Radiology

The Current Status of Breast MR Imaging

Part I. Choice of Technique, Image Interpretation, Diagnostic Accuracy, and Transfer to Clinical Practice[1]

Christiane Kuhl, MD

Compared with mammography and breast ultrasonography, contrast material–enhanced magnetic resonance (MR) imaging is a breast imaging technique that offers not only information on lesion cross-sectional morphology but also on functional lesion features such as tissue perfusion and enhancement kinetics. After an enthusiastic start to clinical breast MR imaging in the early 1990s, a variety of difficulties and obstacles were identified that hampered the transfer of the modality into clinical practice, including a lack of standardization regarding image acquisition and interpretation guidelines, a lack of MR-compatible interventional materials, and a lack of evidence regarding its diagnostic accuracy—particularly specificity and positive predictive value, as well as sensitivity for ductal carcinoma in situ. This article is the first of two on the current status of breast MR imaging. The pathophysiologic basis of breast MR and the effects on acquisition technique and diagnostic accuracy, the diverging demands of high spatial and temporal resolution, and the different approaches that exist for image acquisition are reviewed. Advantages and disadvantages of different pulse sequence parameters are discussed to help radiologists make a balanced and informed decision regarding choice of image acquisition protocol. Imaging findings in common benign and malignant changes are described, and current concepts for differential diagnosis, including the MR Breast Imaging Reporting and Data System lexicon, are discussed. Furthermore, obstacles that impeded the technique's transfer into clinical practice are discussed, and the progress made in recent years, especially regarding the development of guidelines, procedural standardization, and MR-guided interventions are outlined.

[1] From the Department of Radiology, University of Bonn, Sigmund-Freud-Str 25, D-53105 Bonn, Germany. Received September 30, 2005; revision requested November 30; revision received January 3, 2006; accepted February 20; final version accepted April 3; final review and update by the author March 19, 2007. **Address correspondence to** the author (e-mail: *kuhl@uni-bonn.de*).

Once invasive breast cancers grow beyond a size of a few millimeters, their high metabolic demand for oxygen and nutrients exceeds the supply brought about by diffusion through the normal vessels of fibroglandular tissue. The gap between demand and supply increases with increasing tumor size and causes hypoxic stress on the tumor cells. This seems to stimulate the release of peptide hormones (growth factors; particularly, vascular endothelial growth factor) that promote the formation of new vessels and/or the sprouting of existing capillaries in the peritumoral stroma—a process referred to as angiogenesis or neoangiogenesis (1–3). The angiogenic activity of cancers yields a dedicated vasculature that supports the tumor and helps maintain its metabolic homeostasis. Angiogenesis is so closely correlated with invasive cancers that it probably constitutes a sine qua non for invasive growth per se. It is this angiogenic activity that constitutes the basis for breast cancer detection and differential diagnosis with breast magnetic resonance (MR) imaging.

The microscopic and macroscopic architecture of the new capillary system differs from that of the normal fibroglandular vasculature: Large endothelial fenestrations give rise to increased capillary leakage; arteriovenous shunting is observed, and the perfusion of the capillary bed is less (if at all) controlled by regular physiologic mechanisms. It is intuitively plausible that the increased local perfusion and capillary diffusion rates of malignant lesions should be predictive of lesion enhancement at breast MR imaging. There are a variety of published studies that suggest a correlation between the microvessel density of a cancer and its enhancement pattern—yet there are also a number of studies in which no such correlation was found (4–16). This is probably due to the fact that, unlike with computed tomography or other techniques that are based on x-ray absorption, in T1-weighted MR imaging the signal intensity increase that is observable after contrast agent injection (usually referred to as *enhancement*) does not depend linearly on the local amount of contrast agent; thus, signal intensity does not change in linear proportion to the local perfusion or the intravascular space (17). The amount (or concentration) of contrast agent is only one factor that contributes to enhancement; other factors include T1 contrast of the pulse sequence used, baseline T1 relaxation time of the different tissues, relaxivity of the contrast agent (ie, its efficacy in shortening T1 relaxation time), and diffusion rate of the contrast agent, to name a few.

The fact that it is not only vessel density that determines enhancement may explain why enhancement per se is by no means pathognomonic for cancer but can be found in a variety of benign changes and even in normal breast parenchyma in the presence of hormonal stimulation (18,19). In addition, angiogenic activity is found not only in malignant tissues but also in other conditions such as in inflammatory changes or during wound healing. Still, the close and consistent correlation between invasive growth and angiogenic activity explains the high sensitivity for invasive breast cancer that is afforded by MR imaging; in turn, the weak or inconsistent angiogenic activity that can be associated with invasive lobular cancers and pure intraductal cancer explains the diagnostic difficulties in detecting these latter conditions (as will be discussed later).

Essentials

- Breast MR imaging provides tissue information on high-spatial-resolution cross-sectional morphology, functional information on perfusion and capillary leakage, and tissue T1 and T2 relaxation times, all of which can be used for diagnosis of breast cancer and differential diagnosis of enhancing lesions.
- Breast MR protocols should be designed to enable the analysis of all this information: Just as in contrast-enhanced MR angiography, breast MR protocols must compromise on diverging demands of high temporal resolution (acquisition speed) and high spatial resolution.
- Breast MR imaging is currently the most sensitive modality for invasive breast cancer, while for diagnosis of ductal carcinoma in situ, MR and mammography offer complementary information.
- Although the specificity and positive predictive value of breast MR are equivalent to those of mammography, the work-up for a lesion detected only on MR images is much more demanding than that for a mammographic abnormality; therefore, there is great demand for further improvements in the distinction of benign and malignant changes.
- Substantial advances have been made over the past decade on the definition of technical requirements for image quality assurance, the definition of interpretation guidelines and an MR BI-RADS lexicon, and the development of MR-guided minimally invasive biopsy procedures.

Choice of Imaging Technique

Breast MR imaging provides information on a wealth of physical and physiologic tissue features. The ideal pulse sequence protocol for breast MR should provide all (or as much as possible) of this information and make it available for differential diagnosis (see Table). While the specific parameters of the pulse sequences may be chosen at the discretion of the individual radiologist, there are some basic requirements that

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Abbreviations:
ACR = American College of Radiology
BI-RADS = Breast Imaging Reporting and Data System
DCIS = ductal carcinoma in situ
FOV = field of view
GRE = gradient echo
3D = three-dimensional
2D = two-dimensional

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need to be observed. These requirements are largely dictated by the specific enhancement patterns of benign and malignant breast lesions.

