Innhold:

• Hva er tomosyntes?
• Tomosyntes i klinisk utredning
• Tomosyntes i screening
• Tomosyntes: Erfaringer fra Oslo Tomosynthesis Screening Trial (OTST)
• Konklusjon

Disclosure:

Oslo Tomosynthesis Screening Trial
Equipment and support for additional reading provided by Hologic, Inc.
Tomosynthesis (”3D Mammography”)
A) Conventional linear tomography

B) Tomosynthesis with a digital detector:

- Multiple images are acquired
- Tomosynthesis provides tomograms of the entire object
Digital Breast Tomosynthesis (DBT / “3D mammography”): ACQUISITION

- X-ray tube moves through a proscribed arc of excursion
- Fifteen low-dose projection images are acquired during a 4-second sweep
- Images are reconstructed into stack of images spaced at 1 mm apart
- Total dose same as 2D
A) Potential role of DBT in the clinical setting

- Microcalcifications:
  - FFDM slightly more sensitive than DBT for detection
    (Spangler ML: AJR 2011;196:320)
  - Demonstrated with equal or greater clarity on DBT
    (Kopans D: Breast J 2011;17:638)
- Tumor size assessment:
  - DBT superior to FFDM
    (Fornvik B: Acta Radiol 2010;51:240)
  - Specificity increased when used adjunctively with FFDM:
    (Poplack SP: AJR 2007;189:616)
    (Gur D: AJR 2009;193:586)
- Mass characterization:
  - Superior cancer visibility and conspicuity
    (Andersson I: Eur Radiol 2008;18:2817)

i.e., DBT might have a great potential in mammography screening!!
Tomosynthesis: Potential for increased specificity

Clinical studies showing lower call-back rate:

- Bernardi D: Breast Cancer Res Treat 2012;133:267-271
- Michell MJ: Clin Radiol 2012;67:976-981
- Poplack SP: Am J Roentgenol AJR 2007;189:616-623
- Rafferty EA: Radiology 2013:266:104-113
DBT in European mammography screening and potential for increased specificity

European guidelines for quality assurance in mammography screening

**Performance indicator “Recall rate”**

<table>
<thead>
<tr>
<th></th>
<th>Acceptable level</th>
<th>Desirable level</th>
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<tbody>
<tr>
<td>Initial screening examinations</td>
<td>&lt; 7 %</td>
<td>&lt; 5 %</td>
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<tr>
<td>Subsequent screening examinations</td>
<td>&lt; 5 %</td>
<td>&lt; 3 %</td>
</tr>
</tbody>
</table>
B) Potential role of DBT in mammography screening

Invasive lobular carcinoma (ILC) : 2 mm, gr. 1
(+ LCIS 20 mm and ALH / LCIS)
Indication for tomosynthesis: Dense breast parenchyma

Tubular carcinoma 6 mm

<table>
<thead>
<tr>
<th>Reader Arm</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score (NBCSP)</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>1</td>
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</table>
OTST: Cancer right breast

Radiologist

Score (NBCSP)

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<thead>
<tr>
<th>Radiologist</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
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<tr>
<td></td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
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</table>
Indication for tomosynthesis: Fatty breasts ??

Oslo Tomosynthesis Screening Trial

<table>
<thead>
<tr>
<th>Radiologist</th>
<th>A</th>
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<td>4</td>
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</table>
Images to be included:
- One view TOMO (mlo)?
- One view 2D + one view TOMO?
- Two view 2D + one view TOMO?
- Two view TOMO?
- Two view 2D + two view TOMO?

Why do we need 2D (+ TOMO):
- 2D should maximize mc detection (TOMO: ”Thin-slice-effect”)
- Comparison with priors is facilitated if currents includes 2D
- Externals may request current 2D

Experience from experimental clinical studies so far:
Two view FFDM  2D (MLO + CC) plus two view TOMO (MLO + CC) is optimal !
However: This means a ”double” radiation dose !

Synthetic C-Views may substitute for FFDM images (when combined with tomosynthesis) without additional radiation dose !!
Do you see the distortion?
Do you see the distortion?

