# DBT: A Better Mammogram for Screening

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## Background: Benefits of Screening Mammography

- Detection of smaller tumors, with less lymph node metastasis, lower stage
  - less likely to need chemotherapy, radiation and other more severe treatments
  - the benefit of detecting cancer at an earlier stage leads to less-toxic and better tolerated treatments
- Recurrence also less likely when a cancer is found and treated at an early stage

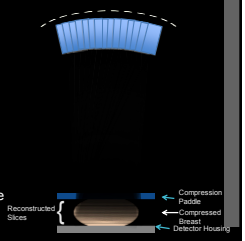
Pische D. et. ... cting to Screen Women Between 40 and 49 Years Old With Mamm... What is the Impact on Treatment Morbidity and Potential Risk Re... m J Roentgenol 2014 202:2, 282-288.

## DBT Technology

- Several manufacturers have developed tomosynthesis technology
  - Have applied different methods to develop and perform tomosynthesis
- Manufacturers vary: the arc of movement, num... of exposures, continuous or pulsed exposu... exposure parameters, dose, effective size ... pixels, X-ray source/filter source, single or binne... 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



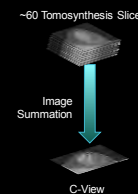

Courtesy of Hologic

## DBT can i... prove visibi... y by reducing tissue superimposi... n


Courtesy of Hologic

## Further Development: Hologic Synthesized 2D Image

- How does it work?
  - Perform a standard tomosynthesis scan (existing system)
  - Reconstruct tomosynthesis slices (existing system)
  - Synthesize 2D image (C-View)
    - Similar to Maximum Intensity Projection (MIP) as done with MRI images




Courtesy of Hologic

## Early DBT Screening Studies

| | Author, year | Recall Rate 2D (%) | Recall Rate DBT (%) | CDR/1000 2D | CDR/1000 DBT | Absolute CDR |
|---|---|---|---|---|---|---|
| Prospective | Ciatto, 2013 | 4.5 | 3.5 | 5.3 | 6.1 | 2.8 |
| | Skaane, 2013 | 6.1 | 5.3 | 6.1 | 8.0 | 1.9 |
| | Friedewald, 2014 | 10.7 | 9.1 | 4.2 | 5.4 | 1.2 |
| Retrospective | Rose, 2013 | 8.7 | 5.5 | 4.0 | 5.4 | 1.4 |
| | McCarthy, 2014 | 10.4 | 8.8 | 4.6 | 5.5 | 0.9 |
| | Sharpe, 2016 | 7.5 | 6.1 | 3.5 | 5.4 | 1.9 |

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

## Screening Study Results are Important

- Improvement in outcomes shown by screening studies address many of the concerns regarding mammography screening:
  - False positives (low specificity)
  - Missed cancers (low sensitivity)
  - Overdiagnosis (DCIS ra' s)

## Synthetic View Performance: A Review of the Literature

| Author | 2D/DBT CDR | s2D/DBT CDR | 2D/DBT Recall | s2D/DBT Recall |
|---|---|---|---|---|
| Aujero et al. | 6.4 | 6.1 | 5.8 | 4.3 |
| Skaane et al. | 7.8 | 7.7 | FP score 4.6 | FP score 4.5 |
| Freer et al. | 6.9 | 5.9 | 6.39 | 5.52 |
| Zuckerman et al. | 5.45 | 5.03 | 8.8 | 7.1 |
| Bernardi et al. | 8.5 | 8.8 | FP recall 3.97 | FP re |
| Ambinder et al. | 5.25 | 5.57 | 7.63 | 7.06 |

*Estimated CDR did not differ between integ ed 2D/3D (range, 5.03 to 8.8/1000 screens,*

Adapt m Houssami et al.

## DBT Outside the United States

- DBT still very much under investigation around the world:
  - Oslo Trial
  - STORM-2
  - BreastScreen Trial
  - To-Be Trial

## Oslo Tomosynthesis Screening Trial: Skaane 2018

- Os' omosynthesis Screening Trial
  ospective, population based, two year trial which compared FFDM alone to FFDM plus DBT on the basis of:
  - Recalls
  - Specificity
  - Cancer detection rate
  - Interval cancer rate

Skaane, P. et al. Breast Cancer Res Treat (2018) 169: 489.

