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Computer-Aided Diagnosis in Breast Magnetic Resonance Imaging

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OUTLINE

ABSTRACT

In this paper, we review the role played by breast magnetic resonance imaging in the detection and diagnosis of breast cancer. This is followed by a discussion of clinical decision support systems in medicine and their contributions in breast magnetic resonance imaging interpretation. We conclude by discussing the future of computer-aided diagnosis in breast magnetic resonance imaging. ***Mt Sinai J Med 78:000–000, 2011.*** © *2011 Mount Sinai School of Medicine*

Key Words: breast imaging, breast magnetic resonance imaging, clinical decision support systems, computer-aided diagnosis.

Screening• mammography is currently the most effective imaging modality for the early detection of breast cancer.[1] A mammographic examination is a projection radiography procedure in which the resulting image (mammogram) represents the projection of the 3-dimensional (3D) structure of the breast onto a 2-dimensional (2D) image plane. Reasonably good lesion conspicuity, low cost, and ease of use have made screening mammography the practical, first-choice modality for the detection of breast cancer in asymptomatic women. Recent technological improvements have made possible digital, high-resolution (<100 μm per pixel), full-field mammograms at an acceptable radiation dose. Yet, mammography is not perfect. A major problem with mammography is that it is a 2D imaging modality. The projection of the 3D tissue structures of the breast onto a 2D image plane can cause out-of-plane tissue structures to overlap one another and mask cancers, thus making detection difficult. The problem posed by overlapping out-of-plane tissue structures in the breast is especially prevalent in women with dense breasts, because dense tissue may obscure cancers. Anatomical noise due to overlapping out-of-plane tissue structures also leads to additional mammographic views and sonographic examinations. In some cases, biopsies are performed, subjecting women to additional monetary, physical, and emotional costs. Studies have indicated that the

Reasonably good lesion conspicuity, low cost, and ease of use have made screening mammography the practical, first-choice modality for the detection of breast cancer in asymptomatic women.

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positive predictive value of mammography ranges between 10% and 30%.[2–4]

Yet, mammography is not perfect. A major problem with mammography is that it is a 2D imaging modality. Studies have indicated that the positive predictive value of mammography ranges between 10% and 30%.

To achieve higher breast cancer detection sensitivity and to reduce the number of unnecessary biopsies during routine screening, other 3D and 4D (3D + an additional time dimension) imaging technologies such as ultrasound and magnetic resonance imaging (MRI) are used as adjuvant imaging technologies to mammography. Ultrasound has been used in clinical practice for more than a decade now. Ultrasound is particularly effective for distinguishing between cysts and solid lesions,[5] but it is also valuable for characterization of masses, staging, and guiding biopsies. Breast MRI has also received considerable attention because of its ability to detect cancers not visible on mammography, particularly in dense breasts.[6] However, due to the many practical advantages offered by mammography, such as ease of use and low cost, ultrasound and MRI are used primarily as adjuvant modalities in routine screening.

In addition to the development of new breast imaging modalities, imaging informatics is playing

To achieve higher breast cancer detection sensitivity and to reduce the number of unnecessary biopsies during routine screening, 3D and 4D (3D plus an additional time dimension) imaging technologies such as ultrasound and magnetic resonance imaging are used as adjuvant imaging technologies to mammography. In addition, imaging informatics is playing an increasingly important role in the efficient and efficacious interpretation of breast imaging studies.

an increasingly important role in the efficient and efficacious interpretation of breast imaging studies. In particular, clinical decision support systems, commonly known in radiology as computer-aided diagnosis systems, are essential for modern imaging modalities to reach their full potential. In this review, we summarize the role played by breast MRI in the detection and diagnosis of breast cancer. Subsequently, we introduce clinical decision support systems and review the contributions of these systems in breast MRI interpretation. We close with a discussion of the future of computer-aided diagnosis for breast MRI.

BREAST MAGNETIC RESONANCE IMAGING

In MRI, the nuclear magnetic resonance signal from the hydrogen nuclei of the tissue is imaged.[7,8] Nuclear magnetic resonance refers to the phenomenon in which, under the application of an external static magnetic field and a radiofrequency pulse at "Larmor frequency," the magnetic dipole moment of the hydrogen protons changes orientation.[7] The recovery times of the longitudinal and the transverse component of the magnetic dipole moment capture the unique biophysical characteristics of the tissue, and, hence, can be used to provide contrast on the image between different constituent structures of the breast. The recovery of the longitudinal component is characterized by a time constant (T1), and the recovery of the transverse component is characterized by a time constant (T2). The durations for which the external magnetic and radiofrequency fields are applied is governed by pulse sequences. By appropriately combining the pulse sequences, it is possible to generate a series of T1 and T2 signals that can then be spatially encoded using a 3D encoded magnetic field to produce 3D examinations of the breast tissue.[8] However, despite the 3D images generated by MRI, the contrast is still insufficient to visually distinguish between normal and abnormal structures within the breast. Functional imaging techniques that demonstrate the differences in the microcirculatory characteristics of diseased and healthy tissue can be used to provide better visual contrast between the normal and the abnormal structures within the breast. This concept is the driving force behind the development and the clinical use of dynamic contrast-enhanced breast MRI (DCE-MRI).[8]

