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Abbreviated protocol breast MRI: The past, present, and future

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ABSTRACT

Breast MRI has been shown to be the most sensitive examination in the detection of breast cancer. However, given the high associated costs, its use in the screening setting has traditionally been limited to those who are at high-risk for breast cancer. Abbreviated protocol breast MRI is capable of reducing the traditional costs associated with breast MRI, while maintaining diagnostic accuracy and cancer detection, and therefore a potential future screening tool for breast cancer in a broader population of women than just those at high-risk. New techniques, such as Ultrafast breast MRI, are able to not only shorten the traditional breast MRI acquisition and interpretation time, but also provide kinetic information.

1. Background

Breast cancer is the second most common cancer in American women and is the second leading cause of cancer death in women. There is a 1 in 8 chance that a woman will develop breast cancer in her lifetime [1]. Mammography has been the screening test for the early detection of breast cancer for several decades. However, mammography has several limitations – including its lower sensitivity in dense breasts, detection of non-calcified breast cancers, and potential over diagnosis of biologically irrelevant cancers.

The use of breast MRI (bMRI) has increased over the past decade [2–5]. Breast MRI has been shown to be the most sensitive imaging modality for the detection of breast cancer (both invasive and DCIS) [6–8]. Breast MRI addresses several of the standard limitations of mammography as it is not effected by breast density and it relies on contrast enhancement. In addition, bMRI is thought to detect the more biologically relevant cancers, as it detects those with angiogenic activity. Despite these advantages, there are limitations of bMRI, such as high direct and indirect costs [9,10]. The acquisition time for bMRI ranges from 20 to 60 min [11–15]. The long acquisition times increase cost and in addition may cause patient discomfort. In the American College of Radiology (ACR) Network 6666 trial, 25.4% of women stated that inability to tolerate the long acquisition time due to claustrophobia and 18.2% of women stated the long acquisition time leading to time constraints, as main reasons they refused MRI screening [16].

Screening bMRI has been limited to women at high-risk for breast cancer, in part due to the high associated costs. Women at high-risk for breast cancer are defined as those with a lifetime risk of > 20% of breast cancer, patients with a BRCA1 or BRCA2 gene mutation, patients with a first degree relative with a BRCA mutation who are themselves untested, patients with a history of chest wall radiation between ages 10–30, and patients with Li-Fraumeni, Cowden, or Bannayan-Riley-Ruvalcaba Syndrome [17]. In addition, the American College of Radiology (ACR) recently updated the recommendation for bMRI screening. In addition to the aforementioned patient populations, bMRI screening is now also recommended in women with personal histories of breast cancer and dense breast tissue and/or those with a personal history of breast cancer diagnosed before the age of 50. Also, bMRI should be considered in women with personal histories of breast cancer not mentioned prior, or patients with lobular carcinoma in situ (LCIS) or atypia on previous biopsy [18].

Recently, many studies have looked at ways to decrease the costs of traditional bMRI to make it more accessible, while maintaining diagnostic accuracy. The high cost of bMRI is secondary to it being time consuming both to perform and to interpret. Standard bMRI protocols are variable, but tend to include a localizer, a T1-weighted(W) non-fat saturated sequence, a T2W fat saturated sequence, T1W fat saturated pre-contrast, and multiple T1W fat saturated post-contrast sequences. In addition, post-processing subtraction images and maximum intensity projection (MIP) images are also obtained and interpreted. An approach to address the traditional high cost of bMRI has been to decrease the time of the acquisition protocol and interpretation time, by using an abbreviated protocol (AP) bMRI [19].

