

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

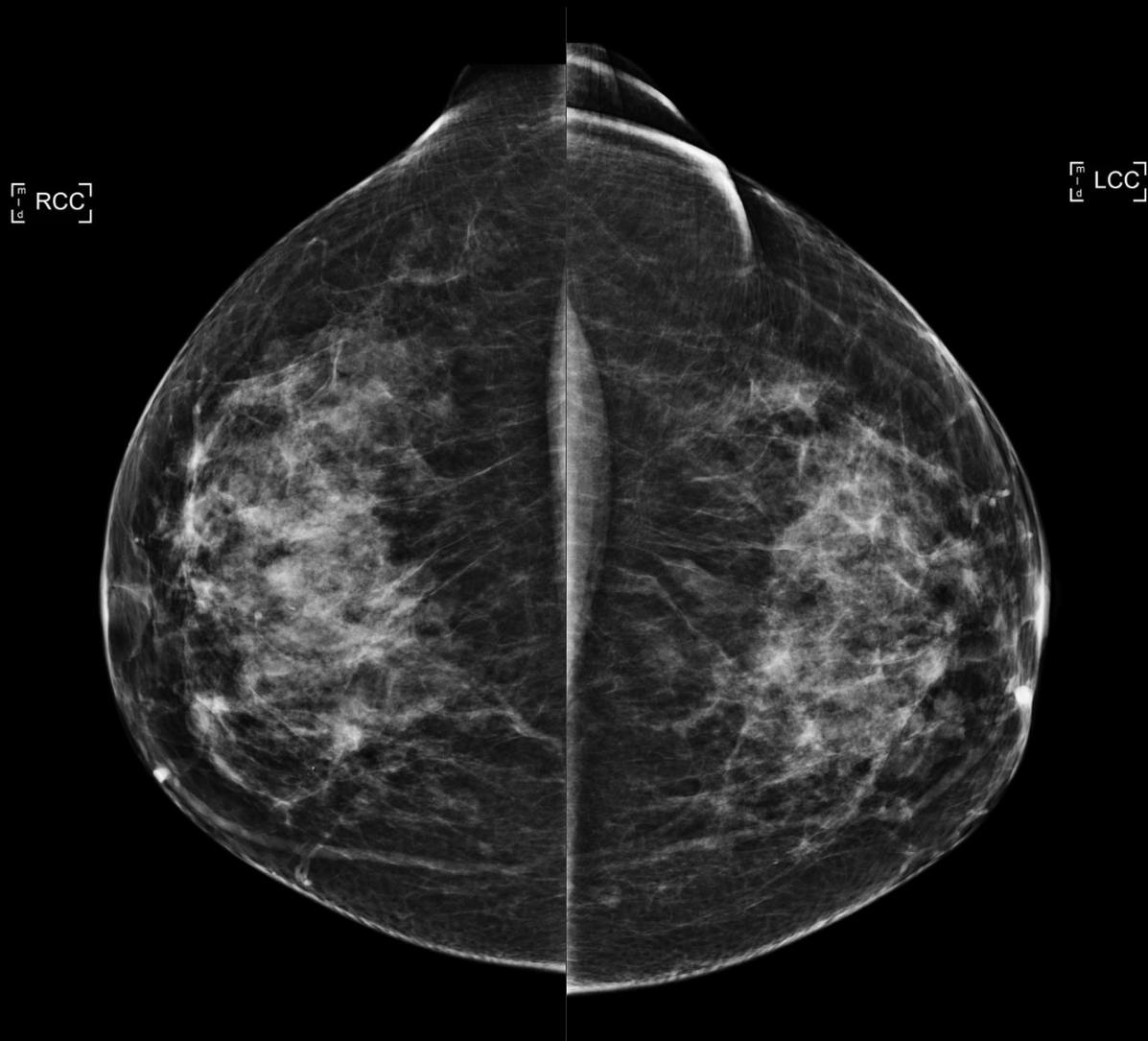
# Case presentation

47 yo with heterogeneously dense breasts present for annual screening mammogram.

