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Assessment of MRI-detected lesions on screening tomosynthesis in patients with newly diagnosed breast cancer

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Abstract

Objectives—The purpose of this study is to retrospectively evaluate the presence of screening digital breast tomosynthesis (DBT) correlates for suspicious lesions detected on pre-operative staging magnetic resonance imaging (MRI) in patients with newly diagnosed breast cancer.

Methods—After approval from the institutional review board (IRB), screening DBTs on breast cancer patients with BI-RADS 4 or 5 staging MRI exams between 8/1/17 and 8/1/18 were assessed for presence of DBT correlates for suspicious MRI findings. The pathology of the index lesion, type of additional MRI finding (mass, non-mass enhancement, or focus), correlative finding on tomosynthesis (mass, asymmetry/focal asymmetry, distortion, or calcifications), size on MRI and tomosynthesis, breast density, and pathology of the additional lesion were recorded. The chi-square test of association was used unless otherwise specified. Confidence intervals for proportions were estimated using the Wilson's score method.

Results—17/70 (24%) of additional lesions seen on pre-operative MRI exams in patients with newly diagnosed cancer had a mammographic correlate on corresponding screening DBT. There was no significant relationship between the presence of a mammographic correlate and the type of MRI finding (mass, NME, or focus), breast density, size of lesion, pathology of index cancer, or pathology of the additional lesion ($p=0.05$).

Conclusions—76% of additional lesions seen on pre-operative staging MRI in patients with newly diagnosed breast cancer are not seen retrospectively on screening DBT. Since about 24% of MRI-detected additional lesions may have a DBT correlate, DBT exams should be reviewed in patients recalled for further workup of findings seen on pre-operative MRI since this may facilitate DBT-guided biopsy of suspicious lesions, which is preferable to MRI-guided biopsy for cost and patient comfort reasons.

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Keywords

MRI; tomosynthesis; breast; cancer; screening

1. Introduction

Pre-operative breast magnetic resonance imaging (MRI) is being commonly used in clinical practice for extent of disease evaluation in patients with breast cancer. MRI reveals mammographically occult ipsilateral disease additional to the known malignancy on average in about 10–15% of patients [1] and contralateral malignancy in about 3–9% of patients [2–6]. This leads to change in surgical and overall treatment planning in breast cancer patients, with some studies reporting a change in surgical management of up to 10–19% of patients with operable primary breast cancer [7, 8]. Hence, breast MRI remains a valuable tool that is very sensitive for detection of additional malignancy in ipsilateral or contralateral breasts of patients with primary breast cancer.

Despite its clinical utility, pre-operative breast MRI remains a controversial diagnostic tool. The lower specificity of breast MRI leads to additional diagnostic studies and benign biopsies [20], which invariably increase patient anxiety and overall diagnostic costs, and may result in increased mastectomy rates [9]. Additionally, many patients have contraindications to MRI, such as extreme claustrophobia, incompatible magnetic devices, and gadolinium allergy. Additionally, breast MRI is not available in every imaging practice, and there is not enough evidence about the role of pre-operative MRI in improving long-term patient outcomes including risk for recurrence [10].

In the past few years, digital breast tomosynthesis (DBT) has become an increasingly utilized tool in screening and diagnostic mammography. Studies have shown that DBT screening reduces recall rate, increases cancer detection rate, and improves diagnostic accuracy [11–15]. Additionally, DBT increases conspicuity of certain features of cancers such as architectural distortion in comparison to full field digital mammography (FFDM) [16]. Although some data suggest that the utility of pre-operative MRI may be diminished in patients screened with DBT [17] and that DBT may increase detection of additional lesions in patients with breast cancer [18], there is limited data overall on the role of pre-operative MRI in the era of tomosynthesis. The purpose of our study was to retrospectively evaluate the presence of screening digital breast tomosynthesis (DBT) correlates for suspicious lesions seen on pre-operative staging MRI exams in patients with newly diagnosed breast cancer.

2. Material and Methods

2.1 Study Subjects, Imaging Technique, and Interpretation

Our Institutional Review Board approved this retrospective Health Insurance Portability and Accountability Act-compliant study.

