# Synthetic/Reconstructed Mammography

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# Background: Breast Cancer Incidence and Screening

US female invasive breast cancer cases were estimated to reach 287,850 in 2022

- Estimated 43,780 deaths from the disease

Death rate has decreased by 37% since mid 1980s, largely attributable to screening

- Falling on average 1.8% each year (2006-2015)

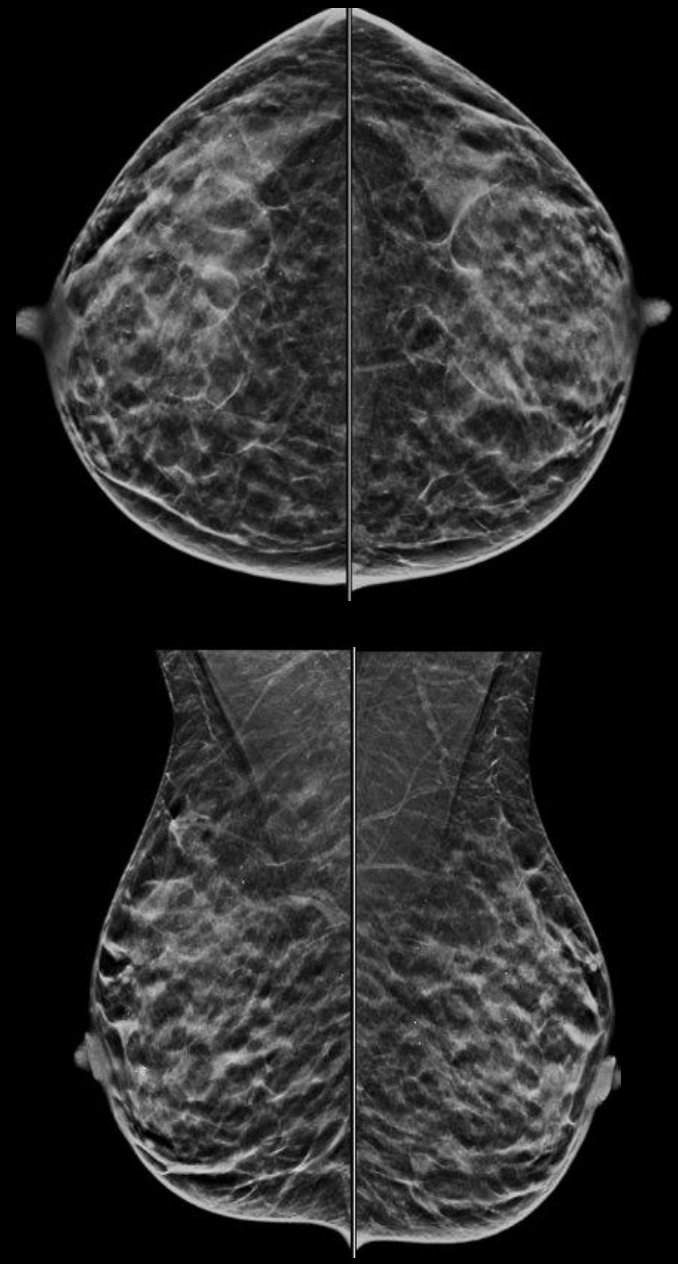
# Background: Mammography

- Annual mammography has shown the ability to reduce mortality from breast cancer at a rate of 15 to 35 percent
- Screening mammograms have been shown to miss up to 20% of breast cancers
  - Up to 50% in dense breast tissue
- Average recall rates for digital mammography range at 8.7-16.2%
  - Recall rates for mammography recommended to be at 10% or less

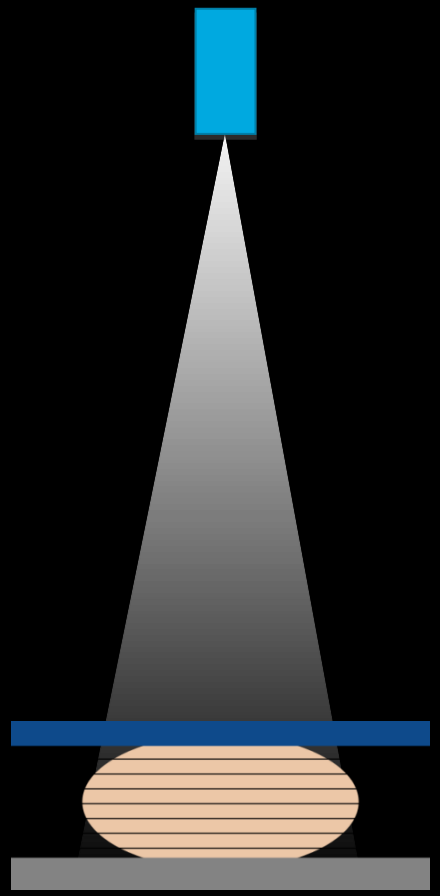
# Shortcomings of Mammography

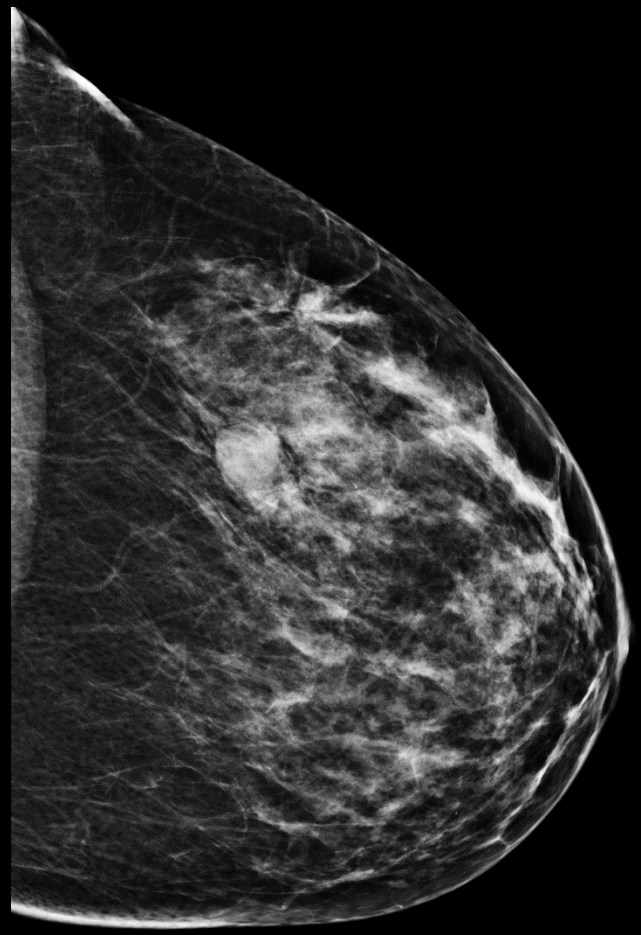
- Tissue superimposition is a major shortcoming of 2D imaging
  - Can obscure a lesion making it more difficult to visualize or rendering it completely mammographically occult
  - Can generate false positives, resulting in unnecessary recalls

- New breast imaging technologies try to address these limitations



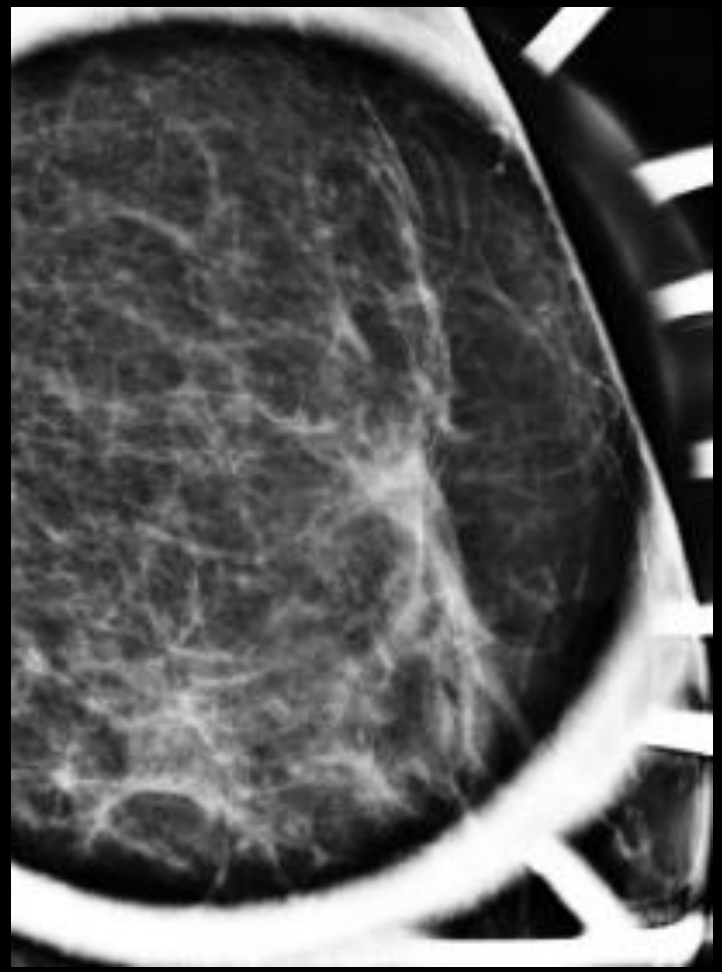
# 2D FFDM image is acquired under the same compression after the projections



