Original Investigation

Synthesized Mammography: The New Standard of Care When Screening for Breast Cancer with Digital Breast Tomosynthesis?

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Rationale and Objectives: This study aims to evaluate the screening performance of digital breast tomosynthesis (DBT) combined with synthesized mammography (SM) vs combined with full-field digital mammography (FFDM).

Materials and Methods: We retrospectively reviewed all screening studies utilizing FFDM + DBT ($n = 7845$) and SM + DBT ($n = 14,776$) between April 1, 2013, and February 15, 2016. Recall rate, biopsy rate, positive predictive value 1 (PPV1), positive predictive value 3 (PPV3), and cancer detection rate (CDR) were compared between the two groups. A generalized linear mixed model specifying the reading radiologist as the random effect and controlling for age was used to compare clinical outcomes between the two groups.

Results: The overall recall rate was significantly lower in the SM + DBT cohort compared to the FFDM + DBT cohort (7.06% vs 7.63%, $P = .04$). There was no difference in biopsy rate, PPV1, PPV3, or CDR between the two groups.

Conclusions: When DBT is performed for screening, the use of SM rather than acquiring an additional FFDM has no significant effect on biopsy rate, PPV1, PPV3, or CDR. We found a decrease in recall rate in the SM + DBT group, which may be related to the learning curve of interpreting DBT. These findings support the use of SM for patients undergoing screening with DBT.

Key Words: Mammography; breast neoplasms; early detection of cancer.

INTRODUCTION

Digital breast tomosynthesis (DBT) is a relatively recent advancement in breast imaging that decreases recall rate and improves invasive cancer detection rate (CDR) (1–6). The US Food and Drug Administration (FDA) initially approved DBT as a screening adjunct to be used in combination with standard full-field digital mammography (FFDM). The primary reasons that DBT was only approved in combination with FFDM were that some findings, such as microcalcifications, are thought to not be well visualized on DBT (7,8), and the standard FFDM examination allows easier comparison to previous examinations.

The disadvantage of combination FFDM and DBT is an approximate twofold increase in radiation dose (9), although the total dose still falls within radiation dose limits set forth by the Mammographic Quality and Standards Act (3 mGy). Concerns regarding increased radiation dose led to the advancement of synthesized two-dimensional mammography (SM). SM is a technique that generates two-dimensional images from the DBT dataset, eliminating the need for a separately acquired FFDM examination and thereby decreasing the radiation dose to the patient (10). The FDA approved replacing FFDM with a specific SM technique (Selenia Dimensions 3D System with C-View Software Module, sponsored by Hologic, Inc., Marlborough, MA) for screening mammography in May 2013.

There have been limited studies comparing SM + DBT to FFDM + DBT. In 2009, one small study using a first version of SM + DBT demonstrated lower sensitivity and similar specificity compared to FFDM + DBT (11). Since then, a few reader studies and prospective studies have shown overall comparable results between the two techniques (12–14). For example, in 2014, Zuley et al. published a retrospective observer performance study of 123 cases concluding that SM was comparable in performance to FFDM. Recently, the first study was published evaluating implementation of SM + DBT in a screening

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population compared to historic screening outcomes of FFDM + DBT (15). Results showed decreased recall rate and radiation dose in the SM + DBT group while maintaining CDR. The purpose of this study was to further validate the use of SM in women being screened with DBT by comparing the performance metrics of SM + DBT to FFDM + DBT in screening asymptomatic women at a large multisite academic center.

MATERIALS AND METHODS

This was an Health Insurance Portability and Accountability Act compliant, institutional review board approved study with a waiver of informed consent. We retrospectively evaluated outcome metrics of two cohorts of patients undergoing breast cancer screening with DBT at multiple sites of a single institution. The first cohort included patients screened with DBT and FFDM from April 1, 2013, to February 14, 2015 ($n = 7845$) and the second included patients screened with DBT and SM from February 15, 2015, to February 15, 2016 ($n = 14,776$).

Four breast imaging locations within the same institution were included in the study. DBT with FFDM was first introduced at a single site on April 1, 2013, and was subsequently introduced at the other three sites on November 15, 2014, February 15, 2015, and January 15, 2015. On February 15, 2015, all imaging sites began using only SM and stopped obtaining a separate FFDM when patients underwent DBT screening examinations.