We performed a review of our breast MRI database for all exams performed on patients with newly diagnosed breast cancer for extent of disease evaluation between the dates of August

1, 2017 to August 1, 2018. Patients who had additional findings identified in the ipsilateral or contralateral breast on the diagnostic MRI (Breast Imaging Reporting and Data System (BI-RADS) 4 or 5 findings) and had a bilateral screening full-field tomosynthesis exam, including bilateral mediolateral oblique (MLO) or mediolateral (ML) and craniocaudal (CC) views with synthetic mammographic (SM) full-field images (Hologic C-View™, Bedford, MA) available from the year of diagnosis and performed within 45 days of the MRI were included in the study. Four patients were excluded from the study as they were either lost to follow up or had incomplete MRI or tomosynthesis exams (secondary to either early abortion of exams or incomplete data archiving in our system).

MRI exams were performed on GE 1.5T HDxt, 1.5T 450W, or 3T 750W MRI scanners (General Electric Healthcare, Milwaukee, WI) with a dedicated breast coil. MRI exams included a T2 axial acquisition, with and without fat suppression pre-contrast and three post-contrast T1 axial series, and a diffusion-weighted imaging (DWI) series. Gadobutrol (Gadovist; Bayer Healthcare, Berlin, Germany) was used as contrast at a dose of 0.1 mmol/kg, power-injected intravenously at 2.0 mL/s. DBT examinations were performed using Hologic Selenia Dimensions digital breast tomosynthesis (Hologic, Bedford, MA). All exams were prospectively interpreted by one of eighteen breast imaging radiologists, nine of whom completed a breast imaging fellowship. One radiologist (the study radiologist) retrospectively reviewed the MRI and DBT exams to assess for DBT correlates for suspicious MRI findings. The study radiologist completed a breast imaging fellowship, with five years of breast tomosynthesis experience and two years of practice in a tertiary breast imaging academic setting at the time of the study.

2.2 Data Collection and Statistical Analysis

A breast imaging fellowship-trained radiologist, not blinded to the outcomes, retrospectively reviewed all BI-RADS 4 or 5 findings recalled on diagnostic MRI exams and reviewed the corresponding screening DBT exams to see if any findings were seen retrospectively, either on SM or tomosynthesis, to correlate with the MRI findings. Using our electronic medical record (EMR) and Picture Archiving and Communication System (PACS), the type of additional MRI finding (mass, non-mass enhancement, or focus) besides the known cancer was recorded along with its size on MRI. The pathology of the index cancer and the additional lesion, if applicable, was also recorded. If a correlative lesion was seen on tomosynthesis retrospectively, the type of finding (mass, asymmetry/focal asymmetry, distortion, or calcifications) and its size on tomosynthesis were also recorded. Breast density was assessed as dense, comprising the BI-RADS heterogeneously dense and extremely dense categories, and non-dense, comprising the BI-RADS almost entirely fatty and scattered areas of fibroglandular density.

The chi-square test of association was used unless otherwise specified. Confidence intervals for proportions were estimated using the Wilson's score method. Analyses were done in R version 3.5.2. A p-value less than 0.05 was considered statistically significant, and all tests were two-sided.

3. Results

A total of 1933 breast MRI exams were performed at our institution during the study period. Out of the 1933 MRI exams performed, 74 exams were assessed as BI-RADS 4 (n=61) or BI-RADS 5 (n=13) in women undergoing breast MRI for evaluation of extent of disease in the setting of newly diagnosed breast cancer. The breast MRI exams were performed at the discretion of the referring provider or surgeon. 70/74 MRI exams met our inclusion criteria and were evaluated in this study (Figure A). The mean patient age was 55 (range 31–78 years). Pathology of the index malignancy was as follows: 5 patients with ductal carcinoma in situ (DCIS), 47 with invasive ductal carcinoma (IDC), 11 with invasive lobular carcinoma (ILC), 5 with invasive mammary carcinoma (IMC), and 2 with malignant phyllodes (Table A). There were 19 non-dense patients (including almost entirely fatty and scattered areas of fibroglandular density) and 51 dense patients (including heterogeneously dense and extremely dense breasts), based on breast tissue density reported on the screening mammogram. On the MRI exams, the fibroglandular tissue was categorized as: 3 almost entirely fat, 22 scattered fibroglandular issue, 29 heterogeneous fibroglandular tissue, and 16 extreme fibroglandular tissue.