## Oslo Screening Trial

| | FFDM | FFDM + DBT |
|---|---|---|
| Recall Rate | 10.3% | 10.7% |
| Cancer Detection Rate (n/1000) | 1.8 | 3.8 |
| Interval Cancer Rate (n/1000) | 2.1 | 2.0 |
| Specificity (%) | 1.8 | 3.6 |

*Addition of DBT resulted in increase in Cancer Detection, Specificity*

## STORM-2 Trial 2016 (Bernardi)

| | Detected cancers, n | CDR per 1000 screens (95% CI) | p value* | Incremental CDR per 1000 screens (95% CI) attributed to integrating 3D screening vs 2D alone† |
|---|---|---|---|---|
| All screening participants (n=9672, analysed as n=9677)‡ | | | | |
| Standard digital 2D mammography | 61 | 6·3 (4·8–8·1) | .. | .. |
| Integrated 2D–3D mammography | 82 | 8·5 (6·7–10·5) | <0·0001 | 2·2 (1·2–3·3) |
| Integrated 2D synthetic–3D mammography | 85 | 8·8 (7·0–10·8) | <0·0001 | 2·5 (1·4–3·8) |

almost all breast cancers detected only at
3D mammography were invasive—thus, there were relatively higher proportions of pT1a–c cancer in those
detected only at 3D mammography compared with those
detected by 2D mammography

## Large amount of the effect of DBT was observed in women younger than 60 years

| | Detected cancers, n | CDR per 1000 screens (95% CI) | p value* | Incremental CDR per 1000 screens (95% CI) attributed to integrating 3D screening vs 2D alone† |
|---|---|---|---|---|
| Stratified by age: | | | | |
| <60 years (n=5745) | | | | |
| Standard digital 2D mammography | 21 | 3·7 (2·3–5·6) | .. | .. |
| Integrated 2D–3D mammography | 36 | 6·3 (4·4–8·7) | <0·0001 | 2·6 (1·3–4·3) |
| Integrated 2D synthetic–3D mammography | 40 | 7·0 (5·0–9·5) | <0·0001 | 3·3 (1·9–5·2) |
| ≥60 years (n=3932) | | | | |
| Standard digital 2D mammography | 40 | 10·2 (7·3–13·8) | .. | .. |
| Integrated 2D–3D mammography | 46 | 11·7 (8·6–15·6) | 0·031 | 1·5 (0·03–3·3) |
| Integrated 2D synthetic–3D mammography | 45 | 11·4 (8·3–15·3) | 0·23 | 1·3 (–0·6–3·3) |

## Large amount of the effect of DBT was observed in those with denser breasts

| | Detected cancers, n | CDR per 1000 screens (95% CI) | p value* | Incremental CDR per 1000 screens (95% CI) attributed to integrating 3D screening vs 2D alone† |
|---|---|---|---|---|
| Stratified by breast density | | | | |
| Density 1–2 (less dense; n=7085) | | | | |
| Standard digital 2D mammography | 41 | 5·8 (4·2–7·8) | .. | .. |
| Integrated 2D–3D mammography | 48 | 6·8 (5·0–9·0) | 0·016 | 1·0 (0·1–2·0) |
| Integrated 2D synthetic–3D mammography | 49 | 6·9 (5·1–9·1) | 0·057 | 1·1 (0·0–2·4) |
| Density 3–4 (more dense; n=2592) | | | | |
| Standard digital 2D mammography | 20 | 7·7 (4·7–11·9) | .. | .. |
| Integrated 2D–3D mammography | 34 | 13·1 (9·1–18·3) | <0·0001 | (1·6–9·0) |
| Integrated 2D synthetic–3D mammography | 36 | 13·9 (9·7–19·2) | <0·0001 | (3·2–10·0) |

## BreastScreen Victoria: Screening Pilot Trial (Houssami)

- Pilot trial comparing tomosynthesis (with synthesized 2D images) and standard mammography screening
- 5018 DBT, 5166 SM in 10146 women

| | Cancer detection rate | Recall Rate | Read Time |
|---|---|---|---|
| DBT | 9.8/1000 | 4.2% | 67 seconds |
| SM | 6.6/1000 | 3.0% | 16 seconds |

Houssami N, et al. Pilot trial of digital breast tomosynthesis (3D mammography) for population-based screening in BreastScreen Victoria. Med J Aust. 2019; doi: 10.5694/mja2.50320. [Epub ahead of print].