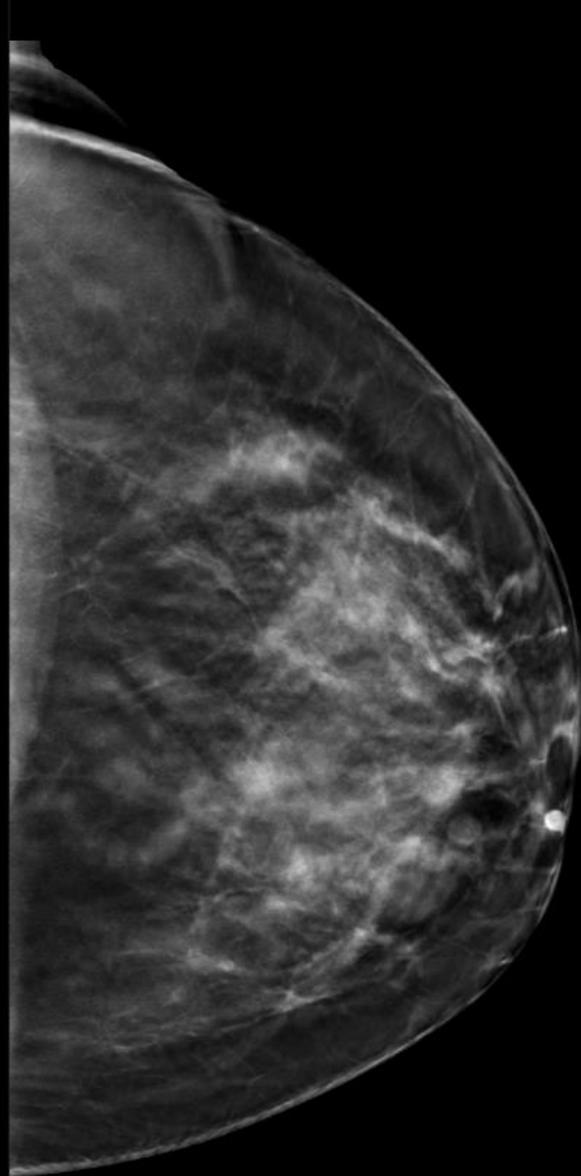
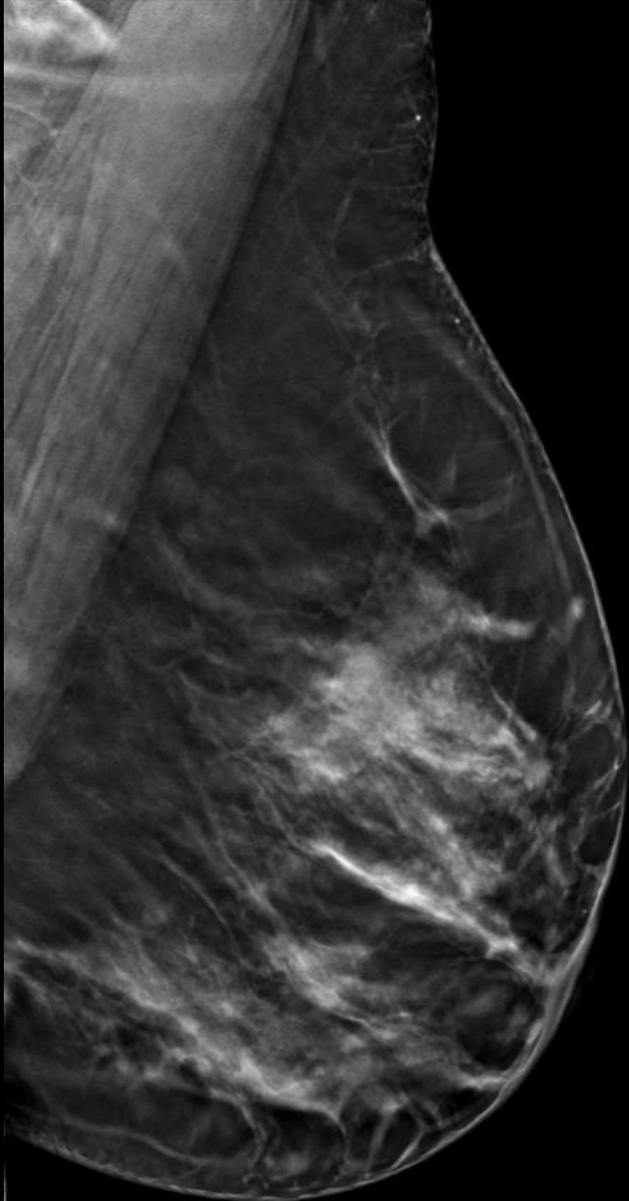
# Case imaging: Full Field Screening