The additional findings recalled on the diagnostic MRI included: 40 masses, 23 non-mass enhancement (NME) lesions, and 7 foci. The mean size of these lesions on MRI was 1.5 cm (range 0.3–10 cm). The mean size by lesion type was: foci 0.4 cm (range 0.3–0.5 cm), masses 1.1 cm (range 0.3–7.2 cm), and NME 2.6 cm (range 0.5–10 cm). 23/70 (33%; 95% CI: 0.23 – 0.44) lesions were contralateral to the breast with known malignancy and 47/70 (67%; 95% CI: 0.56 – 0.77) were ipsilateral to the breast with known malignancy. 17/70 (24%; 95% CI: 0.16 – 0.35) additional lesions seen on MRI were thought to have a correlate on DBT exams (Figure B). 6/23 (26%; 95% CI: 0.13 – 0.46) lesions contralateral to the breast malignancy and 11/47 (23%; 95% CI: 0.14–0.37) lesions ipsilateral to the breast malignancy comprised the 17 MRI lesions that had a correlate on tomosynthesis. For lesions with a correlate on DBT, the mean mammographic size was 1.2 cm (range 0.5–4 cm), which had a high correlation with MRI lesion size (Pearson's $r = 0.95$).

13/40 (33%; 95% CI: 0.20 – 0.48) masses, 4/23 (17%; 95% CI: 0.07 – 0.37) NME, and 0/7 (0%; 95% CI: 0.00 – 0.35) foci had correlates. Of these 17 lesions with DBT correlates, 3 were BI-RADS 5 and 14 were BI-RADS 4 lesions. The mean size on MRI of lesions with DBT correlates was 1.4 cm (range 0.4–4.7 cm). Of these, the average size for masses was 1.1 cm (range 0.4–2 cm) and NME was 2.3 cm (range 1–4.7 cm). The DBT correlates for MRI-detected mass lesions included 2 (15%) focal asymmetries, 4 (31%) architectural distortions, 6 (46%) masses, and 1 (8%) group of calcifications (Table B). All 4 correlates for NME lesions were calcifications. There was no statistically significant difference between the type of MRI finding (mass, NME, or focus) and the presence of a correlate on tomosynthesis ($p=0.1$) (Table A). There was no statistically significant difference between the density of breasts (dense or non-dense) and the presence of a correlate on tomosynthesis ($p=0.24$). There was no statistically significant association between size of the lesion on MRI and presence of a correlate on tomosynthesis (Wilcoxon rank sum test, $p = 0.19$). There was no statistically significant association between the type of index malignancy (IDC/IMC vs. ILC vs. DCIS/others) and the presence of a correlate on tomosynthesis ($p = 0.9$).

12/17 (71%) MRI lesions that had a correlate on DBT had biopsies and the remaining 5 (29%) patients opted for mastectomies. Of these 12 biopsied lesions, 7 (58%) were malignant (3 IDC, 2 DCIS, 1 ILC, and 1 IMC) and 5 (42%) were benign, including the high-risk lesions which were deemed benign. Out of the 53 MRI lesions that had no DBT correlate (Figure C), 24 (45%) underwent biopsies and the remaining 29 (55%) opted for mastectomies. Of the 24 biopsied lesions, 9 (38%) were malignant (3 IDC, 3 DCIS, 2 ILC, and 1 IMC) and 15 (62%) were benign, which included the high-risk lesions. There was no statistically significant association between the pathology of the additional lesion (malignant or benign) and the presence of a correlate on tomosynthesis ($p = 0.17$). Overall, there were 16 additional cancers detected in our study, of which 9/16 (56%) were only visible on MRI and 7/16 (44%) had DBT correlates. When looking at all additional biopsied lesions, there were 20 benign and high-risk lesions and 16 malignant lesions, resulting in a positive predictive value (PPV) for malignancy of 44.4%.

4. Discussion

In our study, 76% (53/70) of additional lesions seen on MRI in patients with newly diagnosed breast cancer did not have a detectable correlate on bilateral screening mammogram exams done with tomosynthesis. Only 24% (17/70) MRI lesions had mammographic correlates. In our study, the presence of a detectable mammographic/DBT correlate was independent of the type of MRI finding (mass, NME, or focus) and MRI size of the lesion, likely secondary to the small sample size. It was also independent of breast density, type of index cancer, or the pathology (benign or malignant) of the additional lesion. Our data suggests that even in the era of tomosynthesis, most additional MRI-detected ipsilateral or contralateral lesions in patients with new breast cancer remain mammographically occult. This study adds to the limited data in the literature about the role of pre-operative MRI in the era of DBT and is unique in that it performs a one-to-one comparison of additional MRI-detected lesions in patients with breast cancer with their respective screening DBT exams.