Setting the General Framework: Temporal and Spatial Resolution

Temporal resolution.—Owing to the more or less transient enhancement of cancers (rapid wash in followed by washout) and the concomitant progressive enhancement of the adjacent fibroglandular tissue, the contrast with which the cancer

Typical Breast MR Imaging Findings in Some Frequent Breast Diseases

Disease Type and Subtype	Lesion Type	Lesion Shape	Lesion Margins	Internal Enhancement	Distribution Symmetry	Initial Enhancement Increase	Delayed Enhancement	Signal Intensity on T2-weighted Images
Invasive cancer								
Ductal	Mass	Irregular	Irregular or spiculated	Rim or heterogeneous	Not applicable	Fast	Washout or plateau	Often low
Lobular	Mass or non-masslike	Not applicable	Not applicable	Heterogeneous	Focal area, asymmetric	About 50% fast, 30% medium, 20% slow	For fast initial enhancement: washout; for slow: persistent	Isointense to fibroglandular tissue
DCIS*	Non-masslike	Not applicable	Not applicable	Clumped or stippled	Segmental or ductal, asymmetric	About 40% fast, 40% medium, 20% slow	For fast initial enhancement: washout; for medium or slow: persistent	Isointense to fibroglandular tissue
Fibroadenoma								
Myxoid	Mass	Round, oval	Smooth	Dark septations or homogeneous	Not applicable	Fast	Persistent	High
Sclerotic	Mass	Round, oval	Smooth	Homogeneous	Not applicable	Slow or absent	Persistent	Very low
Mastopathic changes	Focus or non-masslike	Not applicable	Not applicable	Homo- or heterogeneous	Multiple foci, focal area, regional, diffuse, symmetric	Slow to fast	Persistent or plateau, less often washout	Isointense to fibroglandular tissue
Scar tissue	Mass or nonmass	Irregular	Irregular	None	Not applicable	Absent	Not applicable	Low
Intramammary lymph node†	Mass	Oval or round	Smooth	Central high signal intensity on non–fat-suppressed precontrast T1-weighted images	Not applicable	Fast	Washout	High
Fat necrosis								
Fresh	Mass	Irregular or round	Irregular	Central high signal intensity on non–fat-suppressed precontrast T1-weighted images	Not applicable	Fast	Washout	High
Chronic (oil cyst)	Mass	Round	Smooth	Central high signal intensity on non–fat-suppressed precontrast T1-weighted images	Not applicable	Absent	Not applicable	High

Note.—Findings in individual patients may deviate substantially.

* DCIS = ductal carcinoma in situ.

† Normal, hyperplastic, or metastatic.

is depicted against its background is best only in the early postcontrast phase, 60–120 seconds after contrast material injection, and will deteriorate progressively thereafter (Fig 1).

This is very similar to the situation in contrast-enhanced MR angiography, where image acquisition has to be synchronized with peak arterial (in breast MR, cancer) enhancement and must be completed before venous (in breast MR, fibroglandular) enhancement occurs. If acquisition of the postcontrast images is delayed, it is possible that the lesion-to-parenchyma contrast will be reduced or even cancelled out by the time the contrast-determining lines of k-space are read (20) (Fig 1). With the time-consuming acquisition strategies used to obtain images with very high spatial resolution, one may run the risk of missing breast cancers that have strong washout, particularly if a cancer is situated amid strongly enhancing breast parenchyma (Fig 1). Also, depiction of fine morphologic details of lesion margins (eg, spicules) is best only during the early postcontrast phase, before the washout in cancers occurs and morphologic details are masked by adjacent enhancing fibroglandular tissue. Last, fast dynamic imaging is required to track the different enhancement patterns of lesions in order to use kinetic information for differential diagnosis of lesions with equivocal morphologic features.

