Effect of Breast Cancer Screening Modality Order on Recall, Cancer Detection Rates, and Positive Predictive Value 1 for Women with Multiple Screening Exams

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Background

Background

- Female breast cancer is the leading incident cancer among U.S. women, with an age-standardized rate of 84.9 per 100,000 world-wide[1]
- Screening mammography, as well as improvements in treatment, have resulted in a 40% decrease in breast cancer mortality[2]
- Digital mammography (DM) using 2-dimensional imaging is the primary modality for breast cancer screening[3,4]
- Since FDA approval in 2011, digital breast tomosynthesis (DBT), which uses 3-dimensional imaging, is rapidly being implemented as a replacement to DM-alone screening

Rationale

Multiple studies have reported improvements in population-level outcome metrics for breast cancer screening with the use of DBT vs. DM alone[5-7]

Improvements include:

- recall rate (RR)
- cancer detection rate per 1,000 screens (CDR), and
- positive predictive value 1 (PPV1)

Objectives

- This study aims to evaluate the influence of the most recent mammographic screening modality (DBT vs. DM) on RR, CDR, and PPV1, based on women's prior screening history (DBT vs. DM)

- Accounting for screening modality sequences (DM-DM, DM-DBT, DBT-DM, DBT-DBT), this study is one of the few studies which examines whether DBT performs differently if the prior screening modality is DBT vs. DM

Methods

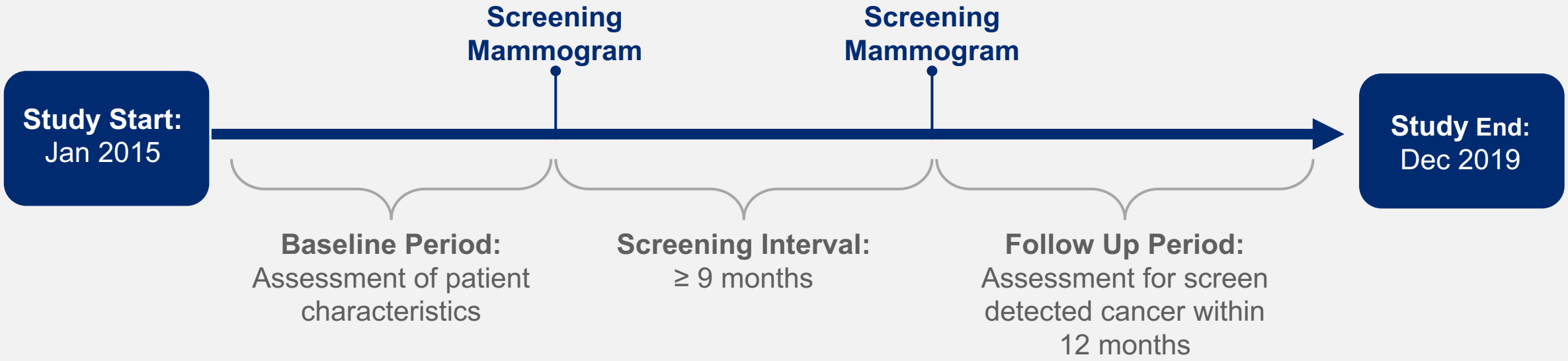
Source Data

- Integrated electronic medical record (EMR), Radiology Information System (RIS), and tumor registry data across 4 large healthcare organizations (Advocate, Sanford, Penn, Solis) were used

Cohort Criteria

- Women with ≥ 2 screening mammography exams, ≥ 9 months apart between 2015-2019 were included in the study

- Women with prior history of breast cancer or breast implants excluded



Analysis

- Patient characteristics described overall and by screening modality sequences:

  Prior screening-last screening: DM-DM, DM-DBT, DBT-DM, DBT-DBT

- RR, CDR, and PPV1 compared across screening modality sequences:
  - RR calculated as percent BI-RADS score of 0, 4, or 5 of total screened
  - CDR calculated as number of cancers detected per 1,000 screened
  - PPV1 calculated as percent cancers detected/recalls.