The findings in our study are supported by other studies in the literature. Kim et al. [19] demonstrated in a reader study of patients with known breast cancer that MRI with FFDM has higher sensitivity for malignancy than tomosynthesis with FFDM, but MRI with FFDM has higher false positive rates than tomosynthesis FFDM. Similarly, in our study, MRI was more sensitive than DBT for additional cancer. 16 additional cancers were found in our study, of which 9/16 (56%) were only seen on MRI and 7/16 (44%) had a DBT correlate on retrospective examination. For all additional biopsied lesions, MRI had a positive predictive value (PPV) for malignancy of 44.4% (16/36). The PPV for malignancy in this study is within the documented 42–70% PPV range for breast MRI in the literature [21].

Mariscotti et al. [22] showed that 64% of additional lesions seen on breast MRI in patients with newly diagnosed cancer, that had no sonographic correlate, had a DBT correlate. Additionally, they showed that these findings seen by DBT were more likely to be masses (41%) or distortion (34%). In our study, only 17/70 (24%) of findings seen on MRI were retrospectively seen on DBT. The lower percentage of correlates seen on DBT in our study may be secondary to due to our small sample size and differences in workup, as the DBT

performed in Mariscotti's study [22] was a diagnostic DBT after a MRI on patients who did not have a sonographic correlate for the MRI finding. Similar to the Mariscotti study [22], majority of the correlates seen on DBT in our study were masses (35%) or architectural distortion (24%). Additionally, in our study, 13/40 (33%) masses, 4/23 (17%) NME, and 0/7 (0%) foci had DBT correlates, suggesting that masses seen on MRI were more likely to have DBT correlates than NME or foci, although this relationship was not statistically significant likely due to our small sample size. Similarly, lesions with DBT correlates were more likely to be malignant than benign, 58% (7/12) vs 42% (5/12) of biopsied lesions respectively, but this relationship was also not statistically significant. We hypothesize that these relationships did not reach statistical significance due to our small sample size.

There are a few limitations of our study. This is a retrospective, single-institution study with a relatively small number of cases. The DBT cases were reviewed by a single unblinded reader retrospectively, and the applicability of these findings prospectively is unknown. A significant number of patients in this cohort went to mastectomy and MRI findings of additional lesions could not be correlated directly with pathology, limiting our overall evaluation of the true rate of malignancy in our study. We did not evaluate all DBT exams, such as diagnostic images, in this study. We also did not assess for sonographic correlates of additional lesions seen on MRI. Additionally, lesions besides the index malignancy that were prospectively thought to be suspicious on DBT before the MRI was performed would not have received a BI-RADS 4 or 5 assessment on subsequent MRI and were not included in this study. We did not evaluate if some findings were seen on DBT and/or SM in comparison to DBT only. Lastly, we had a relatively high rate of mastectomy in this patient cohort, 29% in the group with DBT correlates and 55% in the group without DBT correlates. We believe that this rate is a result of selective performance of pre-operative MRI in patients with breast cancer who are likely to have multicentric or multifocal disease, as decided by the referring provider or surgeon. Due to the typical advanced extent of disease in these patients, the additional lesions may have been more conspicuous on tomosynthesis than in other patients, potentially biasing our results.

In conclusion, our study demonstrates that a significant number (76%) of additional lesions seen on MRI in patients with newly diagnosed cancer are not retrospectively seen on screening DBT. Hence, MRI remains a critical tool for evaluating extent of disease in the age of tomosynthesis. This is independent of the type of MRI finding (mass, NME, or focus), breast density, size of lesion, type of index cancer, or the pathology (benign or malignant) of the additional lesion. Although not statistically significant, mass lesions on MRI and lesions with malignant pathology are more likely to be seen on DBT, and the DBT correlates for mass lesions on MRI are more likely to be masses and architectural distortions whereas correlates for NME are likely to be calcifications. Since about 24% of additional lesions are retrospectively seen on DBT in our study, we suggest that it is worthwhile to retrospectively look at the screening DBT in patients recalled for workup of additional lesions seen on staging MRI. If a DBT correlate is seen and no sonographic correlate is visualized, a DBT-guided biopsy can be performed and a more costly and time-consuming MRI-guided biopsy can be avoided.