Dynamic contrast-enhanced MRI images are acquired before, during, and after the injection of a contrast agent. Gadolinium diethylenetriamine pentaacetic acid is a commonly used intravenous contrast agent.[8] Diffusion of the contrast agent through an

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organ is governed by the kinetic properties of the tissues. The accumulation of the contrast agent in the target tissue shortens the T1 and T2 relaxation times of the protons in the hydrogen nuclei, which affects the resulting signal intensity in the T1- and T2-weighted images. Because contrast agent uptake and washout is a function of time, DCE-MRI images are acquired sequentially.

The typical DCE-MRI protocol in most hospitals involves acquiring precontrast and postcontrast images using T1-weighted pulse sequences with good fat suppression. The timing of pulse sequences is designed such that the microcirculatory characteristics of diseased and healthy tissue are accurately captured. This is achieved by adopting a pulse sequence design in which the resulting temporal resolution of the DCE-MRI series is about 1 to 2 minutes.[9] The reason for using T1-weighted pulse sequences with good fat suppression is that the gadolinium-based contrast-agent compound affects the T1 relaxation time of the protons in the hydrogen nuclei more than the T2 relaxation time.[9] This causes the enhancing lesions to appear brighter than the fibroglandular tissue and fat in T1-weighted postcontrast images.[9] By contrast, on the T2-weighted images there is darkening of breast tissue and lesions, with the exception of cysts that appear the brightest on T2-weighted images. Breast-tissue analysis is usually carried out on T1-weighted images because these images best portray enhancing lesions. Figures 1 and 2 illustrate examples of precontrast and postcontrast T1-weighted DCE-MRI images. Note the enhancing mass in the postcontrast T1-weighted image in Figure 1 and the enhancing malignant process in the postcontrast T1-weighted image in Figure 2.

DCE-MRI exams are usually performed using MRI systems that operate at 1.5 Tesla (T), although 3.0 T systems are commercially available. The advantage of using systems operating at 3.0 T is that they provide a higher signal-to-noise ratio than systems operating at 1.5 T. Kuhl *et al.* conducted a study in which they prospectively compared contrast-enhanced MRI at 1.5 T and 3.0 T in the same 37 patients.[10] Their results showed that the images acquired at 3.0 T had overall higher image quality scores than those acquired at 1.5 T.[10] The higher spatial resolution at 3.0 T also resulted in an increased confidence in the differential diagnosis of enhancing lesions.[10] Also available are MRI systems with parallel imaging techniques. Parallel imaging techniques facilitate bilateral breast imaging and help to reduce the time and the costs associated with breast MRI.[9]

Another recent development in the use of MRI for breast cancer diagnosis is magnetic resonance

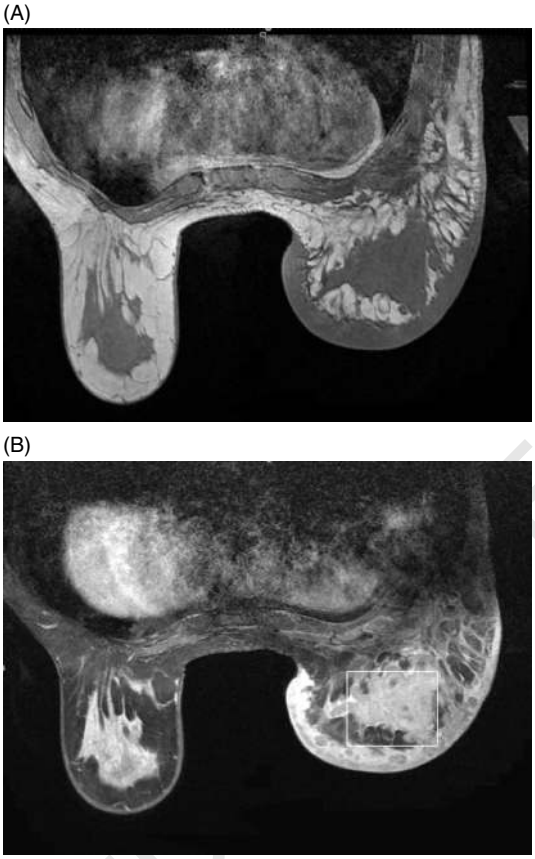

Fig 1. A 33-year-old woman with a known left breast invasive cancer with a lobular growth pattern underwent a staging MRI. (A) T1-weighted axial MRI shows a large mass in the left breast at 6:00 with associated skin thickening. (B) Axial T1-weighted postcontrast MRI shows the large nodular enhancing mass (white box) in the left breast 6:00 region with associated enhancing nodular skin thickening. **Abbreviations:** MRI, magnetic resonance imaging.

