Hacia la imagenología tomográfica de mama
Futuro y presente

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Towards Tomographic Breast Imaging

2 D  2+ D  2.2 D  3 D

Standard Mammography  Stereoscopic Mammography  Digital Tomosynthesis  Dedicated Breast CT

(Is your optical system can handle it!)

Digital Mammography Improvements

Detection in some patient subgroups (DMIST)

Digital Mammography Improvements

Workflow
Digital Mammography Improvements

Contrast-enhanced imaging

29% of cancers missed by “overlying tissue”

STEREOSCOPIC DIGITAL MAMMOGRAPHY
Benign Mass

Note shift

Translated X-ray source

X-ray beam limits

Lesions of Interest

Detector

These two images are shown separately to each eye
High Risk Screening Study
N = 1298 cases

<table>
<thead>
<tr>
<th></th>
<th>Mammo</th>
<th>Stereo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>12/19</td>
<td>13/19</td>
</tr>
<tr>
<td>Recall rate</td>
<td>12.9%</td>
<td>9.6%*</td>
</tr>
</tbody>
</table>

Stereoscopic Mammography
Promising Results

Stereoscopic Mammography
Cheap!
(and fast!)

Stereoscopic Mammography
Too little, too late?
Stereoscopic Mammography

In Memoriam: The Death of 3D TV

So long 3D TV, we’ll see you in another thirty years.

The elephant in the room with 3D were the glasses, no one really wanted to wear them whilst sitting in their reading room. ~ Dead.

TV Technology Trends: The Death of the 3D TV

Digital Breast Tomosynthesis

Recall

Lesion of Interest

Detector

This information is used to reconstruct the volume

Courtesy of Hologic Inc.
Recall

Courtesy of Hologic Inc.

Find the 8 differences...
**Benefits**

Mammography++
- System
- Workflow
- Interpretation
- Dose

...but with some discrimination of vertical position!

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**(Some) Screening Trials**

<table>
<thead>
<tr>
<th>Trial</th>
<th>N</th>
<th>Cancer Det Rate Δ</th>
<th>Recall Rate Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>STORM-2</td>
<td>9,672</td>
<td>DM: +35%</td>
<td>DM: +16%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Synth: +40%</td>
<td>Synth: +30%</td>
</tr>
<tr>
<td>OSLO</td>
<td>25,547</td>
<td>+30%</td>
<td>-13%</td>
</tr>
<tr>
<td>MALMÖ</td>
<td>14,848</td>
<td>+30%</td>
<td>+43%</td>
</tr>
</tbody>
</table>
Implementation?

An adjunct to mammography?

Or a replacement of mammography?

Do we need two views?
Or is **one** view enough?

One-view breast tomo: *feasible?*

**Retrospective studies**
- Gennaro 2010: 1v tomo = 2v DM
- Svane 2011: 1v tomo = 2v DM
- Svahn 2012: 1v tomo > 2v DM
- Wallis 2012: 1v tomo = 2v DM

**Malmö Breast Tomosynthesis Screening Trial (MBTST)**
- Lång *et al* 2016: 1v tomo > 2v DM
  - +43% increase in cancer detection rate

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**Study design**

*6 readers from 3 different institutions*

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**Does 1-view experience matter?**

<table>
<thead>
<tr>
<th>3 readers &lt; 3 years</th>
<th>3 readers &gt; 3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Sensitivity**

*Less experienced, significant increase respect to 1v tomo, p < 0.05*

![Sensitivity Diagram](image)

**Specificity**

*Less experienced, significant decrease respect to 1v tomo, p < 0.05*

![Specificity Diagram](image)

**Case-based ROC**

Average all readers

1v tomo not significantly different

![Case-based ROC Diagram](image)

**JAFROC analysis**

NO statistical difference between 1v DBT and the rest of modalities, p = 0.08

![JAFROC Analysis Diagram](image)
Limitations
Not screening population
1/3 were recalls seen with 2-view mammo
One vendor

Conclusion
Perhaps enough

SYNTHETIC MAMMOGRAMS

Mammogram Orig. Synthetic Tomo Slice

### Recall Rates

<table>
<thead>
<tr>
<th></th>
<th>DBT + FFDM</th>
<th>DBT + Synthetic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>False Positive Rate</td>
<td>% Detected Cancers</td>
</tr>
<tr>
<td>1st Generation</td>
<td>53.1</td>
<td>83.5</td>
</tr>
<tr>
<td>2nd Generation</td>
<td>45.6</td>
<td>87.3</td>
</tr>
</tbody>
</table>