- RR and CDR were compared by modality of only the last screen (DM, DBT)

- Multivariable logistic regressions performed separately for RR and CDR, controlling for site, age, and breast density, by both screening modality sequence and by modality of the last screen

Results

Screening Modality Patterns

- 255,969 women contributed 346,832 DBT and 165,106 DM screens

  By sequence:

  - DBT-DM=4,411
  - DM-DM=35,890
  - DM-DBT=58,302
  - DBT-DBT=157,366

  By last screen: DM=40,301, DBT=215,668

- Distribution of screening modality sequences differed across sites (Table 1)

Patient Characteristics

- Patient characteristics were not notably different between modality sequence groups (Table 1) with exception of:
  - Those screened with DBT-DBT more likely to be older, compared to all other sequences (DM-DM, DBT-DM, DM-DBT)
  - Those screened with DBT-DBT less likely to identify as Black and be post-menopausal, compared to all other sequences (DM-DM, DBT-DM, DM-DBT)
  - Those screened with DM-DBT had longer screening interval on average and more likely have a screening interval of >= 15 months and >=24 months, compared to all other sequences (DM-DM, DBT-DM, DBT-DBT)

Table 1: Patient Characteristics by Screening Modality Pattern

		DBT-DBT (N=157,366)	DBT-DM (N=4,411)	DM-DBT (N=58,302)	DM-DM (N=35,890)	Total (N=255,969)	P-Value
Age (categorical)	40-44 years	16,525 (10.5%)	345 (7.8%)	6,123 (10.5%)	2,035 (5.7%)	25,028 (9.8%)	<.001*
	45-49 years	21,940 (13.9%)	537 (12.2%)	8,927 (15.3%)	3,747 (10.4%)	35,151 (13.7%)	
	50-59 years	47,365 (30.1%)	1,360 (30.8%)	19,105 (32.8%)	10,697 (29.8%)	78,527 (30.7%)	
	60-69 years	44,363 (28.2%)	1,353 (30.7%)	16,527 (28.3%)	11,881 (33.1%)	74,124 (29.0%)	
	70-79 years	27,210 (17.3%)	816 (18.5%)	7,637 (13.1%)	7,531 (21.0%)	43,194 (16.9%)	
Race	Black	14,248 (11.9%)	1,260 (32.0%)	11,152 (24.8%)	9,121 (27.2%)	35,781 (17.7%)	<.001*
	Caucasian	95,663 (79.8%)	2,359 (59.9%)	29,289 (65.1%)	21,588 (64.5%)	148,899 (73.6%)	
	Asian	5,417 (4.5%)	173 (4.4%)	2,202 (4.9%)	1,131 (3.4%)	8,923 (4.4%)	
	Other	4,589 (3.8%)	148 (3.8%)	2,342 (5.2%)	1,651 (4.9%)	8,730 (4.3%)	
	Unknown	37,486	471	13,334	2,400	53,691	
Menopause	Post-menopause	87,122 (79.7%)	2,432 (86.5%)	31,644 (86.6%)	20,417 (84.5%)	141,615 (81.9%)	<.001*
	Pre-menopause	22,241 (20.3%)	381 (13.5%)	4,895 (13.4%)	3,736 (15.5%)	31,253 (18.1%)	
	Unknown	48,040	1598	21,780	11,738	83,156	

**Chi-Square Test*
***Analysis of Variance*

Table 1: Patient Characteristics by Screening Modality Pattern (Con't)

