Abbreviated breast MRI for breast cancer screening: introduction and review of the literature

By Dr. L Heacock

Screening mammography decreases breast cancer mortality and increases the detection of early stage, more easily treated breast cancer [1]. While mammography is the mainstay of breast cancer screening [2,3], it has known limitations in evaluating patients with dense fibroglandular breast tissue [4] and has been shown to preferentially detect slower-growing, low-grade cancers or ductal carcinoma *in situ* [5,6]. More biologically relevant, fast growing cancers are often masked by benign breast tissue on mammography [5,6].

BREAST MRI ADVANTAGES

The limitations of screening mammography are easily overcome by the use of breast MRI, which has been shown to demonstrate high sensitivity compared to other screening modalities [7-10] with increased detection of high-grade invasive cancers compared to mammography and ultrasound [6]. This is due to the superior tissue contrast offered by MRI and the physiologic uptake of gadolinium contrast, which exploits the rapid wash-in and wash-out of contrast observed due to angiogenesis in breast cancer. However, widespread use of breast MRI has been limited to those patients considered at high (>20%) lifetime risk of breast cancer [1], despite its cancer detection rate of 14.6-16.0 cancers per 1000 women in this high risk group compared to 7.7 per 1000 women when compared to mammography and ultrasound screening alone [2]. Further studies have shown that women at intermediate lifetime risk (15-20%) of breast cancer can similarly benefit from breast MRI [1, 3], with recent studies even suggesting average risk women may benefit from a screening MRI every 2-3 years [14]. Despite these benefits, even 42.1% of high risk women offered a free screening breast MRI as part of the American College of Radiology Imaging Network (ACRIN) 6666 study declined to participate [4]. A subsequent analysis of breast MRI utilization demonstrated only 1.5% of women with high lifetime risk have ever had a breast MRI [5].

DRAWBACKS OF BREAST MRI

Despite the clear benefits of breast MRI in cancer screening, the cost, patient tolerance of the exam, and accessibility remain key issues. An growing number of women at increased risk of breast cancer who might benefit from breast MRI have high deductible insurance plans [6] for which an MRI co-pay may be a prohibitive expense. The prone positioning traditionally used for breast MRI is difficult for many women to tolerate, leading to motion degradation and patient reluctance to undergo future breast MRI. Finally, socioeconomic disparities have been observed in screening breast MRI, with nonurban residents traveling further to obtain it [7].

RATIONALE FOR ABBREVIATED MRI AND BASIC PRINCIPLES

Abbreviated breast MRI (AB-MRI), in which only a selected number of sequences and post-contrast imaging is acquired, exploits the high sensitivity of breast MRI while reducing table time and reading time to maximize availability, improve patient tolerance and accessibility of breast MRI. First described in 2014 by Kuhl *et al,* [8], AB-MRI has rapidly become integrated into many practices and academic institutions.

Kuhl *et al* introduced the first clinical study of an abbreviated MRI protocol for breast cancer screening, which included a non-contrast T1 weighted and first post-contrast T1 weighted sequence, subtraction images and a single maximum intensity projection (MIP) image [8]. This abbreviated protocol was performed in 606 screening MRI in 443 women at mildly to moderately increased risk of breast cancer. All 11 breast cancers were identified on both abbreviated and full protocols with equivalent diagnostic accuracy, while the interpretation of MIP images alone missed one cancer. Kuhl et al demonstrated the specificity (94.3% v 93.9%) and positive predictive value (PPV) of abbreviated versus full diagnostic protocol (24.4% v 23.4%) were equivalent, with both reduced image acquisition time (17 minutes vs. 3 minutes) and radiologist interpretation time. Average interpretation time of the abbreviated protocol was 28 seconds for first post-contrast images and 2.8 seconds for the MIP image alone.

Kuhl's proposed abbreviated protocol is in contrast to the American College of Radiology (ACR) accreditation requirements for breast MRI, which include a scout localizer, a T2-weighted sequence and pre-contrast, early post-contrast and delayed post-contrast T1-weighted images. Many breast imaging centers acquire at least three post-contrast sequences to generate time signal intensity curves [3, 9]. In contrast, the essential sequences for abbreviated breast MRI

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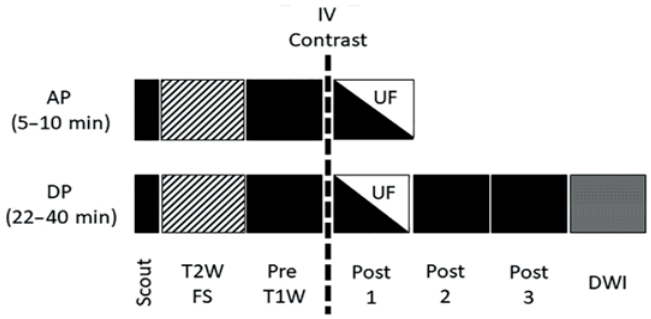