Figure 1

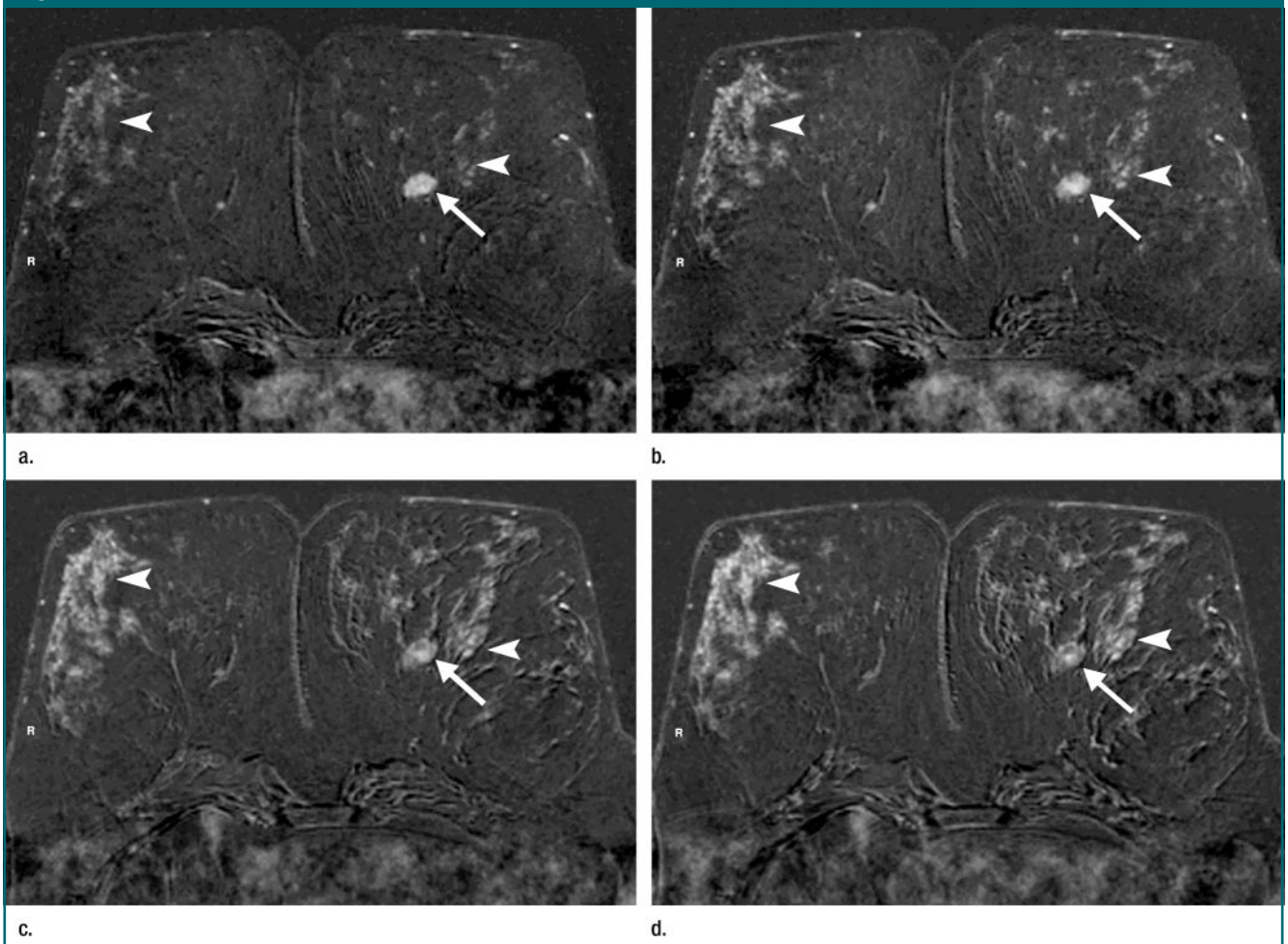


Figure 1: **(a–d)** Standard dynamic protocol for bilateral dynamic subtracted breast MR imaging in a 53-year-old patient with invasive ductal cancer. Images were obtained with transverse two-dimensional (2D) gradient-echo (GRE) pulse sequence (repetition time msec/echo time msec, 270/4.6; flip angle, 90°) before and nine times after bolus injection of contrast material. Pulse sequence has relatively high temporal resolution (69 seconds per dynamic acquisition) and relatively limited spatial resolution (matrix, 256 × 256; field of view [FOV], 320 mm; voxel size, 1.25 × 1.25 × 3 mm, or 4.69 mm^3). The same section is displayed throughout the dynamic series, from 69 seconds after injection (**a**) through the fourth scan obtained 4 minutes 36 seconds after injection (**d**). Note that contrast between cancer (arrow) and normal fibroglandular tissue (arrowheads) on both sides is best on **a,** very early in postcontrast phase. Owing to strong washout effect of the cancer and progressive signal intensity increase of normal parenchyma, the cancer may even be overlooked on **d,** and assessment of fine morphologic details will not be feasible on this delayed postcontrast image owing to lack of contrast between cancer and normal tissue.

In terms of breast MR imaging, "fast" means a temporal resolution of less than 120 seconds per acquisition, ideally about 60 seconds per acquisition. Although initially suggested (21), there is no evidence to support an even higher temporal resolution—that is, to achieve even faster acquisitions (22). There are a number of studies on pharmacokinetic modeling and multicompartment analyses of time-resolved breast MR imaging (23–26), but each failed to demonstrate superiority compared with "regular" dynamic MR imaging and a detailed morphologic analysis. In this author's experience, there is no relevant additional diagnostic information attainable with a reduction in acquisition speed to below the 60-second level. Most important, it is probably disadvantageous if acquisition speed is increased at the expense of necessary spatial resolution (20).

To use enhancement kinetics for differential diagnosis, dynamic imaging is needed. This means that one acquires the same image stack once before and several (four to five) times after bolus injection of the contrast agent.

Spatial resolution.—Detailed high spatial resolution is the other prerequisite for diagnosing breast cancer with the aid of MR imaging. This is in close agreement with mammography or breast ultrasonography (US), where for the past several years attempts have been made to further improve the visualization of morphologic details. High spatial resolution is important because some of the most powerful diagnostic criteria that are in use for differential diagnosis are based on lesion morphology—specifically, margins and internal architecture (27,28). In breast MR, however, acquisition speed and spatial resolution are diverging demands. Any increase in spatial resolution (eg, an increase in the size of the acquisition matrix) is associated with an increase in acquisition time.

All pulse sequence protocols that are in use today have to compromise with regard to these diverging demands. We recommend setting the time per dynamic acquisition to a maximum of 60–120 seconds and investing all remaining imager capacity into spatial resolution. The largest imaging matrix that is achievable within this acquisition window should be used. A true (ie, noninterpolated) acquisition matrix of 512 × 512 should be used for bilateral transverse or coronal imaging (with FOV of 320–350 mm), and an imaging matrix of at least 256 × 256 should be used for unilateral imaging (FOV, 180–200 mm). These specifications should translate into an in-plane pixel size on the order of 0.5 × 0.5 to 0.8 × 0.8 mm and a through-plane pixel size (section thickness) of 1–3 mm. With state-of-the-art MR systems, these matrices are acquired fast enough to allow arterial phase imaging and to track the time course of enhancing lesions.

Choice of Pulse Sequence Type: 2D GRE or 3D GRE?

All contrast-enhanced breast MR pulse sequences use some sort of T1-weighted (GRE) sequence (eg, fast field echo, fast low-angle shot, magnetization-prepared rapid GRE). Spin-echo, inversion-recovery, and echo-planar imaging are not suitable, for various reasons. The GRE pulse sequence comes in many subtypes: It can be 2D multisection or three-dimensional (3D), fast (turbo) or regular, spoiled or nonspoiled. Three-dimensional imaging indicates that phase encoding, frequency encoding, and section encoding are all achieved by applying suitable gradients during image acquisition. For 2D imaging, section encoding is achieved by means of selective excitation. Compared with 2D imaging, 3D imaging has the inherent advantage of stronger T1 contrast: 3D imaging uses a shorter repetition time than does 2D multisection imaging and has a higher inherent signal-to-noise ratio, which therefore allows thinner sections (or partitions) to be acquired. Accordingly, most groups use 3D GRE for breast imaging. For non–fat-saturated subtracted dynamic breast MR at 1.5 T, however, we recommend the use of a 2D GRE sequence. The reason is that with the 3D acquisition mode, phase errors can accumulate in all three dimensions, which can cause in-plane blurring (unsharp contours) and difficult-to-read artifacts on subtracted images. The GRE pulse sequence should be spoiled to avoid any confounding T2 contrast. All pulse sequences should use the shortest possible repetition time, a large flip angle (larger with longer repetition times: usually 90° for 2D and about 25°–50° for 3D GRE) and a short echo time, which should be set in phase (4.6 msec at 1.5 T) for non–fat-saturated subtracted protocols. The same receiver settings must be used for pre- and postcontrast imaging: No new receiver adjustment is allowed in between the dynamic acquisitions.

Choice of Imaging Plane: Sagittal, Transverse, or Coronal?

