Why implementing abbreviated breast MRI is a good idea: perspectives from North America

By Dr. B. E. Dogan

Breast magnetic resonance imaging (BMRI) has been used with increasing frequency over the past 10 years because of its well-documented high sensitivity for detecting breast cancers, especially those that are occult on conventional imaging. Compared with other screening modalities, such as X-ray mammography and ultrasonography, MRI has a substantially higher diagnostic sensitivity and cancer yield and lower interval cancer rates [1-6]. In large patient populations, BMRI screening cancer yields, range from 2.6% to 9.3% [1-11], with a large number of patients having benign outcomes. Since BMRI is also used as an advanced diagnostic test, clinical MRI protocols usually utilize multiple sequences to best characterize and establish the extent of malignant disease, but these additional sequences result in longer scan and overall table times. In diagnostic imaging centers, the acquisition time for BMRI protocols ranges from 20–60 minutes depending on the sequences used [6-11].

BMRI has become an established modality for breast cancer screening mainly for women with an elevated familial risk of breast cancer. For high-risk women (e.g. those with hereditary gene mutation carriers or whose lifetime breast cancer risk is greater than 20%), the American Cancer Society recommends yearly BMRI screening in addition to mammography beginning at age 30 years [12]. However, the large number of screening MRI studies resulting from this regimen have given rise to substantial health care cost-related concerns that may limit access to high-quality MRI screening for women with a familial risk of breast cancer. Furthermore, the long acquisition time of BMRI can increase the study cost, compromise patient comfort, and decrease image quality (IQ). In the American College of Radiology (ACR) Imaging Network 6666 trial, women cited their inability to tolerate the long scan time owing to claustrophobia (25.4%) and the long scan time leading to "time constraints" (18.2%) as the primary reasons they refused MRI screening [13].

ABBREVIATED MRI TECHNIQUES

Prior efforts to demonstrate a shorter MRI scan to be adequate for annual high-risk screening have been retrospective in nature. In a recent single-site study of women with a mildly to moderately increased breast cancer risk, Kuhl *et al.* [14] showed that separate interpretations of the images from a complete BMRI protocol and of a subset of images containing only the pre-contrast and the post-contrast arterial phase had equivalent diagnostic accuracy and negative predictive value. All of the invasive cancers were less than 1.0 cm in size, and there were no axillary metastases identified clinically or at sentinel lymph node biopsy. The negative predictive value of the Abbreviated MRI was 99.8%. The mean acquisition time was three minutes for the Abbreviated MRI versus 17 minutes for the full DCE-MRI. The specificity and positive predictive value of Abbreviated MRI was equivalent to the full protocol.. Although this and later studies [15,16)] provided a framework for expanding screening MRI (in a manner similar to the screening mammography versus diagnostic mammography concept), they did not evaluate protocols containing a T2-weighted sequence, which is one of the minimal requirements of ACR BMRI accreditation [17]. In addition, these retrospective reader studies do not reflect the true clinical scenarios in which substantial table time for field shimming and repeat series may be required due to the use of the conventional chemical shift selective fat saturation methods in both T2-weighted and dynamic contrast-enhanced (DCE) T1-weighted imaging.

Therefore, there is a need to develop a short screening breast MRI protocol that includes a bright- fluid

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ABBREVIATIONS

AB-MRI	Abbreviated Breast MRI
ACR	American college of Radiology
BMRI	Breast MRI
DBT	Digital breast tomosynthesis
DCE	Dynamic contrast enhanced
ECOG/ACRIN	-Eastern Cooperative Oncology Group; Amer. College of Radiology Imaging Network
eFlex	3D fast Dixon dual echo spoiled gradient echo sequence
FSE	Fast spin echo
FSGPR	Fast spoiled gradient echo
FTED	Fast triple Echo Dixon
IDEAL	Iterative decomposition of water and fat with echo asymmetry and least-squares estimation
IQ	image quality
SBMRI	Short breast MRI
SOC MRI	Standard of Care MRI
VIBRANT	Volume imaging for breast assessment

T2-weighted sequence and a fast T1-weighted dynamic sequence with consistent fat saturation and image quality similar to standard of care (SOC) MRI protocols. Over time, Abbreviated MRI protocols have evolved to include a fluid-bright series, with any contrast-enhanced protocol that takes less than 10 minutes to perform being accepted as Abbreviated.

In our work [18], we assessed the feasibility of using a short BMRI (SBMRI) protocol that produces high-quality BMRI images, including pre-contrast fast fat-saturated Dixon-based T2-weighted sequence, which is in compliance with the ACR accreditation requirements for BMRI [17] to screen patients at high risk for breast cancer, and compared our protocol with SOC-MRI. We selected a high-risk patient population because they commonly undergo multiple annual breast MRI exams in their lifetime and are the subgroup of patients most likely to benefit from a shortened screening MRI concept.

