Contrast-Enhanced Spectral Mammography compared to breast MRI for evaluation of the extent of disease in newly diagnosed breast cancer

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This article summarizes the results of a recent study comparing the diagnostic performance of MRI and Contrast-Enhanced Spectral Mammography (CESM) for the detection of index and secondary cancers in women with newly diagnosed breast cancer. The results indicate that, in such patients, CESM has a sensitivity equal to that of MRI and a PPV greater than that of MRI,

Breast cancer is the most common non-cutaneous malignancy among women in the United States and worldwide, with an incidence of 233 per 100,000 in the United States and 362 per 100,000 in the European Union [1].

While mammography and breast ultrasound are considered as gold standards for the initial detection and diagnosis of breast cancer, dynamic contrast-enhanced breast magnetic resonance imaging (MRI) has the highest overall sensitivity for detecting breast cancer, with a reported sensitivity of 90% [2]. MRI depicts both lesion morphology and perfusion behavior and is well suited for identifying multifocal (more than one cancer site within the same quadrant), multicentric (more than one cancer site among different quadrants), and contralateral breast cancer. Accordingly, MRI is the imaging modality of choice for evaluating newly diagnosed breast cancer [3, 4]. In our practice, women with dense breasts, mammographically occult breast cancer, and invasive lobular carcinoma are referred routinely for MRI to evaluate the extent of disease for treatment planning.

However, the specificity of MRI is limited [5], as both benign and malignant lesions can enhance [6]. Additional sequences such as non-fat saturated T1, T2 or short tau inversion recovery (STIR), and diffusion weighted imaging have been added to MRI protocols to help improve lesion characterization, with nevertheless imperfect specificity and additional trade offs of longer scan times, lower throughput, longer interpretation times, and overall higher costs. For the patient, the limited specificity of MRI is especially problematic for treatment planning, since additional suspicious enhancing lesions detected on MRI warrant targeted biopsy to confirm malignancy prior to any change in management, often resulting in delayed treatment [7-9].

Recently, a few studies have evaluated bilateral contrast-enhanced spectral mammography (CESM) as an alternative to MRI, citing its similar ability to depict lesion morphology and perfusion, while doing so with faster imaging acquisition, equal sensitivity for detecting index cancers [10, 11], superior specificity [10], and lower cost. CESM has been used both for screening and diagnostic indications, including evaluation of newly diagnosed breast cancer.

The purpose of our retrospective study was to compare the diagnostic performances of MRI and CESM for detection of index and secondary cancers in women with newly diagnosed breast cancer, using histology or imaging stability as the reference standards.

We studied a cohort of women with newly diagnosed breast cancer who underwent both MRI and CESM as part of routine clinical evaluation between March 2014 and October 2015 (n = 52). The majority of these women first underwent MRI and were subsequently referred for CESM as part of "second look" diagnostic imaging in conjunction with targeted breast ultrasound (n = 46). The minority of these women were diagnosed with breast cancer at outside institutions without prior imaging available; they first underwent CESM as part of diagnostic imaging in conjunction with targeted breast ultrasound prior to MRI (n = 6).

MRIs were performed in the prone position without breast compression on a 1.5 Tesla scanner (Siemens

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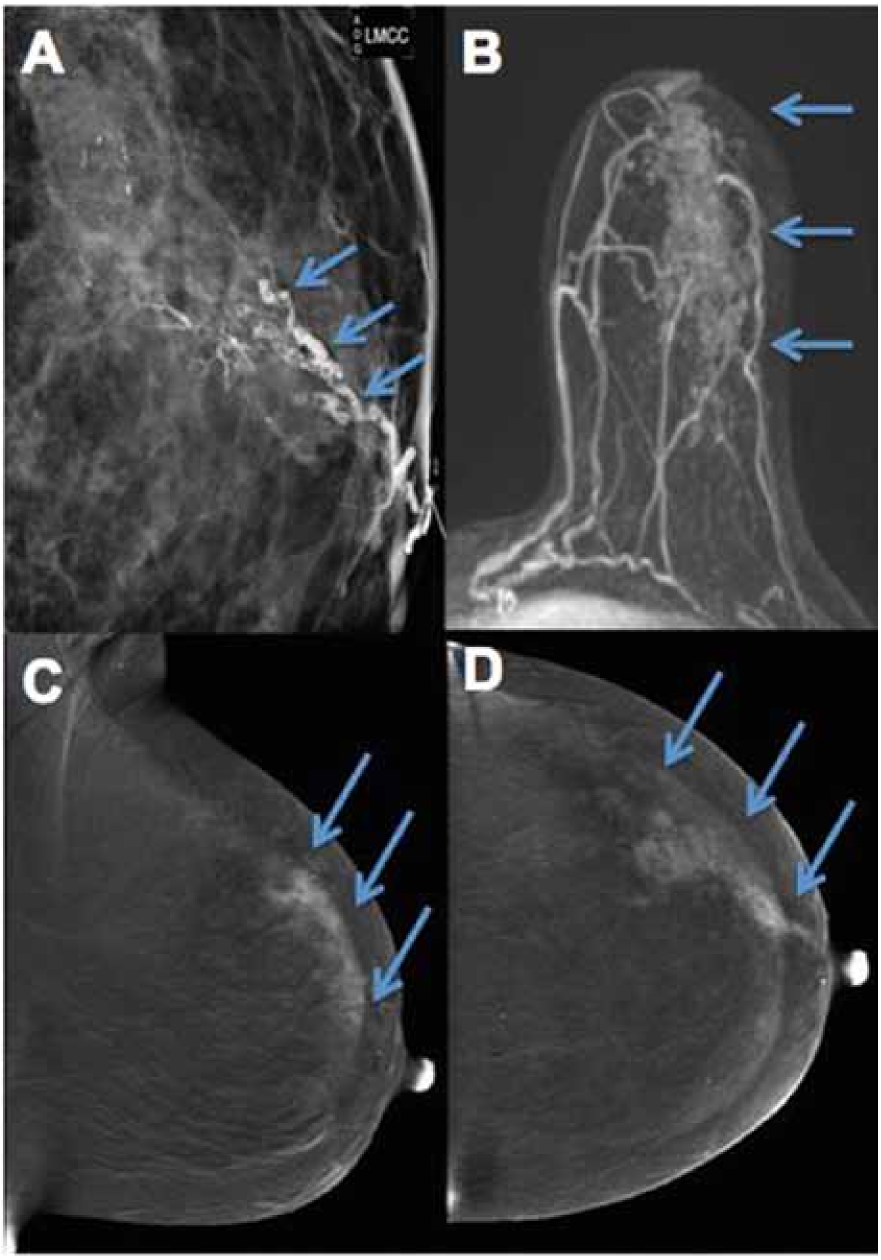