Not easy to detect on the tomosynthesis MLO view!
OTST: Radial scar (+ fibrocystic changes)

Distortion obvious on tomosynthesis CC view!
Synthetic 2D generation:

Tomosynthesis reconstructed slices

Synthesized Projection

Synthetic 2D image (called C-View by Hologic) shows a roadmap of the important features from tomosynthesis slices
Synthetic 2D image
C-views and diagnostic performance:

Do we see the same on C-View as on conventional 2D FFDM and tomosynthesis (3D)?
Invasive ductal carcinoma  9 mm
Invasive lobular carcinoma (ILC) G1, 12 mm (+ DCIS G3)

Synthetic 2D image

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<th>C</th>
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<tr>
<td>Score (NBCSP)</td>
<td>1</td>
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<td>3</td>
<td>4</td>
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</tbody>
</table>
Microcalcifications

Synthetic 2D (C-view):
Highlighting

Tomo:
"Thin-slice-effect"
Oslo Tomosynthesis Screening Trial: DCIS gr. 1, 40 mm

Conventional 2D vs. Synthetic 2D + tomosynthesis
Tomosynthesis in the Oslo Breast Cancer Screening Program (DBT)

This study is currently recruiting participants.

ClinicalTrials.gov Identifier: NCT01248546

- Estimated Enrollment: 25,000
- Study Start Date: November 2010
- Estimated Primary Completion Date: December 2012
  (Final data collection date for primary outcome measure)

Oslo Tomosynthesis Screening Trial:

- Part of the Norwegian Breast Cancer Screening Program
- Age group 50-69 years
- Two-view (CC and MLO) mammography
- Independent double reading with consensus (arbitration)
- 5-point rating scale (1=normal/benign; 2-5=positive score)
- On-line reporting directly into the database of the Norwegian Cancer Registry
Oslo Tomosynthesis Screening Trial (OTST)

Screening:
FFDM (2D) + TOMO (3D)

FFDM: Independent double reading

FFDM + TOMO: Independent double reading
Oslo Tomosynthesis Screening Trial (OTST)

Screening: FFDM (2D) + TOMO (3D)

FFDM: Independent double reading

Arm A: FFDM: Single reading

Arm B: FFDM + CAD: Single reading

Arm C: FFDM + TOMO: Single reading

Arm D: CompView + TOMO: Single reading

Concensus / Arbitration meeting
(for all cases with a score of 2 or higher in at least one arm)
DBT: Breast cancer screening in women with dense breast parenchyma:

OTST: Batch reading "combo mode" (FFDM + DBT)
Hanging protocol step 1 - 4
OTST: Batch reading "combo mode" (FFDM + DBT)
Hanging protocol step 5 - 8
Mean interpretation time* (sec.) for study arm A – D for the 7 radiologists

One year "Interim analysis"
Average interpretation time:
- Arm A: 45 sec.
- Arm C: 91 sec.
(Skaane P et al.: Radiology 2013)

Radiologist 1 2 3 4 5 6 7
Arm
A = 49  B = 58  C = 88  D = 82
A = 49  B = 58  C = 88  D = 82

*Outliers (interpretation times < 20 sec. and > 200 sec.) excluded
Oslo Tomosynthesis Screening Trial (OTST): First year results *

Women 2D + (2D+3D): n = 12,631
Malignancy: n = 130
Malignancy rate: 1.03%

Excl. 10 women with malignancy:
- 2 palp. cancer (clin recall)
- 3 Interval cancers (IC)
- 5 Lymphomas/metastases

Arm A (2D): n = 12,621
Cancers: n = 77
Cancer detection rate: 0.61%

Arm C (2D + 3D): n = 12,621
Cancers: n = 101
Cancer detection rate: 0.80%

Relative increase in cancer detection (2D+TOMO) vs. (2D): 31%

* Skaane P et al.: Radiology 2013; 267: 47-56
Oslo Tomosynthesis Screening Trial (OTST): First year results

Cancer detection in the 4 arms stratified on the mammographic features

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Circumscri. mass</td>
<td>2</td>
<td>7</td>
<td>0</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>0</td>
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<tr>
<td>Spiculated mass</td>
<td>15</td>
<td>28</td>
<td>13</td>
<td>30</td>
<td>33</td>
<td>42</td>
<td>9</td>
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<tr>
<td>Distortion</td>
<td>12</td>
<td>8</td>
<td>15</td>
<td>5</td>
<td>9</td>
<td>20</td>
<td>11</td>
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<tr>
<td>Asymm. density</td>
<td>2</td>
<td>4</td>
<td>4</td>
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<td>4</td>
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<td>Calcifications</td>
<td>3</td>
<td>26</td>
<td>4</td>
<td>25</td>
<td>28</td>
<td>29</td>
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<tr>
<td>Calc + density</td>
<td>10</td>
<td>4</td>
<td>8</td>
<td>6</td>
<td>7</td>
<td>14</td>
<td>7</td>
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<tr>
<td>Total</td>
<td>44</td>
<td>77</td>
<td>44</td>
<td>77</td>
<td>90</td>
<td>119</td>
<td>29</td>
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</tbody>
</table>

