

# Clinical Performance of Synthesized Two-dimensional Mammography Combined with Tomosynthesis in a Large Screening Population<sup>1</sup>

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## Purpose:

To compare the clinical performance of synthesized two-dimensional (s2D) mammography combined with digital breast tomosynthesis (DBT) with that of full-field digital mammography (FFDM) alone and FFDM combined with DBT in a large community-based screening population by analyzing recall rate, positive predictive value, and cancer detection rate.

## Materials and Methods:

This was a retrospective study approved by the institutional review board and was HIPAA compliant with waiver of informed consent. A total of 78810 screening mammograms from October 11, 2011, to June 30, 2016, were retrospectively collected. Of these, 32076 were FFDM, 30561 were DBT-FFDM, and 16173 were DBT-s2D mammograms. Diagnostic performance of FFDM, DBT-FFDM, and DBT-s2D mammography was compared. Statistical significance was determined by using the Pearson  $\chi^2$  test and was expressed as odds ratios and related confidence intervals determined by means of logistic regression analysis with pairwise comparisons.

## Results:

Recall rates were significantly lower with DBT-s2D mammography (4.3%, 687 of 16173) when compared with DBT-FFDM (5.8%, 1785 of 30561; odds ratio, 0.72; 95% confidence interval: 0.65, 0.78;  $P < .0001$ ) and when compared with FFDM alone (8.7%, 2799 of 32076; odds ratio, 0.46; 95% confidence interval: 0.43, 0.51). The cancer detection rate was similar among FFDM alone (5.3 of 1000 screening examinations), DBT-FFDM (6.4 of 1000 screening examinations), and DBT-s2D mammography (6.1 of 1000 screening examinations) with no significant difference (FFDM vs DBT-FFDM,  $P = .08$ ; FFDM vs DBT-s2D,  $P = .27$ ). The percentage of invasive cancers detected was significantly higher with DBT-s2D mammography (76.5%) than with DBT-FFDM (61.3%,  $P = .01$ ), and positive predictive values with DBT-s2D mammography (40.8%) were significantly higher than those with DBT-FFDM (28.5%,  $P < .0001$ ).

## Conclusion:

Screening with DBT-s2D mammography in a large community-based practice improved recall rate and positive predictive values without loss of cancer detection rate when compared with DBT-FFDM and FFDM alone.

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**A**fter the U.S. Food and Drug Administration (FDA) approved digital breast tomosynthesis (DBT) combined with full-field digital mammography (FFDM) in 2011, the efficacy of this technology was evaluated in multiple large-scale studies. Most of these studies reported a reduction in the rate of women recalled for further examination (recall rate), reduction in the rate of false-positive results, and increases in the cancer detection rate with the use of DBT-FFDM when compared with FFDM alone (1–7). Despite the reported clinical advantages of DBT-FFDM, one disadvantage is that DBT-FFDM

requires a second radiation exposure to the breast. Although this dual exposure during DBT-FFDM acquisition does not exceed the recommended American College of Radiology Mammography Quality and Standards dose limit of 3.0 mGy per breast per view (8), adding DBT to FFDM increases radiation dose by 39%–45% while also slightly increasing time spent in breast compression (9–13). To address this situation, some manufacturers developed methods to generate synthesized two-dimensional (s2D) images, which are maximum intensity projections created from the DBT image set, from the DBT acquisition data (DBT-s2D) to reduce the increased radiation dose to the patient. This goal is in line with the principle of as low as reasonably achievable, or ALARA, a guiding philosophy in radiation protection (14). The total radiation dose from a single DBT acquisition is slightly higher than that for FFDM alone (1.45 mGy vs 1.2 mGy, respectively) (9,15).

In 2013, the U.S. FDA approved an improved version of s2D software to be used instead of FFDM as an adjunct to DBT in breast cancer screening, reporting that DBT-s2D mammography is noninferior to FFDM alone and suggesting that DBT-s2D mammography may be more effective for breast cancer

screening than FFDM, with the added benefit of limiting radiation exposure (15). Empowered by this, radiologists in several imaging centers across the country who already were using the approved DBT option (DBT-FFDM) transitioned to DBT-s2D mammography and eliminated the separate conventional two-dimensional FFDM acquisition. This decreased patient dose and time in breast compression. Results of a few studies (11–13,16,17) since have shown favorable clinical performance with DBT-s2D when compared with DBT-FFDM. For example, results of a prospective double-reader study from Italy, the screening with DBT or standard mammography-2, or Storm-2, study (11), showed that both DBT-s2D and DBT-FFDM allowed detection of more cases of breast cancer than did FFDM alone. However, the study showed a significant increase in the false-positive results rate with sequential reading of DBT-s2D and DBT-FFDM images when compared with FFDM alone. Authors of other studies (12,13,16,17), including prospective, retrospective, and multireader studies, reported comparable clinical performance for detection of cancer with DBT-s2D mammography to