Figure 1. Comparison of a typical abbreviated breast MRI protocol (AP) to a typical diagnostic breast MRI protocol (DP). At a minimum, the AP should include pre- and first post-contrast T1-weighted images, with generated subtraction images and maximum intensity projection (MIP) image if desired. T2-weighted images are required for American College of Radiology (ACR) MRI accreditation requirements. Ultrafast imaging and diffusion weighted imaging can be included in either AP or DP as part of a multiparametric protocol. Abbreviations: DWI = Diffusion weighted imaging, FS = Fat saturated, Post 1 = first post-contrast T1-weighted, Pre T1W = Pre-contrast T1-weighted, T2W = T2 weighted, UF = ultrafast. [37]
Above figure adapted from Figure 6, Reference 37 Heacock et al. Radiol Clin North Am

include at a minimum only a single series of T1-weighted pre- and post-contrast imaging, which does not meet current ACR accreditation standards. Both abbreviated and full protocols often include subtraction and maximum intensity projection (MIP) images [Figure 1].

SUMMARY OF LITERATURE TO DATE

Multiple variations on Kuhl's basic protocol have been tested in the literature. Subsequent early studies on known biopsy-proven cancer and cancer-enriched populations demonstrated the similar high sensitivity of first post-contrast (FAST) images for the detection of breast cancer, with mean sensitivities ranging from 86-99.6% [10-13]. Although Kuhl's original study reported a fast interpretation time (3 seconds) for MIP images, the decreased sensitivity of MIP image interpretation alone in subsequent studies demonstrated that optimal interpretation includes evaluation of FAST images [10]. These early retrospective studies also reported substantially faster image acquisition and interpretation times for abbreviated protocols compared to prior full breast MRI protocols. Cancers proven to be difficult to visualize in abbreviated protocols were more likely to be low-grade invasive cancers, DCIS, or axillary lesions [10, 12]. Grimm *et al.* evaluated a second post-contrast acquisition did not significantly improve sensitivity or specificity [13].

As T2-weighted images are required for ACR breast MRI accreditation, the value of T2-weighted imaging in an abbreviated breast MRI remains a topic of interest. Heacock *et al.* [12] investigated the role of T2-weighted imaging in AB-MRI and found that it improved perceived lesion conspicuity in a known cancer cohort but did not change the cancer detection rate (CDR). Image acquisition time increased by 5 minutes but with increased interpretation times of 10-15 seconds [12]. Stahl *et al.* prospectively assessed the impact of each full breast MRI protocol sequence and concluded that T2-weighted imaging improves breast cancer screening [14]. Other studies [8, 10, 15] demonstrating comparable diagnostic accuracy between AB-MRI without T2-weighted images and full diagnostic MRI protocols suggest that T2-weighted sequences may not add significant benefit. However, as few of these studies were carried out in a pure screening population, it is possible that

Reference	Ultrafast	Standard temporal resolution						Sens	Spec	Max AUC
		Pre-T1W	FAST T1W	Second/ delayed post T1W	T2W	Sub	MIP			
Platel et al 2014 [38]	Y	Y	Y	N	N	Y	Y	NA	NA	0.87
Kuhl et al 2014 [8]	N	Y	Y	N	N	Y	Y	100%	94.3%	NA
Mann et al 2014 [36]	Y	N	N	N	N	N	N	90%	67%	0.812
Mango et al 2015 [10]	N	Y	Y	N	N	Y	Y	93-98%	NA	NA
Grimm et al 2015 [13]	N	Y	Y	Y	Y	Y	N	86-89%	45-52%	NA
Harvey et al 2016 [27]	N	Y	Y	N	N	Y	Y	100%	94%	NA
Heacock et al 2016 [12]	N	Y	Y	N	Y	Y	N	97.8-99.4%	NA	NA
Moschetta et al 2016 [22]	N	Y	Y	N	Y	Y	Y	89%	91%	NA
Abe et al 2016 [34]	Y	Y	Y	N	N	Y	N	85%	79%	0.89
Machida et al 2017 [23]	Y	Y	Y	N	N	N	N	87.1-93.5%	83.4-91.7%	NA
Chen et al 2017 [19]	N	Y	Y	N	N	Y	Y	92.9-93.8%	86.5-88.3%	NA
Petrillo et al 2017 [15]	N	Y	Y	N	N	Y	Y	99.5%	75.4%	NA
Panigrahi et al 2017 [25]	N	Y	Y	N	N	Y	Y	81.8%	97.2%	NA
Romeo et al 2017 [26]	N	Y	Y	N	Y	Y	N	99%	93%	NA
Oldrini et al 2017 [39]	Y	Y	Y	N	Y	Y	N	93.1%	70.8-83.3%	NA
Choi et al 2017 [40]	N	Y	Y	N	Y	Y	Y	100%	89.2%	NA
Oldrini et al 2018 [24]	N	Y	Y	N	N	Y	N	100%	95.1%	NA
Lee-Felker et al 2019[29]	N	Y	Y	N	N	Y	Y	99%	97%	NA