		DBT-DBT (N=157,366)	DBT-DM (N=4,411)	DM-DBT (N=58,302)	DM-DM (N=35,890)	Total (N=255,969)	P-Value
Breast Density	Almost entirely fatty (A)	14,332 (9.1%)	248 (5.6%)	4,253 (7.3%)	2,616 (7.3%)	21,449 (8.4%)	<.001*
	Scattered fibroglandular densities (B)	70,941 (45.1%)	1,828 (41.4%)	26,789 (45.9%)	18,384 (51.3%)	117,942 (46.1%)	
	Heterogeneously dense (C)	60,420 (38.4%)	1,952 (44.3%)	23,310 (40.0%)	12,777 (35.6%)	98,459 (38.5%)	
	Extremely dense (D)	11,667 (7.4%)	383 (8.7%)	3,959 (6.8%)	2,075 (5.8%)	18,084 (7.1%)	
	Unknown	43	0	8	39	90	
Institution	Advocate	33,563 (21.3%)	3,007 (68.2%)	22,634 (38.8%)	25,134 (70.0%)	84,338 (32.9%)	<.001*
	Sanford	25,371 (16.1%)	347 (7.9%)	3,938 (6.8%)	6,190 (17.2%)	35,846 (14.0%)	
	Solis	76,731 (48.7%)	676 (15.3%)	23,391 (40.1%)	2,626 (7.3%)	103,424 (40.4%)	
	UPenn	21,738 (13.8%)	381 (8.6%)	8,356 (14.3%)	1,941 (5.4%)	32,416 (12.7%)	

**Chi-Square Test*
***Analysis of Variance*

Table 1: Patient Characteristics by Screening Modality Pattern (Con't)

		DBT-DBT (N=157,366)	DBT-DM (N=4,411)	DM-DBT (N=58,302)	DM-DM (N=35,890)	Total (N=255,969)	P-Value
Screen Interval (continuous, days)	Mean (s.d.)	426.3 (107.3)	426.6 (92.5)	477.9 (159.0)	427.8 (86.1)	438.3 (120.4)	<.001**
	Median (Q1-Q3)	385 (370-430)	390 (371-442)	409 (373-512)	394 (371-448)	391 (371-448)	
24 Month Screen Interval (categorical)	<24 months	152,072 (96.6%)	4,320 (97.9%)	52,949 (90.8%)	35,334 (98.4%)	244,675 (95.6%)	<.001*
	>=24 months	5,331 (3.4%)	91 (2.1%)	5,370 (9.2%)	557 (1.6%)	11,349 (4.4%)	
15 Month Screen Interval (categorical)	<15 months	142,048 (90.2%)	3,989 (90.4%)	45,936 (78.8%)	32,568 (90.7%)	224,541 (87.7%)	<.001*
	>=15 months	15,355 (9.8%)	422 (9.6%)	12,383 (21.2%)	3,323 (9.3%)	31,483 (12.3%)	
12 Month Screen Interval (categorical)	<12 months	7,377 (4.7%)	205 (4.6%)	1,589 (2.7%)	1,452 (4.0%)	10,623 (4.1%)	<.001*
	>=12 months	150,026 (95.3%)	4,206 (95.4%)	56,730 (97.3%)	34,439 (96.0%)	245,401 (95.9%)	