### Advances in Knowledge

- Synthesized two-dimensional (s2D) mammography combined with digital breast tomosynthesis (DBT), when compared with full-field digital mammography (FFDM) combined with DBT, had a lower recall rate (4.3% [687 of 16173] and 5.8% [1785 of 30561], respectively;  $P < .0001$ ) and a maintained cancer detection rate (6.1 of 1000 vs 6.4 of 1000, respectively;  $P = .71$ ) in our population.
- The percentage of invasive cancers detected was significantly higher with DBT-s2D mammography than with DBT-FFDM (76.5% [75 of 98] vs 61.3% [119 of 194] respectively,  $P = .01$ ).
- No significant difference was observed between the number of in-situ cancers detected per 1000 with DBT-s2D mammography than with DBT-FFDM (1.4 per 1000 vs 2.1 per 1000, respectively;  $P = .1$ ).
- The false-positive rate was significantly lower with DBT-s2D mammography than with DBT-FFDM (3.6% [589 of 16173] vs 5.2% [1591 of 30561], respectively;  $P < .0001$ ), while the positive predictive value of biopsy was significantly higher (40.8% [98 of 240] vs 28.5% [194 of 682], respectively;  $P < .0001$ ).

### Implications for Patient Care

- The results of this study support the conclusion that s2D mammography combined with DBT is an acceptable screening tool when compared with DBT-FFDM in our large community population and may result in improved overall diagnostic performance.
- Screening with s2D mammography combined with DBT will limit radiation exposure to the patient compared with use of both DBT and FFDM, while the number of false-positive findings will likely decrease, and the number of invasive cancers detected will be similar to those found at screening with DBT-FFDM.

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### Abbreviations:

CI = confidence interval  
DBT = digital breast tomosynthesis  
FDA = Food and Drug Administration  
FFDM = full-field digital mammography  
OR = odds ratio  
PPV = positive predictive value  
s2D = synthesized two-dimensional

### Author contributions:

Guarantors of integrity of entire study, M.P.A., R.B., Z.Z., J.S.H.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, all authors; clinical studies, M.P.A., S.C.G., Z.Z., J.S.H.; experimental studies, Z.Z.; statistical analysis, M.P.A., R.B., Z.Z., J.S.H.; and manuscript editing, all authors

Conflicts of interest are listed at the end of this article.

that with DBT-FFDM. The purpose of our study was to determine the clinical performance of DBT-s2D mammography in a large community-based population by analyzing recall rate, positive predictive value (PPV), and cancer detection rates when compared with those of FFDM and DBT-FFDM.

### Materials and Methods

The Institutional Review Board approved this Health Insurance Portability and Accountability Act-compliant study. The requirement for informed consent was waived.

### Equipment and Patients

All patients were imaged with the same system (Selenia Dimensions 2D/3D System; Hologic, Marlboro, Mass) for both DBT and FFDM. The same hardware is capable of FFDM and DBT-s2D imaging. Image processing software (C-View Software Module; Hologic) was used for s2D image acquisition throughout the study time period (15).

We began using DBT in our practice on September 6, 2012. DBT was available to all patients who presented to the main central breast center for screening mammography and was offered to patients at no charge and on the basis of room availability. Subsequently, additional DBT units were acquired to replace end-of-life FFDM units, and DBT continued to be offered at no charge. In January 2016, 1 year after the Centers for Medicare and Medicaid Services decision for reimbursement, an institutional decision was made to charge for DBT. Since that time, patients whose insurance carriers do not cover DBT are informed of the possibility of being responsible for an additional cost, and some patients opt for screening with FFDM alone.

In our institution, s2D mammography was implemented on June 5, 2015, and for 3 months, it was used with DBT-FFDM for a single interpretation. After this time period, ending August 29, 2015 (the trial period), FFDM was no longer routinely performed in patients who underwent DBT screening. Throughout the study period, patients

were able to opt out of the use of DBT and be screened with FFDM alone.