Relative increase in cancer detection using double reading (2D+TOMO=C+D) vs. (2D=A+B): 32%

Arm A: FFDM (2D)
Arm B: 2D + CAD
Arm C: 2D + Tomosynthesis (3D)
Arm D: Synthetic 2D + 3D
<table>
<thead>
<tr>
<th>Study</th>
<th>Population (n)</th>
<th>Study design</th>
<th>Examination mode</th>
<th>Reading mode</th>
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<tbody>
<tr>
<td>Trento/Verona (STORM) 1</td>
<td>7,292</td>
<td>Prospective; paired</td>
<td>2D: 2-view 3D: 2-view</td>
<td>Double; Sequential</td>
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<tr>
<td>Oslo (OTST) 2</td>
<td>12,631</td>
<td>Prospective; paired</td>
<td>2D: 2-view 3D: 2-view</td>
<td>Double; Independent</td>
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<tr>
<td>TOPS Compr. Breast Center, Houston, TX 3</td>
<td>2D: 13,856 3D: 9,499</td>
<td>Retrospective; non-paired</td>
<td>2D: 2-view 3D: 2-view</td>
<td>Single; Independent</td>
</tr>
<tr>
<td>Malmø (MBTST) 4</td>
<td>5,700</td>
<td>Prospective; paired</td>
<td>2D: 2-view 3D: 1-view</td>
<td>Double; Sequential</td>
</tr>
<tr>
<td>Yale University 5 (New Haven, CT)</td>
<td>2D: 8,355 3D: 4,936</td>
<td>Retrospective; non-paired</td>
<td>2D: 2-view 3D: 2-view</td>
<td>Single; Independent</td>
</tr>
</tbody>
</table>

3) TOPS Comprehensive Breast Center, Houston, Texas Rose SL et al.: Am J Roentgenol AJR 2013
4) Malmø Breast Tomosynthesis Screening Trial (MBTST): Interim analysis; presented at Satellite Symposium, ECR Vienna, 2013
5) Yale New Haven University Hospital, New Haven, CT: Interim analysis: presented at the ARRS Annual Meeting, Washington, 2013
<table>
<thead>
<tr>
<th>Study</th>
<th>Popul. (n)</th>
<th>Cancer (n)</th>
<th>Cancer (n / 1,000)</th>
<th>Cancer: Rel. increase (%)</th>
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</thead>
<tbody>
<tr>
<td>Trento/Verona (STORM) 1</td>
<td>7,292</td>
<td>39 59</td>
<td>5.3 8.1</td>
<td>51 %</td>
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<tr>
<td>Oslo (OTST) 2</td>
<td>12,631</td>
<td>90 119</td>
<td>7.1 9.4</td>
<td>32 %</td>
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<tr>
<td>TOPS Compr. Breast Center, Houston, TX 3</td>
<td>2D: 13,856</td>
<td>56     51</td>
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<td>Malmø (MBTST) 4</td>
<td>5,700</td>
<td>- -</td>
<td>4.7 6.8</td>
<td>45 %</td>
</tr>
<tr>
<td>Yale University 5 (New Haven, CT) 5</td>
<td>2D: 8,355</td>
<td>38 25</td>
<td>4.6 5.1</td>
<td>12 %</td>
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<td>3D: 4,936</td>
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Digital Breast Tomosynthesis (DBT)
Conclusions: Tomosynthesis and breast cancer screening

- Tomosynthesis plus synthesized 2D makes combined 2D and 3D ("combo mode") possible with approximately the same radiation dose as conventional 2D FFDM
- Tomosynthesis plus 2D significantly increase the cancer detection rate as compared with 2D FFDM alone
- Tomosynthesis plus 2D has the potential to reduce the recall rate
- The additional interpretation time for tomosynthesis plus 2D as compared with 2D alone is acceptable for implementation in organized high-volume breast cancer screening

Thank you very much for your time!

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