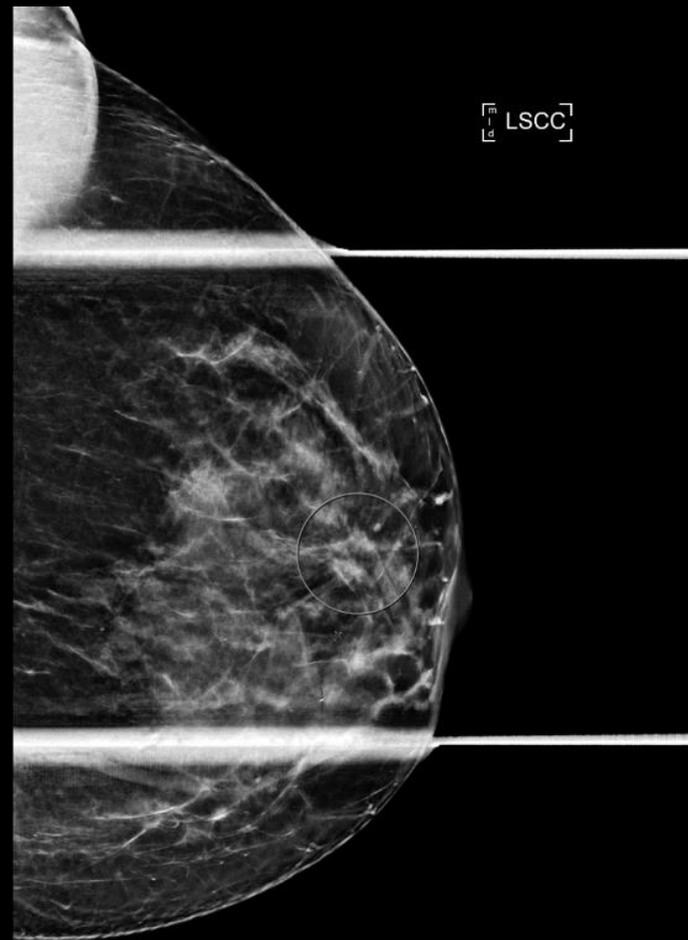
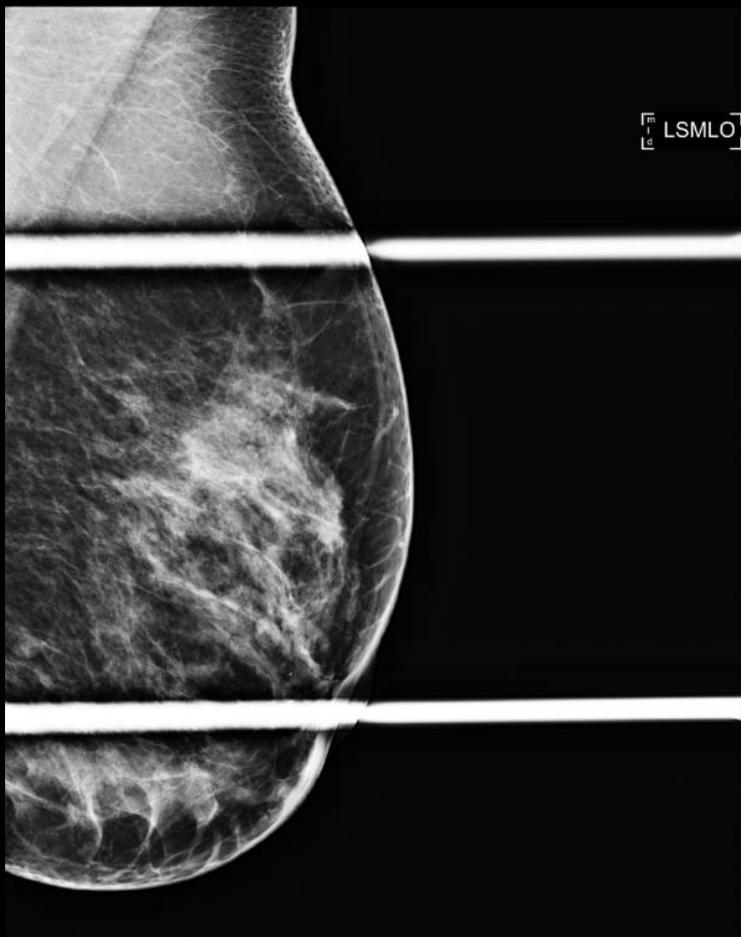
# 2D Full Field Screening