After the installation of DBT and the start of its use in our facility, we saw a steady increase in the percentage of DBT-FFDM screening examinations performed per year. By the end of 2014, 70% (13055 of 18750) of our screening studies were performed with DBT-FFDM (Figure) and by the end of 2015, which includes the time of integration of s2D examination, less than 2% (214 of 15432) of the studies were performed with FFDM alone. By mid-2016, the percentage of FFDM examinations performed was 11% (1058 of 9379). Image specifications for both s2D mammography and FFDM were similar. The detector-reconstructed pixel size for s2D mammography was approximately 0.100 mm  $\times$  0.100 mm, slightly larger than that for FFDM (0.07 mm  $\times$  0.07 mm), and the spatial resolution was 5 line pairs per millimeter with s2D and 9 line pairs per millimeter for FFDM.

### Data Acquisition and Analysis

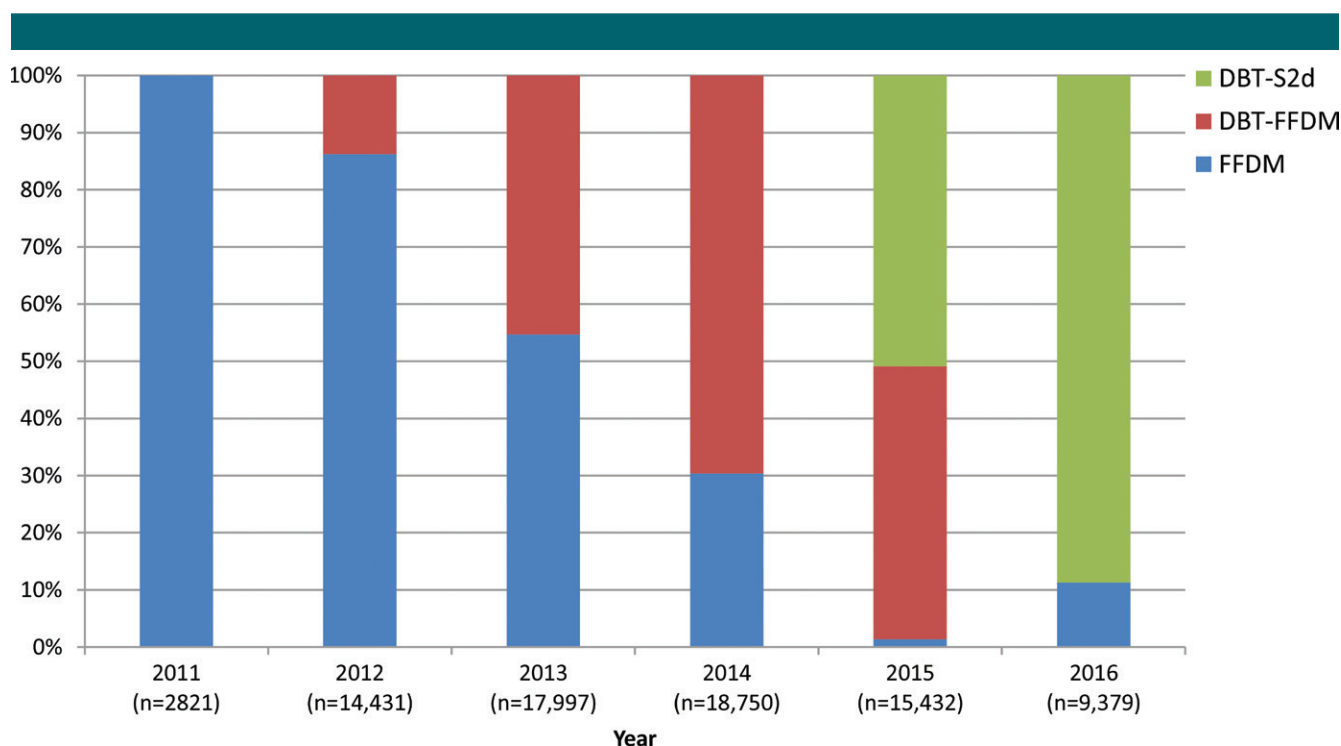
Our institution's radiology information system database and the hospital's electronic medical records were used to collect data retrospectively and to access pathologic reports. Electronic data were available for extraction for October 11, 2011, through June 30, 2016. A total of 90737 screening mammograms were obtained at our main breast imaging center during this time period. Studies read by radiologists not present for all three technology time periods or by readers with less than 1 year of clinical experience were excluded ( $n = 7411$ ). This left 83348 screening mammograms interpreted by five radiologists. Thirty-two screening studies were lost to follow-up and were excluded from data analysis. The studies from our trial period (which included the combination of all technologies) were also excluded from the study ( $n = 4506$ ). This left a total of 78810 screening mammograms. These were separated into three main groups: FFDM, DBT-FFDM, and DBT-s2D examinations. There were 32076 screening mammograms acquired with FFDM alone from October 11, 2011, to June 30, 2016, 30561 screening mammograms