2. Abbreviated protocol MRI: screening

The first to address the concept of an abbreviated protocol bMRI was Kuhl and her group in Germany in 2014 [20]. Their basic concept was to limit bMRI to the early post-contrast phase. This is based on the observation that invasive breast cancers as well as DCIS tend to enhance

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early, while more benign lesions tend to enhance later. Background parenchymal enhancement (BPE) tends to increase with time, so cancers often stand out most from BPE on the early-post contrast phase. Kuhl et al. performed a prospective reader study in which all women underwent a full diagnostic protocol (FDP) MRI. In addition, an abbreviated protocol (AP) was reconstructed from images from the pre- and first post-contrast acquisitions. The AP consisted of a T1W pre-contrast and a single post-contrast T1W sequence. These were subtracted to yield first post-contrast subtraction (FAST) images, which were then fused into a single maximum intensity projection (MIP). The FDP consisted of all the images of AP, as well as the non-subtracted and subtracted images of an additional four post-contrast phases and coronal T1-weighted and axial T2 weighted sequences. Two readers prospectively interpreted the MIP only first, followed by the FAST images, and finally the FDP.

Their study included 443 women, with a total of 606 screening bMRI examinations. The mean age of the women was 54.2 years. Eleven cancers were diagnosed in the 606 bMRI screenings, 4 DCIS and 7 invasive carcinomas. The mean age of patient diagnosed with cancer was 50.9 years. All the invasive cancers were T1 N0 with a median size of 8 mm. All the cancers were diagnosed in the first screen, with a 0% interval cancer rate.

The sensitivity of reading the MIP alone was 90.95%, which did not differ significantly from the AP or FDP both of which had 100% sensitivity. Reading the MIP alone, 10/11 of the breast cancers were detected. The NPV for the MIP was 99.8%, and 100% for the AP and FDP. Specificity of the MIP and FDP did not vary significantly 94.3% vs. 93.9%, and neither did the PPV of AP vs. FDP, 24/4% vs. 23/4% respectively. In addition, the acquisition time of the AP was 184 s, vs. 1024 s for the FP. Average reading time of the MIP was 2.8 s, AP 28 s. The time to read FDP was not measured. This initial proof-of-concept study found that an abbreviated MRI protocol was able to maintain an equivalent diagnostic accuracy and cancer yield compared to a standard breast MRI protocol, while also reducing both image acquisition as well as image interpretation time.

Since this first proof-of-concept study several other investigators have looked at abbreviated bMRI for breast cancer screening [21–27]. These studies have used various bMRI abbreviated protocols which are listed in Table 1. Information on the number of patients, number of examinations, cancer yield, and number of invasive and non-invasive cancers is listed in Table 2. Information on acquisition and interpretation times are provided in Table 3. Select overall results of these studies are provided in Table 4.

Mango et al. performed a retrospective study in 100 consecutive patients with biopsy proven unicentric breast carcinoma (79% invasive, 21% DCIS) visible on bMRI. Four breast radiologists were blinded to the carcinoma location. They assessed an abbreviated protocol bMRI of a first post-contrast T1-weighted image and a subtracted first post-contrast and subtraction MIP images for tumor detection and localization. This was then compared to a full diagnostic protocol of 13 pre-contrast, post-contrast, and post-processed sequences. Ninety-two of the 100 cancers were detected by all readers on the AP bMRI. The mean sensitivity was 96% for the first post-contrast, 96% for the first post-contrast subtraction, and 93% for the subtraction MIP. Given these results, they suggested that the number of sequences necessary for screening may be fewer than the FDP, however the first post-contrast subtraction MIP alone was not sufficient [21].

In contrast to Mango et al., Heacock et al. used an abbreviated protocol that included a T2W sequence. They retrospectively evaluated 107 women with unifocal breast cancer on MRI. Three readers evaluated three varying protocols 1) non-contrast T1-weighted images, T1-weighted first post-contrast images, and T1-weighted first subtraction post-contrast images, 2) images with clinical history and prior imaging, including previous FDP MRIs, 3) addition of pre-contrast T2-weighted images as well as clinical history and prior imaging. With T1W imaging alone (no prior imaging or history) the percent of cancers detected was 97.2% by reader 1, 96.3% for reader 2 and 100% for reader 3. Providing clinical history and prior imaging, increased sensitivities for all readers, 2 of the readers had a 100% detection of cancer and one reader a 98.1% detection. Adding prior imaging and clinical history increased the cancer detection rate for all readers, this information is usually available to radiologists at the time of bMRI interpretation, so these higher sensitivities (100%, 100%, 98.1%) for cancer detection with an AP bMRI are more realistic. With addition of the T2W sequence there was no effect on cancer detection rate, however lesion conspicuity was significantly increased for 2 of the 3 readers. The least experienced reader found T2W imaging helpful in 49.5% of cases, versus the 2 more experienced readers reported it was helpful in < 8% of cases. This suggests that T2W imaging is not necessary for the detection/evaluation of breast cancer, but is helpful particularly for less experienced breast imagers. One of the missed cancers was located in the axilla, which may be a challenging location on AP bMRI. Three of 5 missed cancers were non-mass enhancement (NME), suggesting that cancers presenting as NME may be harder to detect on AP bMRI than cancers presenting as masses [22].