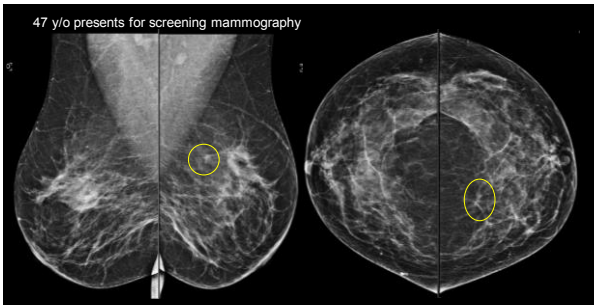
## To-Be BreastScreen Norway Trial: DBT Screening (Aase)

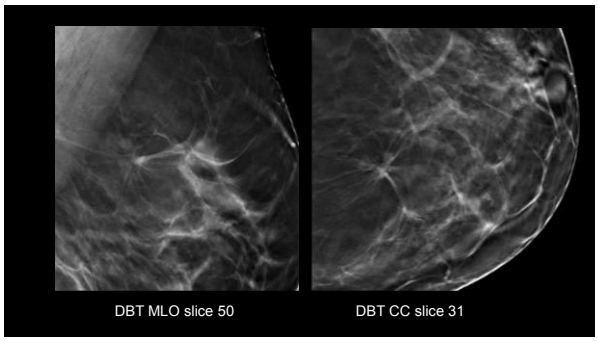
- ıdomized controlled trial in Bergen of DBT (+ synthesized ew) vs. digital mammography
- All screening attendees invited to participate
  - 89% (14,274/15,976) consented during the first year, and were randomized to DBT (*n* = 7155) or DM (*n* = 7119)

| | 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 |
| SM | 3.6% | 3.4% | 3.6% | 41s | 2.95 mGy |

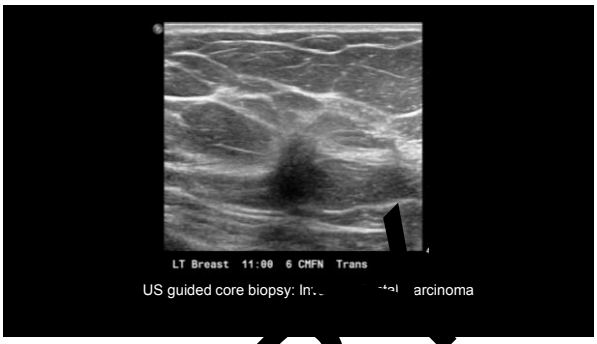
Aase HS, et al. A randomized controlled trial of digital breast tomosynthesis versus digital mammography in population-based screening in Bergen: interim analysis of performance indicators from the To-Be trial. Eur Radiol 2019; 29(3): 1175-1186.

