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Review

Clinical role of breast MRI now and going forward

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Magnetic resonance imaging (MRI) is a well-established method in breast imaging, with manifold clinical applications, including the non-invasive differentiation between benign and malignant breast lesions, preoperative staging, detection of scar versus recurrence, implant assessment, and the evaluation of high-risk patients. At present, dynamic contrast-enhanced MRI is the most sensitive imaging technique for breast cancer diagnosis, and provides excellent morphological and to some extent also functional information. To compensate for the limited functional information, and to increase the specificity of MRI while preserving its sensitivity, additional functional parameters such as diffusion-weighted imaging and apparent diffusion coefficient mapping, and MR spectroscopic imaging have been investigated and implemented into the clinical routine. Several additional MRI parameters to capture breast cancer biology are still under investigation. MRI at high and ultra-high field strength and advances in hard- and software may also further improve this imaging technique. This article will review the current clinical role of breast MRI, including multiparametric MRI and abbreviated protocols, and provide an outlook on the future of this technique. In addition, the predictive and prognostic value of MRI as well as the evolving field of radiogenomics will be discussed.

Introduction

Magnetic resonance imaging (MRI) is an essential tool in breast imaging with multiple clinical indications, including preoperative staging, monitoring of neoadjuvant chemotherapy, differentiation between scar and recurrence, evaluation of breast implants, evaluation of patients with cancer of unknown primary (CUP), and screening of high-risk patients.[1,2] When lesions are found to be suspicious on mammography, digital breast tomosynthesis, or sonography, MRI provides further non-invasive analysis and can obviate unnecessary biopsies.[3] When breast cancer is detected or confirmed, MRI provides concurrent staging of disease for treatment planning. Dynamic contrast-enhanced MRI (DCE-MRI) offers morphological and functional tumour information, with excellent sensitivity and variable specificity for breast cancer diagnosis.[4–6] To

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overcome limitations in specificity and assess more functional data, additional MRI parameters can be combined with DCE-MRI; this approach is defined as multiparametric MRI (MP MRI) and has been successfully implemented in clinical routine. Recent studies demonstrated that MP MRI can provide additional information regarding the hallmarks of cancer, thereby increasing its specificity.[7–9] Diffusion-weighted imaging (DWI) and proton MR spectroscopy imaging (^{1}H-MRSI) are examples of techniques that are already established in breast imaging for providing additional parameters, while newer techniques such as chemical exchange saturation transfer (CEST), blood oxygen level-dependent (BOLD), sodium imaging (^{23}Na-MRI), phosphorus spectroscopy (^{31}P-MRSI), lipid MRSI or hyperpolarised MRI (HP MRI) are still being investigated. Meanwhile, breast MRI is steadily moving to 3 T and even 7 T, as the application of high and ultra-high field strengths can improve diagnostic accuracy of breast cancer detection. Abbreviated MRI protocols for breast cancer assessment and screening are currently being developed.

This article will provide a comprehensive overview of the current and future clinical role of breast MRI. We will explain the concept of MP MRI using established (DCE-MRI, DWI, and MRSI) and emerging pulse sequence techniques (sodium imaging, phosphorus MRSI, lipid MRSI, CEST, BOLD, and HP MRI). High and ultra-high field MRI, abbreviated/fast MRI protocols, as well as the prognostic and predictive potential of MRI will be discussed. In addition, an outlook on the evolving field of radiogenomics in MRI of the breast will be given.

Dynamic contrast-enhanced MRI (DCE-MRI)

DCE-MRI is the backbone of any MRI protocol, enabling the simultaneous assessment of tumour morphology and semi-quantitative enhancement kinetics that evaluate neoangiogenesis as a tumour-specific feature.[4,7] Cancers typically develop abnormal vasculature and increased vessel permeability to support its high metabolic demand for oxygen and nutrients.[10] At present, DCE-MRI is generally recognised as the most sensitive imaging modality and aids in the non-invasive differentiation of benign and malignant lesions, while it may obviate unnecessary breast biopsies.[6,11,12]

In 2003, the American College of Radiology (ACR) introduced the Breast Imaging-Reporting and Data System (BI-RADS) MRI lexicon to standardise breast MRI reports worldwide; a revised version was released in 2013.[13] This lexicon provides a standardised terminology for breast MRI findings, report structure, and classification system. The final BI-RADS category determines the probability of malignancy and is based on the most suspicious finding in each breast. A BI-RADS category 0 is assigned when the examination is incomplete, while category 1 indicates a negative examination, category 2 a benign, and category 3 a probably benign lesion. A BI-RADS category 4 suggests that the finding is suspicious enough to justify biopsy, while category 5 is highly suggestive of malignancy, and category 6 is assigned in the case of a histologically verified malignancy.

In DCE-MRI, when a contrast agent is administered, different enhancement kinetics can be identified. A slow, continuous enhancement curve (type I) is attributed to a benign lesion. A medium or strong enhancement followed by a plateau or persistent enhancement (type II) is indicative of either a benign or malignant lesion. A fast initial enhancement and wash-out (type III) is typically seen in malignancies, due to increased vascular permeability, density, and interstitial fluid.[14] According to several studies and recommendations in the revised BI-RADS lexicon, the combination of functional and morphological information is necessary for the optimal evaluation of breast lesions.[4]

The ACR recommends that the morphology of lesions should be reported using standardised BI-RADS descriptors. Larger tumour size, spiculate or irregular margins and shape, a wash-out curve or heterogeneous enhancement are descriptors that most strongly indicate malignancy.[4,15–17] In contrast, typically benign morphological features include round or oval shape, circumscribed margins, dark septa, and homogeneous slow-to-medium/persistent enhancement.[15,18] With 97–100% of histologically confirmed benign lesions showing smooth margins, this feature has the highest predictive value for the presence of a benign lesion.[18,19] For non-mass-like enhancement, benign lesion criteria include cystic changes, and diffuse bilateral enhancement.[20] According to a modified interpretation scheme, a lesion should be assigned a BI-RADS category 4 if both shape and margin are suspicious but enhancement kinetics suggest a benign lesion, or if lesion shape and margin are both non-suspicious but a wash-out is observed.[21] Although DCE-MRI aids in the differentiation between benign and malignant breast lesions, needle biopsy is still generally recommended for newly diagnosed BI-RADS 4 or 5 lesions.

When cancer is detected, DCE-MRI can be used for simultaneous assessment of disease extent, satellite lesions, and multifocal, multicentric, and bilateral disease. DCE-MRI seems particularly more useful than mammography and ultrasound for evaluating invasive lobular cancer (ILC), ductal carcinoma in situ (DCIS), multifocal/multicentric disease, and lesions with a suspected associated extensive intraductal component (EIC; Fig 1).[22,23] If additional suspicious lesions are found on preoperative MRI, histopathological verification before alteration of treatment strategies is mandatory. Although DCE-MRI improves the pre-treatment assessment of disease, it remains controversial whether or not it improves overall or disease-free survival.[24]

DCE-MRI can be performed at different field strengths from 1.5 to 7 T, and so far has yielded excellent results for the assessment of breast cancer, with a sensitivity of up to 99% and a specificity of up to 97%.[9,14,25,26] Its relatively high rate of false-positives occurs due to a significant overlap between benign and malignant lesions, and may result in additional work-up and unnecessary breast biopsies. To reduce background enhancement of normal parenchyma and hence the rate of false-positives, DCE-MRI should ideally be performed in the second week of the menstrual cycle.[27]