Grimm et al. looked at 48 high-risk patients undergoing screening bMRI. They selected MRIs to include 50% normal, 25% benign, and 25% malignant (8 IDC, 1 ILC, and 3 DCIS). Three breast imaging radiologists were presented two different AP-bMRI protocols as detailed in Table 1. After a one month waiting period a FDP bMRI was also reviewed which included a T1W non-fat saturated sequence as well as 3–4 post contrast T1W sequences in addition to what was included in the AP bMRI protocols. Overall sensitivity was 86% for AP 1, and 89% for AP 2, compared to 95% sensitivity of the FDP. In both abbreviated protocols the cancer missed was a recurrent IDC in a mastectomy patient on the chest wall. The specificity of AP 1 was 52%, AP 2 was 45%, and FDP was 52%. The addition of more post-contrast sequences did not increase specificity, therefore they concluded multiple post-contrast series may not be necessary. Also in their study, they aimed to compare interpretation times between FDP and AP, surprisingly there was no difference between AP 1 and the FDP (2.98 vs. 2.95 min). The authors suggested that this may be that radiologists aren't using the more delayed sequences even when these sequences are provided, or alternatively the radiologists interpreting the AP may have spent more time reviewing this protocol to be more confident when lacking traditional sequences [23].

A recent prospective study by Dogan et al. evaluated the feasibility of an AP bMRI with image quality complying with the American College of Radiology (ACR) accreditation requirements. Twenty-three high-risk women underwent a standard-of-care (SOC) bMRI and a separate short breast MRI protocol. Each patient underwent a SOC MRI and 1–7 working days later underwent a separate short bMRI protocol. The short bMRI protocol consisted of a single T2W fast spin-echo triple-echo Dixon T2 sequence and a 3D dual-echo fast spoiled gradient-echo two-point Dixon sequence for volumetric T1W imaging prior to and after contrast as the dynamic sequence. Three radiologists with breast MRI expertise assessed the image quality by rating images for fat saturation, artifact severity, and quality of normal anatomic structures. The short-protocol bMRI took 9.42 min to acquire with an average table time of 13.92 min versus 22.09 min for the SOC MRI acquisition time and 35.87 min for table time. The SOC MRI had significantly worse motion artifact ($p < 0.01$) than the short-protocol. There was no significant difference in the evaluation of normal structures, or assessment of enhancing lesions between the 2 protocols. The authors concluded in this prospective study that this short protocol breast MRI, with an acquisition time of 10 min, including at T2W sequence is feasible and at least equivalent to a SOC MRI [28].

A recent review of 6 of these studies [20–25] by Chor and Mercado [19] found an overall average time to perform FDP bMRI of approximately 24 min (range, 16–40 min), and average time for AP of 9 min (range 3–15 min). In addition, 5 of the 6 studies showed a shortened interpretation time. Overall, the AP bMRI is able to greatly reduce both

Table 1
Fast abbreviated breast MRI protocols.