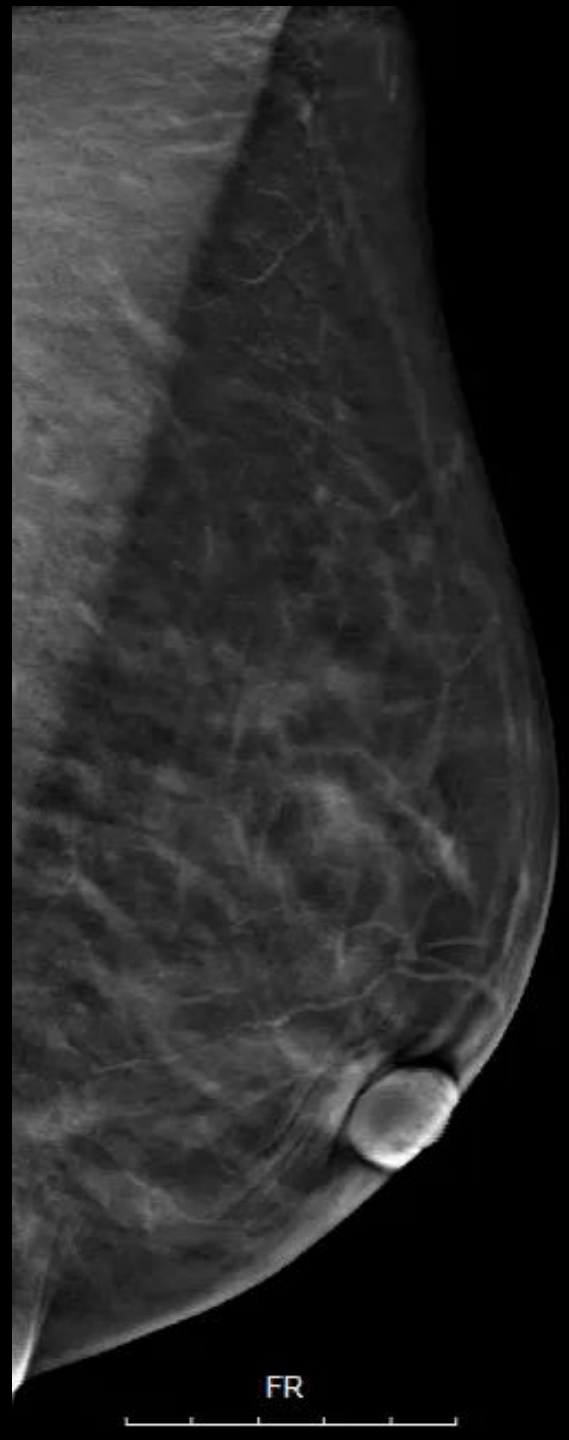


2D mammogram

Courtesy of Hologic



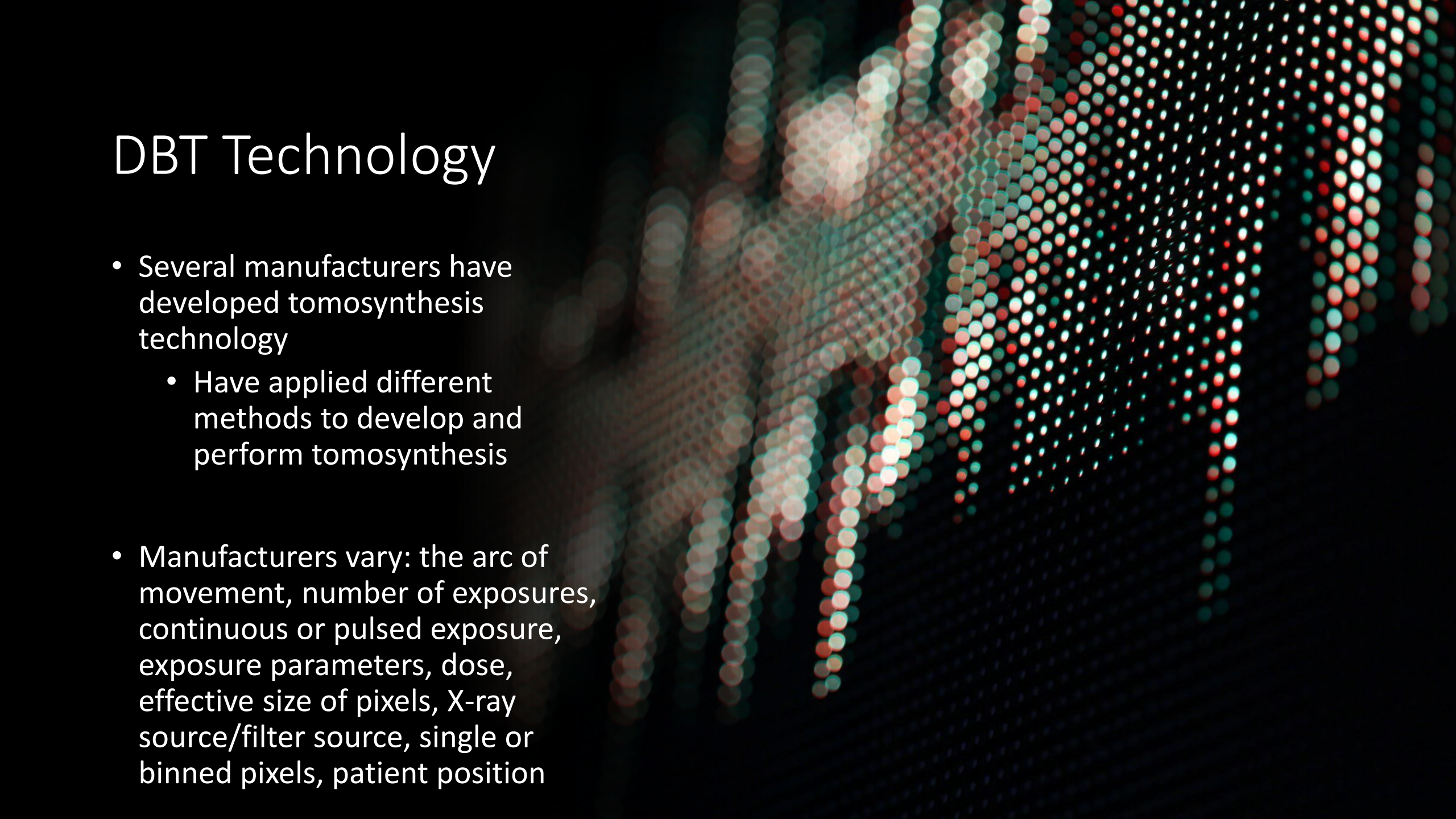
Overlap



# DBT Technology

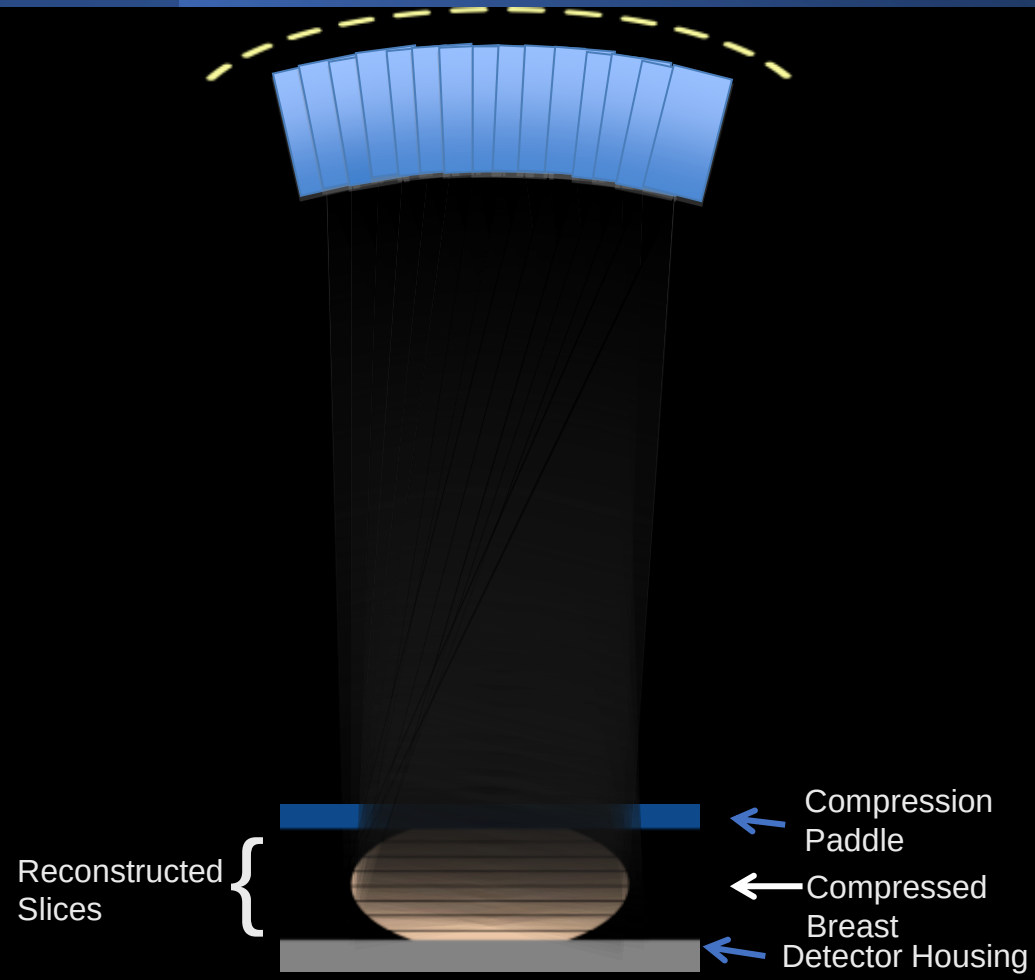
- Several manufacturers have developed tomosynthesis technology
  - Have applied different methods to develop and perform tomosynthesis

- Manufacturers vary: the arc of movement, number of exposures, continuous or pulsed exposure, exposure parameters, dose, effective size of pixels, X-ray source/filter source, single or binned pixels, patient position



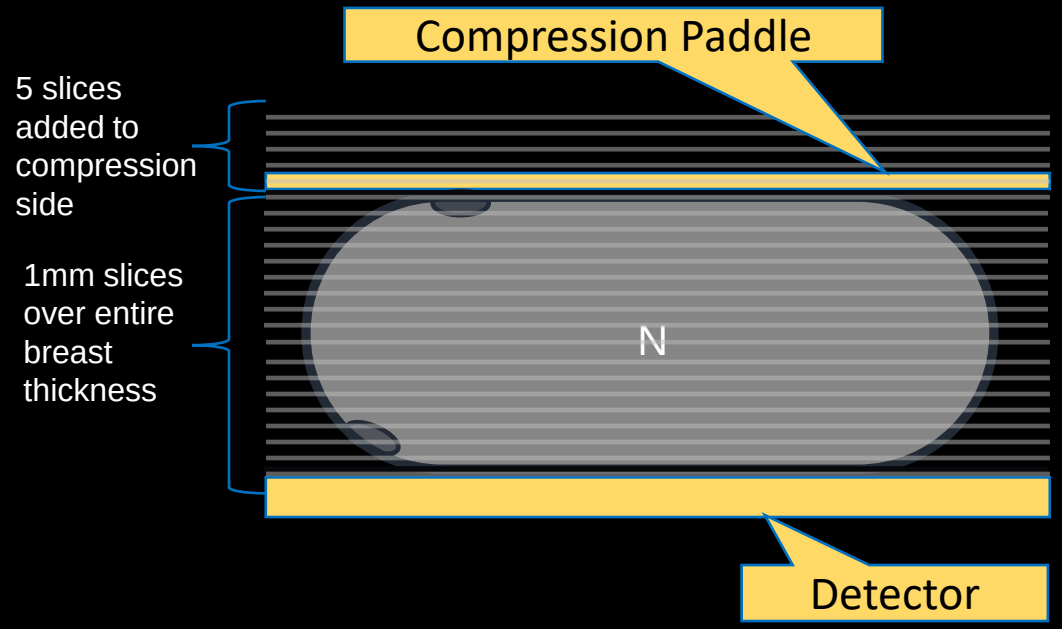
# DBT Principles: Hologic

- X-ray tube moves in an arc across the breast
- A series of low dose images are acquired from different angles to create a tomosynthesis image set
- A 2D image is acquired by an additional exposure, or generated from the tomosynthesis image set without an additional exposure
- Total dose is within allowable limits



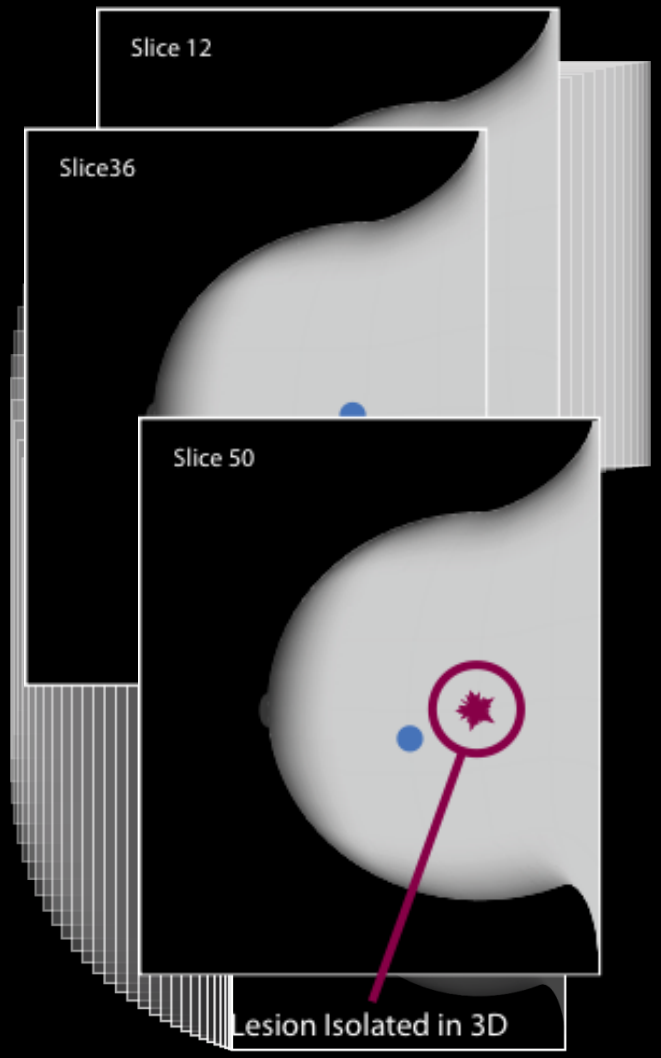

Courtesy of Hologic

# Reconstruction




- Tomosynthesis projections reconstructed into 1 mm slices for entire thickness of breast
- Additional five (5mm) are added at the compression side, to assure the entire breast is reconstructed
  - Takes into account uncertainties of compression thickness

# DBT can improves visibility by reducing tissue superimposition




Courtesy of Hologic

# Background: DBT Advantages and Disadvantages

Decreased recall rates

Improved cancer detection rates

Improved visualization

Increased dose with Combination DBT

- Synthetic views when used in place to 2D brings dose back down

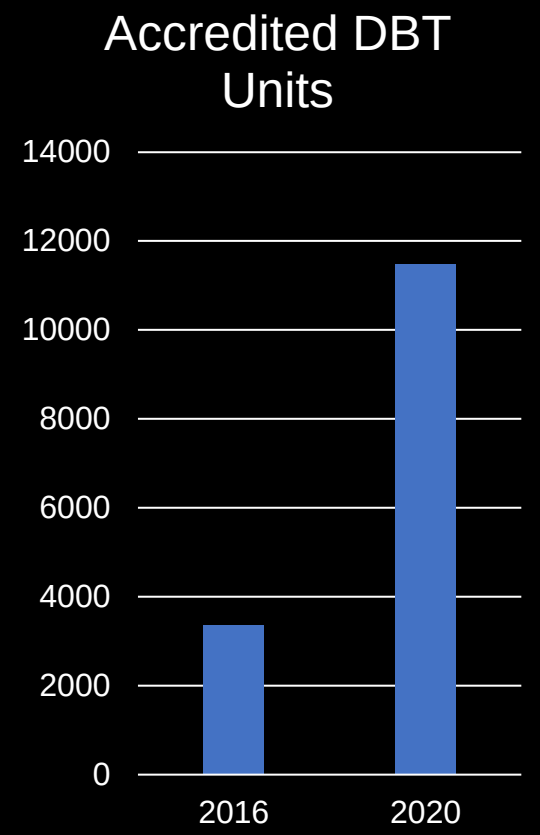
Increased reading time – though decreases with experience

Increased IT and storage needs

Hooley RJ, Durand MA, Philpotts LE. Advances in Breast Imaging AJR 2017;208

# DBT Use in the United States

| | June 2016 | April 2023 |
|---|---|---|
| Total certified facilities | 8,740 | 8,832 |
| Total accredited units | 16,155 | 24,825 |
| Certified facilities with FFDM | 8,506 | 8,829 |
| Accredited FFDM units | 12,508 | 13,348 |
| **Certified facilities with DBT** | **2,444** | **7,601** |
| **Accredited DBT units** | **3,362** | **11,474** |




MQSA National Statistics. https://www.fda.gov/radiation-emitting-products/mqsa-insights/mqsa-national-statistics. Accessed February 24th, 2020.

# Early DBT Screening Studies

| Author, year | Recall Rate 2D (%) | Recall Rate DBT (%) | CDR/1000 2D | CDR/1000 DBT | Absolute CDR |
|---|---|---|---|---|---|
| Ciatto, 2013 (multicenter) | 5.5 | 3.5 | 5.3 | 8.1 | 2.8 |
| Friedewald, 2014 (multicenter) | 10.7 | 9.1 | 4.2 | 5.4 | 1.2 |
| Skaane, 2013 (single center) | 6.1 | 5.3 | 6.1 | 8.0 | 1.9 |
| Rose, 2013 (single center) | 8.7 | 5.5 | 4.0 | 5.4 | 1.4 |
| McCarthy, 2014 (single center) | 10.4 | 8.8 | 4.6 | 5.5 | 0.9 |
| Sharpe, 2016 (single center) | 7.5 | 6.1 | 3.5 | 5.4 | 1.9 |

*General consensus of studies – increased breast cancer detection, reduced recall rate*

Hooley, R. J., Durand, M. A., & Philpotts, L. E. (2017). Advances in digital breast tomosynthesis. American Journal of Roentgenology, 208(2), 256-266.