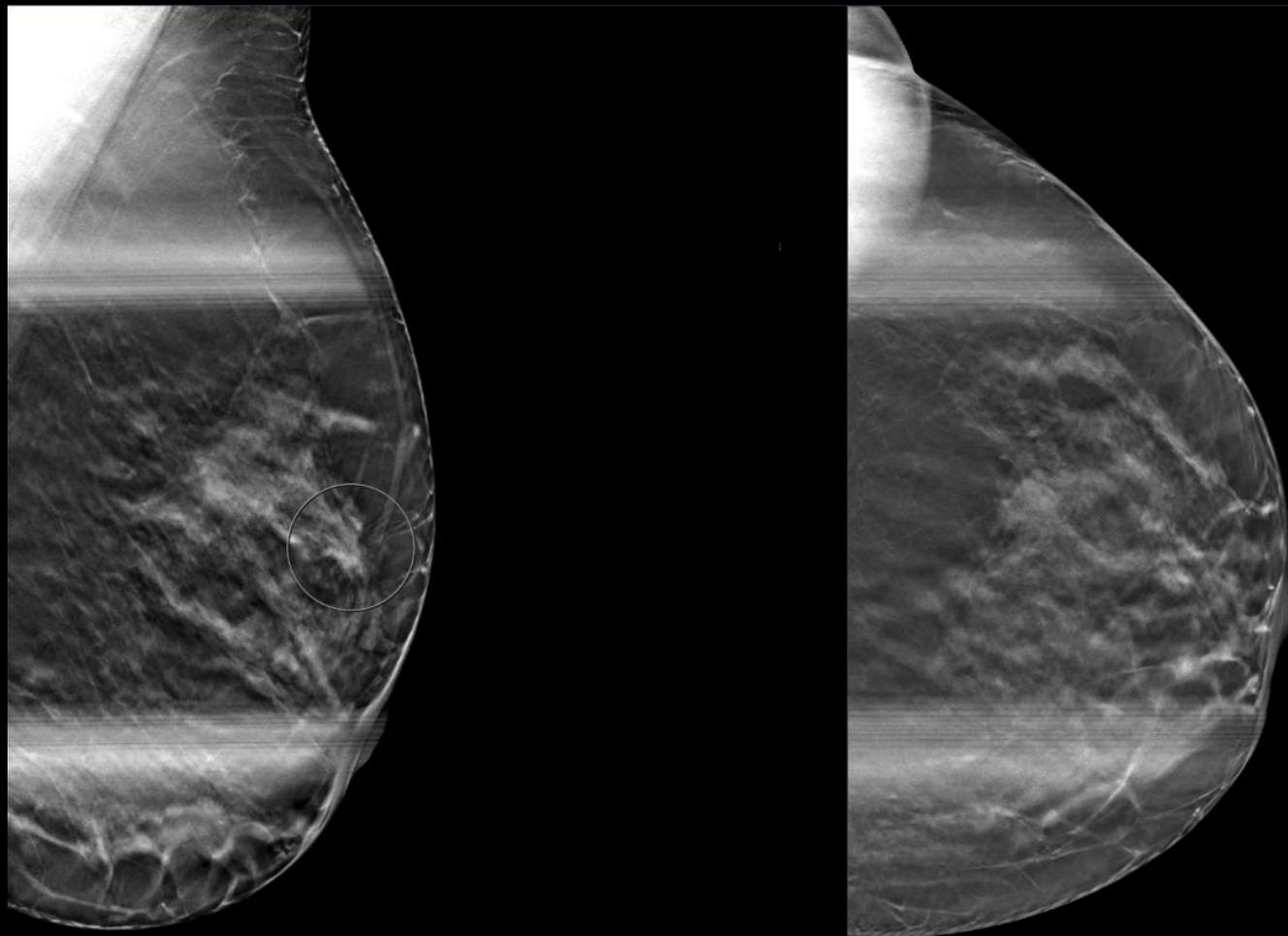
# 3D Tomo Screening



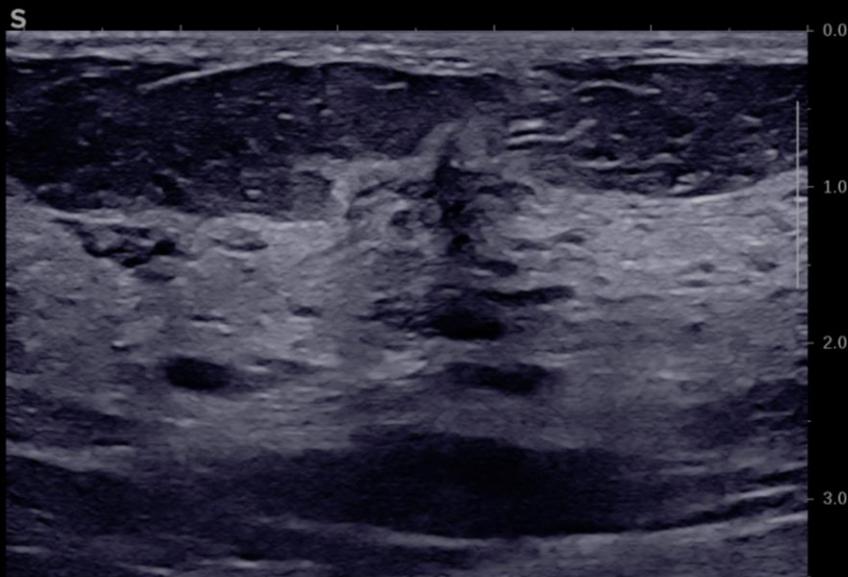