47 y/o presents for screening mammography

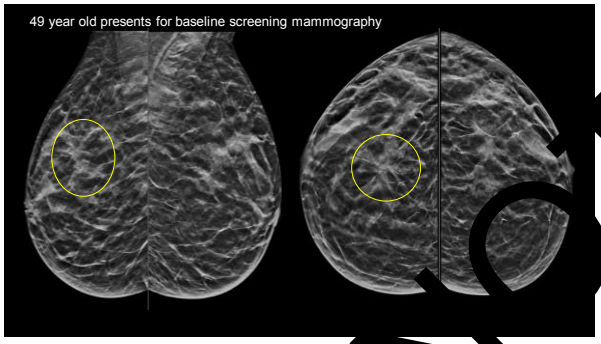


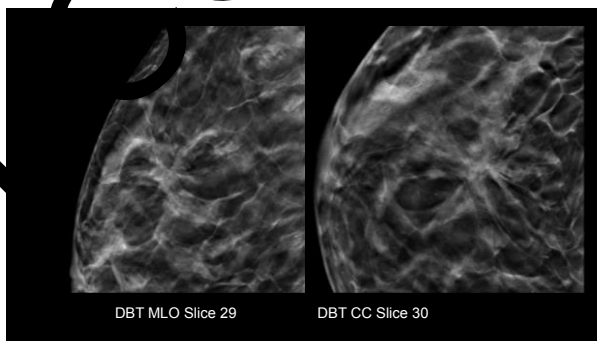


DBT MLO slice 50 DBT CC slice 31




US guided core biopsy: In... ...tal arcinoma

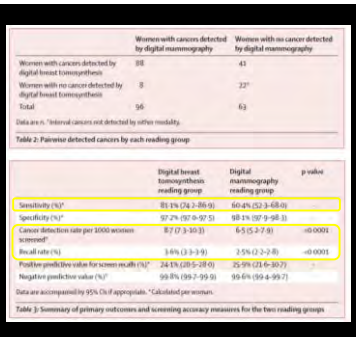


DBT MLO Slice 29 DBT CC Slice 30


Ultrasound guided biopsy: Invasive Lobular Carcinoma

One-view DBT vs. Two-view DM (Malmo Trial): Zackrisson 2018



| | Women with cancers detected by digital mammography | Women with no cancer detected by digital mammography |
|---|---|---|
| Women with cancers detected by digital breast tomosynthesis | 88 | 41 |
| Women with no cancer detected by digital breast tomosynthesis | 8 | 22* |
| Total | 96 | 63 |

Data are n. *Interval cancers not detected by either modality.

Table 2: Pairwise detected cancers by each reading group

| | Digital breast tomosynthesis reading group | Digital mammography reading group | p value |
|---|---|---|---|
| Sensitivity (%)* | 85·1% (76·2–89·9) | 60·4% (52·3–68·0) | |
| Specificity (%)* | 97·2% (97·0–97·5) | 98·1% (97·9–98·3) | |
| Cancer detection rate per 1000 women screened* | 8·7 (7·3–10·3) | 6·5 (5·2–7·9) | <0·0001 |
| Recall rate (%) | 3·6% (3·3–3·9) | 2·5% (2·2–2·8) | <0·0001 |
| Positive predictive value for screen recalls (%)* | 24·1% (20·5–28·0) | 25·9% (21·6–30·7) | |
| Negative predictive value (%)* | 99·8% (99·7–99·9) | 99·6% (99·4–99·7) | |

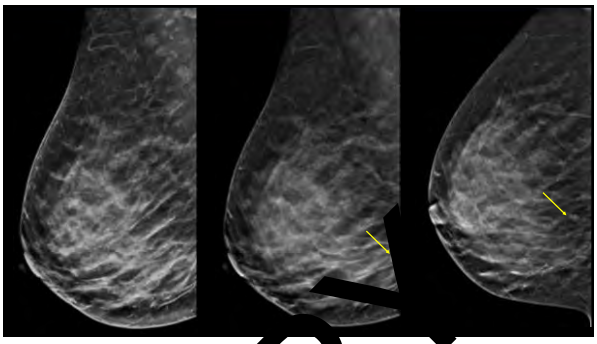
Data are accompanied by 95% CIs if appropriate. *Calculated per woman.

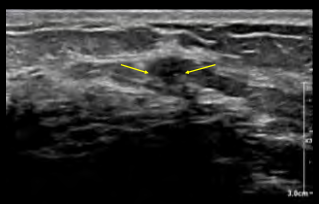
Table 3: Summary of primary outcomes and screening accuracy measures for the two reading groups

## DBT Impact on Screening in Patients <50: Rose 2018

- Model adjusted rates per 1000 screenings (Full Field Digital Mammography (FFDM) vs. FFDM + DBT)
  - Recall rate decreased (117 to 108), biopsy rate increased (13.5 to 16.6), and cancer detection rate increased (1.9 to 2.6)
  - Patients with dense breast tissue
    - Recall rate decreased (135 to 132), biopsy rate increased (16.0 to 20.5), cancer detection rate increased (2.1 to 3.5)

Rose SL, Shisler JL. Tomosynthesis Impact on Breast Cancer Screening in Patients Younger Than 50 Years Old. AJR 2018; 210: 1-4.






