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REVIEW ARTICLE

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Magnetic Resonance Imaging in Breast Cancer Screening and Diagnosis

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Abstract

The purpose of this article was to evaluate the diagnostic and screening effectiveness of breast MRI (BMRI) protocols for detecting breast cancer. The current review was based on prior research published in English databases such as PubMed and ScienceDirect in scientific articles published between 2010 and 2020 with the keywords "breast cancer MRI," "diagnostic," "dense breast," "risk factors," and "imaging." BMRI is the most sensitive imaging modality for detecting breast cancer. Annual BMRI is recommended for screening women who are at high risk for breast cancer in addition to mammography. Abbreviated MRI, with shorter image acquisition and interpretation times, increases the availability of breast MRI and reduces the costs. Unenhanced MRI parameters such as DWI are under investigation to be added to abbreviated MRI protocols. It seems feasible to offer a cost-effective screening breast DCE-MRI to a broader population.(**International Journal of Biomedicine. 2022;12(1):89-94.**)

Key Words: breast cancer • MRI • imaging protocol

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Abbreviations

BMRI, breast MRI; **CESM**, contrast-enhanced spectral mammography; **DCE-MRI**, dynamic contrast-enhanced MRI; **DWI**, diffusion-weighted imaging; **MRI**, magnetic resonance imaging; **PEM**, positron emission mammography: **SPECT**, single-photon emission computerized tomography.

Breast cancer is the most commonly diagnosed cancer among women and the second most prevalent of all malignancies, accounting for 12% of all cancer-related deaths. In a lifetime, a woman also has a 13% chance of acquiring breast cancer.[1-4] In 2021, an estimated 2.3 million women were diagnosed with breast cancer worldwide, with 30.4% of those dying from the disease.[1,5] Breast cancer is caused by a variety of factors, including modern lifestyle (breastfeeding and age at first birth, smoking, and alcohol consumption), hormonal, breast cancer family history, obesity or overweight, null parity or late pregnancy, menstrual history, aging, previous benign breast tumor, and exposure to carcinogenic agents (radiation or chemicals). A hereditary genetic mutation is thought to be responsible for 5% to 10% of breast cancers.[6,7] Breast cancer type 1 (*BRCA1*) and breast cancer type 2 (*BRCA2*) genes are tumor suppressor genes discovered in the 1990s. These genes play an important role in DNA repair, cell cycle control, and overall genomic stability.[8] It was reported that *BRCA1* and *BRCA2* mutation carriers are responsible for 1 in 400 and 1 in 800 women breast cancer in the United States, in that order.[8] Recent estimates suggest that 55 to 65% of *BRCA1* mutation carriers and approximately 45% of *BRCA2* mutation carriers will develop breast cancer by age 70. [9-11]

Breast cancer incidence rates varied widely depending on economic situations and lifestyle. For example, in affluent countries, the incidence is 89.7 cancer cases per 100,000 women in EU countries, whereas, in developing countries, such as Africa, the incidence is 19.3 cancer cases per 100,000 women.[1,12] Dietary impacts along with reproductive factors (first childbirth, lower parity, and shorter nursing) can partly explain the difference in breast cancer incidence between

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developing and developed countries.[13] It is worth noting that the incidence is also rising in emerging countries. One of the most likely reasons for the rise in cancer incidence in emerging countries is that all countries now have superior diagnostic imaging technology, which means that more cancer cases are recognized and diagnosed appropriately. Furthermore, today's culture is well informed about the early identification of breast cancer by self-examination and consultation with a qualified physician for additional investigations. Furthermore, from the 1940s through the 1980s, the average life duration of the global population increased.

The purpose of this article was to evaluate the diagnostic and screening effectiveness of breast MRI protocols for detecting breast cancer.

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Imaging Modalities for Breast Cancer Screening

All health care providers worldwide endorse breast cancer control which involves prevention, early diagnosis, effective treatment with minimal side effects, and palliative health care and rehabilitation.[13] Early detection of breast cancer plays an important role in the treatment and control of the disease.[14]

Currently, there are 3 imaging modalities for breast cancer screening: mammography, MRI, and ultrasound.