Table 1. Summary of sequences included in various abbreviated MRI protocols and the reported sensitivity, specificity and area under the curve (AUC) for that protocol. Studies that used an ultrafast sequence had a temporal resolution of less than 10 seconds and were run both before and after contrast injection. [37]
Abbreviations: AUC, Area under the curve; FAST, first post contrast; Max, Maximum, MIP, Maximum intensity projection; N, No; Pre-, Pre-contrast; Sens, Sensitivity; Spec, Specificity; Subs, Subtraction images; T1W, T1-weighted; T2W, T2-weighted; Y, Yes
Above Table adapted from Table 1 ref 37, Heacock et al. Radiol Clin North Am.

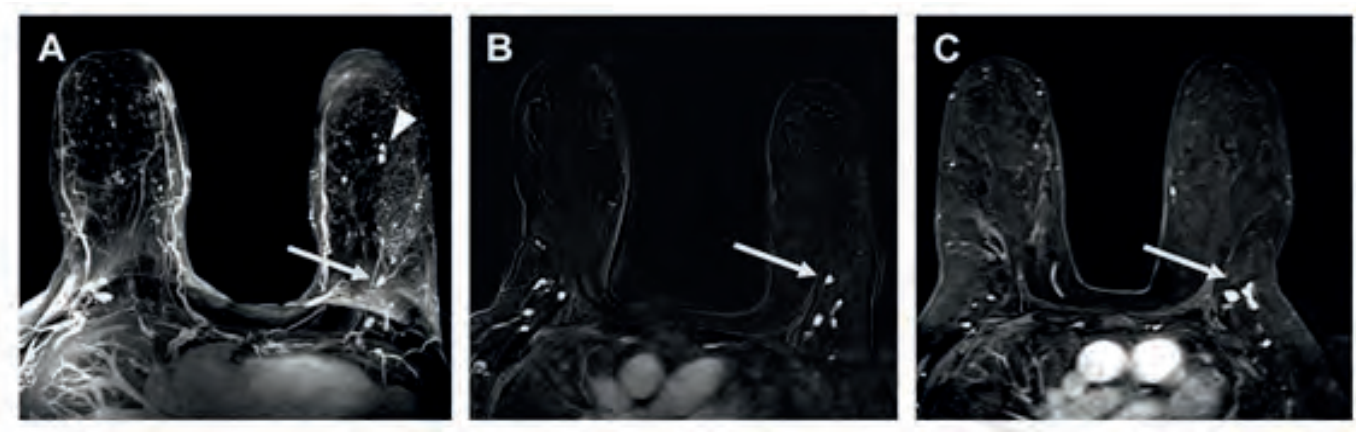

Figure 2. A 56-year-old woman with a personal history of atypia and a strong family history of breast cancer, presenting for high-risk screening. An oval, homogenously enhancing 0.8-cm mass in the left breast at 2:00 (arrow) seems to be a benign axillary lymph node on MIP image (A), but is slightly anterior to axillary lymph nodes on corresponding first postcontrast subtraction images (B). However, the mass is new compared with prior MR imaging (C). MR imaging-guided biopsy yielded metaplastic carcinoma. Arrowhead denotes a previously biopsied left breast benign masses. Axillary lesions are a known pitfall of MIP interpretation; this area should be reviewed carefully on first postcontrast images.
Above figures adapted from Figure 6, ref 37, Heacock et al. Radiol Clin North Am.

the added value of T2-weighted imaging may be most valuable in increasing specificity and biopsy positive predictive value.

Gadolinium-based intravenous contrast remains essential to abbreviated breast MRI. Studies evaluating noncontrast sequences alone, including diffusion weighted imaging (DWI) show sensitivities of 40-78% [16-18] in breast cancer enriched screening populations. These low sensitivities compared to those observed in contrast-enhanced studies demonstrate that DWI and similar noncontrast techniques remain inferior in breast cancer detection. However, adding DWI to a multiparametric contrast-enhanced abbreviated protocol has the potential to improve specificity and sensitivity [19].

The groundwork laid in these prior studies led to the landmark prospective ECOG-ACRIN trial EA1141, "*Comparison of abbreviated breast MRI and DBT in breast cancer screening in women with dense breasts*" [20]. This multicenter study compared digital breast tomosynthesis (DBT) with same day abbreviated breast MRI in asymptomatic, average-risk women with dense breasts, with an overall cancer detection rate of 15.2/1000 women compared to the DBT overall cancer rate of 6.2/1000 women. No invasive cancer was detected by DBT alone. AB-MRI increased short-term follow-up recommendations (BI-RADS 3) compared to DBT (7.5% vs. 1.2%); however, 10.1% of DBT exams required additional imaging (BI-RADS 0) compared to 0% of AB-MRI. Additional analysis is ongoing [21].