# DBT Performance- Radiology 2022

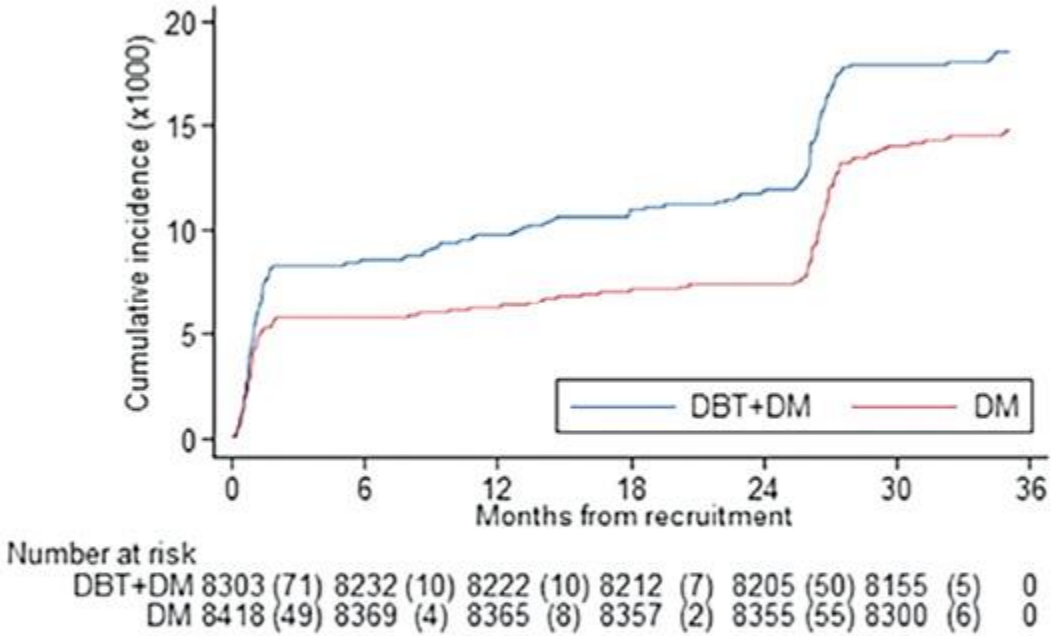
Randomized trial comparing breast cancer incidence and interval cancers after DBT plus mammography (DM) vs. mammography alone

Women attending screening were randomized to one round of DBT plus DM (experimental arm) or to DM (control arm)

All were rescreened with DM after 12 months (women aged 45–49 years) or after 24 months (50–69 years)

Pattacini P, et al. A Randomized Trial Comparing Breast Cancer Incidence and Interval Cancers after Tomosynthesis Plus Mammography versus Mammography Alone. Radiology 2022; online first.

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




Cumulative incidence of breast cancer in women aged 50-69.

- Baseline cancer detection was higher in women undergoing DBT plus digital mammography (DM) versus DM alone (101 of 13 356 vs 61 of 13 521 women; relative detection, 1.7).
- After rescreening with DM after 12 months (in women aged 45-49 years) or 24 months (in women aged 50-69 years), interval cancer incidence was similar in both arms (21 vs 22 cancers; relative incidence, 0.97).
- Cumulative incidence remained higher for women > 50 in the DBT plus DM arm (153 vs 124 cancers; relative incidence, 1.2) but was similar for women aged 45-49 (36 vs 41 cancers; relative incidence, 0.89)

**Pattacini P et al. Published Online:** February 1, 2022
https://doi.org/10.1148/radiol.211132

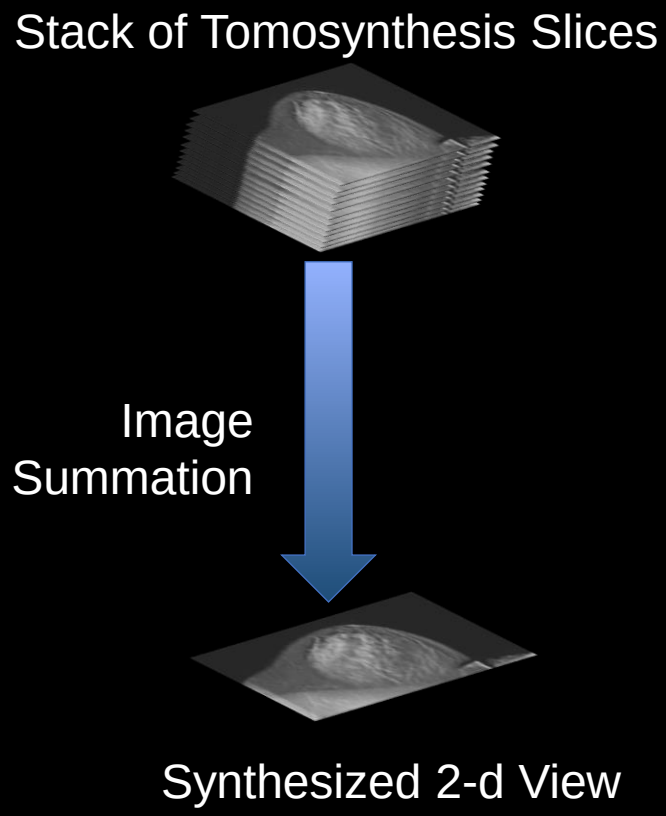
Radiology

- *In women younger than 50 years, benefits of early diagnosis with tomosynthesis plus mammography screening seemed appreciable and could increase diagnosis of slow-growing, invasive cancers for women over age 50*

# Introduction of Synthetic 2D Imaging

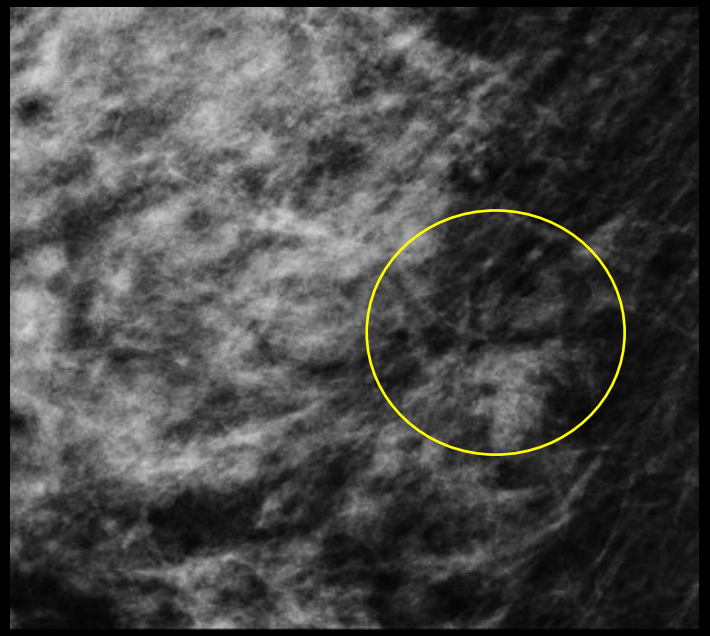
- First to be approved: FDA approved replacing FFDM with C-View (Hologic, Inc.) for screening in May 2013

- How does it work?
  - Perform a standard tomosynthesis scan (existing system)
  - Reconstruct tomosynthesis slices (existing system)
  - Results in synthesized 2D image

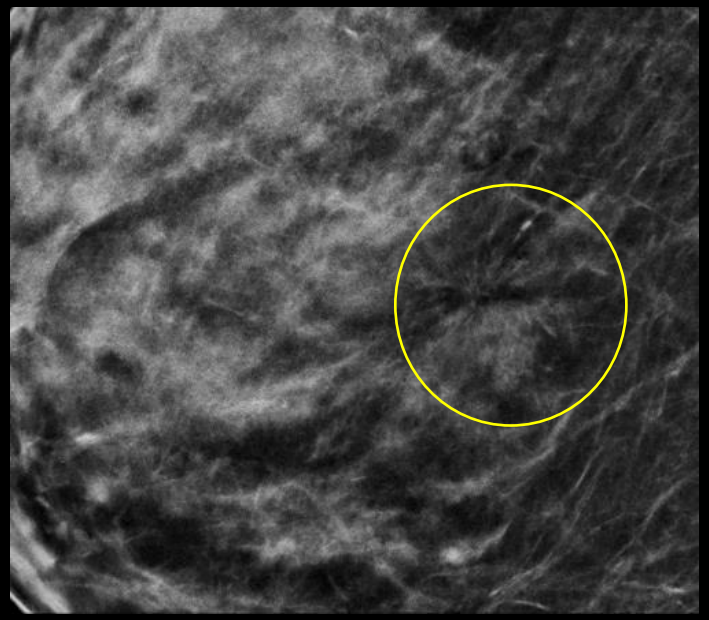


# Synthetic View Algorithm

- Enhances structures i.e. architectural distortions and spiculations; high-contrast features (calcifications)
  - Allows for improved feature visibility



FFDM



Synthetic View

# Versions of Synthesized 2D Images

| | |
|---|---|
| **Intelligent 2D™ software** | • Newest version of synthesized 2D software<br>• Created from high resolution Clarity HD dataset<br>• 70-micron images from 70-micron reconstructions |
| **C-View™ software** | • First version of synthesized 2D software<br>• Created from standard tomosynthesis dataset<br>• 100-micron images from 100-micron reconstructions |
| **Both serve the same purpose** | • Provide 2D image calculated from tomosynthesis dataset<br>• Reduce radiation exposure – eliminates FFDM exposure |

Both used the same way clinically

# Image Resolution

| Image Type | Image Resolution (in µ) |
|---|---|
| Conventional FFDM | 70 |
| C-View™ image | ~100 |
| Intelligent 2D™ image | 70 |

# Dose with Synthesized View

- Incorporating synthetic view in place of FFDM reduces the dose by nearly half
- Substantially less dose than imaging combination mode

Svahn TM, et al. Review of radiation dose estimates in digital breast tomosynthesis relative to those in two-view full-field digital mammography. Breast 2015; 24: 93-99.

# Accuracy of Synthetic View [Simon AJR 2019]

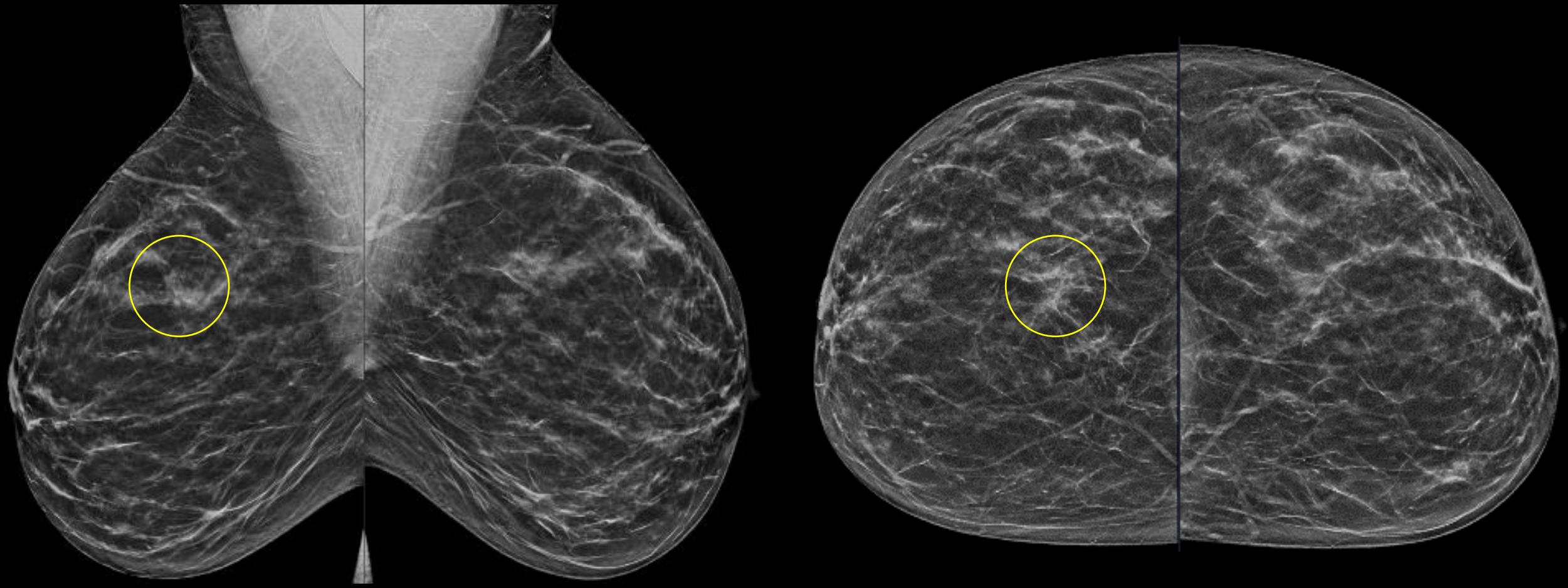
- Assessed the diagnostic accuracy of DBT plus synthetic 2D mammography compared with that of DBT plus FFDM in the U.S. screening population
- No statistically significant difference in diagnostic accuracy between DBT+ Synthesized 2D and DBT+FFDM
- Concluded DBT plus synthetic 2D mammography performs as well as and not worse than DBT plus FFDM in diagnostic accuracy and can be used for decreasing radiation without decreasing performance