**Chi-Square Test*
***Analysis of Variance*

Recall Rates

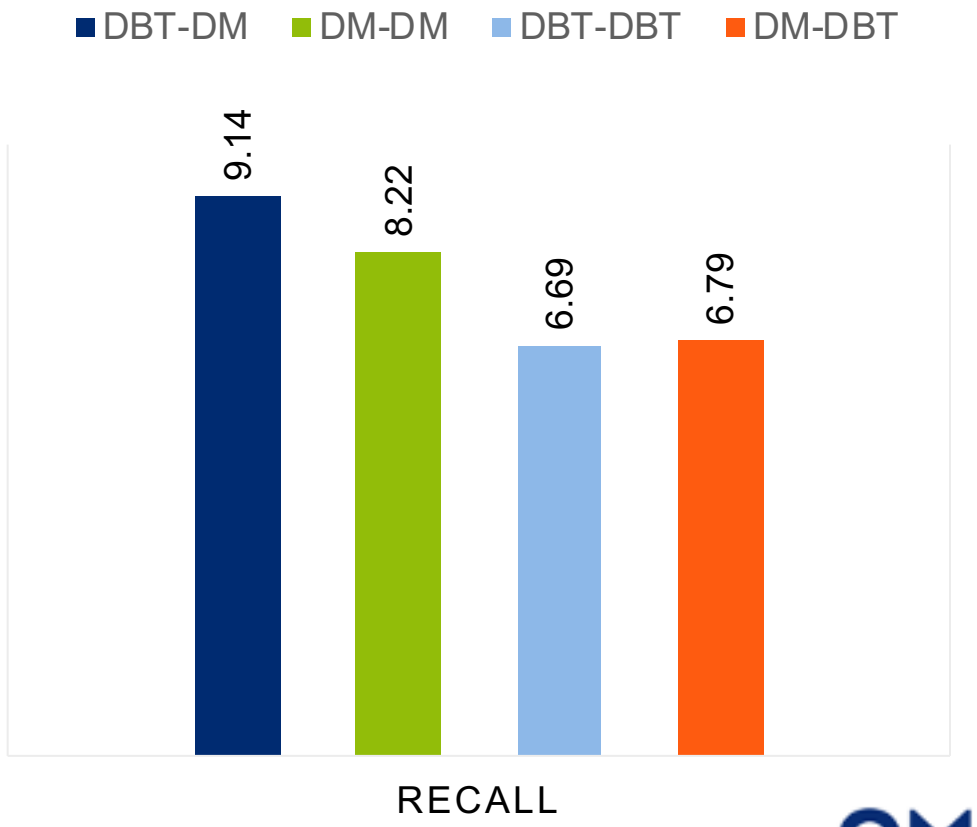
- RRs were lower when DBT was last observed screen, regardless of modality of prior screen (Figure 1)

  By sequence:
  - DBT-DM=9.14
  - DM-DM=8.22
  - DM-DBT=6.79
  - DBT-DBT=6.69

  By last screen:
  - DM=8.32 vs. DBT=6.72

- Among those with DBT as most recent screen, no statistically significant differences were observed in RRs between prior screening with DM vs. DBT (DM: 6.79, DBT: 6.69)