spectroscopy (MRS). In vivo proton magnetic resonance spectroscopy (1H-MRS) can be used to extract information about the biochemical properties of breast lesions. For example, 1H-MRS can be used to detect elevated choline levels, which are typically associated with malignant tissue, but not with benign lesions or normal tissue.[11–14] The exact biological mechanisms that produce elevated choline levels have not yet been identified, but it has been hypothesized that elevated choline is an indicator of increased cell proliferation.[11–14]

It has also been proposed that the choline levels from 1H-MRS could potentially be used to monitor and predict response to cancer therapy. Jagannathan *et al.* conducted the first study to measure treatment response, and they observed that choline levels decreased in 89% of subjects undergoing chemotherapy.[15] Meisamy *et al.* conducted a single-voxel MRS clinical study of 16 patients being

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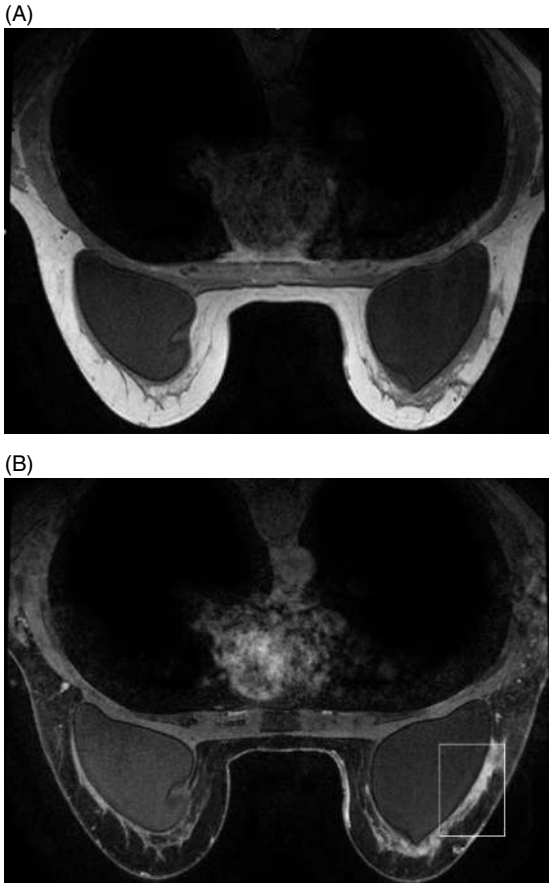

Fig 2. A 60-year-old woman with a known invasive lobular carcinoma in the left breast. (A) Axial T1-weighted MRI demonstrates a low signal region lateral to the left breast prepectoral saline implant, representing the known carcinoma. (B) Axial T1-weighted postcontrast MRI shows an enhancing region (white box) lateral to the implant, representing the malignant process. **Abbreviations:** MRI, magnetic resonance imaging.

treated with neoadjuvant chemotherapy for locally advanced breast cancer.[16] Meisamy *et al.* demonstrated that changes in the total choline level, from baseline to 24 hours after the first dose of therapy, correlated significantly with changes in tumor size. These preliminary results indicate that changes in the choline level within 24 hours after the first dose of treatment could be employed as an early indicator for the prediction of response to therapy for locally advanced breast cancer.[16] Finally, some studies have shown that the inclusion of MRS data can improve the sensitivity and specificity of a diagnostic breast MRI examination. For example, Huang and colleagues added a single-voxel MRS study to a conventional DCE-MRI examination. They reported that the inclusion of MRS increased the specificity of the examination from 62.5% to 87.5%.[17] Even though there have been many encouraging studies that report the potential clinical relevance of MRS, work still needs to be done if MRS has to be used for routine breast cancer diagnosis. Chief areas of concern include a lack of standardization in MRS procedures and the lack of a substantial multicenter clinical trial. Tozaki and Maruyuma provide a nice review on the current status and what the future holds for breast MRS.[18]