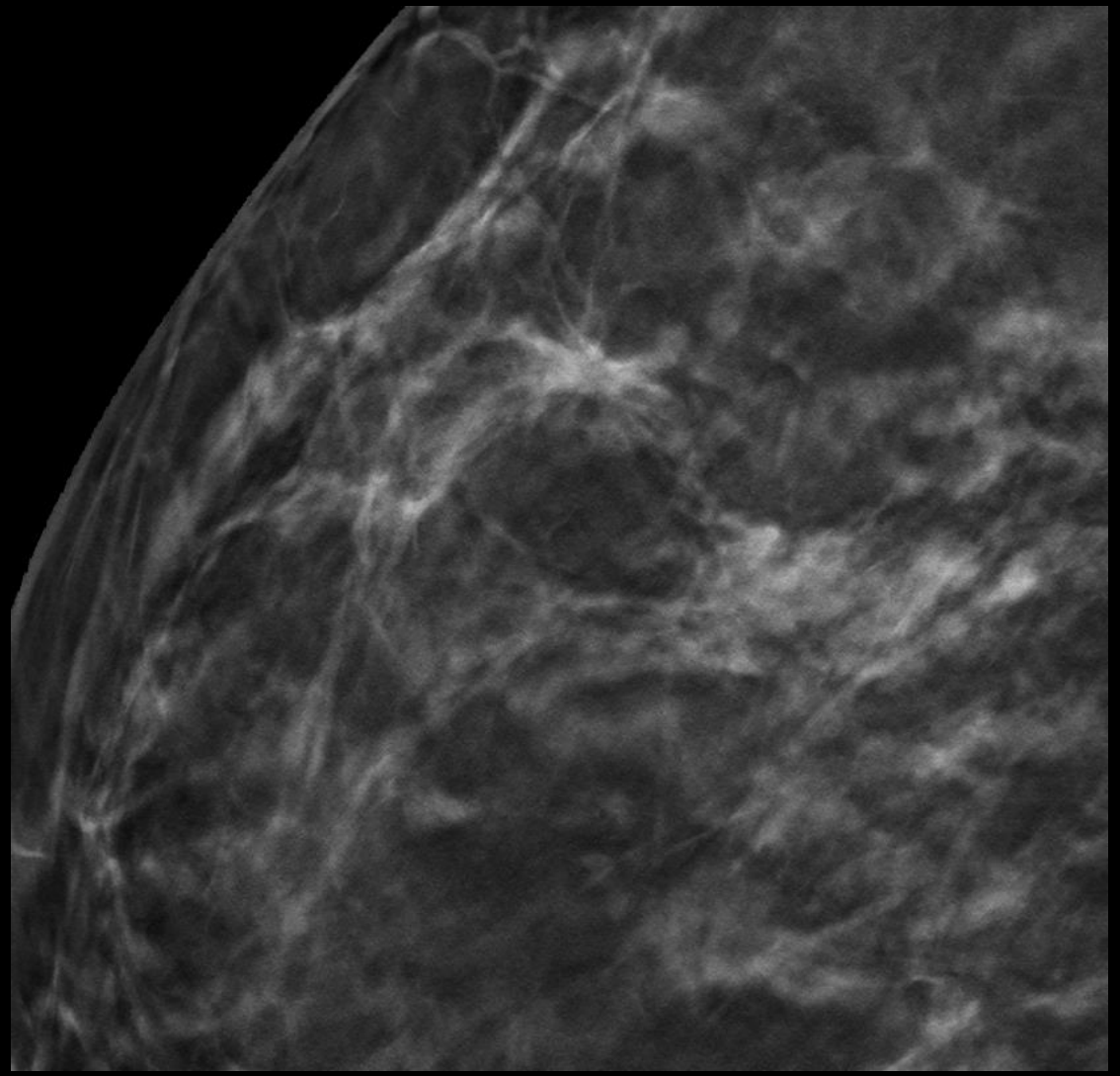
Simon, Katherine, et al. Accuracy of Synthetic 2D Mammography Compared With Conventional 2D Digital Mammography Obtained With 3D Tomosynthesis. American Journal of Roentgenology 212.6 (2019): 1406-1411.

# Architectural Distortion

- Synthesized mammography algorithm enhances appearance of AD
  - Confirmation in both planes and with review of DBT slices can help to avoid false positive recalls
- Choudhery et al [AJR 2017] – PPV for malignancy of 34.6%
- Bahl et al [AJR 2021] – PPV of AD for malignancy lower than for DBT-detected AD than DM-detected AD (50.7% v. 73.6% respectively)

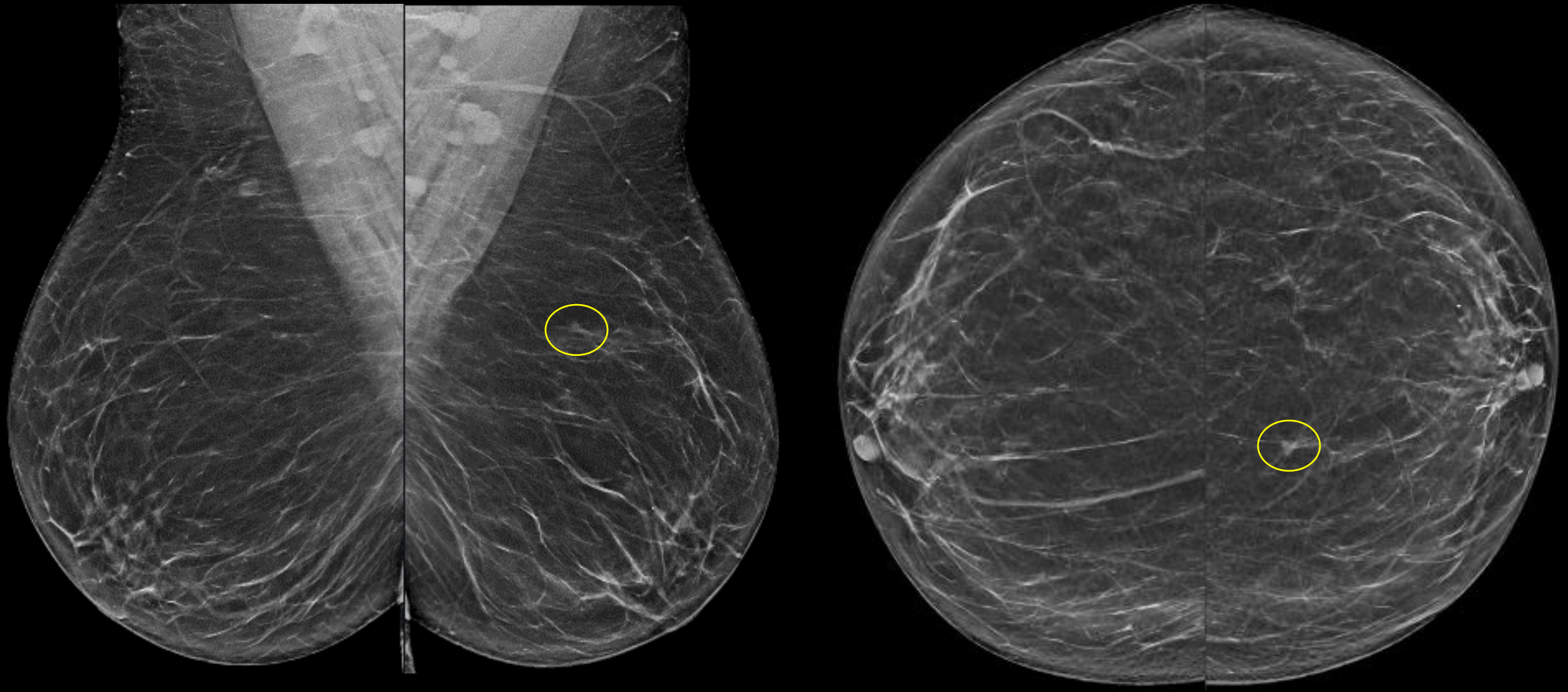
41-year-old presents for routine screening mammography

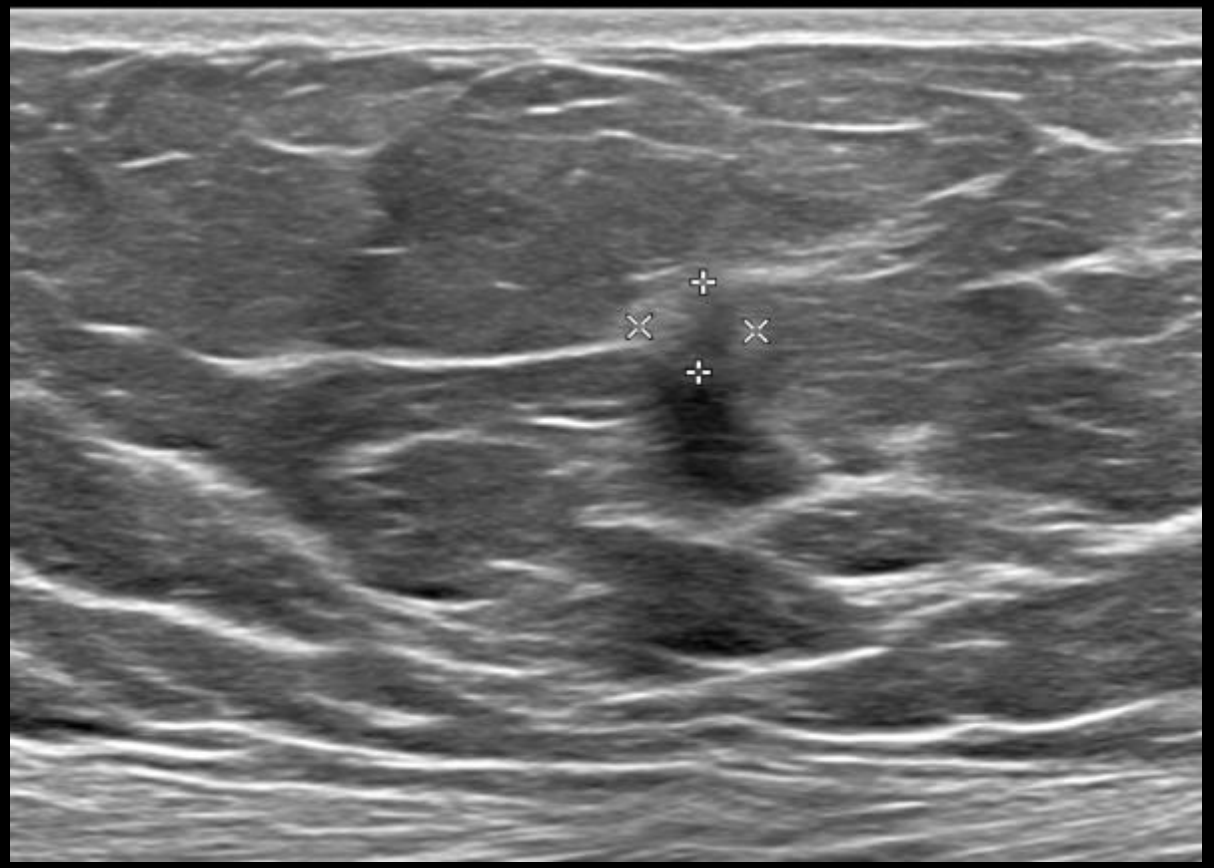




No US correlate – Invasive lobular carcinoma grade 2

58-year-old presents for screening mammography





Left 10:30 Invasive ductal carcinoma grade 2

# The Challenge of DBT-detected AD- JBI 2022

Compared readers' performances when detecting AD on DBT

- determine the risk of malignancy of DBT with SM–detected AD and evaluate imaging features that are associated with malignancy risk

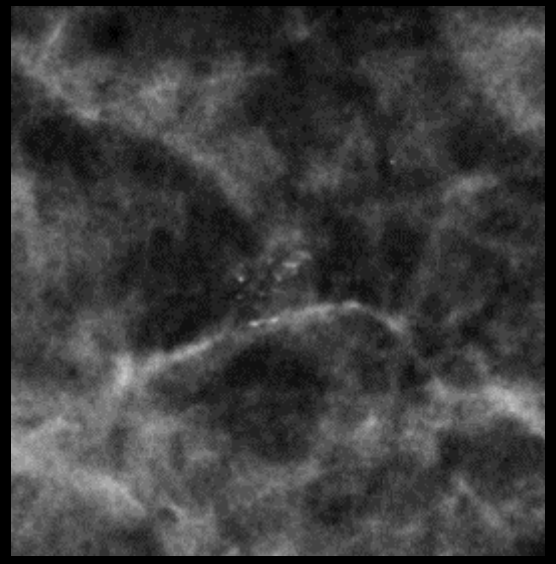
Overall agreement for the presence of AD was fair (0.253)

Majority (55.5%) of the malignant ADs were associated with asymmetries (36.1%), calcifications (11.1%), or both (8.3%), compared to nonmalignant ADs (31.0%; P = 0.038)

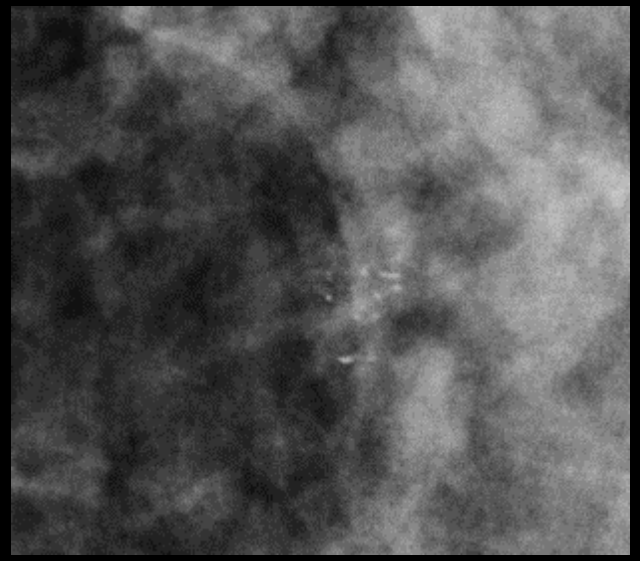
PPV of DBT with SM-detected AD for malignancy was 21.8%, 18.8% for DBT-detected AD, and 26.0% for SM-detected AD (not statistically significant, P = 0.258)

Feliciano-Rivera YZ, et al. The Challenge of Digital Breast Tomosynthesis-Detected Architectural Distortion of the Breast: Inter-reader Variability and Imaging Characteristics That May Improve Positive Predictive Value. JBI 2022; 4(3): 263-272.

