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Research article

Comparison of screening CEDM and MRI for women at increased risk for breast cancer: A pilot study

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ABSTRACT

Objectives: Contrast enhanced digital mammography (CEDM) is a new breast imaging technology increasingly used in the diagnostic setting but its utility in the pure screening setting has not been reported. The goal of this pilot study is to prospectively compare screening CEDM to breast MRI in women with an increased risk for breast cancer.

Methods: In this IRB-approved HIPAA-compliant study, 318 women at increased breast cancer risk were consented (December 2012–May 2015) to undergo CEDM in addition to their scheduled MRI. CEDM was performed within 30 days of screening MRI. CEDM was interpreted blinded to MRI. The reference standard was defined as a combination of pathology and 2-year imaging follow-up.

Results: Data from 307/318 patients were evaluable. Three cancers (two invasive cancers, one ductal carcinoma in situ) were detected at first round screening: MRI detected all three and CEDM detected the two invasive cancers. None of the three cancers was seen on the low energy mammograms which are comparable to conventional mammography. At 2 year imaging follow up, there were 5 additional screen detected cancers and no palpable cancers. The positive predictive value 3 (PPV_3) for CEDM was 15% (2/13, 95% CI: 2–45%) and 14% for MRI (3/21, 95% CI: 3–36%). The specificity of CEDM and MRI were 94.7% and 94.1% respectively.

Conclusions: Both CEDM and MRI detected additional cancers not seen on conventional mammography, primarily invasive cancers. Our pilot data suggest that CEDM could be valuable as a supplemental imaging exam for women at increased risk for breast cancer who do not meet the criteria for MRI or for whom access to MRI is limited. Validation in larger multi institutional trials is warranted.

1. Introduction

Mammography is the only breast imaging examination that has been demonstrated to reduce breast cancer mortality. It is relatively inexpensive and widely available. However, its sensitivity is limited, ranging from 70 to 85% [1–3] overall but is significantly reduced to 30–50% in women with dense breasts which can be attributed to the masking effect of dense breast tissue. Supplemental imaging examinations to overcome the limitation in sensitivity include digital breast tomosynthesis (DBT) and screening ultrasound. Combined mammography and ultrasound can improve sensitivities to 91% [1,4]. DBT detects an additional 1.4–2.5 cancers per thousand women [5] while ultrasound detects approximately 3.5 cancers per thousand women [6].

However, although DBT and ultrasound morphologic imaging increase cancer detection, diagnostic performance can further be

Abbreviations: BI-RADS, Breast Imaging-Reporting and Data System; BPE, background parenchymal enhancement; CI, confidence interval; CEDM, contrast enhanced digital mammography; DCIS, ductal carcinoma in situ; MIP, maximum intensity projection; MRI, magnetic resonance imaging

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significantly improved by functional imaging. Dynamic contrast-enhanced MRI of the breast provides both high-resolution morphologic and functional information on neovascularity as a tumor specific feature. Therefore, MRI often detects cancers which are mammographically and sonographically occult [7,8]. To date, MRI is the most sensitive exam for the detection of breast cancer in both women at average and increased risk [9], yielding 15 cancers for every 1000 women at intermediate (15–20%) or high (> 20%) risk [10]. Multiple studies evaluating imaging of women at intermediate and increased risk for developing breast cancers have demonstrated that in approximately 45% of women, cancers are only detected by MRI [11–13]. Due to these excellent results specific screening programs for high risk women that include both annual mammography and MRI have been developed and are recommended by the American Cancer Society and the European Society for Breast Imaging [9,14]. However, despite this increased ability for cancer detection, MRI may not be an option for every woman at increased risk due to its high cost and low availability.

Contrast enhanced digital mammography (CEDM) is an FDA approved technology which, similar to MRI, is based on the principle of imaging neovascularity. CEDM uses intravenous iodinated contrast to detect breast cancer on a digital mammography platform. Compared to MRI, this technique is relatively inexpensive and potentially more accessible to more women. Previous studies in the diagnostic setting have demonstrated that CEDM is significantly more sensitive and specific than mammography alone in women with abnormal screening mammograms, ultrasound, clinical symptoms and known cancer. Early studies have even demonstrated that the performance of CEDM is superior to that of mammography alone in the diagnostic setting and comparable to the performance of MRI in women with known cancers [15–19]. Moreover, women with dense breasts may particularly benefit from CEDM [20].

To our knowledge, the utility of CEDM in the pure screening setting has not yet been reported. Therefore, we undertook this pilot study to prospectively evaluate and compare screening CEDM to screening breast MRI in women at an increased lifetime risk for breast cancer.