The role of MRI for breast cancer screening in asymptomatic women has been reviewed in many publications (eg,[6,19]). Lehman *et al.* performed a comprehensive review of the role of MRI in breast cancer screening.[6] Screening breast MRI trials in women at high risk for developing breast cancer indicate that breast MRI achieves superior performance in detecting invasive cancers as compared with mammography and ultrasound.[6] Magnetic resonance imaging has been shown to be very effective in detecting mammographically occult cancers, especially in women with dense breast tissue; moreover, the performance of MRI in combination with mammography has been shown to be superior to that of mammography alone.[6]

Screening breast magnetic resonance imaging trials in women at high risk for developing breast cancer indicate that breast magnetic resonance imaging achieves superior performance in detecting invasive cancers as compared with mammography and ultrasound. Magnetic resonance imaging has been shown to be very effective in detecting mammographically occult cancers, especially in women with dense breast tissue.

Breast MRI is recommended by the American Cancer Society to be used as an adjunct modality annually along with mammography for women who have a high risk of breast cancer, such as those with BRCA1 or BRCA2 gene mutations, those who have first-order relatives with BRCA1 or BRCA2 gene mutations, or those with a high risk based on other personal and family history factors.[6] Breast MRI is also used in clinical practice for staging, primarily to determine the extent of the disease in the ipsilateral breast, and for detecting additional cancers in the contralateral breast.[6]

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Whereas MRI has been consistently shown to achieve high sensitivity in screening for invasive cancers when compared with mammography, some earlier studies had reported that ductal carcinoma in situ is more frequently missed on MRI than on mammography. However, as noted by Lehman *et al.*,[6] false-negative MRI examinations in these studies may be attributed to the lower spatial resolution of older MRI systems. More recent studies conducted using high–spatial resolution MRI systems have shown MRI to achieve a higher sensitivity than mammography in detecting DCIS.[20,21]

Higher sensitivity and increased cancer yield from MRI examinations performed on asymptomatic women have spurred the breast-imaging community to explore a much wider role for MRI in breast cancer care. There is considerable debate[22–25] as to whether preoperative breast MRI should be recommended for all patients with newly diagnosed breast cancer. Sardanelli[22] recommended that if MRI is routinely used for all women with newly diagnosed breast cancer, then the MRI examination should be interpreted only after taking into account the results from clinical breast examination, mammography and ultrasound, and fine needle aspiration biopsy. Sardanelli[22] noted that if a lesion is detected on MRI alone, then the hospital or imaging center must be equipped with facilities to perform a core needle biopsy under MRI guidance, and the total time spent on deciding the next course of action after MRI has been performed should not exceed 1 month. In fact, in the latest breast MRI accreditation program requirements issued by the American College of Radiology, it is now mandatory for the hospital to be equipped with facilities or have arrangements with another off-site center to perform a biopsy under MRI guidance.[26]

On the other hand, Solin[23] argued that preoperative MRI had no real benefit in planning the next course of action once a woman was diagnosed with breast cancer on mammography. Solin's recommendation is driven by the initial results from the Comparative Effectiveness of Magnetic Resonance Imaging in Breast Cancer (COMICE) trial,[24] which showed that using preoperative MRI in addition to the standard triple assessment procedure (clinical breast examination, mammography and ultrasound, and fine needle aspiration biopsy or core biopsy) did not significantly reduce reoperation rates when compared with using the standard triple assessment procedure alone. McCaffery and Jansen[25] discussed the complex decision-making process for both patients and care providers when additional information is made available from a breast MRI examination. The same authors made recommendations for educating women about the potential benefits and risks of preoperative MRI, and encouraged the development of evidence-based decision aids to help patients and care providers arrive at optimal treatment choices in the current environment of uncertain evidence.[25]

CLINICAL DECISION SUPPORT SYSTEMS IN MEDICINE

A decision support system is a sophisticated tool that helps a person consider multiple criteria in order to make a choice from among alternatives. Decision support systems are used in a wide variety of domains, including agricultural, business, medical, military, and transportation applications. In the medical arena, clinical decision support systems provide clinicians, staff, patients, and other individuals with person-specific information, intelligently filtered and presented at appropriate times, to enhance health and healthcare.[27] Clinical decision support systems are developed to target different aspects of care, including prevention, diagnosis, and treatment planning.

It is important to emphasize that decision support systems are intended to supplement, not supplant, people in the decision-making process. In other words, such systems are intended to aid a person in choosing from among alternatives; they are not intended to automate the process such that a choice is imposed upon the user. Although some decision support systems are designed to provide specific recommendations for consideration, the user reviews the suggestions and may ultimately reject them in favor of a different alternative. Moreover, many decision support systems are not designed to provide a specific recommendation; rather, they focus on the intelligent filtering and presentation of personalized data.