Since the introduction of mammography about 30 years ago, breast imaging with this method has improved significantly. The sensitivity of screening mammography varied considerably across BI-RADS density codes, from 78% in women with code 1 to 47% in women with code 4.[15] The average specificity of digital screening mammography in the U.S. is 88.9%.[16] Currently, mammography is recommended for breast cancer screening for 50.0 to 74.0 years old females.[17] Previous studies showed that screening decreased mortality up to 30% compared with control patients.[13,17] Breast cancer screening with mammograms was started in Saudi Arabia in 2007 using mammography as the only screening tool.[18] However, despite recent developments in mammographic equipment and techniques, mammography as a diagnostic and screening modality has many limitations.[19] These include the reduced sensitivity in detection lesions in the radiographic dense breast due to tissue overlap and the similarity in the radiographic appearance of cancer lesions and glandular dense tissue.[20]

The sensitivity of breast magnetic resonance imaging (BMRI) in detecting breast cancer is higher than mammography and ultrasonography.[21-23] BMRI includes numerous post-contrast sequences acquired at different time points after the injection of MR contrast. The MRI cost is deemed high, and each MRI scan takes at least 20-25 minutes.[24] At the same time, BMRI has been shown to detect breast cancer at an earlier stage than mammography in high-risk patients.[25] Most studies have found that the sensitivity of MRI ranged from 71%-100% versus 16%-40% in mammography in high-risk populations.[26] Thus, BMRI is now identified as a valuable modality in diagnosing breast cancer.[27] MRI is a very sensitive method to cancer detection, but its specificity (true negative) is low. Dynamic contrast-enhanced MRI (DCE-MRI), which uses injectable gadolinium, has been recognized as the most powerful method for detecting breast cancer. The disadvantages of using MRI are its high cost and scan time. However, in high-risk patients, this method is recommended in addition to mammography.

The diagnostic power of ultrasound imaging is highly dependent on operator proficiency and the correct selection of ultrasound parameters.

Brest MRI

BMRI is an extremely useful tool for identifying and classifying breast lesions, determining the amount of localized illness, assessing response to therapy, and guiding fine-needle aspiration (FNA) biopsy.[28]

The results of mammography and any other past breast imaging should be compared to the MRI findings, as well as the clinical history, physical examination findings, and the results of mammography and any other prior breast imaging.[28] BMRI currently has specific indications, including evaluation of response to treatment, screening in high-risk patients, the study of occult breast cancer, the study of tumor recurrence, and the assessment of breast prostheses. BMRI can also be recommended for the staging of breast cancer, the study of microcalcifications, breast discharge, premalignant lesions, residual tumor in operated patients, or in cases of inconclusive findings by mammography and ultrasound.[29] BMRI was introduced as a potential diagnostic tool for patients with breast cancer as a result of these qualities.[16]

The MRI with contrast agents enhances the sensibility of images in the region of interest. Contrast agents allow improvement to the quality and the follow-up of molecular processes at the cellular and molecular levels of the region under study. For MRI, the more common contrast agents used are gadolinium-based structures.[30]

Other imaging modalities that could be utilized to diagnose breast cancer patients include positron emission mammography (PEM) and single-photon emission computerized tomography (SPECT). PET imaging uses radioactive isotopes that emit positrons (^{18}F, ^{15}O, ^{13}N, or ^{11}C); whereas SPECT imaging uses isotopes that emit gamma photons (^{99m}Tc, ^{123}I, or ^{125}I).

Both PET and SPECT provide information about the physiological activity, such as glucose metabolism, blood flow and perfusion, and oxygen utilization.[31] In recent years, a hybrid imaging modality has come into existence in the form of combined PET and MRI (PET/MRI). PET/MRI combines the unique tissue characterization of MRI with the quantifiable functional and molecular information provided by PET, thereby providing distinct potential clinical advantages over other imaging modalities.[32]

Breast MRI screening

According to the American College of Radiology (ACR),[28] current indications for breast MRI screening include:

(a) high-risk patients- women with greater than or equal to 20% lifetime risk of breast cancer (for example, individuals with genetic predisposition to breast cancer as determined by either gene testing or family pedigree, or individuals with a history of mantle radiation for Hodgkin lymphoma).[33] For high-risk patients, annual screening MRI is recommended in addition to mammography, preferably after risk assessment.

(b) Intermediate-risk patients – women with a moderately elevated risk of breast cancer (15%-20%). Breast MRI may be considered as a supplement to mammography. Annual screening MRI is recommended for women with a personal history of breast cancer and dense tissue or for those diagnosed with breast cancer under the age of 50.[34] A systematic review found that, among women with dense breasts, MRI has a sensitivity of 75–100%, specificity of 78–94%, and a p*ositive predictive value* of 3–33%.[35]

(c) Patients with a newly diagnosed breast malignancy. Bilateral breast MRI for these patients can detect occult malignancy in the contralateral breast in at least 3% to 5% of patients.[36-38]

(d) Patients with breast augmentation. The integrity of silicone implants can be determined by non-contrast breast MRI. Patients having silicone or saline implants and/or free injections with silicone, paraffin, or polyacrylamide gel in whom mammography is difficult may require contrast BMRI. Contrast-enhanced breast MRI screening may be required for patients who have undergone implant reconstruction following lumpectomy or mastectomy for breast cancer.