Grade 1 Invasive ductal carcinoma w/ mucinous features

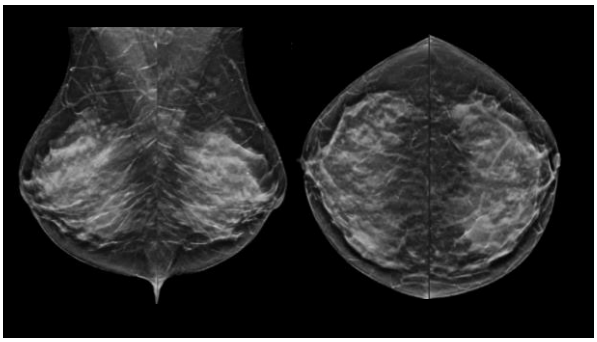
## Screening DBT by Age and Density: Conant 2019

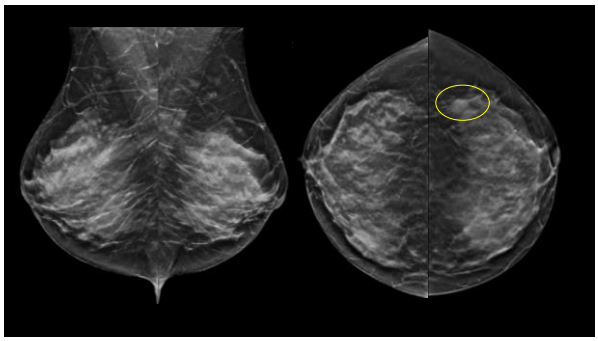
- Retrospective analysis of 96,269 women 40-74 years old who underwent screening using Digital Mammography (DM) and DBT from the Population-based Research Optimizing Screening Through Personalized Regimens (PROSPR) consortium
- Investigated whether DBT screening detects breast cancers that are associated with an improved prognosis and compared detection rates by age and breast density

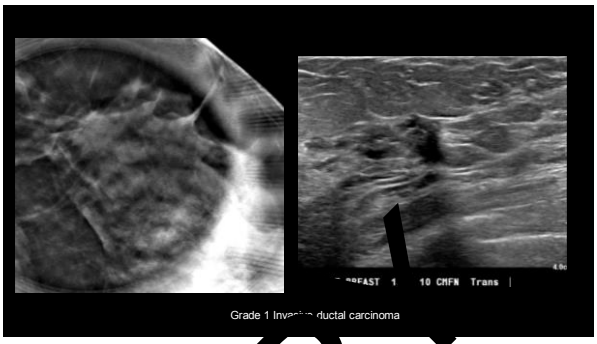
Conant EF, et al. Association of Digital Breast Tomosynthesis vs Digital Mammography With Cancer Detection and Recall Rates by Age and Breast Density. JAMA Oncol. 2019; 5(5):635–642.

## DBT by Age and Density

- Screening with DBT showed across all ages and breast densities:
  - More often node-negative cancers (88.8% DBT vs 81% DM)
  - Lower recall percentage (8.7% DBT vs 11.2% DM)
  - Higher cancer detection rate (5.82/1000 DBT vs 4.42/1000 DM)
  - Higher PPV1 (6.29 DBT vs 3.85 DM)
- **DBT showed the greatest significance in women 40-49**
  - *For women with nondense breasts: CDR for DBT was 1.70/1000 women higher than DM*
  - *For women with dense breasts: CDR was 2.27/1000 women higher than DM*








Grade 1 Invasive ductal carcinoma

## DBT and Dense Breasts: Rafferty 2016

- Compared overall and invasive cancer detection rates and recall rates with and without DBT in patients with dense and nondense breasts

| | Recall Rate/1000 screens | Invasive CDR Nondense | Invasive CDR Dense |
|---|---|---|---|
| FFDM | 90 | 3.0 | 2.9 |
| DBT | 79 | 4.0 | 4.2 |

Improvements were greatest for thos with scattered fibroglandular densities d heterogeneously dense breasts

## DBT Evaluation of Dense Breasts

- Optimal screening regime for evaluation of patients with dense breasts is currently under investigation
- US has so far been the modality of choice for many due to its widespread availability
- With increasing adoption, could DBT take the place over US?