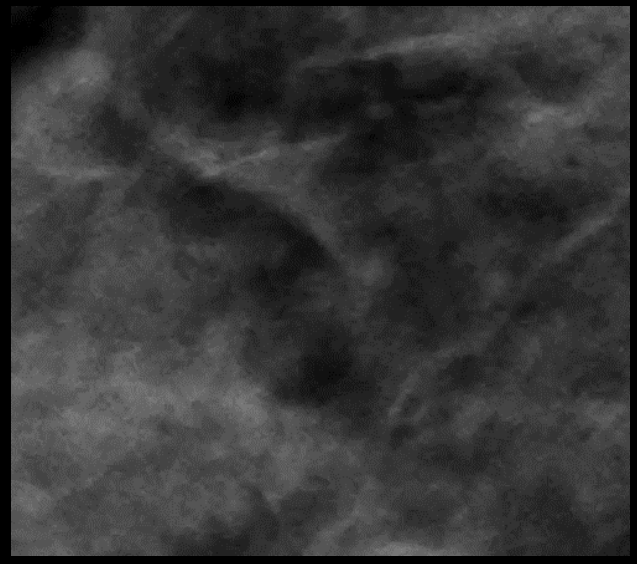
# Calcifications on Synthetic View



Synthetic view MLO



FFDM RMML



MLO DBT slices

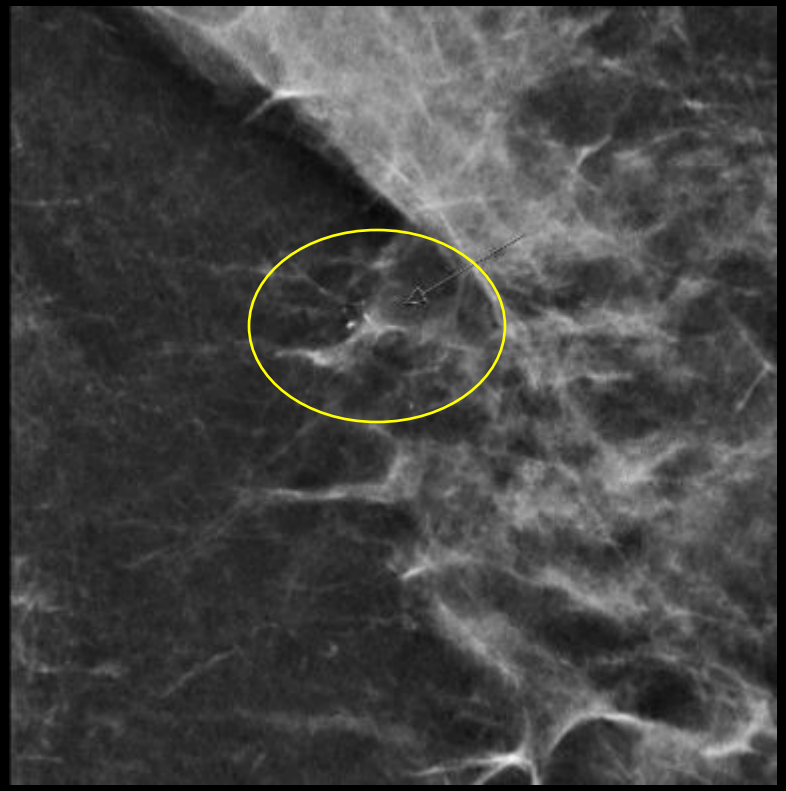
# Pseudo-Calcifications

Algorithm used to generate a s2D image enhances objects above a certain density threshold on s2D - Durand

Pseudo-calcifications are a recognized synthesized mammography artifact

| | |
|---|---|
| When questioning, helpful to confirm identification in both planes, as well as on DBT slices | Pseudo-calcifications will not be identifiable on both planes and may align with ligaments or vessels on tomosynthesis |

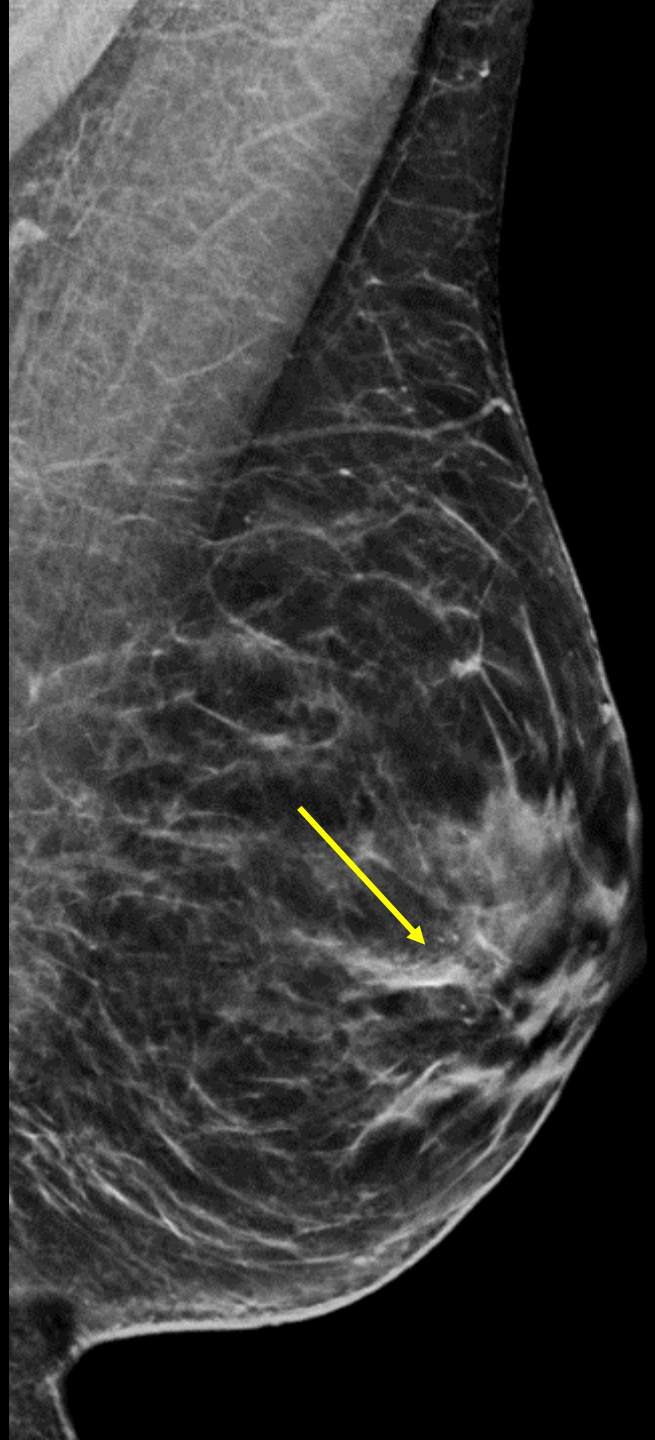
# Pseudo-calcs?

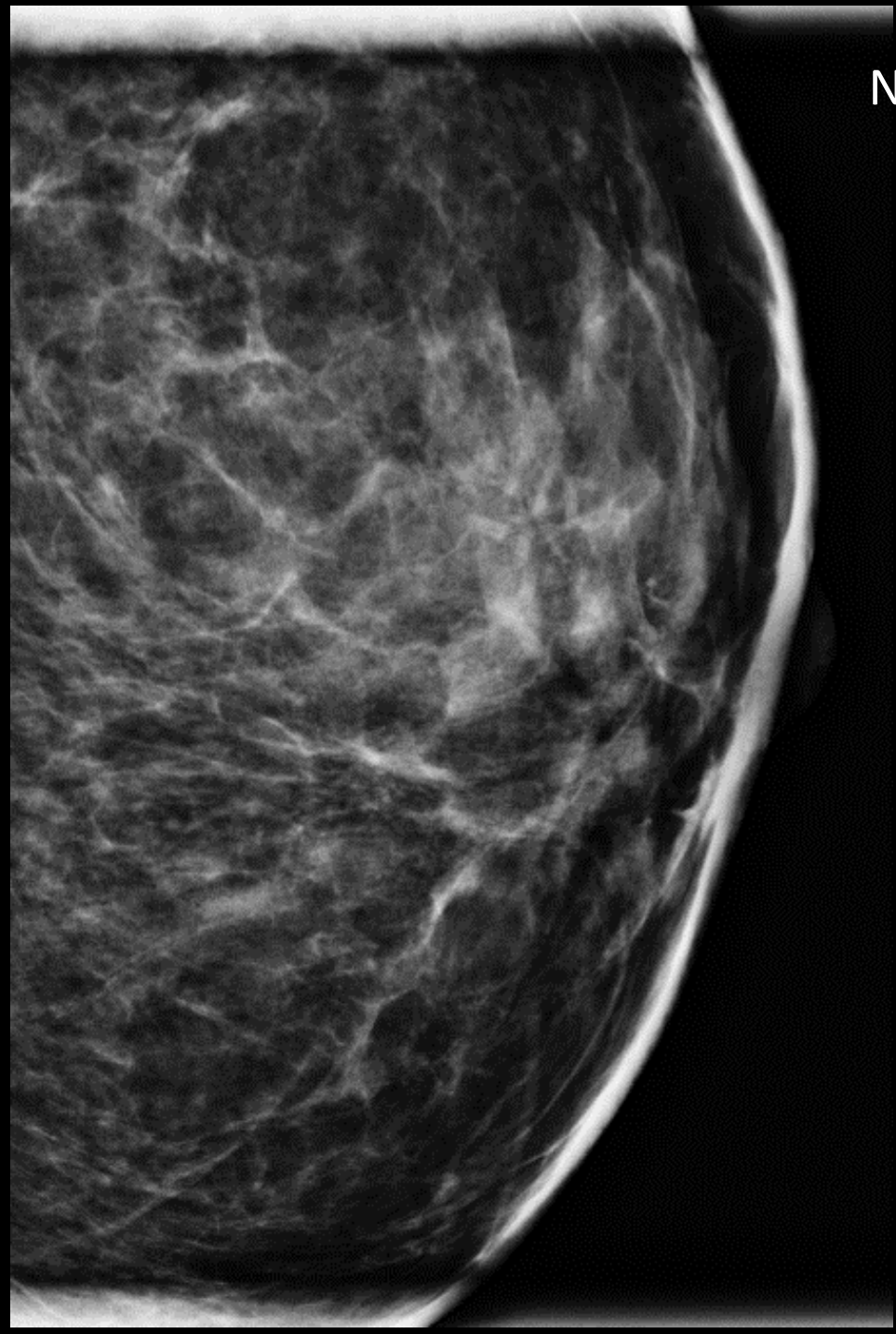


Synthetic view CC

FFDM spot compression CC

Possible area of calcs identified on screening mammogram





No calcs on LMML

# Choi et al. [Eur Radiol 2018]

- No significant difference in lesion conspicuity scores between SM and DM with DBT, or alone
  - No significant differences in readers' AUCs

*DBT with SM may be sufficient for diagnosing microcalcifications, without DM*

Choi JS, et al. Comparison of synthetic and digital mammography with digital breast tomosynthesis or alone for the detection and classification of microcalcifications. Eur Radiol 2018;

# Reader Study- Amorphous Calcifications [Renaldo JBI 2022]

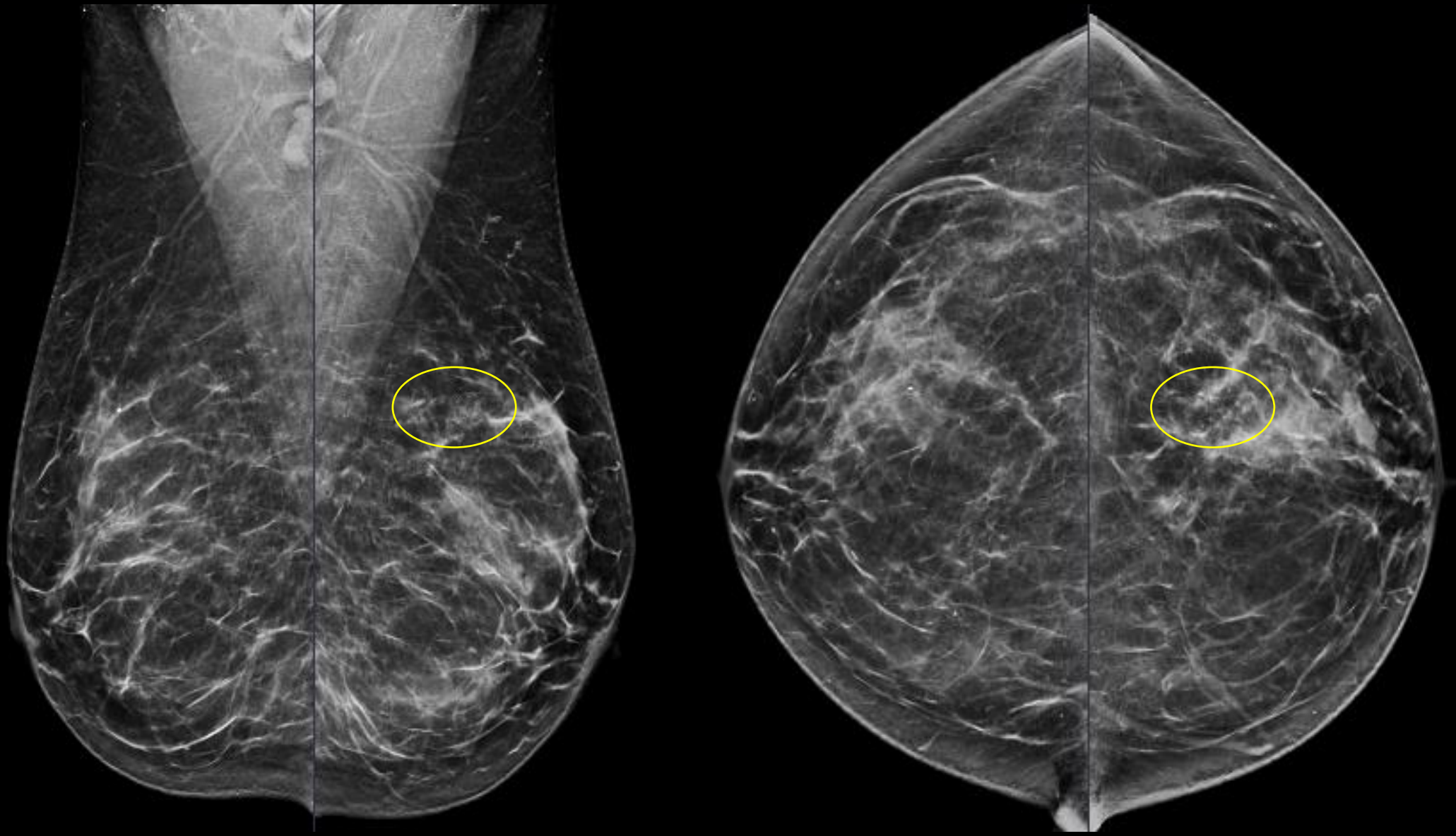
- No difference in detection rates of amorphous calcifications between 2D DM and s2D
- Amorphous calcifications were more visible on s2D than 2D DM
- s2D mammography was not inferior to 2D DM in the identification or assessment of level of suspicion of amorphous calcifications