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Highlights

- Majority (76%) of additional lesions seen on pre-operative MRIs in patients with newly diagnosed cancer did not have a mammographic correlate on corresponding screening DBT.
- There was no significant relationship between the presence of a mammographic correlate and the type of MRI finding (mass, NME, or focus), breast density, size of lesion, type of index cancer, or pathology of the additional lesion ($p \geq 0.05$).
- Only 24% of MRI-detected additional lesions had a DBT correlate. DBT exams should be reviewed in patients recalled for further workup of findings seen on pre-operative MRI.

Fig. A.

Flow chart demonstrating the diagnostic pathways of additional lesions seen on pre-operative breast MRI in patients with newly diagnosed breast cancer.

DBT=Digital Breast Tomosynthesis

MRI= Magnetic Resonance Imaging

Fig. B.

62-year-old woman with newly diagnosed right breast invasive ductal carcinoma with an additional suspicious lesion seen in the right breast. **B.1**, T1 post-contrast subtracted axial image demonstrates mild enhancement in the upper outer right breast, representing the biopsy proven malignancy (circle). The signal void in the center is due to the biopsy clip artifact. **B.2**, T1 post-contrast subtracted axial image demonstrates an additional irregular mass in the slightly lower, outer right breast (circle), suspicious for another site of malignancy. **B.3 and B.4**, Mediolateral oblique (MLO) (C) and craniocaudal (CC) (D) tomosynthesis images demonstrate an irregular mass in the right slightly lower, outer breast (circles) corresponding to the additional finding seen on MRI. Architectural distortion in the upper outer right breast (arrows) represents the site of known newly diagnosed malignancy.

Biopsy of the additional mass in the right slightly lower, outer breast demonstrated invasive ductal carcinoma.

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Fig. C.

54-year-old woman with newly diagnosed left breast invasive ductal carcinoma with an additional suspicious lesion seen in the left breast. **C.1**, T1 post-contrast subtracted axial image demonstrates an irregular mass in the lower inner left breast, representing the biopsy proven malignancy (circle). The signal void in the center is due to the biopsy clip artifact. **C. 2**, T1 post-contrast subtracted axial image demonstrates an additional small mass in the upper inner left breast (circle). **C.3 and C.4**, Mediolateral oblique (MLO) (**C**) and craniocaudal (CC) (**D**) tomosynthesis images demonstrate the known malignancy in the lower inner left breast. No mammographic correlate was seen for the small MRI-detected mass in the upper inner left breast. No ultrasound correlate was seen, and the patient

underwent MRI-guided biopsy of the additional lesion, which showed invasive ductal carcinoma.

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Table A.

Breast and Lesion Characteristics in Patients With and Without DBT Correlates of Additional MRI Lesions Seen on Staging MRIs

	Correlate seen on DBT (n=17)	Correlate not seen on DBT (n=53)	p-value
<i>Breast Density</i>			0.24
Dense	10	41	
Non-dense	7	12	
<i>Pathology of index lesion</i>			0.92
IDC/IMC	12	40	
ILC	3	8	
DCIS	2	3	
Phyllodes	0	2	
<i>Additional lesion type on MRI</i>			0.12
Mass	13	27	
Non-Mass	4	19	
Enhancement			
Focus	0	7	
Additional lesion size on MRI (cm) Mean (Range)	1.36 (0.40 – 4.70)	1.55 (0.30 – 10.00)	0.19*
<i>Pathology of additional lesion</i>			0.17
Benign	6	24	
Malignant	7	9	
IDC	3	3	
IMC	1	1	
ILC	1	2	
DCIS	2	3	

DBT=Digital Breast Tomosynthesis

MRI=Magnetic Resonance Imaging

IDC=Invasive Ductal Carcinoma

IMC=Invasive Mammary Carcinoma

ILC=Invasive Lobular Carcinoma

DCIS=Ductal Carcinoma In Situ

* Wilcoxon rank sum test

Table B.

DBT Features of Additional Staging MRI-detected Lesions With DBT Correlates

DBT Feature	n(%)
Average additional lesion size on DBT (cm) Mean (Range)	1.2 (0.5–4)
<i>Mass on MRI</i>	13(100)
Focal asymmetry	2 (15)
Architectural distortion	4 (31)
Mass	6 (46)
Calcifications	1 (8)
<i>NME on MRI</i>	4(100)
Calcifications	4(100)

DBT=Digital Breast Tomosynthesis

MRI=Magnetic Resonance Imaging

NME=Non-mass Enhancement