A Randomized Trial Comparing Breast Cancer Incidence and Interval Cancers after Tomosynthesis Plus Mammography versus Mammography Alone

Jordan Fenner and Umer Ahmed
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Learning objectives

By the end of this journal club, participants will be able to

• Compare advantages of DBT + DM vs DM alone
• Differentiate which patients would be best candidates for screening by DBT + DM vs DM alone
• Be familiar with ongoing research concerning DBT vs DM
Module Outline

I. Case
II. Background
III. Article Overview
IV. Clinical Questions
V. Key Points
Case presentation

47 yo with heterogeneously dense breasts present for annual screening mammogram.
Case imaging: Full Field Screening
2D Full Field Screening
3D Tomo Screening
Diagnostic work up
Diagnostic: Tomo
Diagnostic: US
Diagnostic Work up: Amorphous Calcifications
• Benefits to including 3D screening images in this patient?

• Other Considerations:
  • Age?
  • Breast density?
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### American College of Radiology

**ACR Appropriateness Criteria®**

**Breast Cancer Screening**

**Variant 1:** Breast cancer screening. Average-risk women: women with <15% lifetime risk of breast cancer.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Appropriateness Category</th>
<th>Relative Radiation Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammography screening</td>
<td>Usually Appropriate</td>
<td>🌟🌟</td>
</tr>
<tr>
<td>Digital breast tomosynthesis screening</td>
<td>Usually Appropriate</td>
<td>🌟🌟</td>
</tr>
<tr>
<td>US breast</td>
<td>May Be Appropriate</td>
<td>🌟</td>
</tr>
<tr>
<td>MRI breast without and with IV contrast</td>
<td>Usually Not Appropriate</td>
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<tr>
<td>MRI breast without IV contrast</td>
<td>Usually Not Appropriate</td>
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<tr>
<td>FDG-PET breast dedicated</td>
<td>Usually Not Appropriate</td>
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</tr>
<tr>
<td>Sestamibi MBI</td>
<td>Usually Not Appropriate</td>
<td>🌟🌟</td>
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</tbody>
</table>
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Article specifics

• Purpose: To compare interval and overall breast cancer incidence after screening with DBT + DM versus DM alone

• Published in Radiology: Breast Imaging

• Randomized Control Trial

• 2018 study: Detection rate was about 90% higher with DBT+DM than with DM alone
Study cohort

• Women aged 45–69 attending screening from March 2014 - August 2017 in one of the three clinics in a province Northern Italy with machines equipped with DBT for a new screening round were eligible for the study
  • n = 26,877

• Exclusion Criteria: Previous breast cancer, inclusion in or eligibility for a hereditary breast cancer surveillance program, pregnancy, previous DBT examination, very large breasts, augmentation prostheses, or language barriers.
Materials and Methods

- Women attending screening were randomized to one round of DBT + DM (experimental arm) or to DM (control arm).
- All were then rescreened with DM after 12 months (women aged 45–49 years) or after 24 months (50–69 years).

Primary outcome:

- Interval cancer incidence (cancers occurring after a negative screening exam and before the next scheduled screening round)
- Cumulative incidence up to the subsequent screening round plus 9 months (21- and 33-month follow-up for women aged 45–49 and 50–69, respectively)
  - Ductal carcinomas in situ are included

Secondary outcomes:

- Detection: # of cancers detected within 9 months of positive screening examination
- Proportion of recalled women: # of women recalled for an assessment out of the total number of screened women
- False-positive results: recalled for assessment but no cancer
- PPV
Women are included in the experimental arm number according to intention-to-treat analysis.
Imaging Protocol

• Both arms underwent standard four-projection DM (L and R CC plus MLO);
• Experimental arm also underwent then four-projection DBT
• In both arms, two radiologists independently read the images; in the event of disagreement, arbitration by a third reader
• In the experimental arm, first, the radiologist read the DBT examination and gave a judgment of positive or negative;
  • DM was presented together with previous mammograms. The radiologist made the final decision about recall at this step, using a dichotomous scale.
  • Women with positive results were recalled for assessment
• Women were actively re-invited for the subsequent screening round unless diagnosed with breast cancer or with a lesion requiring strict follow-up or if they moved to another province or died.
Results

• The mean age ± SD for the women in both arms was 55 ± 7.