The sagittal plane is probably the most natural way to image the breast and will be intuitively familiar to breast surgeons. The technical advantage of the sagittal plane is that a relatively small FOV will be sufficient to cover the breast, which will improve the spatial resolution at a given acquisition matrix (ie, with no acquisition speed penalty). In addition, the FOV can usually be reduced in the craniocaudal direction (rectangular FOV), which will help improve acquisition speed with no penalty in spatial resolution. Because a small FOV is used, the magnetic field across the FOV is relatively homogeneous. This is why active fat suppression works nicely and relatively reliably for sagittal plane protocols. The only disadvantage of the sagittal plane is that far too many sections would be needed to cover both breasts. Accordingly, sagittal imaging protocols have almost always been used only for single-breast imaging.

Recently, bilateral sagittal imaging has become available, but these new techniques rely heavily on parallel imaging. This, in turn, will be associated with a penalty in signal-to-noise ratio and can cause artifacts. If bilateral dynamic imaging is performed in the sagittal plane, radiologists should be aware that this is usually achieved at the expense of signal-to-noise ratio and/or spatiotemporal resolution.

Current bilateral dynamic protocols use the transverse or coronal plane. Compared with transverse images, coronal images have the theoretical advantage

that they can be acquired with a 50% rectangular FOV, which translates to a 50% reduction in acquisition time. However, many more sections are needed to cover the entire fibroglandular volume (including the axillary tail) in the coronal than in the transverse plane, which is why this advantage is at least partly offset. In addition, coronal imaging suffers more from motion artifacts. The reason is that breathing motions occur in the anteroposterior direction, which is the section-encoding direction if coronal imaging is used. When the patient breathes, she "dives" in and out of the imaging plane. This can cause motion and subtraction artifacts that make images very difficult to read. Also, clinically the coronal plane is not helpful in delineating or excluding nipple or chest wall invasion. Accordingly, the transverse plane is preferable if bilateral imaging is desired or required.

Unilateral or Bilateral Imaging?

Breast MR imaging protocols can focus on one breast at a time or include both breasts in the FOV. Bilateral imaging is important in all women undergoing screening (usually women at increased risk for breast cancer) and in all who undergo staging for a known breast cancer (staging of cancer in the ipsilateral breast and screening of the contralateral breast in high-risk patients). Although this is straightforward, there are situations where the clinical question concerns only a single breast—for example, in problem-solving situations. Opponents of the bilateral technique argue that in a patient at average risk who is referred for problem solving of a unilateral finding, inclusion of the opposite breast is equivalent to use of MR imaging for screening, which is not indicated in women at average risk. Also, if bilateral imaging is performed, one has to use a larger FOV to include both breasts. At a given acquisition matrix, this will usually compromise the spatial resolution with which the breast with the questionable finding will be imaged. This in turn may compromise the diagnostic accuracy with which the actual clinical problem can be solved.

These arguments are definitely true. Still, in this author's opinion, there are important reasons to suggest bilateral imaging even in women who are referred for unilateral problem solving: MR imaging of both breasts makes more efficient use of the contrast agent bolus the patient receives and the time she spends in the imager. The approach is comparable to the use of diagnostic mammography in symptomatic patients, in whom mammography is performed not only for the symptomatic breast but also for the opposite breast, although there are no outcome data available to support this. Last, bilateral MR imaging can help avoid diagnostic errors (eg, in patients with non-masslike enhancement or enhancing foci). To categorize these areas or foci, it is very helpful to be able to assess symmetry by comparing with the second breast.

Fat Suppression: Active Fat Saturation or Subtraction?

All breast imaging protocols will necessitate some sort of fat suppression because, after contrast material injection, enhancing lesions may become isointense to adjacent fatty tissue. Active fat suppression, or fat saturation, means that the signal from fatty tissue is specifically eliminated ("knocked out") by additional radiofrequency pulses or by choosing selective water excitation. Both types usually take extra acquisition time and are, therefore, difficult to reconcile with dynamic protocols. In addition, active fat suppression requires a very homogeneous magnetic field across the entire FOV, which is difficult to achieve with bilateral imaging. Therefore, fat saturation is usually used only for nondynamic, unilateral, small-FOV breast imaging in the sagittal plane. With further advancement in MR system components, it can be expected that active fat saturation will also be available for bilateral dynamic imaging.

Subtraction does not require extra acquisition time and is not influenced by magnetic field inhomogeneities, which is why it was (and currently still is) the preferred type of "fat suppression" for dynamic bilateral imaging. The main disadvantage of subtraction is that it may suffer from patient motion: Subtraction errors occur if the precontrast mask and the postcontrast image are not entirely congruent due to even subtle patient motion. With increasing spatial resolution (ie, decreasing pixel size), the probability of such pixel shifts will increase. Therefore, if subtraction is used for high-spatial-resolution, large-matrix imaging, the use of some sort of breast immobilization device becomes crucial. Immobilization should be achieved by gently fixating (not by compressing) the breast in the section-encoding direction. This is the mediolateral direction for sagittal protocols and the craniocaudal direction for transverse protocols. This is important to reduce—and not increase!—the number of sections necessary to cover the breast. Compression should be avoided because it may reduce enhancement of breast cancers (29).

Increasingly, subtraction is also used in addition to fat saturation, because on fat-saturated images some structures may exhibit high signal intensity even before contrast material is administered. This holds true, for example, for fluid-filled ducts or proteinaceous cysts. In these cases, subtraction of fat-saturated images are useful to selectively highlight enhancing structures.

Contrast Material: How Much, How Applied?

For all breast MR studies, T1-shortening contrast agents (gadolinium chelates) are used. While the accepted dose ranges between 0.1 and 0.2 mmol per kilogram of body weight, the majority of groups use a dose of 0.1 mmol/kg. There is only one study of which this author is aware that prospectively investigated the effect of a higher dose (0.2 mmol/kg) and concluded that the higher dose improves sensitivity (30). However, this study stems from a time when neither fat saturation nor subtraction was available, such that cancers had to appear brighter than fatty tissue to be detected reliably, which certainly is an expensive way to highlight enhancing lesions. If some sort of fat suppression is available (subtraction or fat saturation), there is probably no need for the high dose. Also, one can assume that with higher doses, background en-

hancement will become stronger, which may reduce specificity.

