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2D mammography, digital breast tomosynthesis, and ultrasound: which should be used for the different breast densities in breast cancer screening?☆

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ABSTRACT

Purpose: To determine which modalities [2D mammography (2D), digital breast tomosynthesis (DBT), whole breast sonography (WBS)] are optimal for screening depending on breast density.
Methods: Institutional retrospective cohort study of 2013 screening mammograms (16,789), sorted by modalities and density.
Results: Cancer detection is increased by adding WBS to 2D ($P = .02$) for the overall study population. Recall rate was lowest with 2D + DBT (10.2%, $P < .001$) and highest with 2D + DBT + WBS (23.6%, $P < .001$) for the overall study population as well.
Conclusion: Women with dense and nondense breasts benefit from reduced recall rate with the addition of DBT; however, this benefit is negated with the addition of WBS.

1. Introduction

In 2011, the Food and Drug Administration (FDA) approved the first digital breast tomosynthesis (DBT) unit—also known as *3D mammography*—as a breast imaging modality [1–3]. In 2012, several states began adopting mandatory breast density notification laws, and a similar recommendation was introduced at the federal level as well, after studies showed breast density to be an independent risk factor for breast cancer [4,5]; associated notification letters to patients suggest that they consider additional studies to supplement their annual screening mammography. However, those additional studies are not specified, and screening modalities are often ordered based on the experiences of the referring physician or by educated patients that have read about new technologies asking for them directly. For high-risk women (those with a strong familial or genetic predisposition), studies have advocated for the addition of MRI to traditional 2D mammography [6]. For women with intermediate to low or no risk factors, whole breast sonography (WBS) is more often obtained. However, faced with an alphabet soup of options—2D, 3D/DBT, and WBS—the average comer to screening mammography may still be baffled by exactly what testing to have.

A recent widely publicized multicenter study found that the addition of tomosynthesis to screening digital mammography decreased the recall rate for additional imaging and increased cancer detection rates [7]; however, the patient population was not stratified by breast density. In addition, the cost of tomosynthesis has been examined in the dense breasts, suggesting that this modality is a cost-effective technique in this screening population [8]. Other studies have examined the value of WBS in different patient populations, including those with dense breasts [9–11]; however, WBS in combination with DBT has not been well studied. Thus, a logical next step is to investigate how theses modalities—2D mammography, DBT, and WBS—work alone and/or in combination in women across the spectrum of breast densities.

Picture the following common scenario: a woman comes into your office and says, "I am due for my annual screening mammography – what tests should I get?" This research is important because an evidenced-based answer to this question is still pending. Therefore, the purpose of this study was to determine which breast imaging modality (2D, DBT, WBS) or combination of modalities should be used for patients with different breast densities presenting for screening mammography, with the objective of minimizing recall rate and maximizing cancer detection.

2. Methods

2.1. Subjects, criteria, and procedures

This is an Institutional Review Board (IRB)-approved, Health Insurance Portability and Accountability Act (HIPAA) compliant retrospective observational case–control study, with waiver of informed consent obtained.

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All women presenting to our institution for screening mammography from January 1, 2013 to December 31, 2013 were included in the study. Exclusion criteria included women with a previous history of breast cancer and women with a palpable area of concern. Most women had standard 2D digital mammography; however during the study time period, one DBT unit was available for screening purposes, and women with dense breasts (as determined by previous mammogram at our institution) were offered screening with 2D mammography plus DBT by the performing technologist if the unit was available; this determination was not made in advance by any radiologist and specifically not by the radiologist who interpreted the case. In addition, women with nondense breasts requesting DBT were accommodated when possible. As per the request of the referring physician, some women were referred for WBS as well; again, this determination was not made in advance by any radiologist and specifically not by the radiologist who interpreted the case. Approximately one third of these WBS were performed with an automated breast ultrasound machine, while the remaining were performed handheld by a sonographer. The 2D digital mammograms, as well as the whole breast ultrasounds and DBT scans were single reads read by one of 12 radiologists in the women's imaging division; all are fellowship-trained in breast imaging, with experience ranging from 2 to 20 years. If multiple screening modalities were used, they were all performed on the same day and batch read by the same radiologist the following day.

2.2. Definitions

Operational definitions were as follows [12,13]:

- Breast composition (as defined by the American College of Radiology [ACR] Breast Imaging-Reporting and Data System [BI-RADS] Atlas 5th edition) [14]
  - 1: The breasts are almost entirely fatty.
  - 2: There are scattered areas of fibroglandular density.
  - 3: The breasts are heterogeneously dense, which may obscure small masses.
  - 4: The breasts are extremely dense, which lowers the sensitivity of mammography.