We found that SBMRI screening consisting of bilateral high-resolution T2-weighted images, pre-contrast T1-weighted images, and four phases of post-contrast T1-weighted images has a median scan time of 9 minutes and a median table time of 13 minutes. These times are significantly shorter than the scan time and table times achieved with SOC-MRI (30 and 42 minutes, respectively, P<0.0001). Also, compared with the most rigorous standard of care diagnostic breast protocols currently in use, our SBMRI protocol had a drastically shorter overall table time. To our knowledge, this is the first prospective clinical study reporting a SBMRI protocol that included T2-weighted and dynamic T1-weighted sequences that fulfill ACR accreditation criteria and were compared with SOC-MRI in the same patient cohort.

" ...our SBMRI protocol achieved a significantly shorter scan time without compromising image quality ..."

CLINICAL IMPLICATIONS

The clinical implications for these results are as follows: one reason for patient noncompliance in MRI screening programs is the patients' inability to tolerate long scan times. In one study, more than 20% of women reported experiencing discomfort related to the duration, immobility, prone position, or noise associated with undergoing MRI [23]. This finding parallels that of a previous study of women undergoing breast cancer screening, in which MRI scan time, or "lying in the tunnel," was the item most frequently reported (by a statistically significant percentage [21.4%] of patients) as causing "rather" to "extreme" discomfort [24]. Although only 5% of patients discontinue MRI owing to claustrophobia [1], long BMRI scan times can result in the unnecessary administration of sedatives, and this has important sedation risk and cost implications, particularly in the screening setting. With its considerably shorter scan time, the SBMRI protocol proposed in the present study helps mitigate a significant drawback of yearly MRI screening. Besides the reduced acquisition time, the Dixon approach used in our SBMRI protocol obviates the need for any manual shimming, manual center frequency adjustment, or even repeat acquisition that often increase substantially the examination time and/or inconsistency in image quality (IQ) of breast MRI. In turn, the shorter examination time of the SBMRI study were believed to drastically improve patient tolerance and study consistency. Therefore, the proposed SBMRI protocol has the potential to make BMRI screening more widely accessible to patients.

The ability of BMRI to detect early breast cancer (both invasive and *in situ* disease) is directly related to high-quality imaging, particularly with respect to the signal-to-noise ratio and the spatial resolution of the MR image. The detection of early breast cancer (e.g. small invasive cancers and ductal carcinoma *in situ*) requires the simultaneous imaging of both breasts with a high-field MRI unit employing a breast coil and providing high spatial resolution with thin slices and a high matrix (an in-plane resolution of ~1 mm) [17] We found no significant difference in the IQ evaluation of normal breast structures between the Fast Triple Echo Dixon (FTED) and iterative decomposition of water and fat

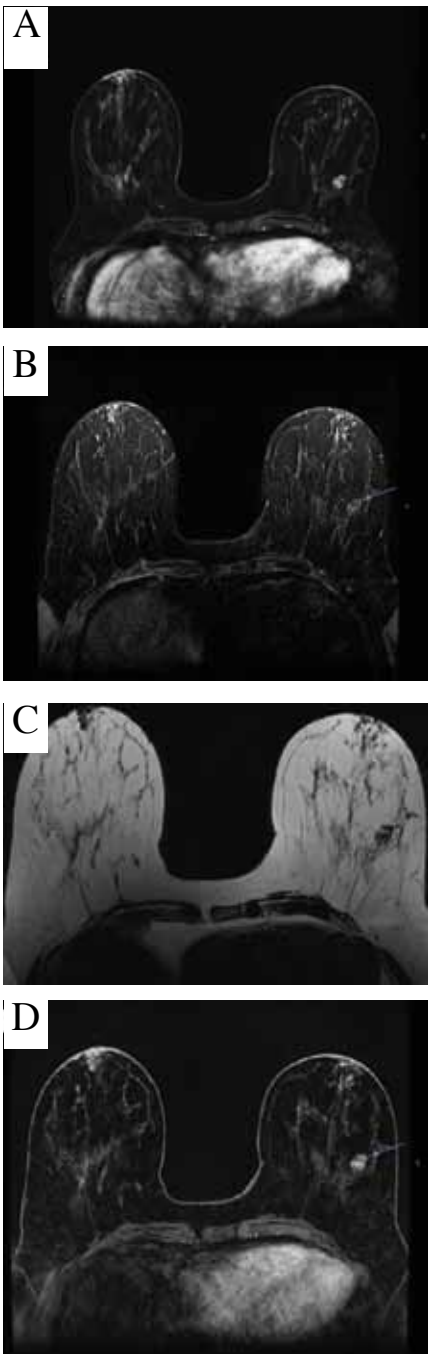

Figure 1. Breast magnetic resonance imaging (MRI) of a 51-year-old woman with a strong family history of breast cancer

(A) A VIBRANT axial image from standard-of-care MRI (SOC-MRI).