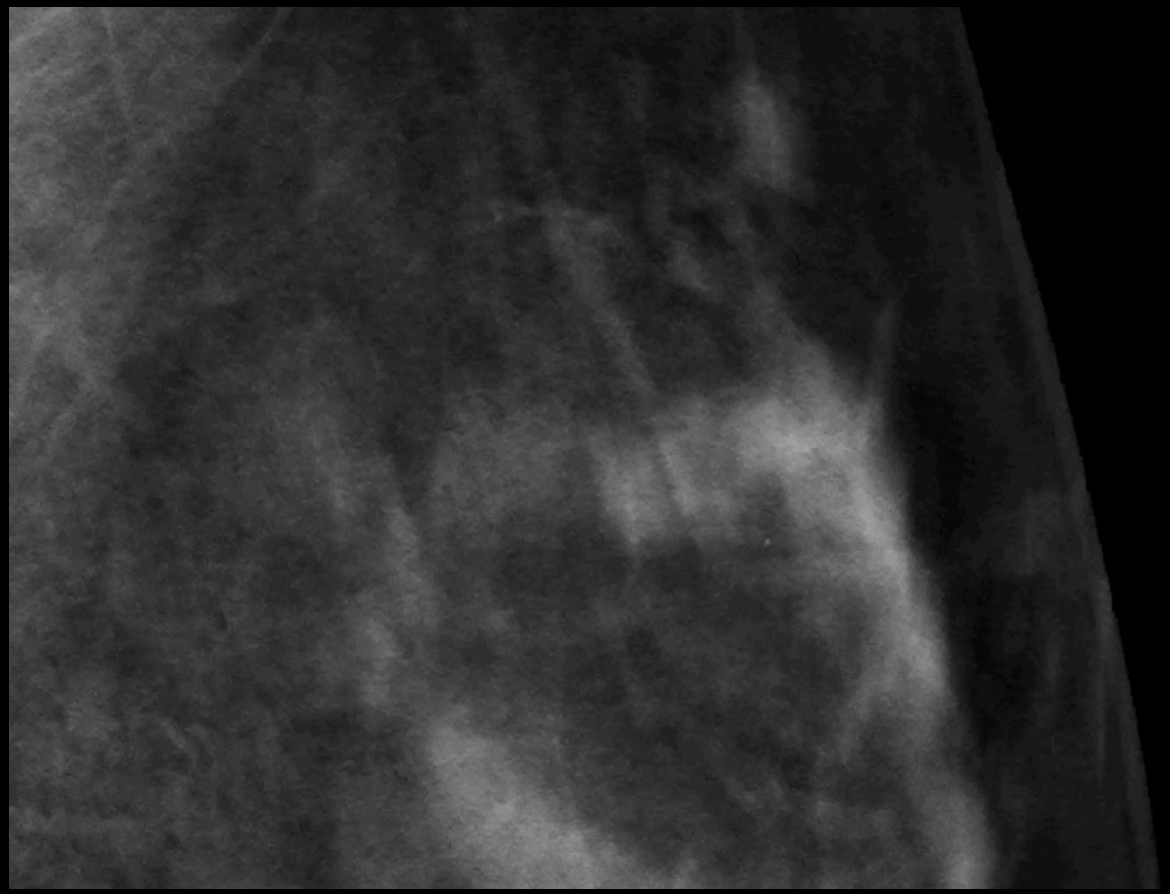
**Table 1.** Concordance Between Calcifications Detected by Radiologist on Screening 2D Digital Mammography (2D) or Synthetic 2D (s2D) Mammography and True Positive[a] Calcifications

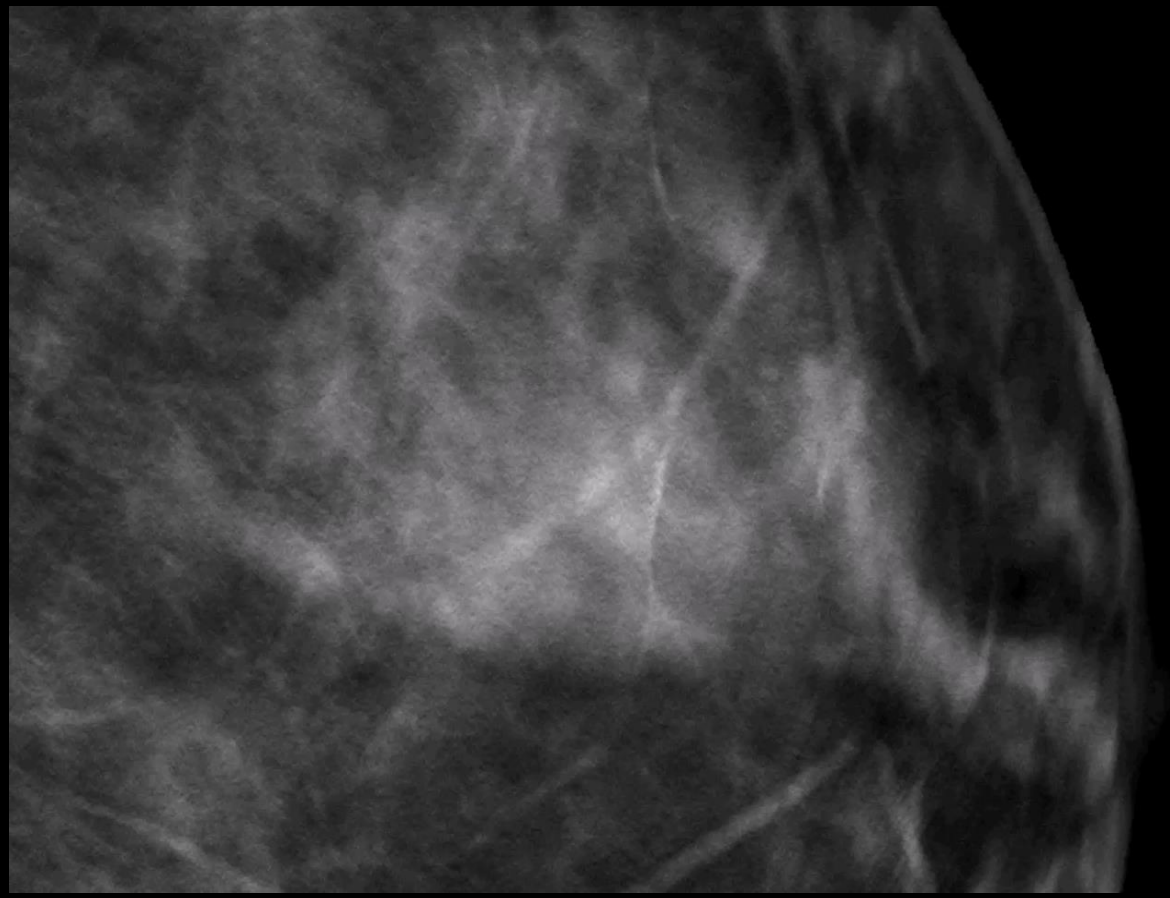
| Reader | Recall Rate on 2D (%) | True Positive[a] Rate on 2D (%) | False Negative[b] Rate on 2D (%) | Recall Rate on s2D (%) | True Positive[a] Rate on s2D (%) | False Negative[b] Rate on s2D (%) | McNemar Test of Concordance of (2D vs. True) vs (s2D vs. True): Chi-square (*P*-value) |
|---|---|---|---|---|---|---|---|
| 1 | 23/36 (63.9) | 23/28 (82.1) | 5/28 (17.9) | 20/36 (55.6) | 20/28 (71.4) | 8/28 (28.6) | 1.29 ($P=0.257$) |
| 2 | 26/36 (72.2) | 25/28 (89.3) | 3/28 (10.7) | 23/36 (63.9) | 22/28 (78.6) | 6/28 (21.4) | 1.29 ($P=0.257$) |
| 3 | 18/36 (50.0) | 18/28 (64.3) | 10/28 (35.7) | 23/36 (63.9) | 23/28 (82.1) | 5/28 (17.9) | 2.78 ($P=0.096$) |
| 4 | 20/36 (55.6) | 19/28 (67.9) | 9/28 (32.1) | 19/36 (52.8) | 19/28 (67.9) | 9/28 (32.1) | 0.09 ($P=0.763$) |
| Combined | 87/144 (60.4) | 85/112 (75.8) | 27/112 (24.1) | 85/144 (59.0) | 84/112 (75.0) | 28/112 (25.0) | 0.00 ($P=1.000$) |

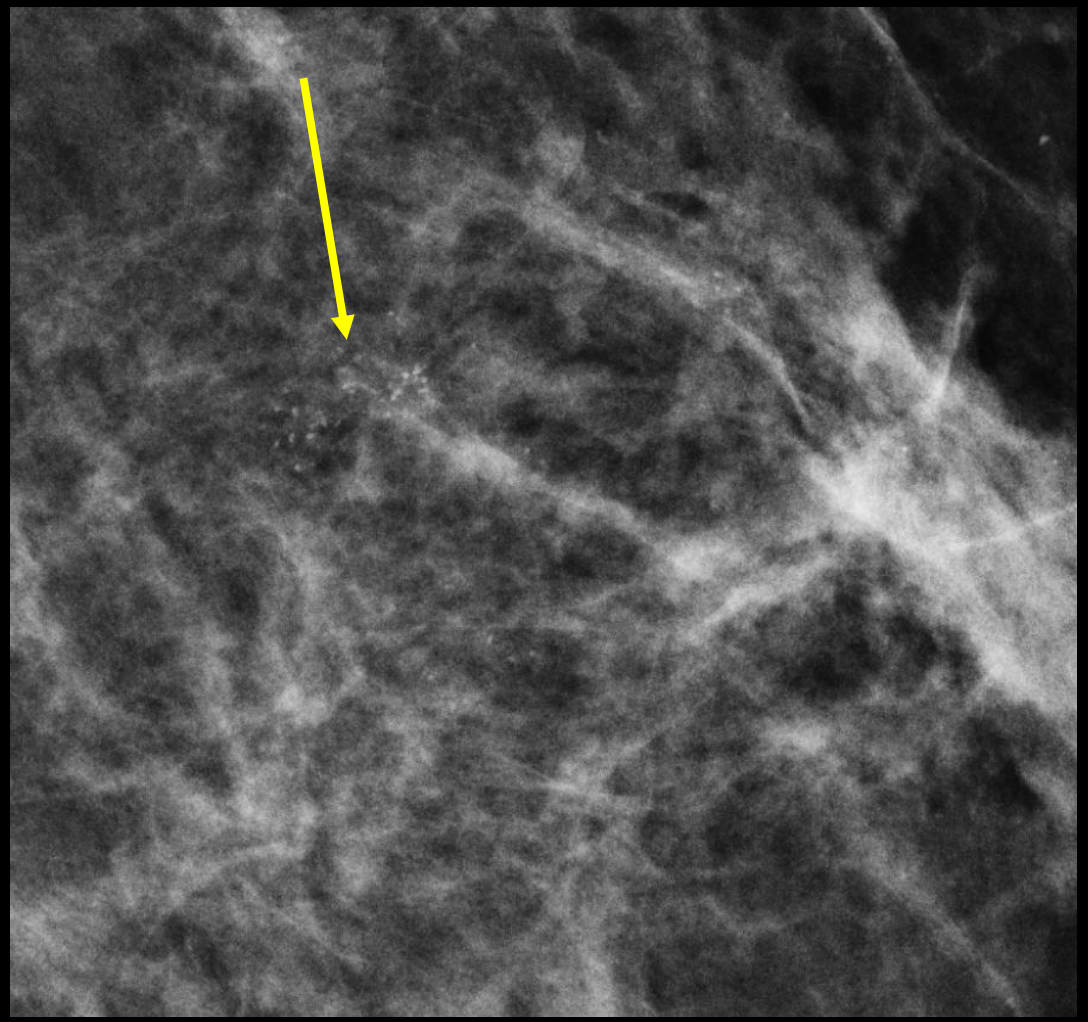
Renaldo A, et al. 2D or Synthetic 2D? A Reader Study of Visualization of Amorphous Calcifications. JBI 2022; 4(1): 19-24.