- Dense breasts: breast composition Categories 3 and 4
- Nondense breasts: breast composition Categories 1 and 2
- Recall rate: screening reports that were given a BI-RADS classification of 0 divided by the total number of screens
- Cancer detection rate: number of cancers following a positive mammogram divided by the total number of screening mammograms

2.3. Data collection

For division records and educational purposes, a list of all biopsy-proven screen-detected breast cancers (ductal carcinoma in situ or any invasive mammary carcinoma) is maintained, and those from the 2013 calendar year were obtained and sorted by breast composition. The assembled study group (all asymptomatic females presenting for screening mammography during the 2013 calendar year) was defined by a search of our electronic health record using natural language processing and sorted by breast composition into subgroups. The age distribution of the patients was consistent with the ACR screening guidelines, with the majority of the patients 40 years old and older. For each subgroup, the recall rate and cancer detection rate, as per the pathology report, was calculated. Subgroups were then further subdivided into subjects who had 2D mammography, 2D + DBT, 2D + WBS, or 2D + DBT + WBS, and the recall rate and cancer detection rate were calculated for each of these "sub-sub groups" as well.

2.4. Statistical tests

The independent variables included breast composition and the breast imaging modalities utilized; the dependent variables (outcomes) were recall rate and cancer detection rate. Recall and cancer detection rates between subgroups and sub–subgroups were compared using the two-sample proportion comparison Z tests. A P value of .05 or less was utilized to determine statistical significance.

3. Results

At our institution during the 2013 calendar year, 16,789 screening mammograms were performed. Table 1 shows the categorization of these 16,789 subjects by breast density; in summary, 65% (10,915/16,789) had dense breasts, and 35% (5,874/16,789) had nondense breasts. Table 2 shows the categorization of these 16,789 subjects according to the breast imaging modalities received; in summary, over a quarter of our screening population (4,632/16,789 = 28%) received an imaging modality in addition to standard 2D mammography.

Of the 16,789 screening mammograms performed, 2888 were recalled, corresponding with an overall recall rate was 17.2%, and 67 cancers were screen detected, corresponding with a cancer detection rate of 4 per 1000 screening mammograms (67/16,789). More specifically, Table 3 shows the recall rate and cancer detection rate stratified by breast density. Notably, the highest recall rate was in subjects with heterogeneously dense breasts, but the highest cancer detection rate was in this category as well.

Table 4 takes it one step further by showing the recall rate and cancer detection rate stratified by not only by breast density but also by imaging modalities received. Looking at the entire screening population overall, 2D + DBT had the lowest recall rate (10.2%, $P < .001$), while 2D + DBT + WBS had the highest recall rate (23.6%, $P < .001$). This was the same in subjects with nondense breasts, with 2D + DBT maintaining the lowest recall rate (8.7%, $P = .03$) and 2D + DBT + WBS having the highest (24.7%, $P = .006$); this trend was demonstrated in subjects with dense breasts as well, with 2D + DBT maintaining the lowest recall rate (10.4%, $P < .001$) and 2D + DBT + WBS having the highest (23.4%); however, this was just shy of statistical significance ($P = .055$).

Looking at cancer detection rates, the addition of WBS significantly increased cancer detection rates ($P = .02$) for the overall population. Breaking up the population by breast density showed a trend toward increase in breast cancer detection with the addition of DBT and WBS, for both dense and nondense breasts; however, these numbers were not statistically significant ($P > .05$).

When the 67 screen-detected breast cancers in 2013 were classified by most invasive component, 46/67 = 69% were invasive (21/67 = 31% were Ductal carcinoma in situ [DCIS]). Table 5 shows that the addition of WBS to 2D mammography increased the detection rate of invasive cancers from 2.3 to 5.1, which was statistically significant ($P = .026$). There was a trend toward increase in invasive breast cancer detection with the addition of DBT to 2D mammography for the overall population; however, these numbers were not statistically significant ($P > .05$). Further stratification by breast densities did not yield any significant differences for invasive cancer detection with regard to the different imaging modalities.

Table 1
Subjects for screening mammography categorized by breast composition

Breast composition	$N = 16,789$
Dense	10,915 (65%)
Nondense	5874 (35%)
Fatty	892 (5%)
Scattered	4982 (30%)
Heterogeneously dense	8912 (53%)
Extremely dense	2003 (12%)