FIGURE 1: RR BY SCREENING MODALITY

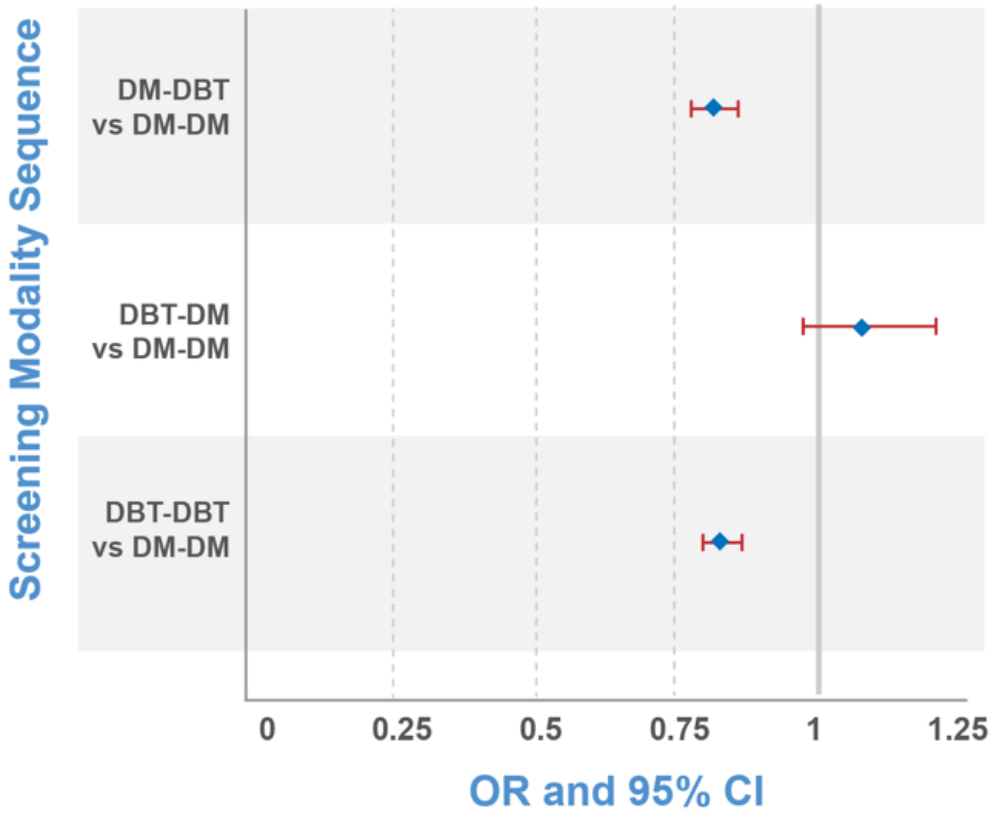


Recall Rates (Continued)

- Compared to those screened with DM-DM, the odds ratios for recall were:
  - DM-DBT: 0.83 (95% CI: 0.79, 0.87)
  - DBT-DBT: 0.83 (95% CI: 0.79, 0.87)
  - DBT-DM : 1.09 (95% CI: 0.97, 1.21)

  when adjusted for site, age and breast density (Figure 2)

FIGURE 2: ODDS OF RECALL BY SCREENING MODALITY SEQUENCE



Cancer Detection Rates

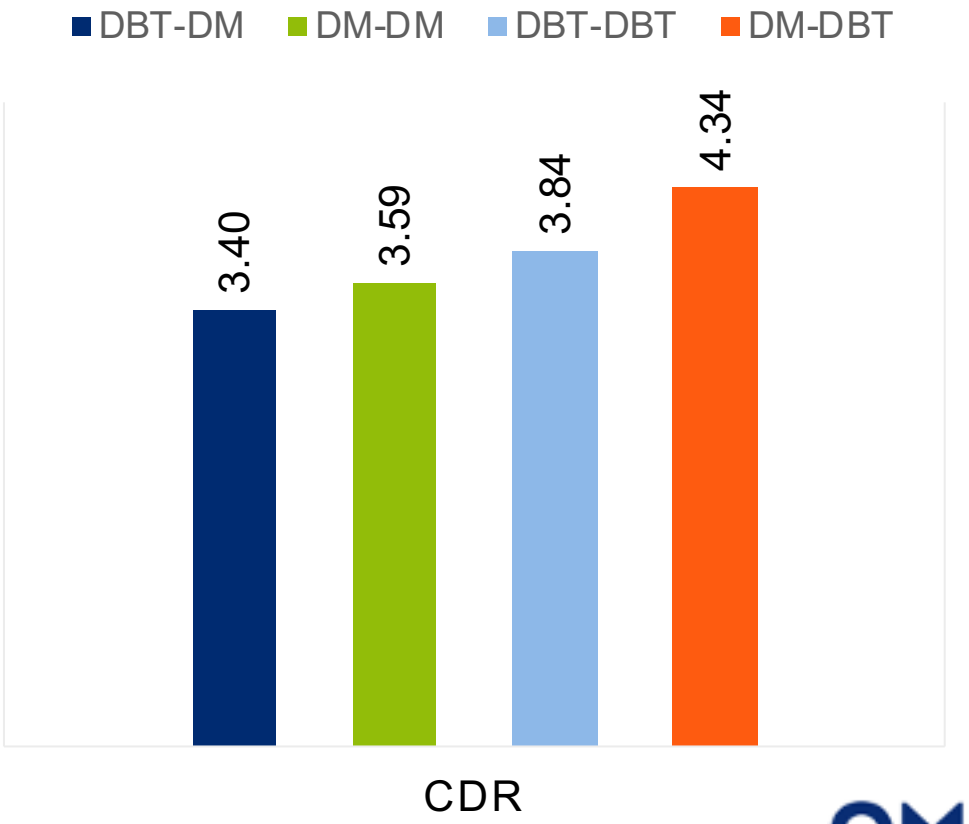
- CDRs/1,000 were higher when most recent screen was DBT, regardless of prior screening modality (Figure 3)