Figure 1. A 43 year-old woman presented for spontaneous bloody left nipple discharge. After inconclusive diagnostic imaging evaluation including mammography and breast ultrasound (not shown), ductography showed multiple irregular filling defects within medium-sized ducts (A, arrows). The patient underwent contrast-enhanced breast MRI and spectral mammography. Both MRI (B, arrows) and CESM (C and D, arrows) show clumped non-mass enhancement in a segmental distribution in the upper outer quadrant of the left breast. MRI-guided core needle biopsy showed ductal carcinoma in situ.

Avanto, Erlangen, Germany) using a dedicated 16-channel breast coil. The following axial sequences were performed: three-plane localizers, non-fat saturated T1, STIR, and pre- and four post-contrast fat saturated T1 at 90 second intervals after intravenous injection of 15 mL gadolinium contrast (Magnevist, Bayer, Leverkusen, Germany) using a power injector at a rate of 2 mL/sec followed by a 20 mL saline flush. Images were reviewed on a dedicated workstation (CADstream, Merge Healthcare Inc., Chicago, IL).

CESMs were performed on a dual energy digital mammography (SenoBright, GE Healthcare Inc., Chicago, IL). Within seven minutes, standard craniocaudal and mediolateral oblique mammographic projections of each breast were obtained at 90 second intervals after a two minute delay following intravenous injection of 90 cc iodinated contrast (Omnipaque 350, GE Healthcare Inc., Chicago, IL) using a power injector at a rate of 3 mL/sec followed by a 10 mL saline bolus. The peripheral intravenous line was disconnected from the injector prior to image acquisition. High and low energy images of each projection were obtained and post-processed automatically for subtraction images by the digital mammography unit. Images were reviewed on a dedicated workstation (GE Healthcare Inc., Chicago, IL).

Clinical MRI reports interpreted in consensus by two of five breast radiologists with two to 17 years of experience with MRI were compared to blinded interpretations of CESMs (both low energy and post-contrast subtraction CESM images) performed independently by two of five breast radiologists with 2.5 years of experience with CESM.

Index cancers were identified based on the presence of a dominant suspicious enhancing mass, non-mass enhancement (NME), or enhancing focus. Suspected secondary cancers were identified based on the presence of additional suspicious enhancing masses, NME, or enhancing foci in the other three quadrants of the ipsilateral breast or in any quadrant of the contralateral breast, with "second look" diagnostic imaging consisting of CESM and targeted breast ultrasound and/or biopsy requested for further evaluation.

When breast conserving treatment was desired, additional suspicious MRI findings were pursued with CESM and targeted breast ultrasound. If CESM and/or ultrasound collaborated the MRI finding as suspicious, targeted biopsy followed. If CESM and/or ultrasound revealed a benign or no correlate for MRI finding, such as a complicated cyst, imaging follow up ensued (MRI for MRI only findings and ultrasound for sonographic correlates). MRI findings, CESM findings, histology results, and/or imaging follow up were recorded.

52 women with 120 lesions were included for analysis (mean age 50 years, range 29 to 73 years). 11 women had one lesion each, 19 women had two lesions each, 17 women had three lesions each, and five women had four lesions each.