Study	Tesla	Protocol 1	Protocol 2	Protocol 3
Kuhl et al. [20]	1.5 T	Subtraction MIP	Protocol 1 PLUS Axial T1W gradient echo pre-contrast Axial T1W gradient echo post-contrast First post-contrast subtracted (FAST) images	
Mango et al. [21]	1.5 T, 3.0 T	Sagittal fat-suppressed T1W Sagittal fat-suppressed 1st T1W post-contrast Sagittal fat-suppressed 1st T1W post-contrast Subtraction Subtraction MIP		
Heacock et al. [22]	3.0 T	Sagittal non-contrast T1W Sagittal 1st post-contrast T1W Sagittal 1st post-contrast T1W Subtraction	Protocol 1 PLUS Clinical history provided Prior imaging	Protocol 2 PLUS Pre-contrast T2W fat-suppressed non-contrast
Grimm et al. [23]	1.5 T, 3.0 T	Fat-saturated pre-contrast T2W Pre-contrast T1W 1st fat-saturated T1 post-contrast	Protocol 1 PLUS 2nd T1W post-contrast	
Harvey et al. [24]		Axial pre-contrast fat-saturated T1W Axial post-contrast fat-saturated T1W Axial post-contrast fat-saturated T1W Subtraction Axial post-contrast fat-saturated T1W Subtraction MIP		
Moschetta et al. [25]	1.5 T	Short T1 inversion recovery (STIR) Turbo-spin-echo (TSE)-T2W Pre-contrast T1-weighted high-resolution isotropic volume (THRIVE) 1st Post-contrast THRIVE		
Oldrini et al. [26]	3.0 T	Sagittal three-dimensional Gradient Echo T1W dynamic VIBRANT pre-contrast 1st Sagittal three-dimensional Gradient Echo T1W dynamic VIBRANT post-contrast Subtraction		
Choi et al. [27]	1.5 T, 3.0 T	Sagittal fat-suppressed T2W fast spin-echo Sagittal T1W fat-suppressed fast spoiled gradient echo pre-contrast Sagittal T1W fat-suppressed fast spoiled gradient echo post-contrast Subtraction images MIP		

performance and interpretation compared to FDP bMRI time while maintaining similar diagnostic accuracy.

3. Ultrafast/accelerated breast MRI

While AP bMRI has shown to have high sensitivity and specificity for the detection of breast cancer, it is not able to provide information on kinetics. This is because the delayed sequences are not acquired, and therefore information on kinetics cannot be obtained. It would be ideal to have a bMRI protocol that is both short, as previous abbreviated protocols have accomplished, but in addition could provide kinetic information, as kinetics provide additional information about breast lesions. To address this, several studies have looked at new Ultrafast/accelerated MRI techniques.

Ultrafast MRI, or accelerated MRI, are techniques that maintain high spatial resolution while decreasing acquisition times, that have recently been introduced for bMRI. View sharing is an acceleration technique in which the central region of k-space is sampled at every point. The outer region of k-space is only partly sampled at every point, and the remaining samples are taken from previous time points (viewsharing), making it possible to image at a high temporal resolution but also maintain diagnostic quality high spatial resolution [29].

Table 2
Select patient and pathology information.

Study	Number of patients	Number of MRI examinations	Cancer detection rate (/1000)	Number of invasive carcinomas	Number of DCIS
Kuhl et al. [20]	443	606	18.2	7	4
Mango et al. [21]	100	100	n/a	79	21
Heacock et al. [22]	107	107	n/a	94	13
Grimm et al. [23]	48	48	n/a	9	3
Harvey et al. [24]	505	568	12.3	5	2
Moschetta et al. [25]	470	470	n/a	69	0
Oldrini et al. [26]	90	90	n.a	25	1
Choi et al. [27]	725	799	15.0	7	5

n/a = not/applicable or information not provided.

Table 3
Acquisition and interpretation times.

	Time to perform[a] (min)		Time to interpret[a] (s)	
	FDP	AP	FDP	AP
Kuhl et al. [20]	17	3	n/a	2.8[b], 28[c]
Mango et al. [21]	30–40	10–15	n/a	44
Heacock et al. [22]	35	12	n/a	25
Grimm et al. [23]	n/a	n/a	177	178.8
Harvey et al. [24]	23.2	4.4	385.8	93
Moschetta et al. [25]	16	10	360	120
Oldrini et al. [26]	n/a	n/a	329[d], 142[e]	247[d], 59[e]
Choi et al. [27]	n/a	8.5	n/a	n/a

n/a = not/applicable or information not provided.
[a] Mean unless range given or otherwise stated.
[b] Protocol 1.
[c] Protocol 2.
[d] Junior reader.
[e] Senior reader.