44-year-old presents for routine screening mammography









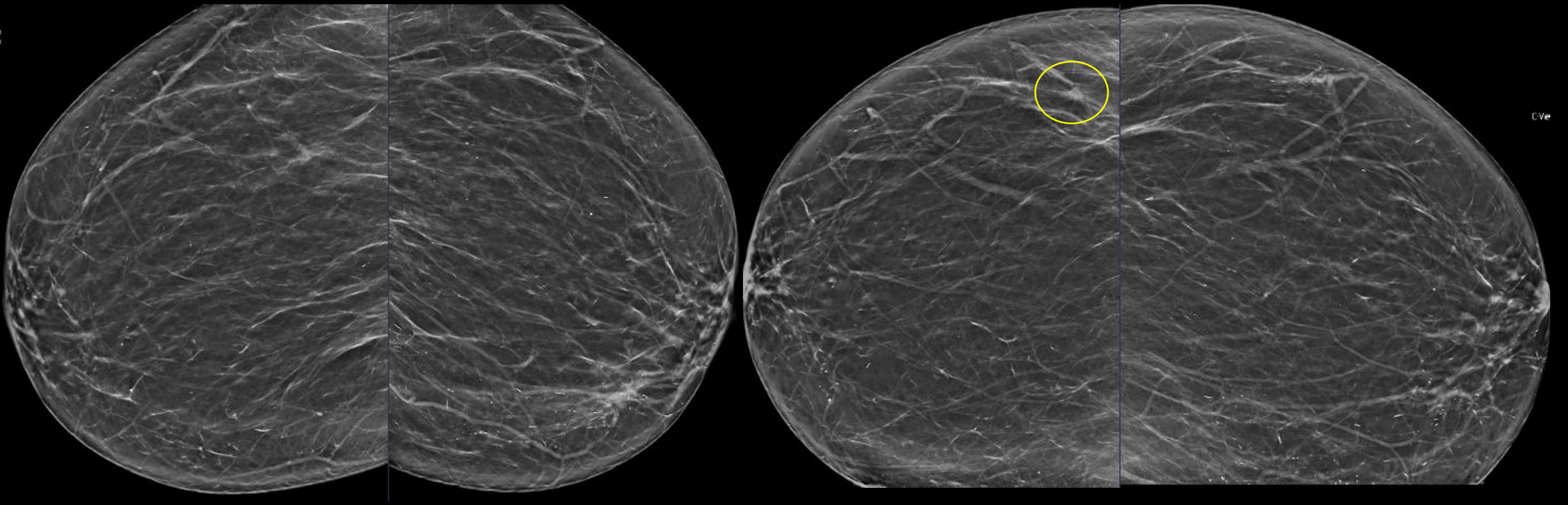
Left 12:30 intermediate grade DCIS cribriform and micropapillary types

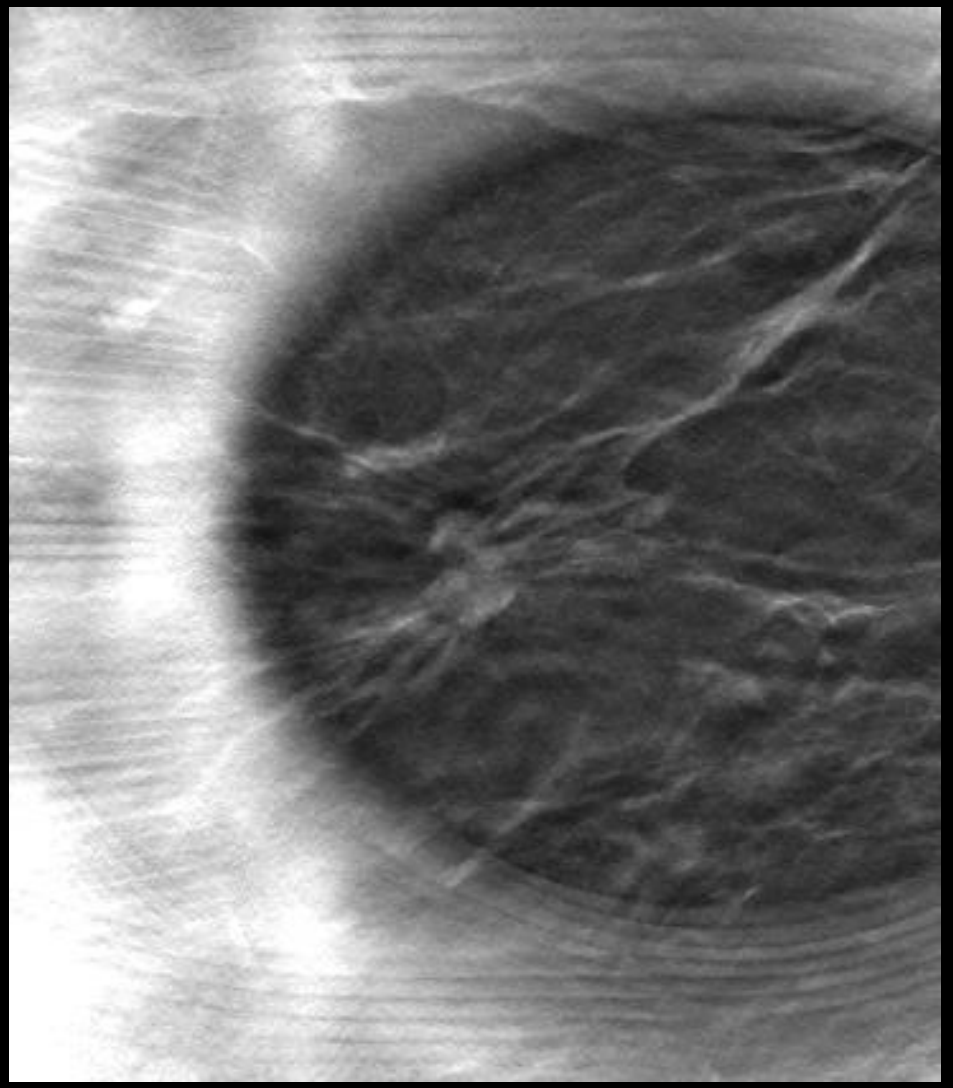
# Subtle Masses and Calcification clusters [Mackenzie Eur Radiol 2022]

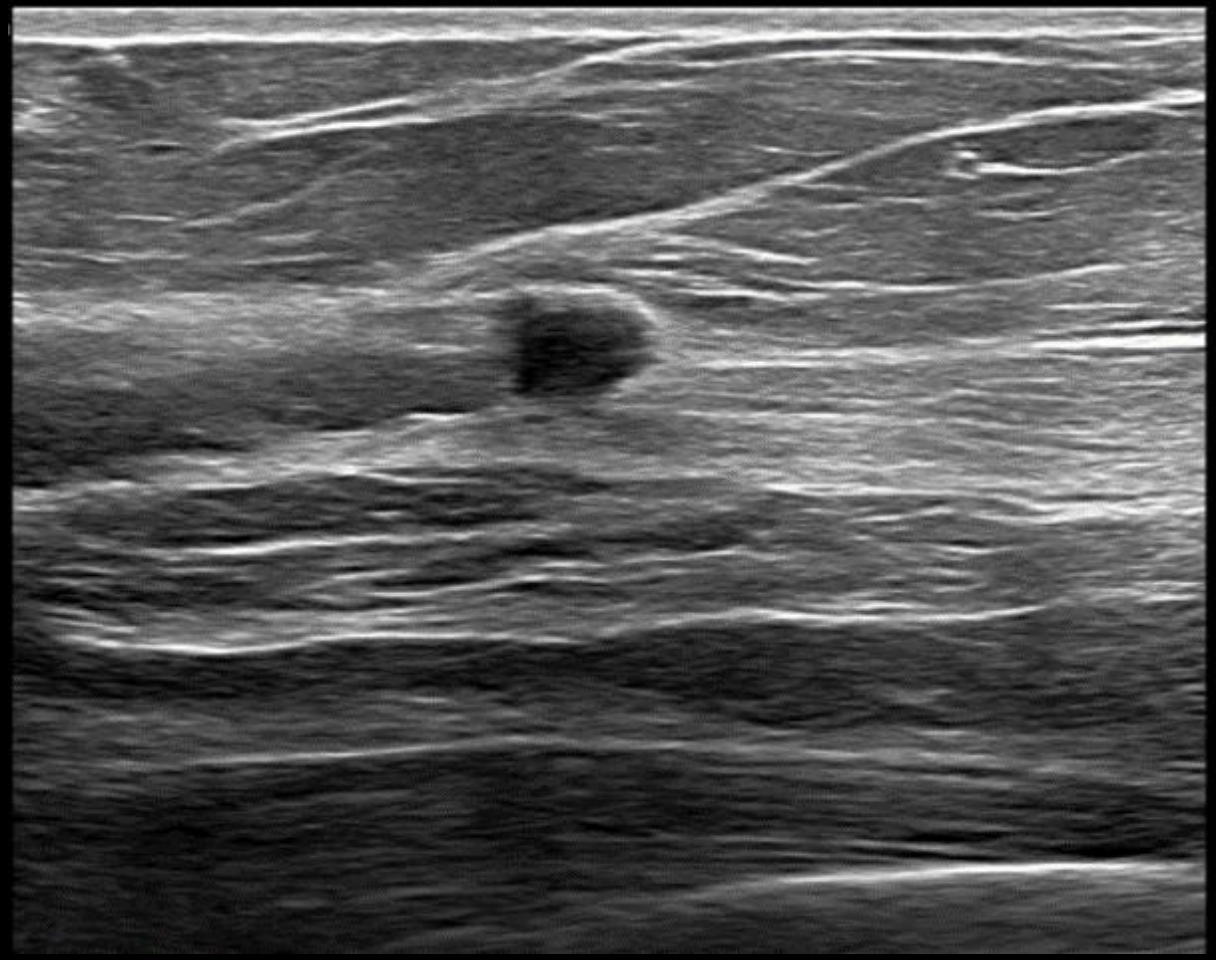
- Study designed to compare the detection of subtle lesions (calcification clusters or masses) when using the combination of DBT and SM with DM alone or combined with DBT
- Study found
  - detection of masses was significantly better using DBT than DM alone
  - detection of calcification clusters (grouped) was not significantly different between DM and SM combined with DBT

Mackenzie A, et al. Virtual clinical trial to compare cancer detection using combinations of 2D mammography, digital breast tomosynthesis, and synthetic 2D imaging. Eur Radiol 2022; 32: 806-814.

58-year-old presents for screening mammography







Right 9:00 – Invasive mammary carcinoma grade 2

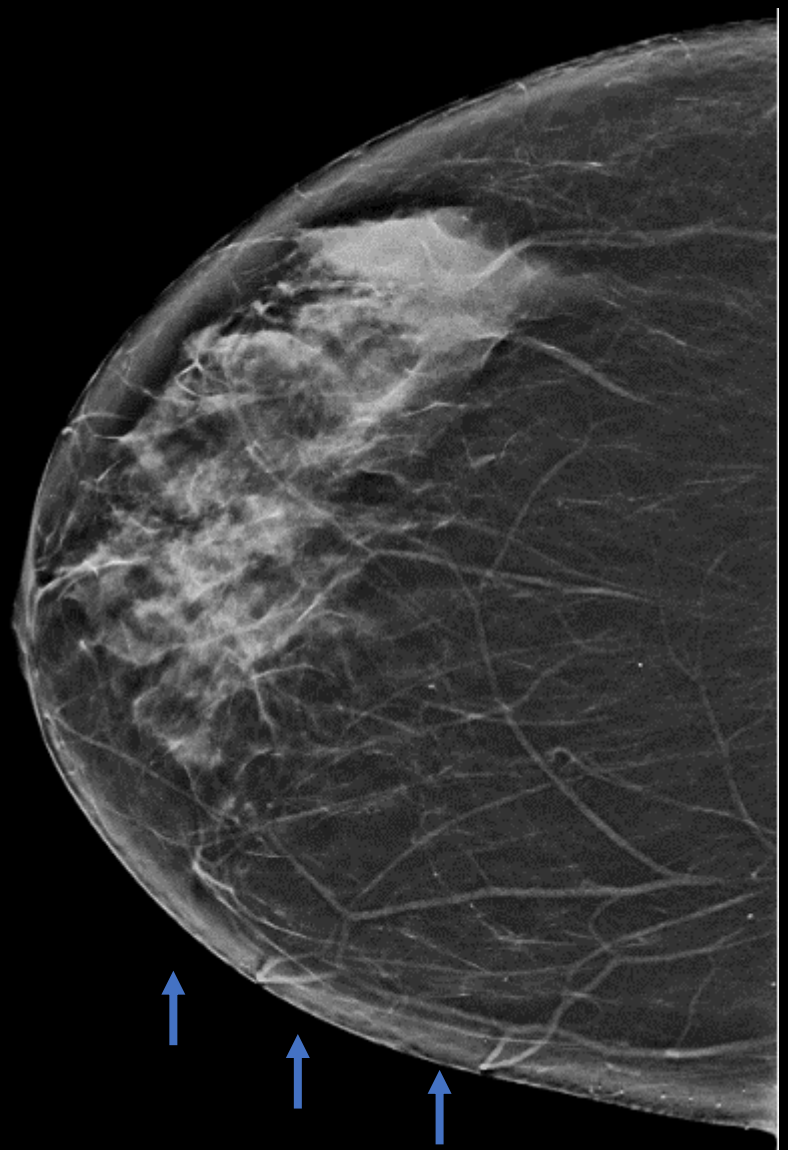
# Limitations of Synthesized Mammography