The contrast material should be injected via an intravenous catheter placed in an antecubital vein before the patient is positioned in the coil. The patient must not be moved in and out of the magnet for the injection, to prevent motion and unnecessary time losses in the early postcontrast phase. The contrast agent is injected with a power injector at a rate of 3 mL/sec, followed by a 20-mL saline flush. We manually start the first postcontrast acquisition after the volume of contrast material has been injected (ie, during the application of the saline flush). There is no need to wait between the injection and the start of the postcontrast series: With the typical 1–2-minute temporal resolution protocol, there is no risk to starting imaging too early, and a delay would unnecessarily postpone the first postcontrast acquisition. A waiting time may be needed only for very fast or fast (turbo) protocols with "low-high" profile order (protocols that acquire the low-contrast–determining k-space lines first). However, these types of pulse sequences are, in this author's view, not suitable for breast imaging. One should establish a standard course of action regarding the timing of the injection and the start of the first postcontrast series—and stick to it. One should, however, keep in mind that many other factors (patient age, heart rate, ejection fraction, overall circulation time) differ substantially between patients and may have a far greater influence on between-patient variations in contrast enhancement. Standardizing one's technique means one should do one's bit to prevent additional between-patient variations.

Kinetic Analysis

Kinetic data can be evaluated by visually assessing the lesion enhancement pattern, by placing a region of interest (ROI) to obtain kinetic curves, and by using a computer-aided detection system. ROIs should be placed with wide window settings into the area that exhibits strongest enhancement on the first postcontrast image. ROIs should include not more than 3–4 pixels, and care should be taken to ensure that the ROI is within the lesion throughout the entire dynamic series. If this is not accomplished, "fake" washout curves will be obtained if the lesion moves out of the prescribed ROI after the first postcontrast image. In addition, visual analysis of the nonsubtracted images is performed, with standardized window settings, to obtain an impression of the overall lesion enhancement pattern.

To quantify enhancement, the increase in signal intensity relative to baseline precontrast signal intensity is measured. For example, a lesion with precontrast signal intensity of 300 arbitrary units and postcontrast signal intensity of 450 arbitrary units has early phase enhancement of 50% ([450 − 300]/300).

The University of Bonn Breast MR Imaging Protocol

We obtain a localizer series that consists of four image stacks in the transverse and coronal planes and in the sagittal plane over the left and the right breast to exactly demonstrate the spatial extent of the fibroglandular tissue of the entire breast. Technicians are trained to place the image stack of the dynamic series to cover precisely the fibroglandular volume as visualized on the localizer image; to achieve this, the stack is angled in two or even three planes, if necessary. We obtain non–fat-suppressed T2-weighted turbo spin-echo images, with 33–35 sections and a full 512 × 512 imaging matrix. The contrast-enhanced dynamic series consists of 31 sections, with a section thickness and anatomic location that exactly match with the T2-weighted images to allow an accurate comparison of a pixel's signal intensity on T1- and T2-weighted images. We use a 2D GRE sequence (280/4.6; flip angle, 90°) with one precontrast and four postcontrast acquisitions. Acquisition time is 3.5 minutes for the T2-weighted pulse sequence and 9 minutes for the entire dynamic series. The patient time in the magnet is usually around 15 minutes. We do not routinely acquire images in additional planes because, in our experience—particularly in cases of breast cancer—the washout phenomenon will yield only poor image contrast. Instead, maximum intensity projections or multiplanar reconstructions of the early postcontrast subtracted images are rendered to enable visualization of the lesion in the sagittal or coronal plane, if desired.

Hardware: Magnets and Coils

The diverging demands of high spatial resolution and adequate temporal resolution explain why breast MR imaging is technically demanding and clearly benefits from advanced image acquisition strategies (eg, parallel imaging), strong gradients, and high magnetic field strength. Accordingly, if one has a choice, breast imaging patients should be scheduled for the most powerful magnet—with *powerful* referring to gradient strength, gradient rise and ramp time, and field strength. A field strength of less than 1.5 T should be avoided because the signal-to-noise ratio decreases in proportion to field strength, and this, in turn, may well compromise diagnostic accuracy. In recently published studies (31,32), the majority of cancers that went undetected at MR imaging were imaged with 1.0-T systems. Also, the in-phase echo time at 1.0-T is long (7 msec), which will inherently compromise acquisition speed. Breast MR imaging should not be performed with systems operating at even lower field strength. A higher field strength (eg, 3.0 T) may be useful to further improve spatial and temporal resolution; however, at the time this article was written, there is little evidence regarding the added clinical value of high-field-strength MR imaging over that of 1.5-T imaging.

It should go without saying that breast MR must be performed, without exception, with a dedicated breast surface coil. Multielement coils provide higher signal-to-noise ratio and offer the advantage of the ability to use parallel imaging techniques.

Differential Diagnosis and Breast MR Imaging

MR imaging depicts with high spatial resolution the cross-sectional anatomy of lesions; in addition, MR provides functional information related to tissue perfusion and diffusion, as well as information on tissue T1 and T2 relaxation

times. This is in contrast to purely structural imaging modalities such as mammography and breast US.

For differential diagnosis of enhancing lesions in breast MR imaging, we analyze morphologic information (type of enhancement, mass shape and margins, distribution of non-masslike enhancement, internal architecture), kinetic information (initial enhancement increase and delayed phase enhancement), and information related to lesion signal intensity on T2- and T1-weighted precontrast non–fat-suppressed images (33–35).

Basic Concept of the MR BI-RADS Lexicon

When interpreting breast MR imaging studies, the first step is to determine the type of a given lesion according to the following categories in the American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS) for MR imaging. A lesion is classified as *(a)* a mass, *(b)* an area of non-masslike enhancement, or *(c)* a focus.

A mass is a space-occupying tumor that has three dimensions. Usually, it has a visible correlate on precontrast T1- or T2-weighted images. Indeed, the definition of a mass is quite comparable to the term used in mammography.

Non-masslike enhancement means that enhancement occurs in an area of the fibroglandular tissue that otherwise appears normal on precontrast images. There is no space-occupying effect. The enhancing area usually has no correlate on fat-suppressed or non–fat-suppressed T2-weighted images.