Table 4
Sensitivity and Specificity of FDP vs. AP.

	Sensitivity (%)		Specificity (%)	
	FDP	AP	FDP	AP
Kuhl et al. [20]	100	100, 90.9[a]	93.9	94.3
Mango et al. [21]	n/a	96, 93[a]	n/a	n/a
Heacock et al. [22]	n/a	97.8[b], 99.4[c],99.4[d]	n/a	n/a
Grimm et al. [23]	95	86[b], 89[c]	52	52[b], 45[c]
Harvey et al. [24]	n/a	100	n/a	n/a
Moschetta et al. [25]	92	89	92	91
Oldrini et al. [26]	100[e], 100[f]	100[e], 100[f]	91.5[e], 94.4[f]	91.5[e], 95.1[f]
Choi et al. [27]	n/a	100	n/a	89.2

n/a = not/applicable or information not provided.
[a] MIP only.
[b] Protocol 1.
[c] Protocol 2.
[d] Protocol 3.
[e] Junior reader.
[f] Senior reader.

This enables both morphologic and kinetic characteristics of breast lesions to be obtained on bMRI in shorter acquisition times.

Mann et al. performed early work in ultrafast MRI. Their study included 160 patients with 199 abnormalities, 95 benign and 104 malignant. They used a view-sharing sequence called time-resolved angiography with stochastic trajectory (TWIST). Curves from the TWIST data were shown to readers who determined the maximum slope (MS) of contrast enhancement versus time curve between lesions. The goal of their study was to compare MS with curve type defined by BIRADS. All of the 199 enhancing lesions were visible on the standard VIBE series and TWIST, with a relative sensitivity of 100%. The MS allowed discrimination between benign and malignant lesions significantly better than BIRADS curves (AUC 0.829 vs. AUC 0.692 respectively, $p = 0.036$). They concluded that ultrafast bMRI allows detection of breast lesions as well as classification with high accuracy using MS [30].

Platel et al. [31] evaluated a set of features extracted from kinetics of contrast agent imaged at 100 s (ultrafast) view-sharing MRI protocol to see how these features measured compared to commonly used features for standard bMRI. The protocol produces five regular high spatial-resolution T1W acquisitions with a series of 20 ultrafast view-sharing acquisitions during contrast uptake. Their study included in 137 patients with 154 enhancing abnormalities, 83 of which were malignant and 71 benign. They found that the classification performance when combing morphologic features and kinetics was significantly better for the ultrafast technique. The classification performance of kinetics alone derived from the ultrafast TWIST (100 s) was significantly higher than performance of the kinetics from the lengthier (510 s) VIBE acquisition.

Abe et al. [32] performed a retrospective study of 60 patients with 62 total lesions, 33 malignant and 29 benign lesions. In their MRI ultrafast imaging protocol, whole-breast 3D images are acquired with high temporal resolution (7 s) using a higher than usual sensitivity-encoded (SENSE) acceleration factors and lower than usual spatial resolution. In their clinical practice, the ultrafast acquisition is performed in the early phase of contrast enhancement for one minute. The goal of their study was to compare the diagnostic parameters on ultrafast images with those on standard images as well to compare the diagnostic accuracy of the two approaches in determining benign from malignant lesions. They used a computer-aided detection (CAD) to obtain initial enhancement rate and signal enhancement ratio (SER) by identification of a voxel with highest signal intensity in first phase of standard imaging. From that voxel, the enhancement rate of each time point of ultrafast acquisition and AUC of kinetic curve from zero to each time point of ultrafast imaging were obtained. They referenced to the time point when the aorta began to enhance as C1 and subsequent time points as C2, C3, and so on. They found statistically significant differences between malignant and benign lesions in enhancement rate at C2–C6 ($p \leq 0.0001$) and in kinetic AUC at C2–C6 ($p \leq 0.001$). Based off their results they suggested that kinetic assessment of ultrafast imaging may be comparable to standard imaging. In addition, they comment that ultrafast imaging is faster and able to reduce effects such as patient motion causing misregistration on subtraction images. Also, they expect background parenchymal enhancement (BPE) to be less on ultrafast imaging, given that the images are obtained earlier, increasing the conspicuity of lesions compared to BPE.

