Only 3 studies were prospective (Oslo, STORM, Malmo)
- Majority of retrospective studies had concurrent DM screening
  - potential for bias in screened cohorts
- There has been little data on false negatives....

University of Pennsylvania Data

Method:
- Three consecutive years DBT screening
  - Population level analysis (each year of screening)
  - Patient level analysis (each round of screening)
  - Comparison with cancer registry data for false negatives

Results from Penn consecutive years of DBT screening

<table>
<thead>
<tr>
<th>Metric</th>
<th>Year 0 DM</th>
<th>Year 1 DBT</th>
<th>Year 2 DBT</th>
<th>Year 3 DBT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recall rate (%)</td>
<td>10.4</td>
<td>8.8</td>
<td>9.0</td>
<td>9.2</td>
</tr>
<tr>
<td>Cancer rate/1000</td>
<td>4.6</td>
<td>5.5</td>
<td>5.8</td>
<td>6.1</td>
</tr>
<tr>
<td>PPV1</td>
<td>4.4</td>
<td>6.2</td>
<td>6.5</td>
<td>6.7</td>
</tr>
<tr>
<td>Interval CA/1000</td>
<td>0.7</td>
<td>0.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Population-level Cancer and Biopsy rates, PPV1 by year

- Cancer/1000
- Invasive cancer/1000
- Interval cancer/1000
- Biopsy %
- PPV1
What about first round, “Prevalence Effect”?

Breast Cancer Research and Treatment – on-line 3/1/16

PROSPR consortium (BWH-D, UVI, UPenn)

- DM and DBT cases 2011-15 (142,883 DM and 55,998 DBT studies)
  - Patient level data
    - Reduction in recall (8.7% vs 10.4% p<0.0001)
    - Increase in cancer detection (5.9 vs 4.4/1000, p= 0.0026),
      - 34% increase in cancers overall
      - 27% invasive cancers
    - Trend in decrease in false negatives (0.46 vs 0.6/1000)

Breast Cancer Research and Treatment – on-line 3/1/16

- DM and DBT cases 2011-15 (142,883 DM and 55,998 DBT studies)
  - Patient level data
    - Reduction in recall (8.7% vs 10.4% p<0.0001)
    - Increase in cancer detection (5.9 vs 4.4/1000, p= 0.0026),
      - 34% increase in cancers overall
      - 27% invasive cancers
    - Trend in decrease in false negatives (0.46 vs 0.6/1000)

Cancer Detection (per 1000) by Age

Tomosynthesis Outcomes by Density Category

<table>
<thead>
<tr>
<th>Author Year</th>
<th>Mean Age</th>
<th>Number of Dense Patients</th>
<th>Change in Cancer Detection Rate (per 1000)</th>
<th>Change in Recall Rate (per 1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prospective Trials</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciatto 2013</td>
<td>58</td>
<td>1,215</td>
<td>+2.5</td>
<td>-26</td>
</tr>
<tr>
<td>Lang 2016</td>
<td>56</td>
<td>3,150</td>
<td>+3.8</td>
<td>-</td>
</tr>
<tr>
<td>Bernardi 2016</td>
<td>58</td>
<td>2,592</td>
<td>+5.4</td>
<td>+10.5</td>
</tr>
<tr>
<td>Palijiova 2016</td>
<td>51</td>
<td>3,211</td>
<td>+4</td>
<td>-</td>
</tr>
</tbody>
</table>

| Retrospective Trials |
| Joe 2013       | 54       | 4,000                    | +4.4                                       | -36.8                            |
| McCarthy 2014  | 55       | 5,056                    | +3.8                                       | -19.4                            |
| Conant 2016    | 57       | 9,265 (21,131)           | +2.1                                       | -22.1                            |
| Rafferty 2016  | -        | 84,243                   | +1.4                                       | -18.4                            |

Adapted from Houssami N, Turner MA. Breast 2016: 141-145.
Fat Scattered Hetero Extreme
Cancer Detection (per 1000) by Density Category

What about False Negatives?