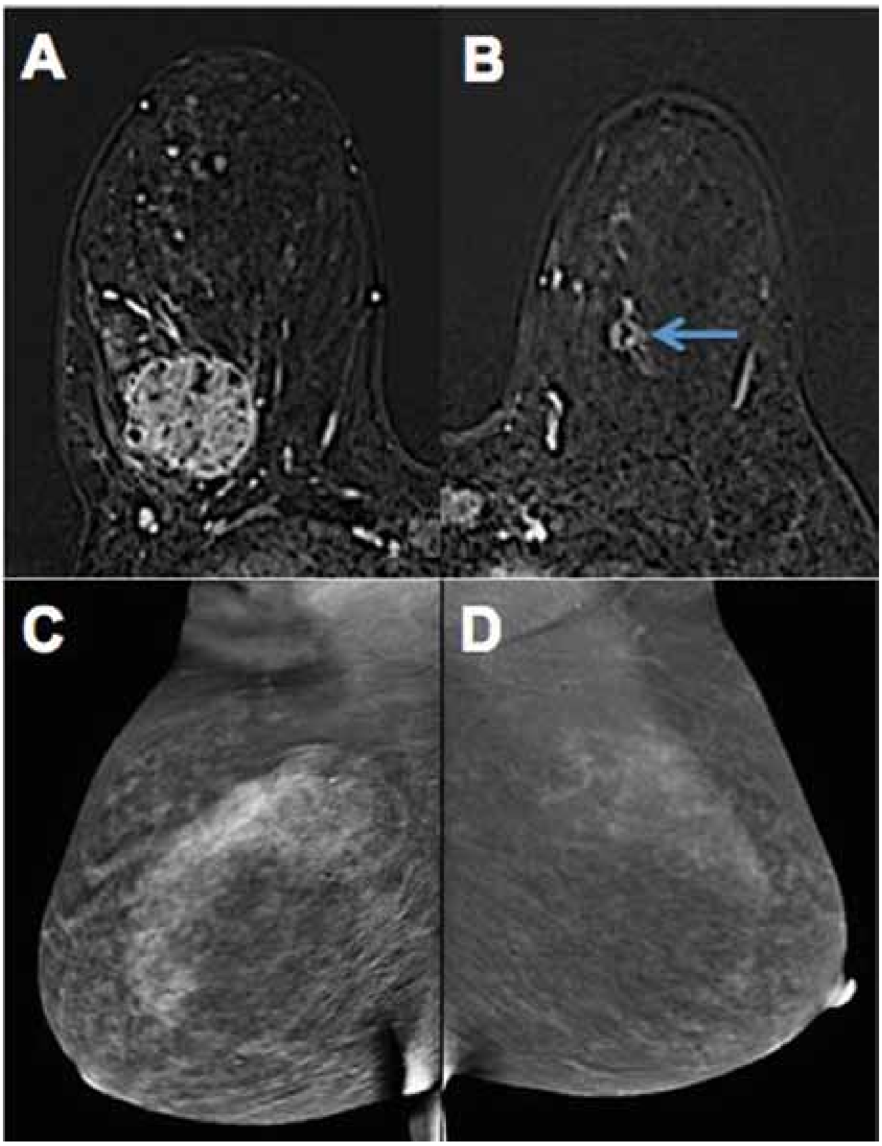

Figure 2. A 46 year-old woman presented with a right breast palpable abnormality at the 9:00 position. After diagnostic mammography and breast ultrasound showed a suspicious 4.5 cm mass at the 9:00 position of the right breast (not shown), ultrasound-guided core needle biopsy yielded invasive carcinoma of no special type. Contrast-enhanced breast MRI showed the biopsy-proven cancer at the 9:00 position of the right breast (A), as well as a rim-enhancing mass at the 11:00 position of the left breast (arrow, B) without correlate on CESM (C, D) or targeted second look breast ultrasound. MRI-guided biopsy yielded fibrocystic change.

In our study, CESM had similar overall sensitivity (94% (66/70) versus 99% (69/70)), significantly higher PPV (93% (66/71) versus 60% (69/115), $p < 0.001$), and significantly fewer false positives than MRI (five versus 45, $p < 0.001$) for overall cancer detection. These MRI false positive lesions resulted in 21 additional core needle biopsies, one surgical excisional biopsy, and ten prophylactic contralateral mastectomies. The excisional biopsy and prophylactic contralateral mastectomies did not result in additional cancer diagnosis. CESM also had similar secondary cancer detection compared to MRI (100% (11/11) versus 91% (10/11)).

CONCLUSION

CESM is a promising imaging modality with the potential to depict lesion morphology and perfusion with faster imaging acquisition, equal sensitivity [Figure 1], superior PPV for cancer detection [Figure 2], and lower cost compared to MRI. The superior PPV of CESM may help expedite treatment planning for women with newly diagnosed breast cancer. CESM can be integrated into routine diagnostic imaging and is valuable for extent of disease evaluation in women with newly diagnosed breast cancer. If these findings are confirmed, more women will have a high quality diagnostic option when MRI is not available or when contraindications for MRI exist.

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