Pineda et al. [33] used another ultrafast technique where all images were acquired with standard uniform Fourier sampling and high sensitivity-encoding (SENSE) acceleration factor. They evaluated 23 patients with enhancing lesions, 18 malignant and 15 benign. Malignant lesions included: 8 primary IDC, 4 satellite IDC, 4 DCIS, and one metaplastic carcinoma. Time of arrival (TOA) maps was created to see the time at which lesions began enhancing. The average TOA was much shorter ($p < 0.01$) for malignant lesions than for benign lesions, malignant lesions enhanced more rapidly and earlier than benign lesions. They suggested that their results show that ultrafast imaging may provide novel information related to contrast media dynamics at early time points that may be clinically useful. In addition, similar to Abe et al., they suggest ultrafast imaging may detect enhancement of lesions early, prior to the appearance of BPE. This would be helpful particularly in patients with moderate and marked BPE, which is often seen in young women.

In conclusion, these studies indicate that kinetic information for accurate breast cancer diagnosis may be obtained along with morphologic information with the AP bMRI.

4. The EA1141 Trial

The EA1141 Trial entitled “Comparison of Abbreviated Breast MRI and Digital Breast Tomosynthesis in Breast Cancer Screening in women with Dense Breasts” is a prospective multi-center trial which was initiated in November 2016, involving international sites. Asymptomatic women ages 40–75 years old with dense breast tissue (BI-RADS density C or D) with no breast-cancer related risk factors, will get a digital breast tomosynthesis (DBT) and abbreviated MRI (AB-MRI) in a randomized order for 2 consecutive years. After this they will return to regular mammography screening for 3 years. The abbreviated breast MRI protocol does not require specific pulse sequences to be used, it is up to the individual site to decide on the sequences, but the acquisition time is required to be < 10 min. The cancer detection rate achieved by DBT vs. AB-MRI will be compared in the same females in the first/

prevalence and second/incidence screening round. PPVs will be compared. In addition, types of cancers and their biologic profiles of cancers found by AB-MRI vs. DBT will be compared, by using genomic profiling studies on screen detected cancers [34].

5. Limitations of abbreviated protocol breast MRI and Ultrafast/accelerated breast MRI

There are limitations to abbreviated protocol breast MRI and the Ultrafast breast MRI techniques. The main limitations include: cost, access to breast MRI, and the requirement of IV gadolinium [35].

Breast MRI is a costlier exam than screening mammography. As addressed earlier, AP bMRI should reduce cost by reducing magnet time as well as interpretation time. To the best of my knowledge the cost of an abbreviated protocol bMRI as well as the reimbursement are yet to be determined. A secondary aim of the EA1141 Trial will be to address cost related issues by performing a comparative cost analysis for DBT and AP MRI.

Breast MRI facilities are less accessible than mammography facilities. Travel times to facilities with breast MRI have been reported to be longer than those to mammography facilities. In addition, longer travel times may be associated with sociodemographic factors such as rural residence and lower educational attainment [36].

The use of intravenous (iv) gadolinium is another limitation. In recent years concern over iv gadolinium-based contrast agents (GBCAs) administration has grown. Repeated exposure to gadolinium based contrast agents has been shown to be associated with neuronal tissue deposition, even in the setting of normal renal function [37]. This is of less concern with macrocyclic GBCAs than linear GBCAs, as linear agents appear to cause greater MRI signal changes [37–39]. However, the clinical significance of this, if any, remains unknown [38,39].

6. Conclusion

Abbreviated protocol bMRI has been to shown to be a lower cost method compared to traditional FDP protocol bMRI, while maintaining sensitivity for breast cancer as well as specificity. The AP bMRI should make bMRI screening more readily available to women beyond just those at high risk for the development of breast cancer. In addition, new ultrafast techniques, are able to accomplish the short protocol time while maintaining spatial resolution, and providing kinetic information. Ongoing research, including the EA1141 Trial, is currently further evaluating these promising techniques.

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