Additional reprint and journal issue purchases

- Should you wish to purchase additional copies of your article, please click on the link and follow the instructions provided: https://caesar.sheridan.com/reprints/redir.php?pub=10089&acro=MSJ

- Corresponding authors are invited to inform their co-authors of the reprint options available.

- Please note that regardless of the form in which they are acquired, reprints should not be resold, nor further disseminated in electronic form, nor deployed in part or in whole in any marketing, promotional or educational contexts without authorization from Wiley. Permissions requests should be directed to mailto: permissionsus@wiley.com

- For information about ‘Pay-Per-View and Article Select’ click on the following link: http://www3.interscience.wiley.com/aboutus/ppv-articleselect.html
Required Form for Authors
Authorship Responsibility, Financial Disclosure, and Assignment of Copyright

Please PRINT names of all authors here:

Each author must read and sign this form dealing with (1) authorship responsibility, (2) financial disclosure, (3) copyright transfer. An author who was a US federal employee when this work was conducted and prepared for publication, must sign statement (4) instead of statement (3).

1. Authorship Responsibility
I certify that I have participated sufficiently in the conception and design of this work, and the analysis of the data (where applicable), as well as the writing of the manuscript, to take public responsibility for it. I believe that the manuscript represents valid work. I have reviewed the final version of the manuscript and approve it for submission for publication. Neither this manuscript nor one with substantially similar content under my (our) authorship has been published or is being considered for publication elsewhere, except as described in a separate attachment. Furthermore, I agree to produce the original recorded data on which the manuscript is based for examination by the Editor-in-Chief and/or his assignees should such records be requested.

2. Financial Disclosure
I certify that I have no affiliation with or financial involvement in any organization or entity with a direct financial interest in the subject matter or materials being discussed in the manuscript (e.g., employment, consultancies, stock ownership, honoraria), except as disclosed in a separate attachment.

3. Copyright
In compliance with the Copyright Revision Act of 1976, the signature of each author on this form shall indicate and be evidence of agreement and mutual understanding with The Mount Sinai Journal of Medicine, in consideration of the further action of the Journal to review and edit the manuscript being submitted, to transfer, assign, and convey all copyright ownership, including any and all rights incidental thereto, exclusively to The Mount Sinai Journal of Medicine if this work is published in the Journal.

4. US Federal Employees
I was an employee of the US government when this work was conducted and prepared for publication; therefore, it is not protected by the Copyright Act and copyright ownership cannot be transferred.

Return your form to: Steven Kyritz, Mount Sinai Journal of Medicine, c/o John Wiley & Sons, Inc., 111 River Street, Mail Stop 8-01, Hoboken, NJ 07030. E-mail: skyritz@wiley.com
Computer-Aided Diagnosis in Breast Magnetic Resonance Imaging

Gautam S. Muralidhar, MS,1 Alan C. Bovik, PhD,2 Mehul P. Sampat, PhD,3 Gary J. Whitman, MD,4 Tamara Miner Haygood, PhD, MD,4 Tanya W. Stephens, MD,4 and Mia K. Markey, PhD1,5

1Department of Biomedical Engineering, University of Texas at Austin, Austin, TX
2Department of Electrical and Computer Engineering, University of Texas at Austin, Austin, TX
3Department of Neurology, University of California at San Francisco, San Francisco, CA
4Department of Diagnostic Radiology, University of Texas MD Anderson Cancer Center, Houston, TX
5Department of Imaging Physics, University of Texas MD Anderson Cancer Center, Houston, TX

OUTLINE

BREAST MAGNETIC RESONANCE IMAGING

CLINICAL DECISION SUPPORT SYSTEMS IN MEDICINE

Computer-Aided Detection and Diagnosis in Magnetic Resonance Imaging

FUTURE OF COMPUTER-AIDED DIAGNOSIS IN BREAST MAGNETIC RESONANCE IMAGING

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 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.
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 a major 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
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 hospi-
tals 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 charac-
teristics of diseased and healthy tissue are accurately cap-
tured. 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 rea-
son 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 enhanc-
ing 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 differen-
tial 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
spectroscopy (MRS). In vivo proton magnetic reso-
nance 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 typi-
cally associated with malignant tissue, but not with
benign lesions or normal tissue.11–14 The exact bio-
logical 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 mea-
sure treatment response, and they observed that
choline levels decreased in 89% of subjects under-
going chemotherapy.15 Meisamy et al. conducted a
single-voxel MRS clinical study of 16 patients being

DOI:10.1002/MSJ
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.

G. S. MURALIDHAR ET AL.: COMPUTER-AIDED DIAGNOSIS IN BREAST MRI

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. 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.
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., 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.

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 as to whether preoperative breast MRI should be recommended for all patients with newly diagnosed breast cancer. Sardanelli 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 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.

On the other hand, Solin 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, 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 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.

**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. 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”

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

...does not adequately describe the range of decisions that must be made, some authors have adopted the more specific terminology of computer-aided...
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. In the context of CAD systems in breast imaging, 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. Several commercially available CAD systems for breast MRI 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.

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. The primary intended benefit of CAD for breast MRI is to help radiologists interpret exams more efficiently. 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.

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.

Wu and Markey have written a comprehensive review of CAD methods for breast MRI. 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...
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 Markey8 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 frame 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.

DOI:10.1002/MSJ
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. 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. 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
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, hypechoic 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 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.

DOI:10.1002/MSJ
evaluation and diagnosis. Although this has been an area of active research,\textsuperscript{30–41} 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.\textsuperscript{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,\textsuperscript{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.\textsuperscript{31}

ACKNOWLEDGMENTS

The authors would like to thank Dr. Jason Stafford for his valuable input in preparing this review.

DISCLOSURES

Potential conflict of interest: Nothing to report.

REFERENCES


DOI:10.1002/MSJ


Q1. A subtitle was supplied along with the article title. We have deleted the subtitle. Please confirm if fine.
Q2. Please confirm there are no disclosures to report.
Q3. Please add date the material was accessed.