The third type of configuration is a focus, which is defined as an enhancing area of less than 5 mm that is too small to be further characterized. In the majority of cases, these foci will be due to a focal proliferation of the glandular tissue (so-called focal adenosis). "Size does matter" is the humorous conclusion of a retrospective analysis by Liberman and co-workers (36): They found that the frequency of malignancy increased significantly with lesion size. In their cohort of 666 consecutive lesions identified on breast MR images alone, only one (3%) of 37 foci proved to be malignant. However, it is important to understand that the classification of a lesion type as a focus, per se, does not imply categorization of the lesion as benign—rather, it is the implicit acknowledgment of the fact that, compared with mammography and high-frequency breast US, the spatial resolution of current MR imaging protocols is limited, which limits our ability to classify small enhancing foci. A focus may correspond to a very small invasive breast cancer, DCIS, a papilloma, a small fibroadenoma, an intramammary lymph node, and so forth. One has to accept that further management of a focus depends on other findings in the same or the opposite breast (symmetry is always reassuring), on corresponding findings from mammography or US, on the personal risk status of the patient—in short, on the entire picture. With the fast technical progress that is being made with breast MR, one can anticipate that the definition of what constitutes a focus (enhancement too small to be characterized) is a moving target and will change with our ability to acquire breast MR studies with higher spatial resolution.

While a focus is too small to be amenable to a further analysis, the situation is different for masses and areas of non-masslike enhancement. These types of lesions are subjected to careful analysis of their morphology, enhancement kinetics, and signal intensity patterns on T1- and T2-weighted images (Table).

The distinction between masslike enhancement and non-masslike enhancement is important because it marks a crossroads for further differential diagnosis. The distinction is comparable, including in its diagnostic implications, to the mammographic distinction between a mass and calcifications (ie, calcifications without accompanying mass): In a mass, the differential diagnostic consideration is either invasive breast cancer or a benign solid tumor (eg, fibroadenoma). In non-masslike enhancement, the main differential diagnosis is between intraductal or diffuse (eg, lobular) cancer and mastopathic changes (focal adenosis), hormonal stimulation, or inflammatory changes.

The distinction between mass and non-masslike enhancement initiates two diagnostic pathways that each require a different set of diagnostic criteria. For masses, shape and margins are assessed, but for non-masslike enhancement this is not done. Instead, the distribution of enhancement is assessed, with major emphasis on whether it is oriented along the distribution of the milk ducts (ductal or segmental enhancement) or not (linear, focal, regional or in multiple regions, diffuse). While enhancement kinetics are useful for the further differential diagnosis of morphologically equivocal masses, they may be misleading and should, therefore, not be used (or used only in the positive case) for the further classification of non-masslike enhancement. The reason is that in non-masslike enhancement, the differential diagnosis includes DCIS and lobular cancers—two disease states known to exhibit inconsistent angiogenic activity. Symmetry is helpful in further characterization of non-masslike enhancement but is not usually assessed in masses. Bilateral symmetric non-masslike enhancement in any distribution is more often caused by benign changes than by malignant lesions.

The analysis of enhancement kinetics (early increase, delayed enhancement) is achieved either by visually assessing the dynamic images (nonsubtracted images or subtracted images with wide window settings) or by measuring the signal intensity in a small area of a lesion and tracking its course over the dynamic series to yield the kinetic curve (also referred to as time–signal intensity curve or signal intensity–time course). Early phase enhancement describes the steepness of the first part of the kinetic curve, during the first 1–2 minutes of the dynamic acquisition. It indicates the velocity and degree with which enhancement occurs and may be slow, medium, or rapid.

Delayed phase enhancement is actually a misnomer because it refers to signal intensity changes that occur immediately after the early signal intensity increase, as early as 3 minutes after injection (37). Immediately after the early initial increase, the signal intensity

may *(a)* decline again, yielding a so-called washout curve (type 3); *(b)* exhibit a sharp bend and plateau (type 2); or *(c)* continue to rise after the early phase, yielding persistent enhancement until the delayed postcontrast phase (type 1). The main difference is that in types 2 (plateau) and 3 (washout) curves, peak enhancement (peak brightness of a lesion at visual analysis) is reached early, usually within the first 2 minutes. This is the time course observed in most invasive breast cancers. In persistent kinetics, the enhancement continues until the delayed postcontrast phase, even if the rate at which the signal intensity increases slows. This is the time course observed in most benign changes.

Imaging Findings in Malignant and Benign Breast Lesions

In this context, it is impossible to provide a complete overview on imaging findings in all possible breast diseases; for this purpose, textbooks are available that should be referred to. Instead, the following section is meant to provide a short introduction to the process of differential diagnosis with breast MR imaging.

Invasive cancers.—The typical invasive breast cancer will manifest as a focal mass with an irregular shape and irregular or spiculated margins. The internal architecture (internal enhancement) is heterogeneous, or so-called rim enhancement is seen. Cancers tend to exhibit fast and strong enhancement that peaks in the early postcontrast phase: High signal intensity is seen 1–3 minutes after contrast agent injection. This is followed by a fast yet incomplete signal intensity loss or a signal intensity plateau (Figs 1–3). On non–fat-suppressed T2-weighted images, breast cancers tend to be hypo- or isointense relative to fibroglandular tissue (38–44).

The appearance of rarer types of breast cancer (medullary, mucinous, and lobular cancers) may differ substantially from this "ideal" breast cancer. In particular, lobular invasive breast cancer with a diffuse growth pattern (so-called Indian path–like spreading of cancer cells) will not appear as a focal mass but as non-masslike enhancement. The diffusely infiltrating cancer cells may be fed by means of diffusion of preexisting fibroglandular capillaries, which is why lobular invasive cancers may be accompanied by only weak angiogenic activity. Accordingly, lobular invasive breast cancer may exhibit only weak and persistent (ie, misleadingly "benign") enhancement kinetics (45,46). This is one reason why, in non-masslike enhancement, enhancement kinetics should be used with caution and may be used for differential diagnosis only in the positive case—that is, when rapid enhancement and washout are observed.

Fibroadenomas.—Benign tumors (fibroadenomas) appear as a focal mass with a round or oval shape and smooth margins. The internal enhancement is homogeneous or shows so-called dark septations (Fig 4). These dark septations are caused by the internal lobulated composition of the fibroadenoma. Fibroadenomas can exhibit variable enhancement, depending on the degree of sclerosis or fibrosis and even on hormonal stimulation of the breast. In myxoid fibroadenomas, enhancement is typically rapid and strong. However, unlike in breast cancers, enhancement does not peak in the early postcontrast phase but persists until the late phase. With a 2D GRE pulse sequence, a washout or plateau curve is only occasionally seen. Myxoid fibroadenomas tend to exhibit high signal intensity on non–fat-suppressed T2-weighted images, which may also help reveal dark internal septations. Sclerotic fibroadenomas have the same shape and margin features, but they usually do not enhance markedly and they exhibit extremely low signal intensity on non–fat-suppressed T2-weighted turbo spin-echo images. Fibroadenomas undergoing regressive changes may exhibit a mixture of these findings.