acquired with DBT-FFDM from September 6, 2012, to June 4, 2015, and 16173 screening mammograms acquired with DBT-s2D mammography from August 31, 2015, to June 30, 2016.

Recall rates were determined on the basis of the initial interpretation of the screening examination. Each screening examination was given a Breast Imaging Reporting and Data System, or BI-RADS, score of 0, 1, or 2 at the time of interpretation. Diagnostic studies of women recalled within 180 days of a screening examination (BI-RADS 0) were included for review, and the corresponding recalled screening study was given a final BI-RADS score. At pathologic examination, benign (lobular carcinoma in situ and other high-risk lesions) or malignant results were assigned, and cancers were identified as in situ, invasive, or unspecified. Cancers containing mixed invasive and in situ components at pathologic examination were designated as invasive and not counted twice. Nonprimary breast cancers were designated as unspecified. Clinical performance of FFDM, DBT-FFDM, and DBT-s2D mammography was compared. The outcomes consisted of rates of recall, biopsies recommended, biopsies performed, cancers, invasive cancers, in situ cancers, false-positive results, and PPVs (PPV1 for recalls, PPV2 for biopsies recommended, and PPV3 for biopsies performed).

### Interpretation

Each screening mammogram was interpreted once by one of five American College of Radiology Mammography Quality and Standards-qualified radiologists with experience in interpreting breast imaging of 2–25 years at the start of the study period. All five radiologists were trained in the interpretation of DBT as mandated by the FDA. Radiologists were trained by means of either an on-site course or a Web-based tutorial. Computer-aided detection software was applied to all studies. Comparison with previous studies was made whenever previous studies were available at the time of screening interpretation for all groups.



Graph shows percentage of screening breast examinations of each modality per year included in the study period. Note gradual decrease in percentage of FFDM studies from 2011 to 2015 and corresponding increase in percentage of DBT studies. Sample size (*n*) refers to number of breast examinations.

### Statistical Analysis

Variables were summarized by using means  $\pm$  standard deviations for continuous data and percentages for categorical data. The Student *t* test or the Wilcoxon rank-sum test were used to compare continuous variables, and contingency table analysis ( $\chi^2$ ) was used to compare categorical variables between data for the performance of the types of screening mammograms. Statistical significance was determined by using the Pearson  $\chi^2$  test, and data were expressed as odds ratios (ORs) and related confidence intervals (CIs) with logistic regression analysis with pairwise comparisons. The Bonferroni, Tukey, Dunnett, or Dunn (nonparametric) multiple comparisons test was used to address the multiplicity among the groups of women screened with each modality.

### Results

We included 78810 screening mammograms in the study. Age, race, and

breast density among the populations were compared and were significantly different (Table 1). Categorization of breast density differed among the technology subgroups, with a statistically significant trend toward lower breast density assessment in the DBT-s2D cohort. Similarly, the trend was toward an older population ( $> 60$  years old) in the DBT-s2D group, with a well-matched population of women in the 50–59 years age group. There was no trend in the self-reported white and self-reported black populations, but these differed significantly among the cohorts. There was no significant difference in the self-reported Hispanic, Asian, and other or unknown race categories between the DBT-FFDM and the DBT-s2D cohorts.