Skaane et al., Radiology, Vol 271(2), 2014

### Synthetic Mammograms

Current synthetic 2D image can replace FFDM in combination with DBT

### Radiation Dose DBT/DM from Clinical Studies

- 1-view DBT vs DM = 0.34 – 1.0
- 2-view DBT vs DM = 0.68 – 1.17
- 1-view DBT + DM vs DM = 1.03 – 1.50
- 2-view DBT + DM vs DM = 2.0 – 2.23

Svahn et al., The Breast, 24 (2015) 63-66
Synthetic (?)

1-view DBT  vs  DM  = 0.34 – 1.0
2-view DBT  vs  DM  = 0.68 – 1.17

TO BE ANSWERED...

Remaining questions in DBT

What is a screening DBT exam?

Remaining questions in DBT

Reading time
Remaining questions in DBT

Reading strategy

False negatives: mammo vs tomo

<table>
<thead>
<tr>
<th></th>
<th>Tomo + Mammo -</th>
<th>Tomo - Mammo +</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visibility</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Radiographic appearance</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Interpretative error</td>
<td>3</td>
<td>6</td>
</tr>
</tbody>
</table>

Lint et al, BJ Radiol 2014;87:20140080

Remaining questions in DBT

What after a tomo screen?

Multiple rounds?
DEDICATED BREAST COMPUTED TOMOGRAPHY
Fully-3D SPECT-CT: CT source down

Fully-3D SPECT-CT: CT source up

White arrow points to 16x20cm² CZT-based SPECT camera; orange arrows point to x-ray CT source, with opposed 40x30cm² flat-panel detector; phantom on radiopaque bed.

Spiral BCT

CLINICAL IMAGES

Coronal

Transverse
BCT – Mammo Comparison

Mammo – BCT: Fibroadenoma

He et al., Eur Radiol, 2016

Mammo – BCT: Microcalcifications

He et al., Eur Radiol, 2016
Mammo – BCT: Microcalcifications

He et al, Eur Radiol, 2016

BREAST DOSE

AGD Equivalent to 2-view Mammo

Boone et al, Medical Physics, 2005; 32(12), 3767

Breast CT vs. Mammography

Sechopoulos et al, Medical Physics, 2010; 37(8), 4110.
Breast CT vs. Mammography


Anthropomorphic Phantom

Sechopoulos et al., Radiology, 2008

Dose Variation with Projection Angle

Sechopoulos et al., Radiology, 2008
Relative Organ Dose

<table>
<thead>
<tr>
<th>Organ</th>
<th>50 kVp</th>
<th>80 kVp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>1.75%/0.79%</td>
<td>3.08%/1.58%</td>
</tr>
<tr>
<td>Lung (IL)</td>
<td>1.79%/2.03%</td>
<td>2.93%/3.25%</td>
</tr>
<tr>
<td>Thymus</td>
<td>1.27%</td>
<td>2.35%</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.08%</td>
<td>0.19%</td>
</tr>
<tr>
<td>Uterus/Fetus</td>
<td>0.010%</td>
<td>0.026%</td>
</tr>
<tr>
<td>Clavicle (IL)</td>
<td>1.57%</td>
<td>2.80%</td>
</tr>
<tr>
<td>Rib Cage</td>
<td>4.14%</td>
<td>5.56%</td>
</tr>
<tr>
<td>Sternum</td>
<td>5.16%</td>
<td>7.74%</td>
</tr>
</tbody>
</table>

Sevastos et al., Radiology, 2008

CLINICAL PERFORMANCE

First Results (N=69)

<table>
<thead>
<tr>
<th>Table 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conspicuity of Lesions at Breast CT Compared with Screen-Film Mammography</td>
</tr>
<tr>
<td>Category</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>All</td>
</tr>
<tr>
<td>Lesion type</td>
</tr>
<tr>
<td>Masses or other findings</td>
</tr>
<tr>
<td>Microcalcifications</td>
</tr>
</tbody>
</table>

Breast CT | 5.5 | 10 Mammo

Lindfors et al., Radiology, 2008

Preliminary Results Diagnostic Work-up

16 BI-RADS® 4 or 5 after work-up Bx:
8 malignant lesions
8 benign lesions
15 adequate BCT studies
**Preliminary Results Diagnostic Work-up**