The BRMI can also be used to assess the extent of disease**:**[28] invasive carcinoma and ductal carcinoma in situ (DCIS), invasion deep to fascia, postlumpectomy with positive margins, neoadjuvant chemotherapy

MRI in the additional evaluation of clinical or imaging findings is beneficial for breast cancer recurrence, metastatic cancer, lesion characterization, Postoperative tissue reconstruction, MRI-guided biopsy

Screening of the general population, assessment of false-positive cases, treatment planning, inappropriate uses of breast MRI, and abbreviated (fast) MRI protocols are all examples of other considerations for MRI.

BMRI protocol

T1-weighted imaging

A dynamic T1-weighted contrast-enhanced sequence is the basis for any MRI protocol. A 3D-spoiled gradient echo sequence with a short repetition time, short echo time, and shallow flip angle is used for contrast-enhanced T1-weighted imaging.[28, 39] 3D sequences, with their intrinsically higher SNR and small, nearly isotropic voxel dimensions, have several intrinsic advantages for post-processing purposes over 2D sequences, allowing for a more precise determination of spatiotemporal disease activity. 3D images at 3T may be more robust to B1 variations,[40] and, consequently, allow for improved contrast-enhanced images.

After contrast material administration, the T1-weighted acquisition is repeated to depict enhancing abnormalities.[41] The temporal resolution required for breast MRI is determined by the time course of contrast agent uptake.[42] Peak contrast enhancement in malignant lesions typically occurs between 60 and 120 seconds after injection.[43] It is important to correctly capture the morphology and time-enhancement pattern of enhancing breast lesions.[42] Good fat suppression in both precontrast and postcontrast images minimizes the structured noise of misregistration artifacts in subtracted images, allowing detection of smaller enhancing lesions or nonmasslike lesions with greater reliability.[42]

For images obtained without fat suppression, creating subtraction images from the pre- and postcontrast acquisitions is required.[39] Subtraction images are helpful for acquisitions with fat suppression because they help differentiate truly enhancing structures from lesions with native high signal intensity at T1.[44] Generating maximum intensity projections from these subtracted images aids in rapid lesion detection.[45,46]

According to standard practice, BMRI should depict all enhancing cancers 5 mm or larger in size. Therefore, T1-weighted acquisitions should have a section thickness of no more than 2.5 mm. Much higher resolutions (1 mm isotropic and lower) can be achieved with modern MRI equipment and breast coils without lengthening the acquisition time per volume beyond 90 seconds. This enables for reconstruction in any plane, facilitating the evaluation of lesions, especially the distribution of non-mass lesions.[41] As shown by the success of abbreviated protocols for breast MRI, the acquisition of two T1-weighted acquisitions at the indicated time points (one before and one approximately 90 seconds after contrast material administration) is usually sufficient for lesion detection.[47] All other sequences aim to improve breast lesion distinction and avoid false-positive and false-negative classification.[45]

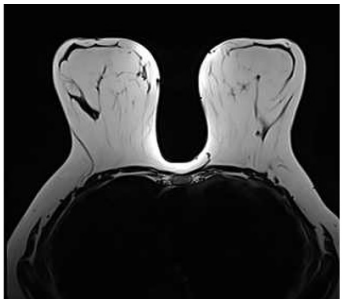

Fig. 1. *BMRI (Dixon protocol) Uuniform fat suppression based on chemical shift .*

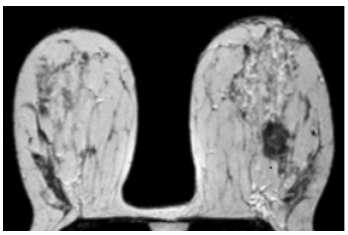

Fig. 2. *T2-weighted BMRI*

Dynamic Evaluation with Time–Signal Intensity Curves

In the previous studies, dynamic analysis has been used to evaluate the permeability of the vessels that supply a lesion.