Recall rates were significantly lower in the DBT-FFDM cohort (5.8%, 1785 of 30561) than in the FFDM alone cohort (8.7%, 2799 of 32076; OR, 0.65; 95% CI: 0.61, 0.69) and were even lower in the DBT-s2D cohort (4.3%, 687 of 16173; OR, 0.72; 95% CI: 0.65, 0.78 for comparison of DBT-FFDM and

DBT-s2D mammography) (Table 2). After adjustment for age, race, and breast density, the lower recall rate observed for DBT-s2D mammography remained significantly lower when compared with that of DBT-FFDM (OR, 0.731; 95% CI: 0.67, 0.80). The false-positive result rate was significantly lower for DBT-FFDM (5.2%, 1591 of 30561) than for FFDM alone (8.2%, 2630 of 2076; OR, 0.61; 95% CI: 0.58, 0.66 for FFDM vs DBT-FFDM) and was even lower for DBT-s2D mammography (3.6%, 589 of 13173; OR, 0.69; 95% CI: 0.62, 0.76 for DBT-FFDM vs DBT-s2D mammography).

The cancer detection rate was similar between the FFDM alone group (5.3 cancers per 1000 screening examinations, 169 of 32076) and the DBT-FFDM group (6.4 of 1000 screening examinations; OR, 1.21; 95% CI: 0.98, 1.48) and between FFDM and DBT-s2D mammography (6.1 of 1000 screening examinations; OR, 1.15; 95% CI: 0.90, 1.48). There was a significant increase in the percentage of invasive cancers

Table 1

## Demographics of Study Population

Variable	FFDM ( <i>n</i> = 32 076)	DBT-FFDM ( <i>n</i> = 30 561)	DBT-s2D ( <i>n</i> = 16 173)	<i>P</i> Values		
				FFDM vs DBT-FFDM	DBT-FFDM vs DBT-s2D	All
Mean age (y)*	56.6 ± 11.7	55.7 ± 11.3	57.3 ± 11.5	.0018	<.0001	.0153
Age (y)						
<40	728 (2.2)	947 (3.1)	365 (2.3)	<.0001	<.0001	.9291
40–49	9542 (29.7)	9277 (30.4)	4361 (27.0)	.0973	<.0001	<.0001
50–59	9516 (29.7)	9382 (30.7)	4796 (29.7)	.0049	.0194	.9770
60–69	7351 (22.9)	7077 (23.2)	4067 (25.1)	.4767	<.0001	<.0001
70–79	3726 (11.6)	3106 (10.2)	2073 (12.8)	<.0001	<.0001	.0001
>80	1213 (3.8)	772 (2.5)	511 (3.2)	<.0001	<.0001	.0005
Race or ethnicity						
White	23 679 (73.8)	23 942 (78.3)	12 254 (75.8)	<.0001	<.0001	<.0001
Black	6174 (19.3)	4896 (16.0)	2984 (18.5)	<.0001	<.0001	<.0001
Hispanic	29 (0.1)	2 (0.01)	0f (0.0)	<.0001	.5474	<.0001
Asian	881 (2.8)	764 (2.5)	411 (2.5)	.0536	.7859	.1872
Other or unknown	1313 (4.1)	957 (3.1)	524 (3.2)	<.0001	.5240	<.0001
Breast density score						
A	1811 (5.65)	1669 (5.46)	981 (6.07)	.3130	.0072	.0623
B	11 014 (43.34)	11 840 (38.74)	6456 (39.92)	<.0001	.0132	<.0001
C	18 031 (56.21)	15 597 (51.04)	7955 (49.19)	<.0001	.0001	<.0001
D	1220 (3.80)	1455 (4.76)	781 (4.83)	<.0001	.7429	<.0001

Note.—Unless otherwise indicated, data are number of patients, with percentages in parentheses. Breast density score A, almost entirely fatty; B, scattered areas of fibroglandular density; C, heterogeneously dense; and D, extremely dense.

\* Data are means ± standard deviation.

detected with DBT-s2D mammography (76.5%, 75 of 98 cancers) when compared with DBT-FFDM (61.3%, 119 of 194 cancers; OR, 2.06; 95% CI: 1.19, 3.56). Also, there was a significant increase in PPV3 with DBT-s2D mammography (40.8%, 98 of 240 biopsies performed) when compared with DBT-FFDM (28.5%, 194 of 682 biopsies performed; OR, 1.74; 95% CI: 1.28, 2.36). PPV1 was significantly higher in the DBT-FFDM group (10%, 194 of 1785 recalls) compared with that in the FFDM group (6%, 169 of 2799 recalls; OR, 1.90; 95% CI: 1.53, 2.35) and was even higher in the DBT-s2D (14.3%, 98 of 687 recalls; OR, 2.59; 95% CI: 1.99, 3.73) than in the DBT-FFDM group. Similar results are shown for PPV2 and PPV3 (Table 2).