To summarize, abbreviated breast MRI has been performed in over 5,400 women in 8 different countries [Table 1] with similar accuracy in contrast-enhanced protocols despite these heterogeneous populations, imaging sequences and equipment [8, 10, 22-27]. The reproducibility of the high accuracy and sensitivity of worldwide protocols highlights the fact that AB-MRI is able to detect biologically aggressive and mammographically occult breast cancer similar to routine breast MRI but with the advantage of decreased imaging time.

LIMITATIONS

The limitations of abbreviated MRI appear similar to those of a full breast MRI protocol. Missed known cancers on AB-MRI are more likely to be DCIS or low-grade invasive cancers [10, 12]. Axillary lesions are a potential pitfall, particularly on review of MIP images (Figure 2) [10, 12]. The lack of delayed postcontrast images inherent to an AB-MRI protocol means that it is less suited to post-neoadjuvant chemotherapy follow up than a full protocol [3, 28], although AB-MRI has shown initial promise in the evaluation of known breast cancers [29].

IMPLEMENTATION CHALLENGES

The major implementation challenges to more widespread use of AB-MRI are those related to reimbursement and workflow optimization. There is still no United States Current Procedural Terminology (CPT) code for AB-MRI, although some breast imaging centers offer a self-pay exam that is not billed to insurance [30]. The cost of this examination varies due to geographic and technical considerations; the goal in self-pay pricing is to offer an examination price that is lower than that of the out-of-pocket deductible for a full breast MRI on high-deductible plans. This is similar to other common cross-sectional screening examinations such as noncontrast CTs for lung cancer screening and cardiac calcium scoring [31].

Clinical workflow optimization remains the other major obstacle to AB-MRI implementation. Early research noting the decrease in AB-MRI image acquisition time referred to what can be called "scan time," (the time it takes to acquire images) which from an operations standpoint is different from the true "table time," or the time from which the patient's intravenous line is placed to the time they are taken off the MRI table. This information is critical to estimating the price point for an abbreviated MR exam and for integrating it into an operations workflow. Borthakur *et al* [32] evaluated full protocol compared to AB-MRI studies in clinical practice and found that the realized gains in patient flow rate (38% for abbreviated MRI compared to a full protocol) were lower than expected based on scan time decrease (65%) because of increased technologist activity time for the AB-MR protocol [32]. This is unsurprising when room setup, patient inflow and exit, IV placement and other considerations are included

when increasing the number of scans performed in the clinical day. Practical considerations when adding AB-MRI to the workflow include keeping the breast coil on the table, duplicating key equipment, and embedding AB-MRI hours into the MRI schedule [31, 33].

FUTURE DIRECTIONS

Clinical research, including the recent EA1141 trial, have shown the promise of AB-MRI protocols in breast cancer screening, particular in increased risk women and women with dense breast tissue. However, further research is still needed and ongoing. An important upcoming study is the planned ECOG-ACRIN PRISM: PRImary Screening with MRI Prospective randomized trial, which will compare DBT and whole breast screening MRI to abbreviated MRI. Additional large-scale clinical trials are ongoing in evaluating AB-MRI in BRCA mutation carriers (Clinicaltrials.gov Identifier: NCT03475979) and in women post breast conservation therapy (NCT03664778). The use of AB-MRI in preoperative MRI staging, evaluating neoadjuvant chemotherapy response, or problem-solving remains unclear and under investigation.

Other novel research protocols include the incorporation of ultrafast imaging acquired immediately post-injection to evaluate wash-in kinetics as a substitute for traditional wash-out time signal intensity curves, which cannot be evaluated in AB-MRI [34-36], and the development of multiparametric protocols. Future directions will likely incorporate deep learning tools for lesion detection, background parenchymal enhancement analysis, and synthetic MRI reconstruction.

CONCLUSION

AB-MRI has the potential to increase patient tolerance and breast MRI screening accessibility to women with intermediate and high lifetime risk of breast cancer, while decreasing scan time and cost. Worldwide studies to date have shown high sensitivity and accuracy for breast cancer screening, including multicenter data demonstrating AB-MRI has improved cancer detection when compared to DBT. These and ongoing studies have proven the utility of AB-MRI in breast cancer detection; reimbursement and clinical implementation remain current challenges to be overcome. Although further research is needed and ongoing, AB-MRI has the potential to transform breast cancer screening in the future.

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Figure 2 (adapted from Figure 6, Heacock et al Radiology Clinics NA)