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The relationship of breast density in mammography and magnetic resonance imaging in high-risk women and women with breast cancer

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ABSTRACT

Purpose: To evaluate the relationship between mammographic breast density (MBD), background parenchymal enhancement (BPE), and fibroglandular tissue (FGT) in women with breast cancer (BC) and at high risk for developing BC.
Methods: Our institutional database was queried for patients who underwent mammography and MRI.
Results: Four hundred three (85%) had BC and 72 (15%) were at high risk. MBD ($P = .0005$), BPE ($P < .0001$), and FGT ($P = .02$) were all higher in high-risk women compared to the BC group.
Conclusions: Higher levels of MBD, BPE and FGT are seen in women at higher risk for developing BC when compared to women with BC.

1. Introduction

Mammographic breast density (MBD) has been shown to be an independent risk factor for breast cancer [1–6]. While digital mammography has improved diagnostic accuracy in patients with dense breasts, sensitivity of mammography remains significantly lower in dense breasts, as low as 70% [7,8]. Decreased sensitivity of mammography is of particular concern to women at high-risk of developing breast cancer. There is well established literature that supports the benefit of screening magnetic resonance imaging (MRI) in women at high-risk for breast cancer. Current screening recommendations for high-risk women may include the use of screening ultrasound and/or magnetic resonance imaging in addition to digital mammography. In its 2007 guidelines for breast cancer screening, the American Cancer Society recommended annual screening MRI as an adjunct to mammography for women at high-risk for breast cancer [9]. MRI has been shown to be an effective screening tool in this group, with sensitivity for cancer detection greater than that of mammography and of mammography and ultrasound combined [10–14].

With an increasing role of screening MRI, attention has turned to whether the amount and degree of enhancing breast tissue; including the proportion of fibroglandular tissue (FGT) and background parenchymal enhancement (BPE) is associated with a risk for breast cancer. FGT can be considered the MRI equivalent of MBD, which is a reflection of the stromal and epithelial tissue components of the breast tissue. Unlike breast density as depicted on mammography, MRI allows for a cross-sectional contiguous slice analysis of FGT [15]. BPE is thought to reflect the vascularity of the fibroglandular tissue and has been shown to be influenced by hormonal changes, including fluctuations in the menstrual cycle, menopausal status and hormone modifying medication [16–30].

Although BPE has been shown not to correlate directly with MBD [31], it similarly represents background noise on imaging, which may affect interpretation and detection accuracy [21,32]. However, the association between BPE and breast cancer has not been as well established as it has for MBD. While a relationship between BPE and breast cancer risk has been suggested [15], other recent studies have demonstrated no increased incidence of cancer with increased BPE [21,32]. There is very limited information regarding the relationship of fibroglandular tissue on contiguous MR images, breast density and BPE in a high-risk population.

Continuing investigation is needed to determine if these MRI imaging characteristics could be used as imaging biomarkers for cancer risk. The purpose of our study was to evaluate the relationship between MBD, and the MRI imaging characteristics of fibroglandular tissue and BPE in high-risk women compared with those undergoing evaluation after being diagnosed with breast cancer and prior to surgery.

2. Materials and methods

2.1. Study population

The Breast Cancer Database was established in January 2010 and includes all patients undergoing definitive breast cancer surgery at our

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institution. The variables collected in this database include personal and family history, screening history, method of diagnosis, stage at diagnosis, details of treatment and outcomes. The High Risk Breast Cancer Consortium was established in January 2011 and includes all patients who do not have breast cancer, but are at an increased risk for developing the disease based on having a strong family history of breast cancer (at least 1 first degree relative) [33,34], BRCA1,2 mutation carriers [35], a history of atypical hyperplasia (AH) and/or lobular carcinoma in situ (LCIS) [36–39]. The variables collected in this database include family history, genetic testing results, screening history, risk reduction strategies, and outcomes. All clinical data are obtained from detailed questionnaires filled out by patients who consented to the database studies and medical chart review. Waiver of authorization and consent was granted by the institutional review board for this Health Insurance Portability and Accountability Act compliant retrospective study.

We queried both longitudinal databases to identify all women who underwent both mammography and breast MRI at our institution. Patients who had either a mammography and/or an MRI performed at an outside institution were excluded from the analysis, as well as patients who didn't have an MRI within 6 months of having a mammogram. Both imaging modalities for the breast cancer patients were performed after diagnosis and before surgery as part of their presurgical workup. The imaging data collected for the high-risk patients were taken from their routine screening protocols. Our screening protocol follows conventional practice and of alternating screening mammography and breast MRI every 6 months [40]. For subgroup analyses, three risk cohorts were formed based on the etiology of breast cancer risk. Group 1 included patients who have >20% lifetime risk with a strong family history of breast cancer and/or who were BRCA 1,2 mutation carriers [9]; Group 2 included patients with intermediate risk who had a history of AH and/or LCIS [9]; and Group 3 included patients who had familial and/or genetic risk (Group 1) as well as history of AH and/or LCIS (Group 2). These three risk groups are not mutually exclusive.

2.2. Mammography and MRI assessments

2.2.1. Mammography imaging technique

All mammography was performed with digital technique using MAMMOMAT Novation DR software (version V8.3, Siemens Healthcare).