Numerous decision support systems, and even more simple decision aids (such as educational videos), are used to assist with different aspects of breast cancer care. The term computer-aided diagnosis (CAD) is used to refer broadly to clinical decision support systems that assist in the interpretation of breast imaging studies. Because the word "diagnosis" does not adequately describe the range of decisions that must be made, some authors have adopted the more specific terminology of computer-aided

The term computer-aided diagnosis is used to refer broadly to clinical decision support systems that assist in the interpretation of breast imaging studies.

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detection and computer-aided diagnosis to help distinguish between the screening and diagnostic roles of medical imaging.

Key questions to consider when designing a decision support system are whose decisions are being supported, what information is presented, when it is presented, and how it is presented to the user.[27] Another way to conceptualize decision support systems is to recognize that their common features are a knowledge base, a means of combining that knowledge with patient-specific information, and a communication mechanism.[27] In the context of CAD systems in breast imaging,[28–31] the knowledge base is typically a rich collection of a variety of patient cases (images) and diagnostic reports. The knowledge from such a collection can be mathematically captured using concepts from statistics and machine learning, and then can be applied to an individual patient to make a prediction regarding the diagnosis. The prediction made by the CAD system can be communicated to the radiologist in a variety of forms, such as the probability of the diagnosis or a yes/no binary recommendation.

Computer-Aided Detection and Diagnosis in Magnetic Resonance Imaging

In breast imaging, CAD systems have been historically developed to assist radiologists in detecting signs of breast cancer on mammography and to reduce the number of false-negative findings.[28–31] Several

In breast imaging, computer-aided detection systems have been historically developed to assist radiologists in detecting signs of breast cancer on mammography and to reduce the number of false-negative findings.

CAD systems for mammography are approved by the US Food and Drug Administration (FDA) for the detection of breast cancer, such as the R2 ImageChecker CAD (Hologic, Inc., Bedford, MA) and SecondLook Digital CAD (iCAD, Inc., Nashua, NH). In contrast, CAD systems that help radiologists analyze breast lesions by performing an automatic evaluation of the lesions are still in the research and development phase and have not yet been approved by the FDA for clinical use.[28–31]

In DCE-MRI, computer-based decision support systems are commercially available for clinical use. Even though these systems are also commonly referred to as CAD systems, their functionality is quite different from those used for x-ray mammography. Commercially available CAD systems for breast MRI assist radiologists by performing certain automated postprocessing tasks, such as image analysis and visualization.[32] The primary intended benefit of CAD for breast MRI is to help radiologists interpret exams more efficiently.[32] The present-day role of decision support systems in breast MRI involves a great degree of human intervention in that the radiologist or imaging technologist controls the postprocessing carried out by the system by providing inputs, and the level of interaction varies with experience in interpreting breast MRI. This is in contrast to

The primary intended benefit of computer-aided detection for breast magnetic resonance imaging is to help radiologists interpret exams more efficiently. The present-day role of decision support systems in breast magnetic resonance imaging involves a great degree of human intervention in that the radiologist or imaging technologist controls the postprocessing carried out by the system by providing inputs, and the level of interaction varies with experience in interpreting breast MRI.

commercial CAD systems in mammography where the systems are used as an "autonomous second reader" for screening mammograms. Examples of commercially available CAD systems for breast MRI include DynaCAD (Invivo, Inc., Orlando, FL) and CADStream (Merge Healthcare Inc., Chicago, IL). It is important to note that there are no commercially available CAD systems for breast MRI that have been approved by the FDA for automatically performing lesion evaluation and for rendering diagnoses.

Wu and Markey have written a comprehensive review of CAD methods for breast MRI.[8] Though the review by Wu and Markey was published in 2006, their summary of the basic CAD workflow for breast MRI is still pertinent. A typical CAD

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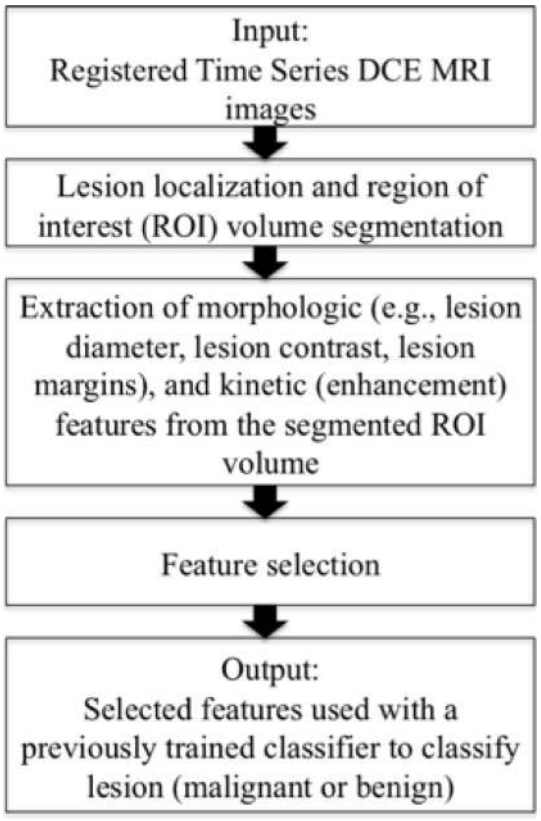