2. Materials and methods

2.1. Patients

This prospective, single-institution study was conducted at a tertiary cancer hospital and was approved by the Institutional Review Board. It was compliant with the US Health Insurance Portability and Accountability Act. Between December 2012 and May 2015, we screened all women > 21 years of age who were scheduled for screening breast MRI because of a history of elevated lifetime risk of breast cancer for eligibility. These patients represented a combination of intermediate risk (high-risk lesions, women with a personal history of breast cancer) and high (greater than 20%) lifetime risk patients including BRCA 1 & 2 carriers and women who had received thoracic radiation when young. Patients with renal insufficiency, a history of allergy to iodinated contrast, or who were pregnant or lactating were excluded from the study. Informed consent was obtained from eligible patients.

We recorded the following patient characteristics: patient age, menstrual status, hormone intake, risk factors for breast cancer including high risk lesions (atypical ductal hyperplasia, lobular neoplasia, radial scars and papillomas), family history of breast cancer, personal history of breast cancer, history of prior radiation to the chest, genetic mutations, breast density and background parenchymal enhancement on both CEDM and MRI.

A portion of this patient population has been previously reported. However, there are no redundant data between those prior studies and this study. In one study [36] we determined the feasibility of using only the low energy images performed as part of the CEDM in 88 women to determine if they were comparable to the patients' recent digital mammograms so that going forward there would be no need to do a separate mammogram when doing CEDM. Of the 88 patients reported, 28 overlapped with the 307 reported herein. Since we only evaluated the low energy images, that study did not discuss sensitivity or specificity in regards to breast cancer screening using CEDM.

A second study [37] compared background parenchymal enhancement (BPE) on CEDM to MRI in 278 women (212 of which are reported in this study). BPE was not specifically evaluated in this study and therefore there is no significant redundancy in data reporting.

2.2. CEDM and MRI technique

2.2.1. CEDM

CEDM was performed within 30 days of MRI using the GE SenoBright mammography unit (Buc, France). Patients were given 1.5 ml/kg body weight of Omnipaque 350 (iohexol, GE, Shanghai, China) through a 20 gauge needle at an injection rate of 3 ml/sec with a maximum injected volume of 150 ml. Once contrast injection was complete, there was a 2.5–3 min delay during which time the patient was positioned for her mammogram. Mammographic imaging was then performed with almost simultaneous low (26–30 kVp) and high (45–49 kVp) energy images. Medio lateral oblique and cranio caudal views of each breast were obtained and completed within 5 min of completion of contrast injection. The total examination time is approximately 8–9 min. The low energy images which were generated were interpreted as the digital mammogram. A recombination algorithm subtracted out the unenhanced breast tissue and provided a subtracted image which highlighted areas of contrast enhancement.

2.2.2. MRI

For the first year of the study, MRI examinations were performed with the patient prone on a 1.5-T or 3.0-T commercially available system (General Electric Medical Systems, Milwaukee, WI) using a dedicated surface breast coil. Integrated Parallel Acquisition Techniques (iPAT) were utilized for imaging both breasts simultaneously. The standard examination included a localizing sequence followed by sagittal fat-suppressed T2-weighted and sagittal T1-weighted sequences. A T1-weighted three dimensional, sagittal fat-suppressed fast spoiled gradient-echo sequence was then performed before and three times 90 s after a rapid bolus injection of gadolinium administered intravenously and followed by a saline bolus. A delayed axial T1 post-contrast sequence and diffusion weighted imaging were also performed. Section thickness was 3 mm with no gap using a minimum matrix of 256 × 256. Unenhanced images were subtracted from the contrast-enhanced images on a pixel-by-pixel basis producing subtracted post-contrast subtraction sequences. Maximum intensity projection images were generated utilizing the first post-contrast and the first post-contrast subtracted data. For the last year and a half, utilizing the same MRI scanners, pre and 3 post-contrast images with subtraction sequences were performed in the axial plane at 1 mm thick isotropic contiguous slices using a 3D VIBRANT sequence. The field of view is 300–360 mm. Localizing images, T2 weighted axial images, T1 non fat saturated images, sagittal reformatted images and sagittal reformatted subtraction images and subtraction maximum intensity projection (MIP) images were also generated.

2.3. Interpretation of CEDM and MRI

CEDM interpretation was randomized to one of four experienced breast radiologists with at least two years of experience interpreting CEDM (R1 n = 77, R2 = 73, R3 = 78, R4 = 79) who read the examinations blinded to the MRI images or reports. Low energy images were read as the patients' routine mammogram with a BIRADS score. Contrast enhanced images were also given a BIRADS score. Final interpretation of CEDM included a combined score of both the low energy images and iodine images and comparison to any available prior