2.2.2. MRI technique

MRI examinations were performed on commercially available systems at 1.5 T (Avanto, Siemens Medical Solutions) or 3.0 T (TIM Trio, Siemens Medical Solutions) using a dedicated surface breast coil (7-Channel Breast Biopsy Array, InVivo Research). Patients were imaged prone, using a standard imaging protocol that included a localizing sequence followed by a sagittal T2-weighted sequence (TR/TE, 7220/84); a sagittal T1-weighted non-fat-suppressed 3D fast spoiled gradient-recalled echo sequence (4.01/1.52; flip angle, 12°; matrix, 384 × 384; field of view, 270 mm; section thickness, 1 mm) followed by the same sagittal T1-weighted fat-suppressed 3D fast spoiled gradient-recalled echo sequence performed before and four times after a rapid bolus injection of 0.1 mmol/L of gadopentetate dimeglumine (Magnevist, Bayer Healthcare Pharmaceuticals) per kilogram of body weight at an injection rate of 2.0 ml/s via an intravenous catheter. Image acquisition began immediately after administration of the contrast material and saline bolus. The first contrast-enhanced dynamic sequence was obtained at approximately 100 s, followed by four additional consecutive sequences (three sagittal followed by one delayed axial). At our institution, pre-menopausal women who undergo a screening breast MRI undergo their breast MRI on Days 7–14 of the menstrual cycle. Pre-menopausal women who are newly diagnosed with breast cancer undergo their breast MRI regardless of their menstrual cycle in an effort to minimize any delays in their breast surgery.

2.3. Image interpretation

2.3.1. Mammographic density

MBD was classified according to the American College of Radiology's categories as almost entirely fatty, scattered fibroglandular, heterogeneously dense breasts, or extremely dense (Fig. 1) [41]. Mammographic breast densities were evaluated on two separate occasions. They were obtained from the original radiology reports. In addition, the mammograms were randomized and a single fellowship-trained breast imaging radiologist with 13 years of experience reassessed the MBD.

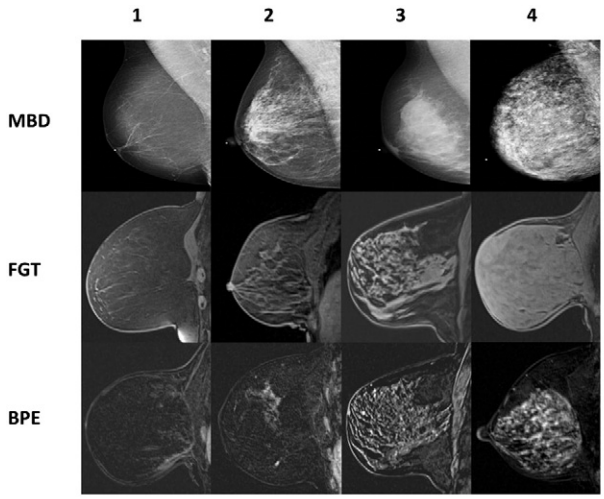
2.3.2. Fibroglandular tissue

FGT is defined as nonfat, non-cystic breast in relation to the total breast volume. The same experienced breast imaging radiologist assessed the amount of FGT parenchyma on contiguous nonfat- and fat-suppressed T1-weighted and T2-weighted images of both breasts. A four-point scale, similar to that used by the American College of Radiology to classify mammographic density, was used to classify the relative amount of FGT as almost entirely fat, scattered fibroglandular tissue, heterogeneous fibroglandular tissue and extreme fibroglandular tissue (Fig. 1) [15]. Since FGT was not included in our reports, this assessment was performed by the radiologist.

2.3.3. Background parenchymal enhancement

BPE is the amount of enhancing fibroglandular tissue. The level of global BPE was assessed using a combination of pre- and the initial post-contrast T1-weighted fat saturated and subtracted images. The volume and intensity enhancement was graded on a four-point scale as minimal, mild, moderate, or marked in accordance with the new Breast Imaging-Reporting and Data System (BI-RADS) categories (Fig. 1) [42]. Both intensity and volume of background enhancement were considered in the assessment. In women who were newly diagnosed with breast cancer, the assessment of the BPE and FGT was performed in the contralateral breast. Similar to the MBD, the BPE were obtained from the radiology reports. In addition a single radiologist retrospectively assessed the BPE.

Evaluation of the MBD, BPE and the amount of FGT was performed by a single radiologist who was blinded to the clinical history. All images were anonymized. The mammograms and breast MRIs were randomized so that the reader did not interpret the breast MRI with knowledge of the mammographic density. In cases where there was disagreement



MBD: 1.) almost entirely fatty, 2.) scattered fibroglandular, 3.) heterogeneously dense, 4.) extremely dense; **FGT:** 1.) almost entirely fat, 2.) scattered fibroglandular tissue, 3.) heterogeneous fibroglandular tissue, 4.) extreme fibroglandular tissue; **BPE:** 1.) minimal, 2.) mild, 3.) moderate, 4.) marked.

Fig. 1. Categories of MBD, FGT and BPE.