[48] This approach is carried out by obtaining a series of T1-weighted acquisitions between 5.0 and 7.0 min after gadolinium administration.[49,50] The peak contrast material accumulation will have passed in the case of leaky vessels, and contrast material is being removed from the lesion. The contrast gradient over the vessel wall will still be positive in lesions with less-permeable vessels, and so the lesion will be enhanced. This is reflected in the shape of the time–signal intensity curves; a persistent increase is most commonly seen in benign lesions, whereas a decrease in the late phase is common in malignant lesions.[41,51] Currently, software programs generate color map overlays of the enhancement curve distribution within a lesion, making it easier to extract diagnostic data. [41]

Abbreviated breast MRI

The abbreviated MRI is a shortened version of the standard MRI, consisting of a single early phase DCE series.[52] Abbreviated MRI, with shorter image acquisition and interpretation times, may increase the availability of breast MRI and reduce the costs. Kuhl et al. and Sheth et al.[34,52] introduced the concept of an abbreviated protocol that consisted of one pre- and one postcontrast T1-weighted acquisition and found equivalent diagnostic accuracy for the abbreviated and full protocols. Abbreviated protocols consisting, for instance, of a pre-contrast and an early post-contrast T1-weighted sequence,[34,45,53-56] or, alternatively, a high-resolution ultrafast dynamic imaging protocol, [56] were found suitable to diagnose breast cancer with high accuracy. However, kinetic assessment cannot be performed with the abbreviated protocol, because multiple sets of post-contrast images are necessary for the generation of kinetic curves. [52] Among women with dense breasts undergoing screening, abbreviated breast MRI, compared with digital breast tomosynthesis, was associated with a significantly higher rate of invasive breast cancer detection.[57] Nevertheless, prospective trials with larger patient numbers are warranted to evaluate the true value of abbreviated MRI for breast cancer screening.[58]

Conclusion

Breast MRI is a useful imaging technique for detecting and evaluating breast cancer. It can be used for cancer screening, staging, and evaluating the response to neoadjuvant treatment. The use of BMRI in the evaluation of breast lesions has been researched in the literature, with various publications demonstrating the importance of the topic. BMRI is recognized as the most precise imaging modality in diagnosing malignancy. because of its high sensitivity to soft tissues and ability to provide more comprehensive diagnostic information to identify benign and malignant breast lesions that are not diagnosed by other imaging modalities such as mammography and ultrasound. The current studies have confirmed that the sensitivity of MRI is up to 80%-97.8%, but the specificity is only 46% to 93.3% in diagnosing breast cancer, leading to high rates of misdiagnosis.[59,50] Imaging with DCE-MRI, a technique that samples the influx of contrast agent in the plaque over time using fast T1-weighted (T1w) imaging sequences, has enabled the quantification of several pharmacokinetic parameters, including endothelial permeability and microvascular volume.[61,62] DCE-MRI provides mainly morphological, and, to some extent, functional information about tumor perfusion and vascularity.[63]

A review article by Xiang et al.[64] identified the performance of CESM and MRI for breast cancer diagnosis. The combined data indicating the pooled sensitivity and specificity of CESM and MRI were 0.97 (95% CI: 0.95–0.98), 0.66 (95% CI: 0.59–0.71), 0.97 (95% CI: 0.95–0.98), and 0.52 (95% CI: 0.46–0.58), respectively. The authors concluded that both CESM and MRI are effective methods for the detection of breast cancer with high diagnostic sensitivity.

Xing et al.[60] showed better accuracy, specificity, and false-positive rate of CESM in breast cancer detection than MRI. Contrast-enhanced spectral mammography displayed a good correlation with histopathology in assessing the lesion size of breast cancer, which is consistent with MRI.

In a study by Luczynska et al.,[65] the main goal of this study was to compare CESM and breast magnetic resonance imaging (MRI) with histopathological results and to compare the sensitivity, accuracy, and positive and negative predictive values for both imaging modalities. The results obtained showed that sensitivity was 100% with CESM and 93% with BMRI. Accuracy was 79% with CESM and 73% with BMRI. Contrast-enhanced MRI has been shown to have a very high sensitivity for detecting breast cancer, although reports for specificity have been more variable.

BMRI is critical for the diagnosis of a variety of breast disorders, and it is the most sensitive medical imaging examination for breast cancer detection and diagnosis when compared to mammography, tomosynthesis, and ultrasound imaging. Annual BMRI is recommended for screening women who are at high risk for breast cancer in addition to mammography. Abbreviated MRI, with shorter image acquisition and interpretation times, increases the availability of breast MRI and reduces the costs. Unenhanced MRI parameters such as DWI are under investigation to be added to abbreviated MRI protocols. It seems feasible to offer a cost-effective screening breast DCE-MRI to a broader population.

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