Fig 3. Flow diagram illustrating the typical processing steps in a CAD system for breast MRI. **Abbreviations:** CAD, computer-aided diagnosis; MRI, magnetic resonance imaging.

workflow for breast MRI, as illustrated by the flow diagram in Figure 3, comprises the following steps: (1) registration of the time series DCE-MRI images to spatially align voxels prior to extracting the kinetic properties, (2) localizing the lesion and segmenting the lesion volume, (3) computing morphological and kinetic properties from the segmented lesion volume, (4) selecting the most important features characteristic of the lesion, and (5) classifying the lesion based on the selected features and providing an opinion on the diagnosis to the radiologist. It is important to note that although the functionality described in steps 1, 2, and 3 is available in present-day commercial CAD systems for breast MRI, steps 4 and 5 are still in a research phase and have not been approved by the FDA for clinical use.[32]

Image registration is the process by which anatomical and functional correspondence is established between the precontrast and the postcontrast images. Image registration is warranted by the relatively long acquisition time of a breast MRI examination (20–40 minutes). Respiratory and cardiac motion, and, to some degree, movement of the patient, are unavoidable during the performance of a breast MRI examination. Due to patient motion, the same coordinates of an image at 2 different time points might correspond to 2 different anatomical structures in the breast. Trying to analyze the morphological and the enhancement properties of an abnormality directly from the MRI data may result in errors due to the spatial displacement of structures between multiple time points. To avoid such errors, it is necessary to perform image registration. Image registration is a well-studied problem in medical imaging,[33] and many algorithms have been developed specifically for breast MRI. The interested reader is referred to Wu and Markey[8] for an overview of image registration algorithms for breast MRI.

Once the images are registered, the next step is to localize and segment the 3D lesion volume from a DCE-MRI exam. Lesion localization can be either automatic or manual and is usually performed using CAD systems. Manual lesion localization entails placing a bounding box known as a region of interest on the contrast-enhanced MRI showing the enhancing lesion. For example, the upper left panel in Figure 4 illustrates an example of a contrast-enhanced MRI showing an enhancing mass, which can be easily localized by placing a region of interest that includes the enhancing region. Lesion localization is also sometimes accomplished with the aid of the subtracted image that is obtained by subtracting the precontrast image from the first postcontrast image after the precontrast and postcontrast images have been registered to compensate for motion errors. Once the lesion has been localized, it ideally needs to be accurately segmented in order to compute morphological and kinetic properties associated with it. Many segmentation techniques have been proposed, and the popular techniques include the use of multiple thresholds to segment the lesion from the background,[34] statistical methods relying on maximum a posteriori estimation of voxel class membership (lesion, nonlesion), and Gaussian mixture models to cluster voxels belonging to ≥ 2 classes (lesion, nonlesion).[35,36]

Once the lesion has been localized (and segmented), the next step is to compute properties that characterize the lesion. These properties include morphological and enhancement (kinetic) properties. Morphological properties are characterized according to the American College of Radiology Breast Imaging Reporting and Data System.[8] Present-day commercial CAD systems have the ability to compute morphological properties such as lesion volume and lesion diameter.[32] The enhancement properties provide additional discriminatory power to distinguish abnormalities from normal regions on an image. The enhancement properties are extracted