Breast CT:
- 8 malignant  ➔ 8 biopsy
- 8 benign  ➔ 5 biopsy
  - 3 no biopsy

---

**BI-RADS c and d density breasts (n = 270 lesions)**

<table>
<thead>
<tr>
<th></th>
<th>MG</th>
<th>US</th>
<th>BCBCT</th>
<th>CE-BCBCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>78.4</td>
<td>81.1</td>
<td>89.2</td>
<td>98.7</td>
</tr>
<tr>
<td></td>
<td>(67.3–87.1)</td>
<td>(70.3–89.3)</td>
<td>(79.8–95.2)</td>
<td>(92.7–100.0)</td>
</tr>
<tr>
<td>Specificity</td>
<td>70.1</td>
<td>82.7</td>
<td>80.1</td>
<td>85.00</td>
</tr>
<tr>
<td></td>
<td>(65.6–75.6)</td>
<td>(80.0–90.3)</td>
<td>(73.8–85.5)</td>
<td>(68.3–80.9)</td>
</tr>
<tr>
<td>AUROC</td>
<td>0.782</td>
<td>0.834</td>
<td>0.846</td>
<td>0.868</td>
</tr>
<tr>
<td></td>
<td>(0.728–0.830)</td>
<td>(0.784–0.876)</td>
<td>(0.798–0.887)</td>
<td>(0.822–0.906)</td>
</tr>
</tbody>
</table>

---

**All patients (N = 442 lesions)**

<table>
<thead>
<tr>
<th></th>
<th>MG</th>
<th>US</th>
<th>BCBCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>93/110</td>
<td>93/110</td>
<td>97/110</td>
</tr>
<tr>
<td></td>
<td>(84.5%)</td>
<td>(84.5%)</td>
<td>(88.2%)</td>
</tr>
<tr>
<td></td>
<td>(76.4–90.7)</td>
<td>(76.4–90.7)</td>
<td>(80.6–93.6)</td>
</tr>
<tr>
<td>Specificity</td>
<td>270/332</td>
<td>288/332</td>
<td>279/332</td>
</tr>
<tr>
<td></td>
<td>81.3 %</td>
<td>86.7 %</td>
<td>84.0 %</td>
</tr>
<tr>
<td></td>
<td>(76.7–85.4)</td>
<td>(82.6–90.2)</td>
<td>(79.6–87.8)</td>
</tr>
<tr>
<td>AUROC</td>
<td>0.829</td>
<td>0.856</td>
<td>0.861</td>
</tr>
<tr>
<td></td>
<td>(0.783–0.875)</td>
<td>(0.820–0.888)</td>
<td>(0.825–0.892)</td>
</tr>
</tbody>
</table>

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**CLINICAL IMPLEMENTATION QUESTIONS**
Questions in BCT

Screening or Work-up?

Questions in BCT

Tissue coverage?

Questions in BCT

0.1% of tumors in Tail of Spence (N=839)

Questions in BCT

Reading time? (reading strategy)
Contrast Enhanced BCT

He et al., Eur Radiol, 2016

Malignant

benign

Courtesy of John Boone, Ph.D.
**Contrast Enhanced BCT Subtraction**

Pre-injection  | Post-injection  | Registered Subtraction

Large arrows point to the same location of a surgically confirmed DCIS lesion in 48yo patient. Small arrow points to posteriorly located biopsy clip. Blobs posterior to breast are chest-wall signals from myocardial uptake of $^{99m}$Tc-sestamibi.

**Towards Tomographic Breast Imaging**

<table>
<thead>
<tr>
<th>2 D</th>
<th>2+ D</th>
<th>2.2 D</th>
<th>3 D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard Mammography</td>
<td>Stereoscopic Mammography</td>
<td>Digital Tomosynthesis</td>
<td>Dedicated Breast CT</td>
</tr>
<tr>
<td>(If your optical system can handle it!)</td>
<td></td>
<td></td>
<td>(Is more always better?)</td>
</tr>
</tbody>
</table>
Towards Tomographic Breast Imaging

2D 3D 4D

Standard Mammography

Dedicated Breast CT

(D is more always better?)

Dedicated Breast CT

FUNCTIONAL!!