## Impact of DBT Screening on Benign Biopsy Rate: UK Screening Programme Sharma 2019

- 4.8% recall rate during study period
- breast cancers detected
- Assessment without DBT – 571 biopsies – 142 cancers
- Assessment with DBT – 298 biopsies – 142 cancers

Biopsy rate from 69% to 36%

Sharma N, et al. The Potential Impact of Digital Breast Tomosynthesis on the Benign Biopsy Rate in Women Recalled within the UK Breast Screening Programme. Radiology 2019; 291(2)

## Tumor Characteristics of Breast Cancers Diagnosed with DBT Screening

- Malmö screening trial reported that the biologic profile of DBT found cancers were similar to those detected at DM
  - No difference between DBT and DM in number of:
    - tumors ≤ 2cm in size (86% [31 of 36] vs 85% [68 of 80], respectively)
    - node negative (75% [27 of 36] vs 74% [59 of 80], respectively)
    - luminal A-like subtype (53% [19 of 36] vs 46% [37 of 81], respectively)

Johnson K, et al. Tumor Characteristics and Molecular Subtypes in Breast Cancer Screening with Digital Breast Tomosynthesis: The Malmo Breast Tomosynthesis Screening Trial. Radiology Sept 2019.

## Benign and Malignant Diagnoses Detection Rates

- Observational data - Vermont Breast Cancer Surveillance System
  - 86,349 DBT screening examinations, 97,378 FFDM screening examinations during 2012–2016
- DBT and FFDM had comparable biopsy rate, benign biopsy rate, and cancer detection rate
- DBT had a lower recall rate vs. FFDM

Fuji MH, et al. Detection Rates for Benign and Malignant Diagnoses on Breast Cancer Screening With Digital Breast Tomosynthesis in a Statewide Mammography Registry Study. AJR 2019; 212(3): 706-711.

## DBT Over Time: McDonald 2016

- Reviewed 23,958 women from 4 consecutive years: before DBT and 3 years following (DM, year 0; DBT, years, 1-3)
- Compared Pre- and Post-DBT implementation, and # of prior DBT screenings:
  - Recall rates
  - Biopsy rates
  - Cancer cases per recalled tients
  - Invasive cancer rates

McDonald ES et al. Effectiveness... ography Outcomes Analysis... 916;2(6):737-743. ...l Breast Tomosynthesis Compared With Digital ...Years of Breast Cancer Screening. JAMA

## McDonald *JAMA Oncol* 2016

| | DM (year 0) | DBT (year 1) | DBT (year 2) | DBT (year 3) |
|---|---|---|---|---|
| Recall Rate (n/1000) | 104 | 88 | 90 | 92 |
| Biopsy Rate (n/1000) | 18 | 20 | 19 | 19 |
| Cancer Detection Rate (n/1000) | 4.6 | 5.5 | 5.8 | 6 |
| Invasive Cancer Rate (n/1000) | 3.2 | 3.8 | 4.1 | 1 |
| PPV (%) | 4.4 | 6.2 | 6.5 | |

*Continued increase in cancer detection and PPV*

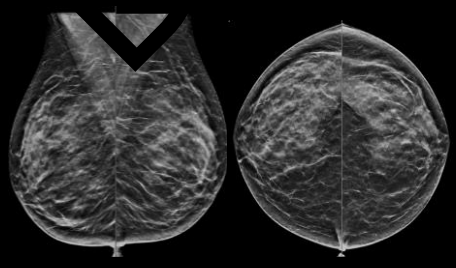
## DBT for Consecutive Screening Rounds: Hovda 2019

- Retrospectively studied the early performance measures of DBT versus DM for consecutive screening rounds
- 35,736 women screened in BreastScreen Norway from 2008–2016, with at least two consecutive screening examinations

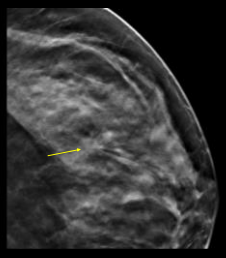
| | DM after DM | DBT after DM | DM after DBT | DBT after DBT |
|---|---|---|---|---|
| Recall Rate | 3.6% | 2.3% | 2.3% | 1.9% |
| CDR | 4.6/1000 | 9.9/1000 | 4.3/1000 | 8.3/1000 |
| PPV1 | 12.9 | 42.0 | 16.2 | 43.5 |

Hovda, T., et al. Screening outcome for consecutive examinations with digital breast tomosynthesis versus standard digital mammography in a population-based screening program. Eur Radiol (2019).