• Interval cancer incidence was similar in the two arms
  • 21 vs 22 cancers; relative incidence, 0.97 [95% CI: 0.53, 1.8]

• Recall at the first round was similar in the two arms
  • 3.8% vs 3.9%; relative recall for DBT plus DM vs DM, 0.99 [95% CI: 0.88, 1.1]

• Detection was 70% higher in the DBT + DM arm, with 101 vs 61 cancers found
  • Relative detection, 1.7 [95% CI: 1.2, 2.3]

• PPV was higher in the DBT + DM arm (19.8%) than in the DM arm (11.7%)
Results (cont)

- Subgroup analysis
  - In the 45–49 age group, interval cancers (3 vs 8) and cancers detected at the second round (9 vs 18) were fewer in the DBT + DM arm than in the DM arm
    - relative incidence of interval cancer, 0.38 [95% CI: 0.10, 1.4]; relative detection, 0.50 [95% CI: 0.23, 1.1]
  - Cumulative incidence remained higher in the DBT+DM arm in women over 50
    - 153 vs 124 cancers; relative incidence, 1.2 [95% CI: 0.99, 1.6]
  - Cumulative incidence similar in the two arms in women aged 45–49
    - 36 vs 41 cancers; relative incidence, 0.89 [95% CI: 0.57, 1.4]
  - In the 11,948 women with dense or very dense breast tissue (BI-RADS category C or D) interval cancers detected lower in DBT + DM arm
    - 14 vs 15 cancers; relative incidence, 0.93 [95% CI: 0.45, 1.9]
Discussion

- DBT + DM shows benefit over DM alone as a screening test for detection and PPV, consistent with other studies
- DBT + DM in women < 50 and women with denser breasts advanced the time of diagnosis of cancers that would have occurred in the near future
- Tumors detected by DBT + DM but undetectable at DM in women > 50 would not have progressed to symptomatic disease in the next 2 years or to cancer detected at screening with DM after 2 years
- Ongoing trial in the UK: randomizing to two rounds of DBT OR DM, with regular DM screening for all thereafter
  - Will be able to tell more about types of breast cancer that can be detected with DBT vs DM
But wait . . . (Limitations)

• DBT + DM has higher radiation dose than DM alone
  • Mean glandular dose: 1.36 mGy for DM and 1.88 mGy for DBT (Gennaro et al., 2018)
  • Can generate synthetic 2D image based on DBT

• Underpowered: final sample was only 67.2% of the planned size (26,877 instead of 40,000)

• External validity: Study did not include women with genetic risk factors for breast cancer, women with larger breasts, or those with implants. Participants all from one province of Italy.

• Availability: “Of the 670 respondents, 200 (29.9%) reported using DBT, 102 (51%) of DBT users had only a single DBT unit at their practice, and 12 (6%) worked in practices with 7 or more DBT units. Only 11 (5.5%) DBT users worked in practices where all mammography units were DBT units.” (Hardesty et al., 2016)
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Clinical questions now . . .

• Direct comparison of DBT vs DM
• DBT vs DM: effect of screening on breast cancer mortality
Key points

• DBT + DM depicts more cancers than DM alone

• In women < 50 years and those with denser breasts, the benefit of early diagnosis with DBT + DM seemed to be appreciable

• Utility of DBT for screening still being evaluated
CONCLUSIONS AND RELEVANCE  Screening with DBT vs digital mammography was not associated with a significant difference in risk of interval invasive cancer and was associated with a significantly lower risk of advanced breast cancer among the 3.6% of women with extremely dense breasts and at high risk of breast cancer. No significant difference was observed in the 96.4% of women with nondense breasts, heterogeneously dense breasts, or with extremely dense breasts not at high risk.
References