False negative DBT: Not all cancers visible with DBT. 42 yo with lump in left breast.

54 yo with pain, thickening of the right breast

Diagnostic mammogram (2013), ultrasound for rt pain, thickening "negative".
MRI extensive asymmetric NMLE enhancement rt breast. Invasive ductal carcinoma.
What about Dose??

Comparison of DBT Dose

- Hologic DBT has dose boost at > 50mm
- Siemens DBT dose higher than DM for all thicknesses
- GE DBT dose same as DM (uses grid for both modes)

Overview of s2D Reconstruction

DBT image data used to create both 1mm slices for tomo “stack” and s2D images

Multiple, low dose images obtained and then reconstructed
Synthetic 2D is about more than just dose!

Need 2D images for interpretative tasks essential to improved performance of DM/DBT screening:

- **Global assessment of breasts**
  - BI-RADS density assessment
  - Comparison with prior images
  - Assessment of lesions – esp. calc, asymmetries, etc.

- **Efficient, high volume screening**

<table>
<thead>
<tr>
<th></th>
<th>Synthetic 2D</th>
<th>DM 2D</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-calc lesions*(n=73)</td>
<td>74.0% 54/73</td>
<td>72.6% 53/73</td>
<td>0.996</td>
</tr>
<tr>
<td>Observer 1</td>
<td>74.0% 54/73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observer 2</td>
<td>83.6% 61/73</td>
<td>83.6% 61/73</td>
<td></td>
</tr>
<tr>
<td>Observer 3</td>
<td>84.9% 62/73</td>
<td>83.6% 61/73</td>
<td>0.991</td>
</tr>
<tr>
<td>Calcified lesions* (n=14)</td>
<td>92.9% 13/14</td>
<td>85.7% 12/14</td>
<td>0.996</td>
</tr>
<tr>
<td>Observer 1</td>
<td>92.9% 13/14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observer 2</td>
<td>92.9% 13/14</td>
<td>100% 14/14</td>
<td>0.995</td>
</tr>
<tr>
<td>Observer 3</td>
<td>92.9% 13/14</td>
<td>92.9% 13/14</td>
<td></td>
</tr>
</tbody>
</table>

*Analysis performed on 87 cancers seen on either synthetic 2D or digital (DM) 2D.

**Gilbert et al** (online Radial 7/17/15): Accuracy of Digital Breast Tomosynthesis for Depicting Breast Cancer Subgroups in a UK Retrospective Reading Study (TOMMY Trial)

- Multicenter/reader, retrospective study
- Dataset of 7060 cases
  - 2D mammo
  - 2D plus DBT (DBT)
  - s2D plus DBT (sDBT)
- Sensitivity:
  - 87% 2D
  - 89% 2D + DBT
  - 88% sDBT
- Specificity:
  - 57% 2D
  - 70% 2D + DBT
  - 72% sDBT

**Arch. Distortion only on s2D and DBT**

51 yo architectural distortion seen only on s2D/DBT
Pathology: invasive ductal carcinoma.
Synthetic 2D with Tomosynthesis

Pathology: Ductal Carcinoma in situ (DCIS)

Synthetic Imaging: False Positive Calcifications

56 yo at screening.

s2D RCC

Possible calcifications?

DM Magnification: No definite calcifications

Magnification at recall demonstrates no calcifications. s2D reconstruction algorithm may make normal ligaments appear like calcifications.