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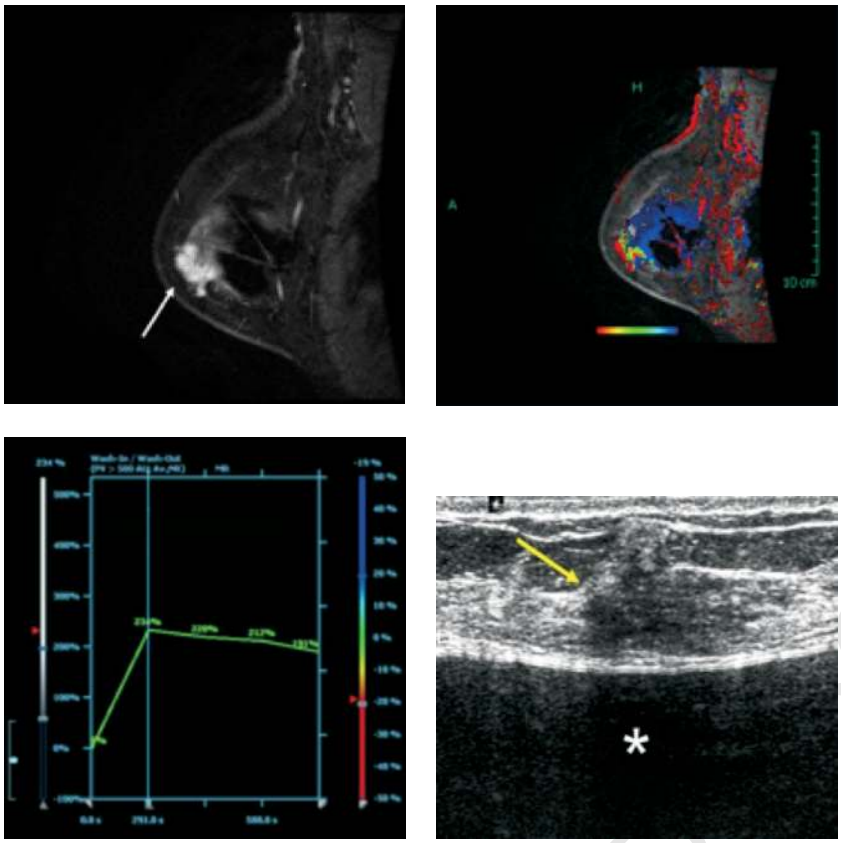

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Fig 4. Breast MRI examination on a 58-year-old woman with implants. Sagittal DCE-MRI shows an enhancing mass (arrow) in the 9:00 region of the right breast (upper left panel). Sagittal CAD color image shows marked enhancement (cursor; upper right panel). Enhancement curve shows rapid wash-in and washout kinetics (lower left panel). Ultrasound performed after the MRI shows an irregular, hypoechoic mass (arrow) anterior to the implant (*) (lower right panel). Ultrasound-guided core biopsy was performed, revealing invasive lobular carcinoma. **Abbreviations:** CAD, computer-aided diagnosis; DCE-MRI, dynamic contrast-enhanced magnetic resonance imaging; MRI, magnetic resonance imaging.

from the "time-contrast enhancement" curve. The time-contrast enhancement curve is a plot of the lesion intensity before and after the administration of the contrast agent versus time.[32] Once the lesion has been localized by the CAD system, the time-contrast enhancement curve can be generated by the system, and this is usually achieved by computing the mean voxel intensity within the same ROI location at different user specified time points (ie, at different user-specified MR series numbers). Some CAD systems also have the ability to automatically identify the most rapidly enhancing voxels and compute the enhancement curves for these voxels.

The idea behind using enhancement curves for diagnosis is that the time-enhancement curves of voxels belonging to the abnormality are usually different from the curves of the voxels belonging to the normal regions of the breast. These findings are due to the difference in the contrast agent uptake and washout of breast abnormalities when compared with the normal anatomical regions of the breast. The enhancement curves usually fall into one of 3 categories. Type 1 enhancement curves typically show a linear increase in the signal along time. The linear increase in Type 1 curves is due to a continuous uptake of the contrast agent, and Type 1 curves have been shown to be associated with a very low probability of cancer.[37] Type 2 and type 3 enhancement curves are characterized by a more rapid linear increase of the signal along time, suggestive of rapid contrast agent uptake. The difference between type 2 and type 3 curves is that a plateau is commonly seen after rapid uptake in type 2 curves, whereas in type 3 curves there is a continuous decrease in the signal along time after rapid uptake, which is suggestive of a washout of the contrast agent. Type 2 curves are shown to be

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associated with a much higher probability of cancer than type 1 curves, whereas type 3 curves are strongly suggestive of cancer.[37] The lower left panel in Figure 4 illustrates the enhancement curve computed using the DynaCAD system for the contrast-enhanced MRI shown in the upper left panel. This enhancement curve is a type 3 curve, as it shows rapid uptake (wash-in) and washout kinetics. Ultrasound performed after the MRI revealed an irregular, hypoechoic mass (lower right panel in Figure 4). Although time-enhancement curve shapes provide valuable insight into the diagnosis of lesions, it is important to note that there is a significant overlap in the wash-in/washout kinetics of benign and malignant lesions. Hence, the enhancement curves are used in conjunction with morphological properties such as lesion shape properties for accurate cancer diagnosis.[37]