4D Breast CT

Tumor Biology Profiling

4D Breast CT

Neoadjuvant chemotherapy treatment planning

4D Breast CT

Response prediction/monitoring
Correct Quantification

4D Noise Filtering

Motion Correction

Motion Correction
**Patient BCT Classification**

[Images of MRI scans showing different tissue types and classifications]

*Courtesy of Dr. Despina Kontos*  
*Cabello et al., IEEE TMI, under review*

---

**4D Breast Phantom**

[Graph showing HU values over time with three lines representing tumor, fibroglandular tissue, and adipose tissue]  
[Image of a 3D reconstruction of a breast phantom]

*Courtesy of Dr. Despina Kontos*  
*Cabello et al., to be presented at RSNA 2017*

---

**Image-based phenotyping**

[Heatmap showing various tissue classifications and densities]

*Courtesy of Dr. Despina Kontos*  
*Cabello et al., to be presented at RSNA 2017*

---

**pCR prediction**

[Graph showing prediction curves for pCR with different markers and conditions]

*Courtesy of Dr. Despina Kontos*
Response Monitoring

Towards Tomographic Breast Imaging

What if

CC+MLO → CC+MLO+ML
**Methods**

Screening with DBT Combo mode

**Results**

- 842 work-ups after screening DBT in previous 30 days
- 266 ML/LM view during work-up
- 133 biopsied cases
- 106 non-biopsied cases
- 121 patients in final cohort
- 28 BI-RADS 3 after work-up and excluded
- 0 patients excluded due to breast implants
- 11 patients excluded due to breast size
- 106 patients excluded follow-up unavailable

**Breast Density**

<table>
<thead>
<tr>
<th>Density</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-dense</td>
<td>42% (51/121)</td>
</tr>
<tr>
<td>Dense</td>
<td>58% (70/121)</td>
</tr>
</tbody>
</table>

**Methods**

Diagnostic work-up with mammo views
### Abnormality

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcifications</td>
<td>31% (38/121)</td>
</tr>
<tr>
<td>Soft Tissue</td>
<td>64% (78/121)</td>
</tr>
<tr>
<td>Both</td>
<td>4% (5/121)</td>
</tr>
</tbody>
</table>

### ROC results – Overall

<table>
<thead>
<tr>
<th>Modality</th>
<th>AUC</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-View DM</td>
<td>0.846</td>
<td>0.787 – 0.905</td>
<td>0.692</td>
</tr>
<tr>
<td>DBT</td>
<td>0.853</td>
<td>0.802 – 0.904</td>
<td></td>
</tr>
</tbody>
</table>

### ROC results – Secondary

No significant difference between:
- Attendings vs. fellows
- Microcalcifications vs. soft tissue
- Non-dense vs. dense breasts

### Abnormality

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>3-View Digital Mammography (%)</th>
<th>Digital Breast Tomosynthesis (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign recall rate</td>
<td>53 (43 – 84)</td>
<td>52 (44 – 76)</td>
<td>1</td>
</tr>
<tr>
<td>Malignant recall rate</td>
<td>74 (50 – 90)</td>
<td>75 (59 – 89)</td>
<td>1</td>
</tr>
</tbody>
</table>
Reading time

3-view DM: 49.4 seconds
DBT: 73.7
p < 0.00001

Limitations

Biased sampling:
Screening with tomo

Unilateral exams
No location

Towards Tomographic Breast Imaging

2 D 2+ D 2.2 D 3 D

Optimal

Standard Stereoscopic Digital Dedicated
Mammography Mammography Tomosynthesis Breast CT

Situation en France

Courtesy of Dr. Patrice Heid
CDMAM Phantom

Gold disc detection

Gold disc detection

QUALITY CONTROL
Screening stopped:

2016: 12 times
2015: 15 times
2014: 5 times

Reasons

• Grid lines clearly visible
• Compression paddle height indication off
• Lines caused by mechanical shocks
• during readout
• Accidental dose increase by service engineer (70% !)

Thickness indication off

Thickness 63 mm
W/Rh 30 kV

Thickness 139 mm
W/Ag 39 kV

Thickness indication off

Thickness 63 mm
W/Rh 30 kV

Thickness 139 mm
W/Ag 39 kV
Lines due to mechanical shocks

Example of grid lines visible

Example of detector problem

Step 1:
Optimal Mammography
Summary
Clinical need to reduce superposition

Stereoscopic mammography
Digital breast tomosynthesis
Dedicated breast CT

Summary
Perhaps....

3 view mammography
**Summary**

Definitely....

Optimized technology at peak performance