(B) Fast T2-weighted sequence in the same (axial) scan plane show corresponding intermediate signal intensity.

(C) A VIBRANT axial "fat-only" image from the same scan location demonstrates internal fat within the lesion, suggesting a benign process.

(D) Early-phase axial dynamic contrast-enhanced MRI obtained 3 years before the MRI studies in A-E confirm the stability of the enhancing mass, which all 3 readers assessed as benign.

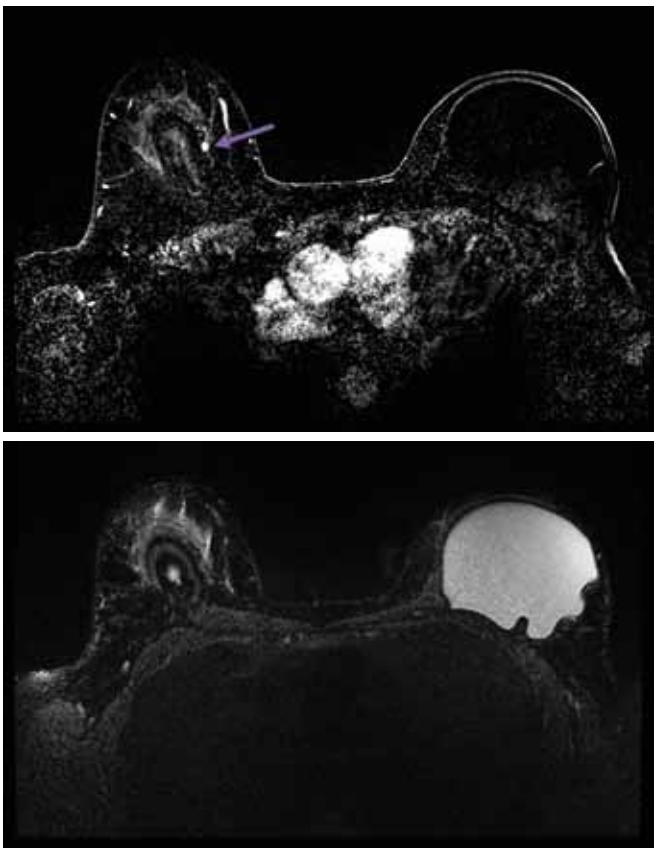

Figure 2. 48 year-old woman with known BRCA1 mutation and a remote history of left breast cancer status post left mastectomy 10 years prior. Axial early subtraction series shows a 3mm enhancing mass in the right breast 1 o'clock position (arrow). On corresponding fast T2 weighted fat saturated image at the same slice location, the lesion is isoechoic and undiscernible. MRI-directed ultrasound-guided needle biopsy showed invasive ductal cancer, ER, PR and HER2 negative (triple-negative).

with echo asymmetry and least squares estimation (IDEAL) sequences or in the assessment of enhancing lesions between the eFLEX and VIBRANT sequences. Therefore, our SBMRI protocol achieved a significantly shorter scan time without compromising image quality Moreover, motion artifact and image blurring were observed significantly less frequently on FTED sequences than on IDEAL sequences, likely owing to better patient tolerance and the reduced scan time, and this contributed to the enhanced IQ of the FTED T2-weighted series.

One of the significant advantages of our proposed protocol compared to those of prior retrospective reader studies [14-16] is that it includes a bright fluid (T2-weighted) series. The T2-weighted image set helps differentiate T2-hyperintense benign pathology from malignant pathology by allowing correlation of suspicious enhancement on DCE-MRI series (intramammary lymph nodes and fibrocystic changes), thereby helping to increase the specificity of the MRI study. T2-weighted/bright fluid series is a required component of ACR breast accreditation [17]. Furthermore, for patients with suspicious abnormalities on SBMRI, the "fat-only" FTED series can be utilized as needed to help assess possible fat-containing enhancing lesions [Figure 1], such as fibroadenomas, fat necrosis or lymph nodes, without necessitating a second, or "diagnostic," MRI scan. The FTED sequence utilized in our SBMRI protocol uses a set of 3 fast switching bipolar readout gradients during each echo spacing period of fast spin echo (FSE) to produce 3 raw images in a single acquisition. While we do not anticipate a need to review all three image sets (fat only, water only and in-phase) routinely for each patient, each image set can be referenced by the readers during reading as needed to help with the diagnosis.