DCIS.—The typical intraductal cancer (ie, DCIS) appears as asymmetric (unilateral) non-masslike enhancement that typically follows the ductal system; that is, the enhancement has a segmental or linear (ductal) distribution (Fig 5) (47–49). Internal enhancement (internal architecture) is usually heterogeneous, with a so-called clumped or stippled internal enhancement. Enhancement kinetics of DCIS are unreliable for diagnosis; only about 70% of these cancers exhibit rapid early enhancement, and the delayed phase enhancement is variable.

As is the case for mammographic calcifications in a segmental or ductal distribution, segmental or ductal enhancement on MR images suggests the presence of an intraductal pathologic condition, be it a small DCIS or a papilloma (in the presence of ductal enhancement) or a large DCIS or a peripheral papillomatosis (in the presence of segmental enhancement). In turn, diffuse or multiple regional enhancement on MR images has probably about the same diagnostic implication as do diffuse or scattered calcifications on a mammogram.

Benign mastopathic changes.—Benign mastopathic changes, or focal adenosis, the most important differential diagnosis with regard to DCIS, appear

Figure 2

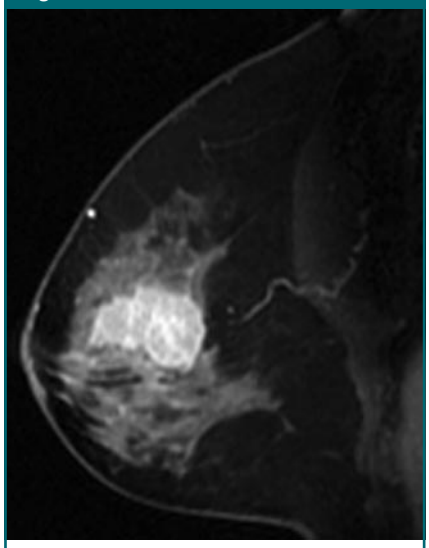


Figure 2: Maximum intensity projection from sagittal unilateral nondynamic actively fat-suppressed breast MR image (morphologic protocol; 8.0/4.2; flip angle, 20°) in a patient with breast cancer. Images were obtained in single postcontrast acquisition with nondynamic 3D GRE sequence with long acquisition time (5 minutes) but high spatial resolution (matrix, 256 × 192; FOV, 190 mm; voxel size, 0.7 × 0.94 × 2.0 [1.32 mm^3]).