# Diagnostic work up



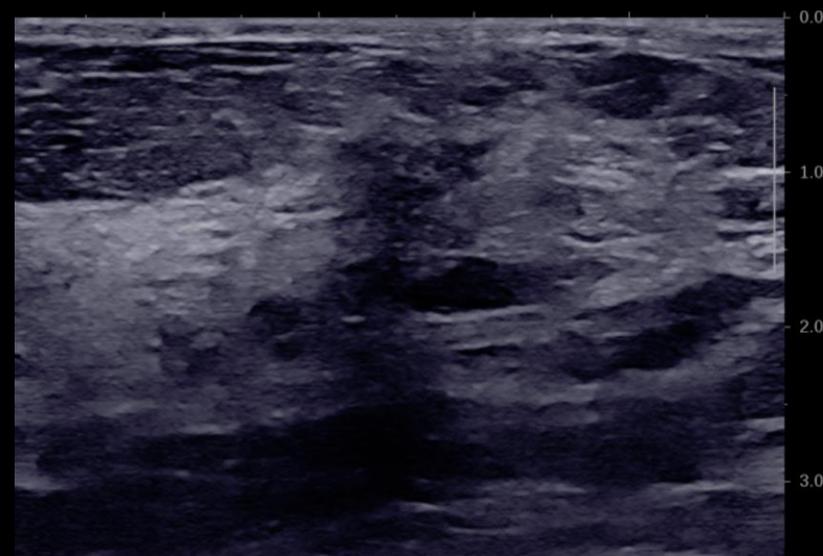
# Diagnostic: Tomo