A statistically significant increased rate of invasive cancers detected at screening mammography was seen with DBT-s2D mammography (4.64 per 1000 examinations) when compared with FFDM (3.21 per 1000 examinations;

OR, 1.45; 95% CI: 1.07, 1.95; *P* = .02). There were no significant differences in invasive or in situ cancers detected at screening mammography with DBT-FFDM versus FFDM or DBT-FFDM versus DBT-s2D mammography. The rates of biopsies recommended and performed were significantly lower in the DBT-s2D group when compared with those in the FFDM and DBT-FFDM groups.

### Discussion

DBT is rapidly becoming a practice-changing technology, because multiple studies show improved sensitivity and specificity in breast cancer screening (1–7). DBT technology is being adopted throughout the United States as newer machines replace the older FFDM units. DBT has been shown to improve patient outcomes for detection of cancer, recall rates, and PPVs. The use of s2D mammography with DBT eliminates the need to perform additional

imaging required with DBT-FFDM and thus limits patient radiation exposure.

At our community-based practice, DBT was initially introduced with the installation of a single DBT unit, so that we screened patients with either conventional two-dimensional FFDM or DBT-FFDM. Over time, we acquired additional DBT units but continued to offer both conventional two-dimensional FFDM and DBT-FFDM to our patients. We inform all women, regardless of breast density, that DBT is available for screening, but some women choose not to undergo DBT and prefer FFDM instead. We theorize that concerns over radiation dose, concerns over cost, and possibly also referring physician and patient education may have been factors that patients weighed if they opted to undergo screening with FFDM alone. There was otherwise no stratification of women according to recommendation of one modality over the other.

We observed continued improvement with each change in screening



Table 2

## Clinical Performance Comparisons of FFDM, DBT-FFDM, and DBT-s2D Mammography

Variable	FFDM vs DBT-FFDM				DBT-FFDM vs DBT-s2D			FFDM vs DBT-s2D	
	FFDM	DBT-FFDM	OR*	P Value	DBT-s2D	OR*	P Value	OR*	P Value
No. of total studies	32 076	30 561			16 173				
No. of recalls	2799 (8.7)	1785 (5.8)	0.65 (0.61, 0.69)	<.0001	687 (4.3)	0.72 (0.65, 0.78)	<.0001	0.46 (0.43–0.51)	<.0001
No. of biopsies recommended	810 (2.5)	737 (2.4)	0.95 (0.86, 1.06)	.36	249 (1.5)	0.63 (0.55, 0.73)	<.0001	0.60 (0.52, 0.70)	<.0001
No. of biopsies performed	761 (2.4)	682 (2.2)	0.94 (0.85, 1.04)	.24	240 (1.5)	0.66 (0.57, 0.77)	<.0001	0.62 (0.54, 0.72)	<.0001
No. of cancers detected†	169 (5.3)	194 (6.4)	1.21 (0.98, 1.48)	.08	98 (6.1)	0.95 (0.75, 1.22)	.71	1.15 (0.90, 1.48)	.27
Proportion of invasive cancers	103/169 (61.0)	119/194 (61.3)	1.02 (0.67, 1.55)	.94	75/98 (76.5)	2.06 (1.19, 3.56)	.01	2.95 (1.07, 8.14)	<.0001
Invasive cancers‡	3.2	3.89	1.21 (0.92, 1.58)	.15	4.64	1.19 (0.89, 1.59)	.23	1.45 (1.07, 1.95)	.0147
Proportion of in situ cancers‡	51/169 (1.6)	65/194 (2.1)	1.34 (0.93, 1.93)	.12	23/98 (1.4)	0.67 (0.42, 1.08)	.10	0.89 (0.55, 1.46)	.6565
PPV1	169/2799 (6.0)	194/1785 (10.9)	1.90 (1.53, 2.35)	<.0001	98/687 (14.3)	1.37 (1.05, 1.77)	.02	2.59 (1.99, 3.73)	<.0001
PPV2	169/810 (20.9)	194/737 (26.3)	1.36 (1.07, 1.72)	.01	98/249 (39.3)	1.82 (1.34, 2.46)	<.0001	2.08 (1.27, 3.40)	<.0001
PPV3	169/761 (22.2)	194/682 (28.5)	1.39 (1.10, 1.77)	.01	98/240 (40.8)	1.74 (1.28, 2.36)	.001	1.96 (1.20, 3.21)	<.0001
No. of false-positive results	2630 (8.2)	1591 (5.2)	0.61 (0.58, 0.66)	<.0001	589 (3.6)	0.69 (0.62, 0.76)	<.0001	0.42 (0.39, 0.46)	<.0001

Note.—Unless otherwise indicated, data in parentheses are percentages. Dunnett adjustment for multiple comparisons was performed for a common control group. False-positive results rate = number of recalls minus number of cancers divided by the total number of studies. PPV1 = number of cancers divided by number of recalls, PPV2 = number of cancers divided by number of biopsies, PPV3 = number of cancers divided by number of biopsies performed.