  By sequence:
  - DBT-DM=3.40
  - DM-DM=3.59
  - DBT-DBT=3.84
  - DM-DBT=4.34

  By most recent screen:
  - DM=3.57 vs. DBT=3.97

- Significantly higher CDRs were seen among those with most recent screen using DBT when prior screen was DM vs. DBT
  (recent screen DM: 4.34, DBT: 3.84, p=0.02)

FIGURE 3: CDR BY SCREENING MODALITY

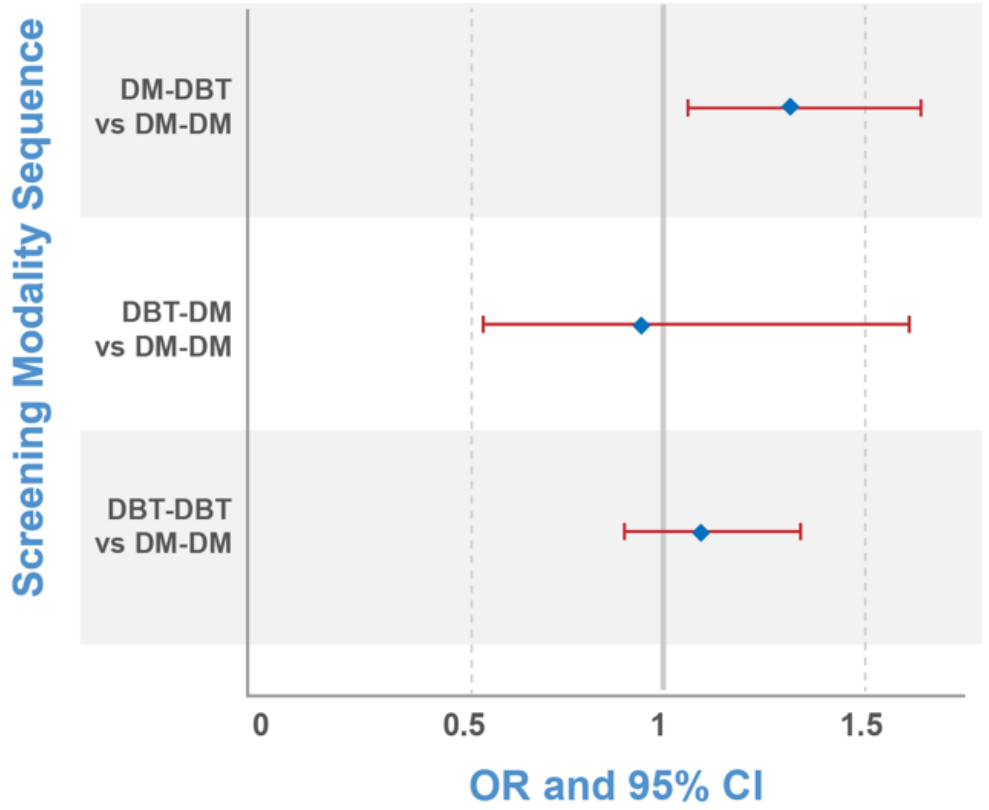


Cancer Detection Rates (Continued)

- Compared to those screened with DM-DM, the odds ratios for cancer detection were:
  - DM-DBT: 1.32 (95% CI: 1.06,1.64)
  - DBT-DBT: 1.10 (95% CI: 0.90,1.35)
  - DBT-DM: 0.94 (95% CI: 0.55,1.61)

  when adjusted for site, age and breast density (Figure 4)