# Diagnostic: US

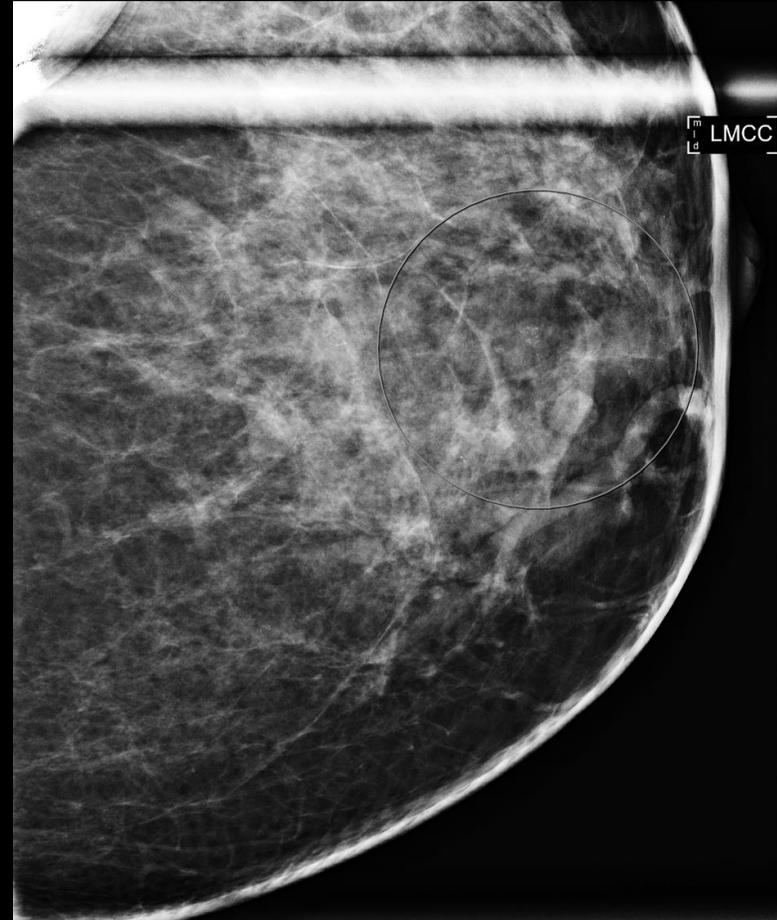
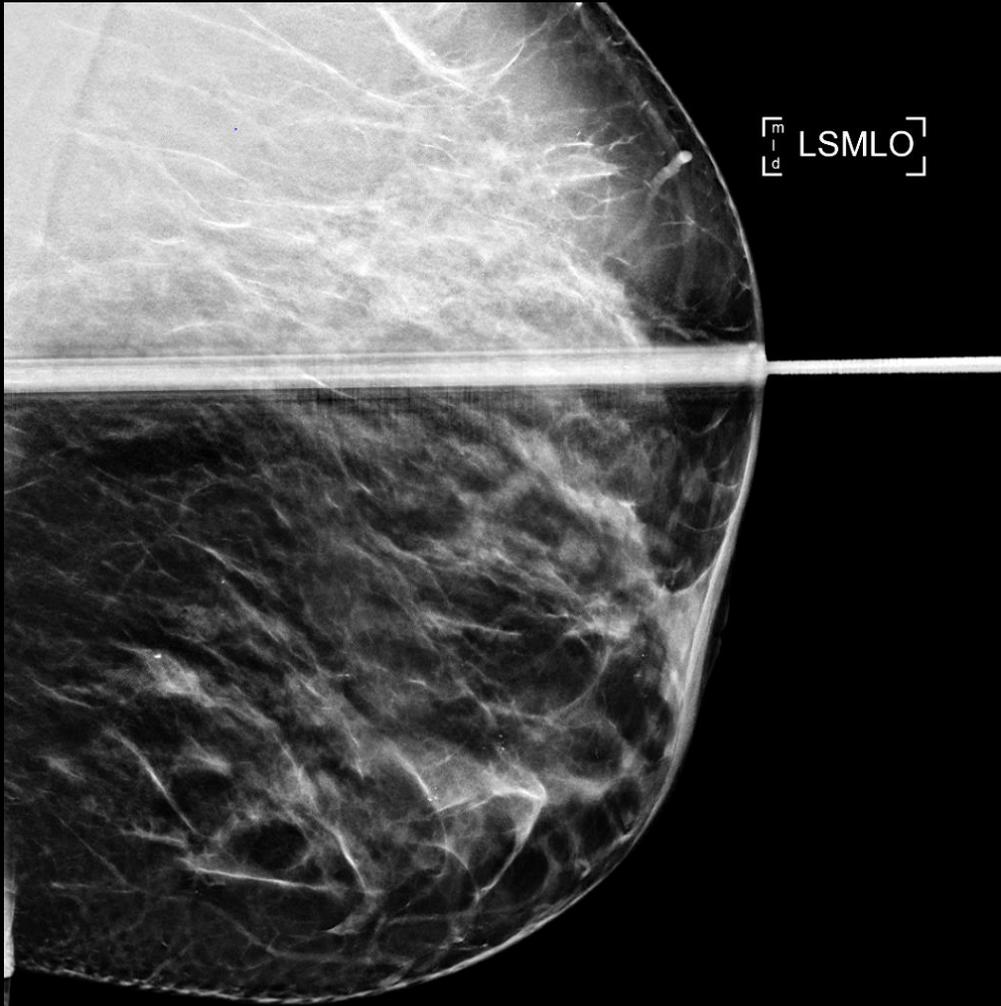