Penn: Integrated s2D over 4 mos. (9/14-12/14)

- Screening:
  - Jan 7th, 2015 began screening all pts with s2D-DBT

Performance outcomes measured
- Recall rate (by lesion type, cancer detection, PPV1)
- Cancer detection
- PPV1, 3

**Performance metrics with s2D?**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Overall recall</th>
<th>Calc</th>
<th>Masses</th>
<th>Asym.</th>
<th>Arch dist</th>
<th>Technical</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM</td>
<td>10.4%</td>
<td>1.8%</td>
<td>2.4%</td>
<td>6.1%</td>
<td>0.7%</td>
<td>0.44%</td>
</tr>
<tr>
<td>DM+DBT</td>
<td>8.8%</td>
<td>1.6%</td>
<td>2.7%</td>
<td>4.5%</td>
<td>1.0%</td>
<td>0.2%</td>
</tr>
<tr>
<td>s2D+DBT</td>
<td>7.1%</td>
<td>1.1%</td>
<td>2.4%</td>
<td>3.1%</td>
<td>1.1%</td>
<td>0.1%</td>
</tr>
</tbody>
</table>

p value (s2D vs DM/DBT): <0.001 0.02 0.31 <0.001 0.70 0.03

**DBT screening dose reduced by 39%**
- Maintained low recall rate (actually continues to decrease)
- Significant changes in calc, asymmetries and technical recalls


---

**s2D Performance metrics continued…**

<table>
<thead>
<tr>
<th>Metric</th>
<th>DM/DBT</th>
<th>s2D/DBT</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy rate (%)</td>
<td>2.0</td>
<td>1.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Cancers/1000</td>
<td>5.45</td>
<td>5.03</td>
<td>0.732</td>
</tr>
<tr>
<td>In situ</td>
<td>1.48</td>
<td>0.9</td>
<td>0.301</td>
</tr>
<tr>
<td>Invasive</td>
<td>3.85</td>
<td>4.10</td>
<td>0.840</td>
</tr>
<tr>
<td>PPV1 (%)</td>
<td>6.2</td>
<td>7.1</td>
<td>0.548</td>
</tr>
<tr>
<td>PPV3 (%)</td>
<td>27.0</td>
<td>18.6</td>
<td>0.026</td>
</tr>
</tbody>
</table>

**s2D maintains benefits of DBT:**
- Increased number of cancers detected per recall (PPV1)
- Sensitivity and specificity similar, thus far...
- Slight decrease in detection of in situ cancers to be monitored


---

**UPenn Data – with s2D as 4th consecutive year…**

Are we “missing” in situ cancers? Is this ok (decreasing overdx) or bad (increasing interval cancers?)

* s2D data is based on initial 6 months of data — not powered for cancer detection...

---

**Aujero et al (2017): More on Synthetic 2D/DBT**

<table>
<thead>
<tr>
<th>Metric</th>
<th>DM/DBT</th>
<th>DM/DBT</th>
<th>s2D/DBT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recall rate (%)</td>
<td>8.7</td>
<td>5.6</td>
<td>6.1</td>
</tr>
<tr>
<td>Cancer detection/1000</td>
<td>5.5</td>
<td>6.4</td>
<td>6.1</td>
</tr>
<tr>
<td>In situ</td>
<td>3.2</td>
<td>3.09</td>
<td>4.64</td>
</tr>
<tr>
<td>Invasive</td>
<td>1.6</td>
<td>2.1</td>
<td>1.4</td>
</tr>
<tr>
<td>PPV1 (%)</td>
<td>6.0</td>
<td>10.9</td>
<td>14.3</td>
</tr>
<tr>
<td>PPV3 (%)</td>
<td>22.2</td>
<td>26.5</td>
<td>48.8</td>
</tr>
</tbody>
</table>

* Screening with s2D/DBT

Aujero MP, et al. Radiology. on line Feb 23
DBT is the “better mammogram”…

Additional outcome data is needed

– Modality based:
  • DBT versus Ultrasound, “abbreviated MR”, Molecular Breast Imaging, Contrast mammography (2D or DBT)

– Larger populations for subgroup analyses:
  • Age, density, screening intervals, etc.

★ Biology, biology, biology…
  • Are additional DBT cancers biologically more aggressive?
  • Surrogate for mortality reduction?

Perelman Center for Advanced Medicine
University of Pennsylvania Medical Center

Thank you!