FIGURE 4: ODDS OF CANCER DETECTION BY SCREENING MODALITY SEQUENCE

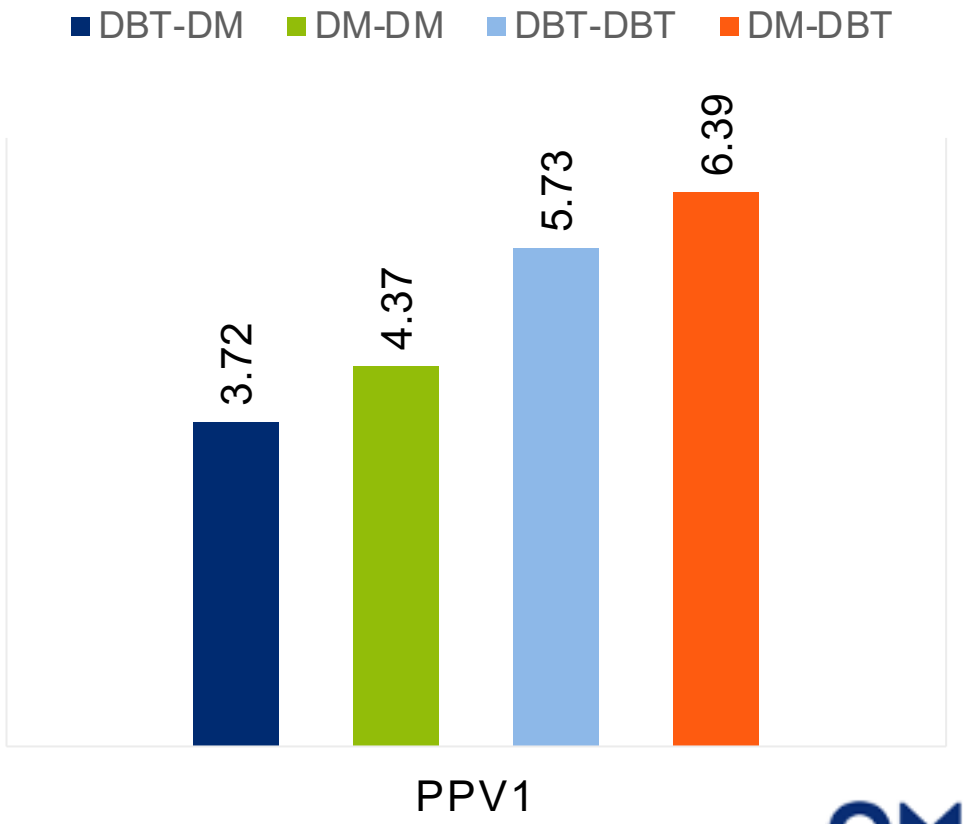


PPV1

- PPV1s were higher when the most recent screen was DBT, regardless of prior screening modality (Figure 5)

  By sequence:
  - DBT-DM =3.72
  - DM-DM=4.37
  - DBT-DBT=5.73
  - DM-DBT=6.39

FIGURE 5: PPV1 BY SCREENING MODALITY



Strengths & Limitations

Strengths

Sample Size

- This study captured a large sample of women undergoing multiple screenings for breast cancer

Patient-Level Data

- Women were individually tracked over multiple years, rather than in aggregate, as in many other multi-year studies

Real-World Data

- The use of real-world data allows for examination of how women are actually screened in practice rather than in an RCT.

Limitations

- Most of the data in this study were captured as part of routine medical practice and therefore, data completeness is variable across sites

- This study uses the diagnosis of breast cancer as reported in cancer registries. Given delays in reporting to registries, data may be incomplete. This may impact cases occurring later in the study which were more likely to be screened using DBT

Conclusions

Conclusions

Lower Recall Rates

- DBT was associated with lower RRs, regardless of the prior screening modality

Higher Cancer Detection Rates

- DBT was associated with higher CDRs, regardless of the prior screening modality

Higher PPV1

- Higher PPV1 for DBT suggests improved detection without increasing recall rates

Expanded use of DBT may benefit women undergoing screening by reducing recall, improving cancer detection, and lowering false positive detections

Future Directions

- Additional studies are planned to assess the associations between screening modality and:
  - Screening interval
  - Tumor size, and
  - Breast cancer stage

Disclosures

- Funding for this study was provided by Hologic, Inc.

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Appendix

Abbreviations

- **CDR** - Cancer detection rate per 1,000 screens
- **DBT** - Digital breast tomosynthesis
- **DM** - Digital mammography
- **EMR** - Electronic medical record
- **PPV** - Positive predictive value 1
- **RIS** - Radiology Information System
- **RR** - Recall rate

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