LT BREAST 12:00 1 cm fn ANTIRADIAL PRE BIOPSY ❄️



LT BREAST 12:00 1 cm fn RADIAL PRE BIOPSY ❄️

# 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.**

Procedure	Appropriateness Category	Relative Radiation Level
Mammography screening	Usually Appropriate	☼☼
Digital breast tomosynthesis screening	Usually Appropriate	☼☼
US breast	May Be Appropriate	○
MRI breast without and with IV contrast	Usually Not Appropriate	○
MRI breast without IV contrast	Usually Not Appropriate	○
FDG-PET breast dedicated	Usually Not Appropriate	☼☼☼☼
Sestamibi MBI	Usually Not Appropriate	☼☼☼

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# Article specifics

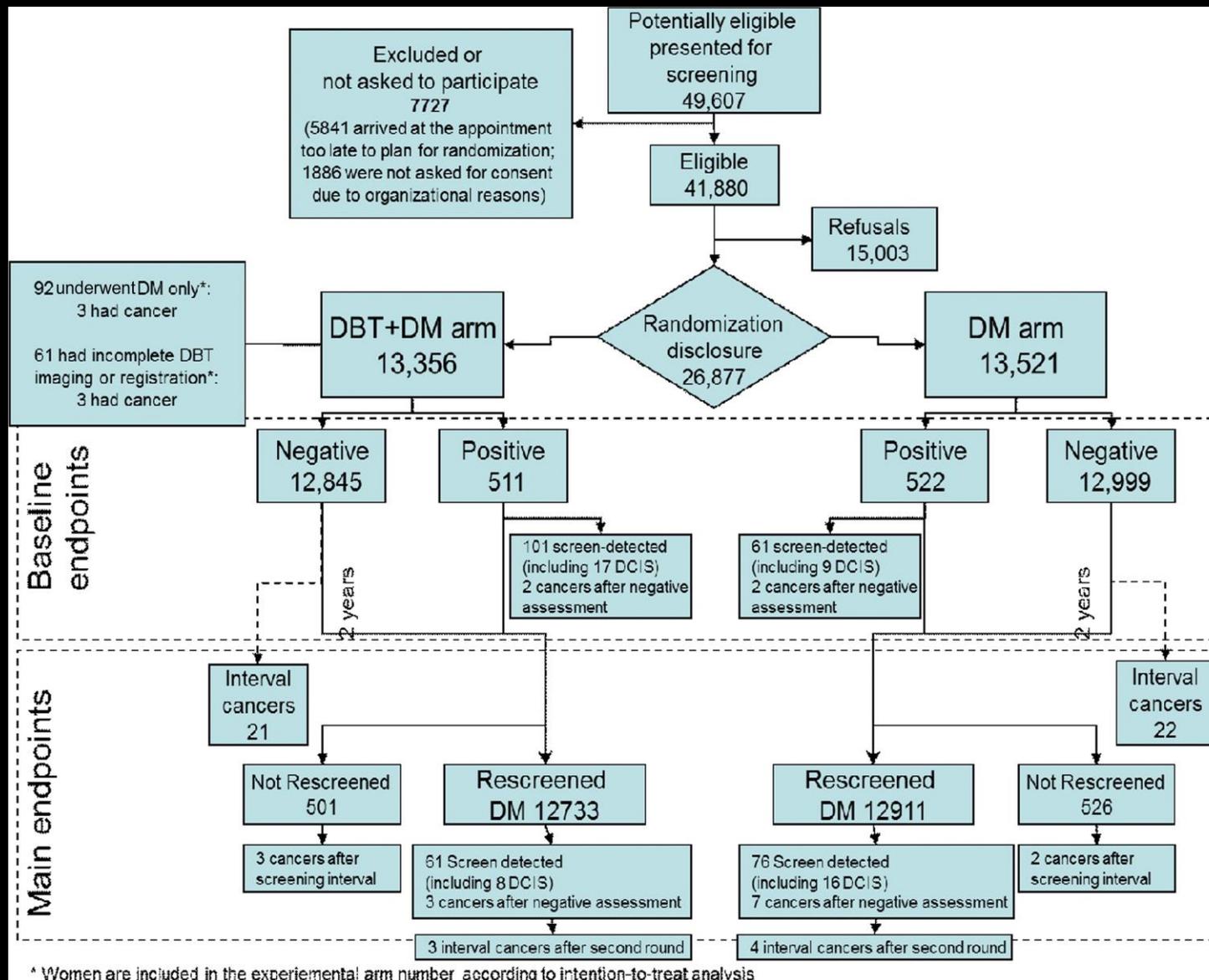
- Purpose: To compare interval and overall breast cancer incidence after screening with DBT + DM versus DM alone
- Published in Radiology: Breast Imaging
- Randomized Control Trial
- 2018 study: Detection rate was about 90% higher with DBT+DM than with DM alone

# 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



# 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  $\pm$  SD for the women in both arms was  $55 \pm 7$ .
- 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

Published this past Tuesday (6/14)!

JAMA | **Original Investigation**