- Artifacts
  - Calcifications – pseudo-calcs
  - Bright-band artifact
  - BBs, coarse calcs, lumpectomy staples
- Difficulty in assessing motion

Durand MA. Synthesized Mammography: Clinical Evidence, Appearance, and Implementation. Diagnostics 2018, 8, 22, doi: https://doi.org/10.3390/diagnostics8020022

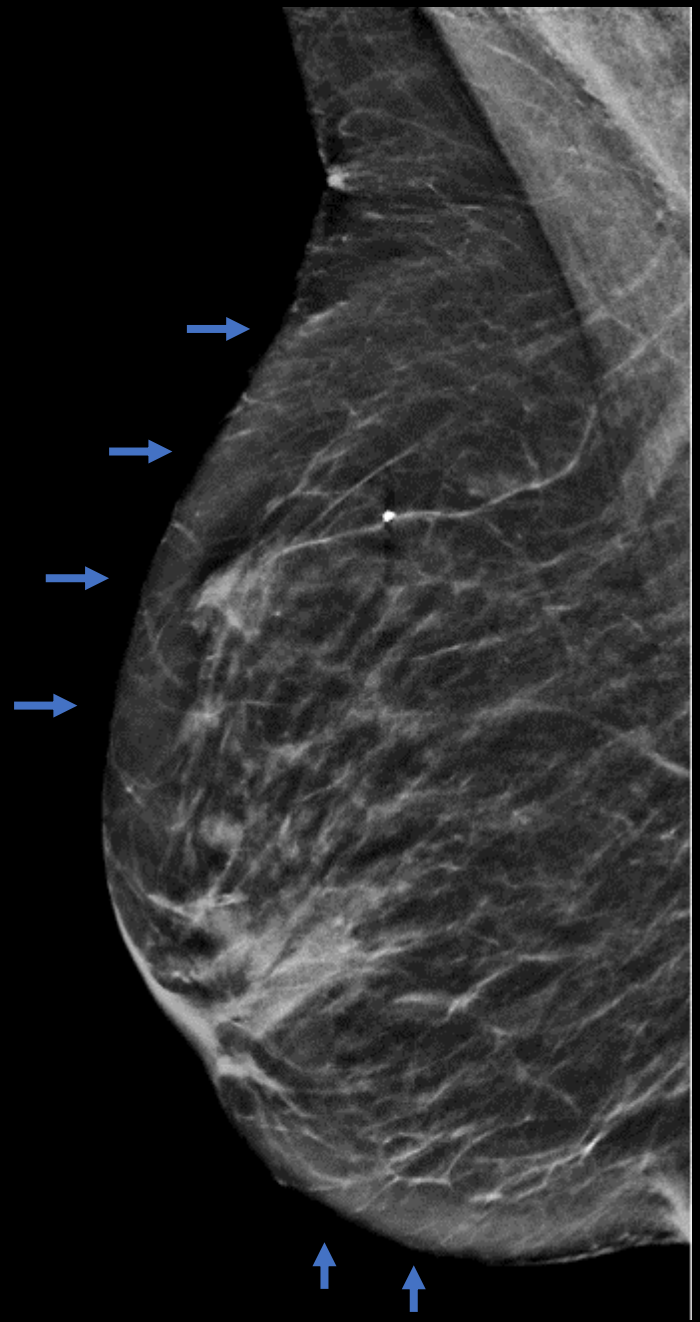
# Synthetic View Artifacts

- Bright-band artifact



# Synthetic View Artifact

- Loss of skin resolution



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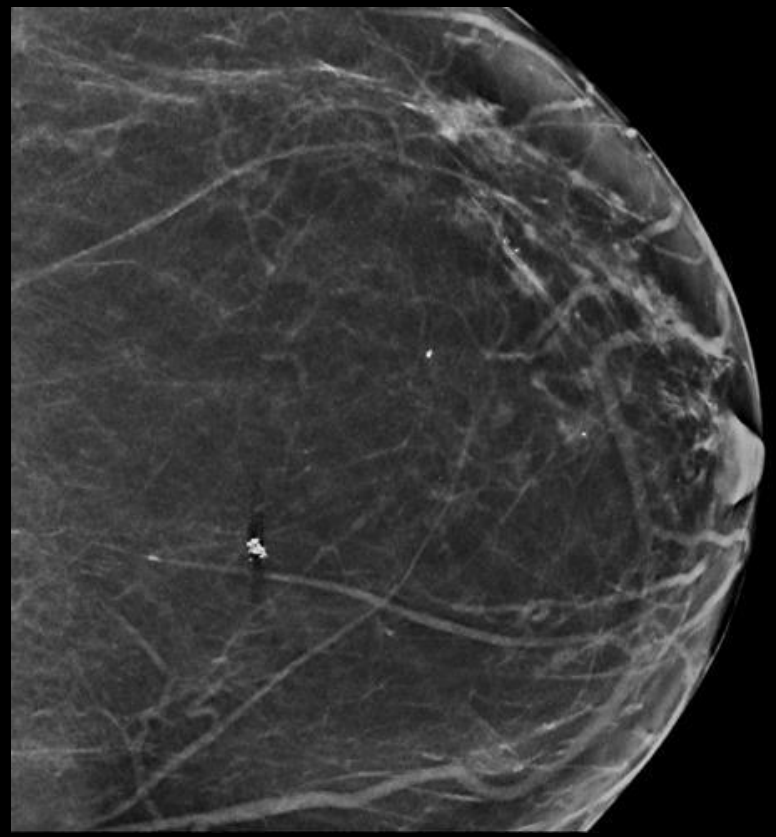
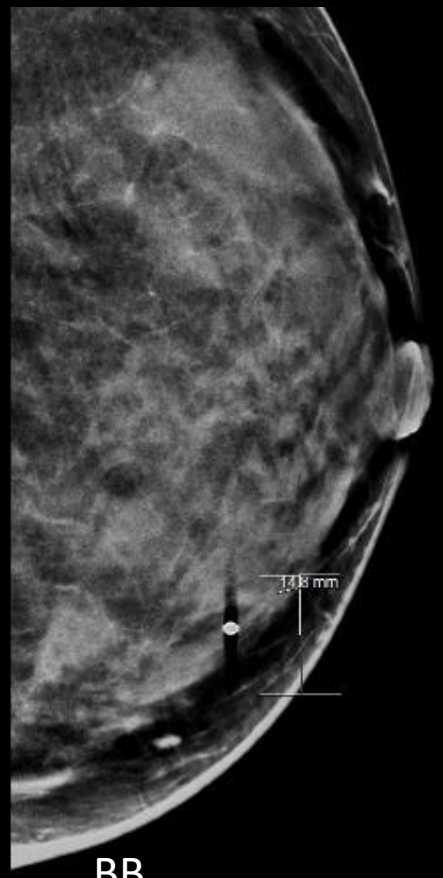


Coarse calcifications




BB

# Can you accurately assess breast density?

| Alshafeiy et al. [AJR 2017; 209: W36-W41] | Conant et al. [Radiology 2017; 283 (3): 673-680] | Haider et al. [JACR 2018; 15.10 (2018): 1430-1436] |
|---|---|---|
| • near perfect agreement ( =0.83) in two-category breast density classification<br>• consensus agreement ( = 0.73) using the four-category BIRADS scale<br>• Individual reader - variability in density categorization | • -strong correlation for percentage density between s2D and 2D (r = 0.92)<br>• the more dense the tissue, greater disagreement<br>• automated density estimates in this study were 1.7% higher on s2D | • substantial interreader agreement with overall κ in 2D of 0.71 and overall s2D κ average of 0.63<br>• minimal density transitions across 2D and s2D which are not statistically |

# Where are we now? [Zuckerman JACR 2020]

- Survey of SBI members in 2018
- 40% reported combined SM and DM use in DBT screens, and 52% reported SM use without DM in the majority of DBT screens
- Reported overall satisfaction with SM was 3.4 of 5 (1-5 scale)

Table 1. Practice characteristics and DBT usage

| Practice Characteristics | Responses |
|---|---|
| Type of practice | |
| Academic | 19% (59 of 312) |
| Private practice | 63% (196 of 312) |
| Hybrid practice | 13% (41 of 312) |
| Other | 5% (16 of 312) |
| Practices with DBT capability | 96% (299 of 312) |
| Years of DBT use | |
| ≤2 | 19% (56 of 299) |
| 2-4 | 39% (117 of 299) |
| 4-6 | 26% (77 of 299) |
| 6+ | 11% (34 of 299) |
| Not answered | 5% (15 of 299) |
| Number of DBT units | |
| 1-3 | 44% (132 of 299) |
| 4-6 | 27% (82 of 299) |
| 7-9 | 13% (38 of 299) |
| 10+ | 15% (45 of 299) |
| Not answered | <1% (2 of 299) |
| Screening examinations | Median = 19,000 |

Zuckerman et al. Survey Results Regarding Uptake and Impact of Synthetic Digital Mammography With Tomosynthesis in the Screening Setting. J Am Coll Radiol 2020;17:31-37.

# Uptake and Use

- Most cited SM advantages were decreased dose (85%) and increased lesion conspicuity (27%)
- The most cited SM disadvantages were calcification characterization (61%) and decreased image quality (31%)

Table 2. SM usage

| Survey Prompts | Responses |
|---|---|
| Respondents with both DBT and SM use by years of SM use | 83% (249 of 299) |
| ≤1 year | 24% (59 of 249) |
| 1-2 years | 27% (68 of 249) |
| 2-3 years | 25% (63 of 249) |
| >3 years | 21% (53 of 249) |
| No response | 2% (6 of 249) |
| Advantages to SM use* | |
| Decreased dose | 85% (182 of 215) |
| Increased conspicuity of lesions | 27% (58 of 215) |
| Increased throughput | 19% (41 of 215) |
| Decreased recall rate | 7% (16 of 215) |
| No advantages or n/a | 5% (10 of 215) |
| Patient preference or marketing advantage | 2% (5 of 215) |
| Disadvantages to SM use* | |
| Calcification characterization | 61% (135 of 220) |
| Missed calcifications | 19% (42 of 220) |
| Overcalling "pseudocalcs" | 24% (52 of 220) |
| Quality of the images | 31% (68 of 220) |
| No disadvantages | 10% (22 of 220) |
| Difficult to compare SM and DM | 9% (20 of 220) |
| Learning curve | 9% (19 of 220) |
| Missed cancers (asymmetries, masses) | 6% (14 of 220) |
| Increased interpretation time | 5% (11 of 220) |
| Administration or billing issues | 2% (4 of 220) |
| Lack of evidence | 2% (4 of 220) |
| Overcall distortion | 0.5% (1 of 220) |

# Zuckerman et al: Multicenter Results of Screening DBT

- Compared multicenter outcomes from breast cancer screening with SM/DBT versus DM/DBT
- Retrospective study of consecutive screening mammograms obtained at two institutions:
  - 34,106 DM/DBT examinations between October 3, 2011, and October 31, 2014, and 34,180 SM/DBT examinations between January 7, 2015, and February 2, 2018, at the University of Pennsylvania
  - 51,148 DM/DBT examinations between January 1, 2012, and May 31, 2016, and 31,929 SM/DBT examinations between June 1, 2016, and March 30, 2018, at the University of Vermont

Zuckerman et al. Multicenter Evaluation of Breast Cancer Screening with Digital Breast Tomosynthesis in Combination with Synthetic versus Digital Mammography. Radiology 2020; 297:545–553.

# Zuckerman Multicenter Results Summary

- Unadjusted recall rate was lower with SM/DBT than with DM/DBT
  - However, after multivariable adjustment, SM/DBT was associated with a slightly higher recall rate compared with DM/DBT

- After multivariable adjustment, SM/DBT was associated with slightly lower specificity compared with DM/DBT

- There was no statistically significant difference in biopsy rate, false-negative rate, cancer detection rate, invasive or in situ cancer detection rate, positive predictive value, or sensitivity for SM/DBT versus DM/DBT overall or within either institution

# To-Be BreastScreen Norway Trial: DBT Screening

- Randomized controlled trial in Bergen of DBT (+ synthesized view) vs. digital mammography
- All screening attendees invited to participate
  - 89% (14,274/15,976) consented during the first year, and were randomized to DBT (n = 7155) or DM (n = 7119)

| | Recall Rate | Recall Rate Non-dense breasts | Recall Rate Dense Breasts | Read Time | Mean glandular dose |
|---|---|---|---|---|---|
| DBT | 3.0% | 2.2% | 3.6% | 1 min 11s | 2.96 mGy |
| DM | 3.6% | 3.4% | 3.6% | 41s | 2.95 mGy |

Aase HS, et al. A randomized controlled trial of digital breast tomosynthesis versus digital mammography in population-based screening in Bergen: interim analysis of performance indicators from the To-Be trial. Eur Radiol 2019; 29(3): 1175-1186.

# Results of TOSYMA Trial: DBT + SM vs. DM [Heindel Lancet Oncol 2022]

TOSYMA was a randomized, open-label, superiority trial done at 17 screening units in two federal states of Germany

Women were randomly assigned (1:1) to digital breast tomosynthesis plus s2D mammography or digital mammography alone

DBT + SM invasive cancer detection rate 7.1 / 1000

- 4.8 / 1000 in the DM group

Heindel W, et al. Digital breast tomosynthesis plus synthesised mammography versus digital screening mammography for the detection of invasive breast cancer (TOSYMA): a multicentre, open-label, randomised, controlled, superiority trial. Lancet Oncol 2022; 23(5): 601-611.

# Summary

- The better mammogram for screening and diagnostic evaluation
  - Reducing recall rates
  - Increasing cancer detection rates
  - Useful for diagnostic imaging and for screening
  - Benefits are sustainable over time

***These findings are still seen with use of synthesized mammography***

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# Thank You

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