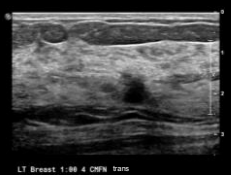
41 year old p... ...nts for screening ...mmography



Subtle DBT finding of A/D on CC view only



Zoomed CC DBT slice 33/62




Invasive ductal carcinoma

## DBT Screening Trial: United States

- Led by Dr. Etta Pisano
- Tomosynthesis Mammographic Imaging Screening Trial (TMIST)
- TMIST is enrolling 165,000 healthy women ages 45 to 74 at 130 sites throughout North America

## TMIST

- Women will be randomized to get either DBT or 2-D screening mammograms for five years
- Each woman will need to agree to let her doctor tell her how often to get screened—either every year or every other year—based on her individual risks for developing breast cancer
- TMIST seeks to stratify women based on risk of developing breast cancer, pinpointing subsets that would benefit most from screening, create a biorepository of blood and buccal smears, and provide a glimpse into overtreatment that may occur in breast oncology
- The trial will help us move toward a more personalized approach that tailors mammography for each woman based on her own genetics and individual risk factors for developing breast cancer

## Summary

- DBT is a valuable tool for screening for breast cancer
  - Has been shown to decrease recall rates and increase cancer detection in a wide range of patient populations, and settings

## References


- American Cancer Society. Cancer Facts & Figures 2018. Atlanta: American Cancer Society; 2018.
- https://seer.cancer.gov/statfacts/html/breast.html
- Plecha D, et al. Neglecting to Screen Women Between 40 and 49 Years Old With Mammography: What Is the Impact on Treatment Morbidity and Potential Risk Reduction? Am J Roentgenol 2017;209:2, 252-258.
- Hooley RJ, Durand MA, Philpotts LE. Advances in Breast Imaging AJR 2017;208.
- Tabár L., et al. Reduction in mortality from breast cancer after mass screening with mammography: randomised trial from the Breast Cancer Screening Working Group of the Swedish National Board of Health and Welfare. Lancet 1985; 1 ( 8433 ): 829-832.
- Tabár L., et al. The Swedish Two-County Trial of mammographic screening for breast cancer: recent results and calculation of benefit. J Epidemiol Community Health 1989 ; 43 ( 2 ) :107 - 114.
- Tabar L, et al , Efficacy of breast cancer screening by age: new results from the Swedish Two-County Trial . Cancer 1995 ; 75 ( 10 ) :2507 - 2517.
- Tabár L., et al. The Swedish Two-County Trial twenty years later: updated mortality results and new insights from long term follow-up . Radiol Clin North Am 2000 ;38 ( 4 ) :625 - 651.
- McDonald ES et al. Effectiveness of Digital Breast Tomosynthesis Compared with Digital mammography: Outcome Analysis From 3 Years of Breast Cancer Screening. JAMA Oncol. Published online February 16, 2016.
- Skaane, P., Sebuødegård, S., Bandos, A.I. et al. Breast Cancer Res Treat (2018) 169: 489. https://doi.org/10.1007/s10549-018-4705-2
- Gilea, C. S., Pourabdollah, S., Ik, V. K., Larson, R., Alper, E., & Khorasani, R. (2017). Comparing diagnostic performance of digital breast tomosynthesis and full-field digital mammography in a hybrid screening environment. American Journal of Roentgenology, 209(4), 929-934.
- Rose SL, Shisler JL. Tomosynthesis Impact on Breast Cancer Screening in Patients Younger Than 50 Years Old. AJR 2018; 210:1-4.
- Aujero, M. P., Gavenonis, S. C., Benjamin, R., Zhang, Z., & Holt, J. S. (2017). Clinical performance of synthesized two-dimensional mammography combined with tomosynthesis in a large screening population. Radiology, 283(1), 70-76.
- Hofvind, et al. Digital Breast Tomosynthesis and Synthetic 2D Mammography versus Digital Mammography: Evaluation in a Population-based Screening Program. Radiology 2018; online ahead of print.


## Thank you!

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Elizabeth Wende Breast Care

Breast Imaging Excellence