## Association of Screening With Digital Breast Tomosynthesis vs Digital Mammography With Risk of Interval Invasive and Advanced Breast Cancer

Karla Kerlikowske, MD; Yu-Ru Su, PhD; Brian L. Sprague, PhD; Anna N. A. Tosteson, ScD; Diana S. M. Buist, PhD; Tracy Onega, PhD; Louise M. Henderson, PhD; Nila Alsheik, MD; Michael C. S. Bissell, PhD; Ellen S. O'Meara, PhD; Christoph I. Lee, MD; Diana L. Miglioretti, PhD

**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

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- Pattacini P, Nitrosi A, Giorgi Rossi P, et al. Digital Mammography versus Digital Mammography Plus Tomosynthesis for Breast Cancer Screening: The Reggio Emilia Tomosynthesis Randomized Trial. *Radiology*. 2018;288(2):375-385. doi:10.1148/radiol.2018172119
- Gennaro G, Bernardi D, Houssami N. Radiation dose with digital breast tomosynthesis compared to digital mammography: per-view analysis. *Eur Radiol*. 2018;28(2):573-581. doi:10.1007/s00330-017-5024-4
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- Kerlikowske K, Su YR, Sprague BL, et al. Association of Screening With Digital Breast Tomosynthesis vs Digital Mammography With Risk of Interval Invasive and Advanced Breast Cancer. *JAMA*. 2022;327(22):2220-2230. doi:10.1001/jama.2022.7672