\* Data in parentheses are 95% CIs.

† Data in parentheses are number of cancers per 1000 screening examinations.

‡ Per 1000 screening examinations.

modality—going from FFDM to DBT-FFDM and DBT-s2D—with a statistically significant decrease in recall rates with DBT-s2D compared with DBT-FFDM or with FFDM alone after adjusting for age, race, and breast density. In addition, early reports that false-positive rates would increase with DBT-s2D or with DBT-FFDM were not seen in our study (12). Instead, similar to the multireader comparison of tomosynthesis with mammography, or TOMMY, trial (16,17), we observed false-positive result rates significantly decrease with the change from FFDM to DBT-FFDM and further decrease with DBT-s2D mammography.

There was a slight increase in the cancer detection rate from the use of FFDM alone to DBT-FFDM and from FFDM to DBT-s2D mammography, but neither was statistically significant. A possible reason that our cancer detection rate did not significantly increase when we made the transition to DBT-FFDM from FFDM alone could be that we started with a high baseline cancer detection

rate with FFDM. Comparable to results of other studies (11–13,18), our cancer detection rate was maintained when we made the transition from DBT-FFDM to DBT-s2D mammography.

Earlier reports that image quality of s2D mammography is inferior to FFDM (19) did not seem to affect the positive clinical performance we observed. This could be explained by the fact that in Nelson et al study (19), the quality comparison between s2D mammography and FFDM was based solely on phantom images. In fact, in addition to further decrease in recall rates with s2D mammography, in our clinical practice we observed a significant increase in the percentage of invasive cancers detected with DBT-s2D compared with that with DBT-FFDM, without loss of in situ cancer detection. This result differs from that of a more recent study by Zuckerman et al (13), who reported no difference in the proportions of invasive and in situ cancers detected.

Categorization of breast density differed among the technology subgroups,

with a statistically significant lower density assessment in the DBT-s2D cohort. We speculate that this difference may in part be due to the perceptual adaptation of readers to the s2D images, which affects the subjective assessment of breast density. For example, concurrent FFDM and s2D images of the same breast may be categorized subjectively as heterogeneously dense and scattered fibroglandular, respectively. This trend toward a lower density category on the basis of s2D mammograms is comparable to cohort characteristics reported by Zuckerman et al (13).

We report several limitations to our study. First, this was a single-institution, single-vendor study, and PPV varied with breast cancer prevalence, which differs per geographic location and limits the generalizability of these results. Second, this was a retrospective study, and given the free text dictation system used at our institution for reporting, complete data regarding availability of prior studies, risk profile, or reason for recall were not available for

full analysis. Furthermore, it is possible that the learning-curve effect influenced the results of our study, because the readers had nearly 3 years of experience with DBT, including a trial period, before s2D mammography was fully implemented. Also, since this was a retrospective review, inpatient comparisons could not be avoided. Thus, women with more than one screening examination during the study time period might have been more or less likely to have obtained screening with the same or different technologies after a previous negative or positive result. Finally, our last accrual date was June 30, 2016, and thus information on true- or false-negative results was not available for complete assessment. Although our results showed that DBT-s2D mammography detected more invasive cancers without a statistically significant loss of in situ cancer detection compared with DBT-FFDM, further research with adequate follow-up time and sample size is needed to elucidate the reasons behind this result. Theoretical considerations include the theory that subtle features of invasive cancers may have been more conspicuous on the DBT-s2D images, and this may have contributed to the increased detection of invasive cancers. It is also possible that in situ cancers are being underdiagnosed. Additional research is necessary to clarify the underlying factors.

In conclusion, the adoption of s2D mammography combined with DBT into screening programs would limit radiation exposure to the patient, and, on the basis of our results, may improve clinical performance compared with that of DBT-FFDM.

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