All images were acquired using the Hologic Dimensions with the required software for C-view. Radiologists underwent the required 8 hours of training for DBT before implementation, or had training for DBT during breast imaging fellowship.

All images were interpreted and reported utilizing the Breast Imaging—Reporting and Data System (BI-RADS) fourth or fifth edition as available (16).

Patient demographic data and mammography findings were acquired from our Mammography Quality Standards Act-compliant radiology information system (MagView versions 6.6 and 6.8). Pathology data were obtained from pathology reports in the electronic medical record (Epic 2016).

Recall rate, biopsy rate, CDR, positive predictive value 1 (PPV1), and positive predictive value 3 (PPV3) (as defined by BI-RADS fifth edition (16)) were calculated for each of the patient cohorts. The distribution of mammographic findings that led to recall were compared between the two groups. CDR was calculated for all cancers combined and then separately for ductal carcinoma in situ (DCIS) and invasive cancers. PPV1 and PPV3 were calculated excluding patients lost to follow-up. Finally, cancer characteristics obtained from pathology were compared between the groups.

Statistical analysis was performed using R (17). A generalized linear mixed model specifying the reading radiologist as the random effect and controlling for patient age was used to compare clinical outcomes between the two groups (18). The chi-square test was used to compare the distribution of recall rates of specific mammographic findings between the two groups. Fisher exact test was used to compare cancer characteristics of the two patient cohorts given the small sample size. A P value of $\leq .05$ was considered statistically significant.

RESULTS

A total of 7845 asymptomatic women underwent screening with FFDM + DBT between April 4, 2013, and February 14, 2015, and a total of 14,776 asymptomatic women underwent screening with SM + DBT between February 15, 2015, and February 15, 2016. After excluding screening recalls for technical issues ($n = 32$ in the FFDM + DBT group and $n = 54$ in the SM + DBT group), a total of 7813 studies were included in the first cohort and 14,722 in the second cohort. From recall recommendation, 2 patients were lost to follow-up in the FFDM + DBT group and 18 patients were lost to follow-up in the SM + DBT group. From biopsy recommendation, six patients were lost to follow-up in the FFDM + DBT group and eight patients were lost to follow-up in the SM + DBT group.

Clinical performance measures are summarized in Table 1. The recall rate was 7.63% (95% confidence interval [CI] 7.04–8.21%) in the FFDM + DBT cohort and 7.06% (95% CI 6.64–7.57%) in the SM + DBT cohort ($P = .04$). The distribution of mammographic findings that led to recall was similar between the two groups, as shown in Table 2 ($P = .09$).

No difference in biopsy rate, PPV1, or PPV3 was found between the two groups (Table 1). The CDR was also similar between the two groups with a total of 41 cancers (CDR 5.25, 95% CI 3.65–6.85) detected in the FFDM + DBT cohort and 82 (CDR 5.57, 95% CI 4.37–6.77) in the SM + DBT cohort ($P = .75$). CDR for DCIS and invasive cancers were also similar between the two groups (Table 1).

We further investigated the types of cancers diagnosed in each cohort (Table 3). The distribution of cancer types was similar between the two groups, with the percentage of DCIS vs invasive cancers being 24.4% and 73.2% in the first cohort and 15.8% and 84.1% in the second cohort ($P = .35$). Note that one case of lymphoma was diagnosed in the FFDM + DBT group. The distribution of invasive cancer types was also similar between the two groups ($P = .27$).

DISCUSSION

Breast cancer screening with combined FFMD + DBT decreases recall rate and improves CDR (1–6) but also increases radiation dose (9). In this study, we found that replacing FFDM with SM in an asymptomatic population being screened with DBT does not affect biopsy rate, PPV1, PPV3, or CDR, and decreased recall rate.

We found similar biopsy rates, PPV1, PPV3, and CDR between the cohort screened with FFDM + DBT and the cohort screened with SM + DBT. This supports a previous study, which similarly found that using synthesized mammography had no effect on these variables (15). In subgroup