Another way of using the enhancement curves for diagnosis is to generate a color overlay on the contrast-enhanced MR image that represents the contrast agent enhancement kinetics in the breast. The color map is generated using a user-specified threshold on the degree of enhancement. The upper right panel in Figure 4 illustrates the color map generated by the DynaCAD system on the contrast-enhanced MRI shown in the upper left panel. The colors assigned by the DynaCAD system to the pixels range from blue (cool) to red (hot), with the color intensity modulated according to the rate of enhancement. In the color map illustrated in the upper right panel of Figure 4, the color blue has been assigned to pixels whose degree of enhancement (wash-in/uptake) was >20%, and the color red has been assigned to pixels whose degree of enhancement (washout) was <20%. Cancerous tissue tends to demonstrate more washout (red). It is important to note that there are minor differences in how the color maps are generated by different commercial CAD systems. For example, CADStream assigns only 3 colors—blue, green, and red—of constant intensity value to the pixels meeting the enhancement threshold. These 3 colors are in one-to-one correspondence with the 3 enhancement curve types, type 1 (blue), type 2 (green), and type 3 (red). This is in contrast to the DynaCAD system, which assigns a range of colors from blue to red with modulated intensities to pixels meeting the enhancement threshold.[32] Although enhancement thresholds can be used to obtain useful diagnostic information, the thresholds must be set with caution, as variations in the enhancement threshold can affect the overall diagnosis.[38]

Once the morphologic and enhancement properties have been extracted from the MRI images, the next step is to select the most discriminatory properties and use classification methods to determine the likelihood of malignancy of a suspicious lesion. This step employs feature selection and classification techniques[8] developed by the machine-learning community in which the term "features" is typically used in place of the term "properties." Feature selection and training of the classifier is usually carried out on a dataset reserved exclusively for training, whereas evaluation of the system is carried out on a previously unseen test/validation data set. The CAD systems for breast MRI are usually evaluated using the receiver operating characteristic (ROC) curve, which is a plot of the sensitivity versus the false-positive fraction. The area under the ROC curve is commonly used to summarize the performance of the classifier. Automatic feature selection and lesion evaluation using classification techniques remains an area of active research.[39–41] Commercially available CAD systems for breast MRI do not have automatic feature selection and lesion evaluation capabilities; this is an area of current research.

FUTURE OF COMPUTER-AIDED DIAGNOSIS IN BREAST MAGNETIC RESONANCE IMAGING

The need to simultaneously image the functional properties of breast tissue along with the anatomical structures has spurred rapid progress in breast MRI. The CAD systems for breast MRI have proven to be valuable in helping radiologists analyze DCE-MRI data and arrive at diagnoses. Yet, challenges remain for breast MRI CAD systems, and they have to be addressed if these systems are to realize their full potential. One of the challenges with commercial CAD systems is errors/delays in diagnosis due to blood vessels being colored on color overlay maps. Colored vessels can mislead or delay radiologists if they are mistaken for tumor. The color maps are generated by assigning colors to all pixels whose degree of enhancement meets the user-specified threshold. Blood vessels whose diameters are >1–2 mm usually meet the enhancement thresholds and are colored, and the color assigned could be one that suggests a rapid washout. The radiologist then has to carefully assess each vessel that is colored in order to completely rule out all suspicious findings. Such false-positive coloring may also pose a problem when determining the extent of disease. Algorithms are needed to identify normal structures such as blood vessels in order to reduce false-positive coloring. There have been ongoing efforts in the research community to develop such algorithms.[42] Breast MRI CAD systems are yet to be used for automated lesion

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evaluation and diagnosis. Although this has been an area of active research,[39–41] this goal can be realized only if a concentrated effort is made toward developing a standardized performance evaluation of these systems involving multiple datasets from multiple vendors and institutions. Whereas the past decade has seen the development of CAD systems focused on individual modalities like mammography and breast MRI, we believe that the true potential of CAD will be realized once these systems are made interoperable across multiple breast-imaging modalities. This is particularly relevant in the current scenario, in which breast imaging is in a transient phase with the advent of new x-ray–based 3D breast-imaging modalities such as breast tomosynthesis, breast computed tomography, and stereoscopic mammography.[43] It is not yet certain which combination of modalities will be used in routine practice in conjunction with mammography. Development of multimodality CAD systems should be model-based,[44] a paradigm focused on the properties of the underlying cancer being detected rather than on the modality with which it is being detected. Finally, CAD systems should be designed to integrate information from multiple modalities while arriving at a diagnostic decision. The focus should be on capturing information that could be useful for assessing disease prognosis.[31]

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Potential conflict of interest: Nothing• to report.

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