The second sequence in our SBMRI protocol was a 3-dimensional fast Dixon dual echo spoiled gradient echo (eFLEX) sequence for volumetric T1-weighted imaging before and after contrast injection. Unlike a conventional 3-dimensional fast spoiled gradient echo sequence, the eFLEX sequence acquires 2 echoes consecutively after each radiofrequency excitation, and the images corresponding to the 2 echoes are post-processed to yield water-only and fat-only images. We elected to use the above two sequences to construct our SBMRI instead of only using IDEAL and Vibrant sequences of SOC MRI due to the following advantages: first, FTED is significantly shorter than IDEAL, and can be applied without the need for a manual fat saturation. Furthermore, none of these sequences require a manual "prescan", which further decreases the patient's table time or the time spent within the magnet bore. Second, both eFLEX and FTED yield a "fat-only" image set, which can be helpful to further characterize an enhancing lesion. Given these advantages, the SBMRI protocol allows a complete and comprehensive MRI protocol to be constructed unlike the "abbreviated" MRI protocol. In the abbreviated MRI concept, the patient may need to return for a more detailed MRI to further characterize the lesion and determine the need for a biopsy. The additional image sets obtained in SBMRI may not be needed for every case; however, they are available for utilization by the radiologist when an abnormality is identified.

ABBREVIATED MRI IN AVERAGE RISK WOMEN

If Abbreviated MRI protocols are adopted successfully, breast MRI may become more widely available to women at average or mildly elevated risk for screening- including women with dense breast tissue or those with a personal history of breast cancer [25]. Like the cancers detected in high risk women, the majority were small, T1 invasive cancers, less than 1.0 cm in size, and over 90% were node negative. The cancers detected were of intermediate (39%) or high histologic grade (43%) with one third of cancers being of the triple negative subtype. The positive predictive value (ppv) of the Abbreviated MRI was 35.7%, well within the range of ppv accepted for mammographic screening (25-40%). Additionally, the interval cancer rate in women undergoing several rounds of screening with Abbreviated MRI was zero. After conclusion of the study, when the women returned to traditional breast cancer screening methods, no cancers were detected by mammography or ultrasound within the first three years, suggesting that Abbreviated MRI screening may have a "protective" effect on subsequent breast cancer detection so that the frequency of AB-MRI screening might be reduced in average risk women, another significant cost saving.

ABBREVIATED MRI FOR SCREENING WOMEN WITH DENSE BREAST TISSUE — THE EA1141 TRIAL

The effect of breast density legislation in the United States has prompted the evaluation of supplemental screening methods for breast cancer detection in women with dense breast tissue who are without other breast cancer related risk factors. The ECOG/ACRIN group is organizing a prospective multicenter trial, the EA-1141 trial comparing abbreviated MRI and DBT in breast cancer screening in women with dense breasts [26]. In this trial, women aged 40-75 with dense breast tissue (BIRADS C or D) but not at increased risk of breast cancer will undergo DBT and Abbreviated MRI in randomized order for two consecutive years. Outcome metrics assessed will be the cancer detection rate (CDR) of the two modalities as well as the histopathological profiles of cancers detected by the two imaging methods. The study will also assess patient reported quality of life as well as their willingness to undergo repeated breast MRI for breast cancer screening. The trial leaves the specific sequences of the abbreviated protocol up to the individual centers and only requires that the scans be obtained in less than ten minutes. Patient accrual has been completed and results are expected within the next year.

" …Abbreviated MRI has the potential to replace mammography as a stand-alone imaging tool for the detection of breast cancer..."

ABBREVIATED MRI IN WOMEN WITH A PERSONAL HISTORY OF BREAST CANCER

Abbreviated MRI has more recently been shown to be of benefit for women with a personal history of breast cancer but no other breast cancer risk factors. Choi *et al.* reported the outcomes of Abbreviated MRI in a cohort of 725 women with a personal history of breast cancer [28]. They found that the diagnostic performance of AB-MRI for women with a history of breast cancer surgery is comparable to that of the full diagnostic MRI protocol, but with the advantages of short examination and interpretation times and low costs.

CONCLUSION

Abbreviated MRI consisting of a single T2 weighted fast spin echo (FSE) triple echo Dixon sequence and a dual echo fast spoiled gradient echo sequence (FSPGR) before and after the administration of contrast, is feasible, and compliant with ACR standards for the accreditation of breast MRI. Sensitivity for breast cancer detection is equivalent to that of full protocol DCE-MRI, but with greatly reduced scan and table times, While cancers detected with Abbreviated MRI are usually small T1, node negative invasive cancers, they often have aggressive histopathological tumor profiles. Given its superior performance and the greatly reduced scan times resulting from the use of abbreviated protocols, Abbreviated MRI has the potential to replace mammography as a stand-alone imaging tool for the detection of breast cancer, not only in high risk women, but in women of average or mildly elevated risk, such as women with dense breast tissue or a personal history of breast cancer.

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