Figure 3

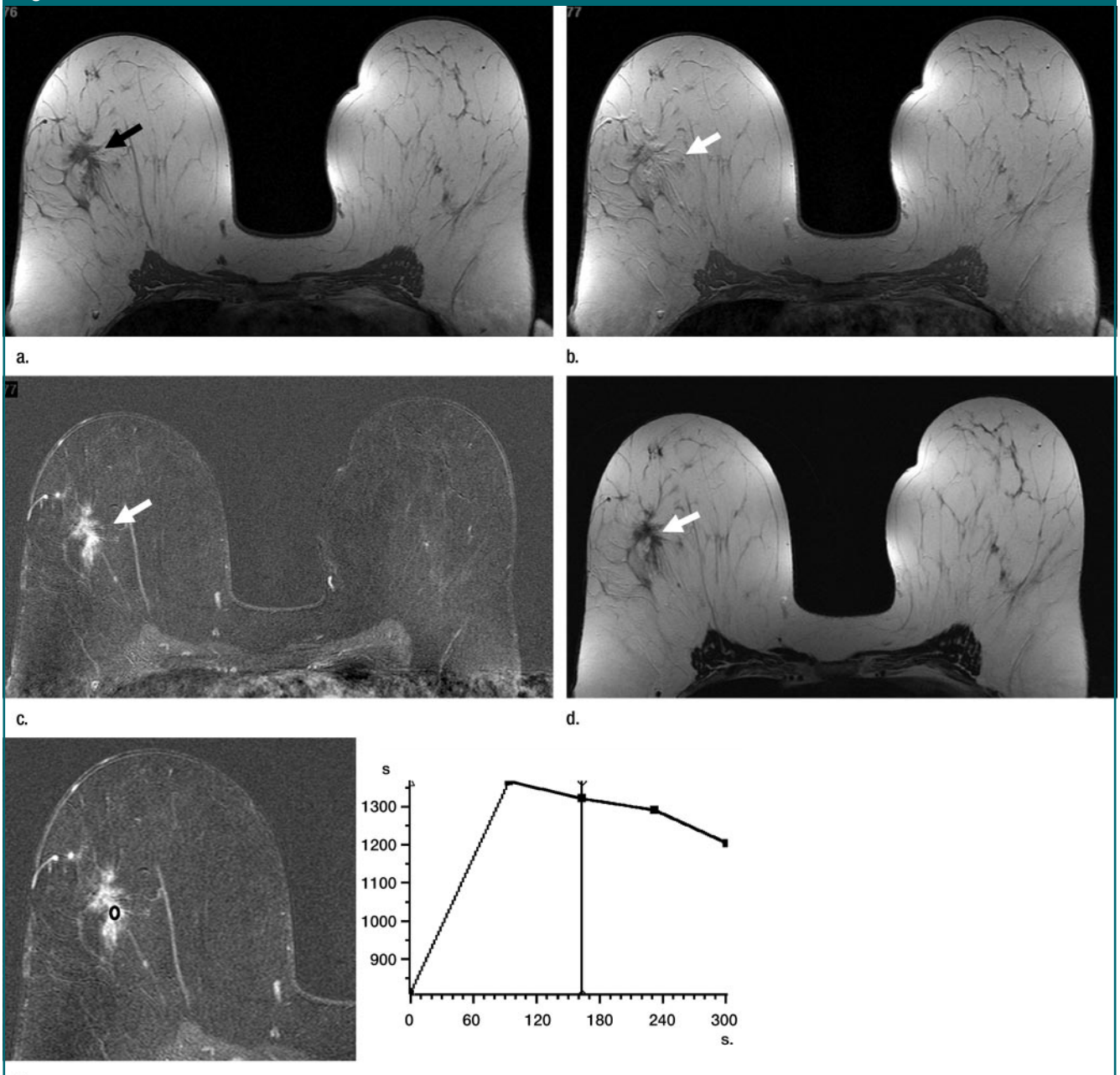


Figure 3: Bilateral dynamic subtracted breast MR images with improved spatial and reduced temporal resolution (modified dynamic protocol: 300/4.6; flip angle, 90°; matrix, 512 × 420; FOV, 320 mm; voxel size, 0.60 × 0.76 × 3.0 mm [1.37 mm^3]; dynamic acquisition time, 110 seconds), relative to those for Figure 1, show lobular invasive cancer (arrow) in 53-year-old patient. **(a–c)** Transverse 2D GRE sequence was performed before and four times after bolus injection of contrast material. Dynamic pulse sequence with moderate temporal resolution and relatively high spatial resolution. Transverse **(a)** precontrast, **(b)** first postcontrast nonsubtracted, **(c)** first postcontrast subtracted, and **(d)** T2-weighted turbo spin-echo (3800/110; turbo factor, 19) images and **(e)** region of interest (black oval on left image) and corresponding time–signal intensity curve of enhancing mass in right breast with irregular shape, spiculated borders, heterogeneous internal enhancement, and fast initial enhancement followed by early washout. Note low signal intensity in **d.** The mass was called BI-RADS category 5, since morphologic and kinetic criteria were both highly suggestive of malignancy.

Figure 4

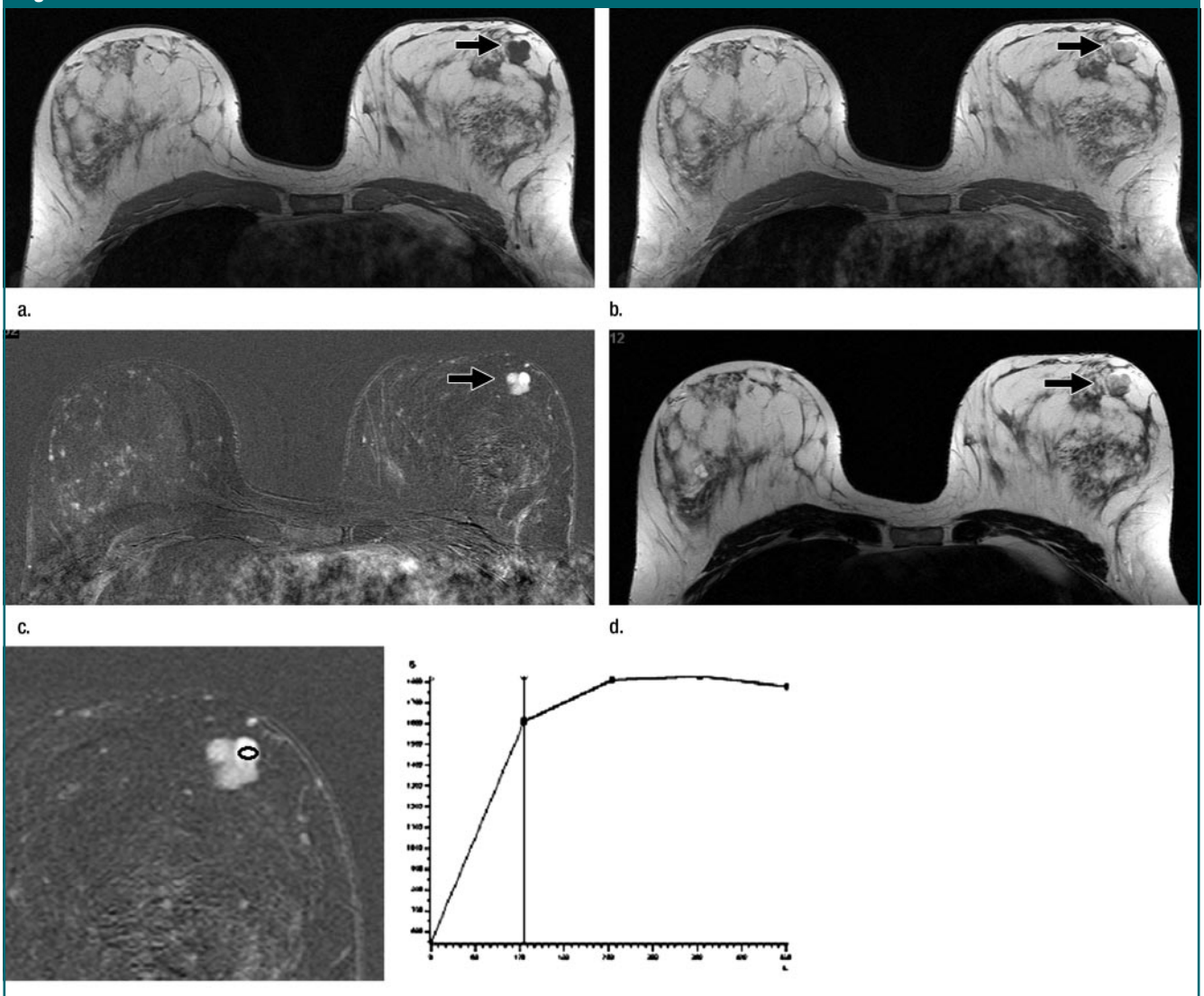


Figure 4: Myxoid fibroadenoma. Same MR pulse sequence parameters as in Figure 3 (modified dynamic protocol) were used to obtain transverse **(a)** precontrast, **(b)** first postcontrast nonsubtracted, **(c)** first postcontrast subtracted, and **(d)** T2-weighted turbo spin-echo (3800/110; turbo factor, 19) images, which show enhancing mass (arrow) in left upper outer quadrant. **(e)** Region of interest (black oval on left image) and the corresponding time–signal intensity curve. Mass has lobulated shape, smooth borders, heterogeneous internal enhancement with dark internal septations, and fast initial enhancement followed by persistent enhancement. Note high signal intensity on **d.** The mass was called BI-RADS category 2, since morphologic and kinetic criteria were concordantly benign.

as enhancing foci or areas of non-mass-like enhancement that usually do not follow the ductal system and appear to be more or less bilaterally symmetric. Enhancement kinetics cannot be used for a further classification—enhancing foci secondary to adenosis frequently exhibit a washout time course.

Normal fibroglandular tissue.—Normal fibroglandular tissue shows highly variable enhancement over the course of the dynamic series. The degree of enhancement depends on the patient's hormonal status and the amount of glandular (vs fibrous and fatty) tissue. The enhancement in presumably normal fibroglandular tissue is referred to as background enhancement. In the ideal case, normal fibroglandular tissue will exhibit no enhancement during the early phase and progressive (persistent) but still faint enhancement in the late phase. However, in women with strong hormonal influence, enhancement in normal fibroglandular tissue may be rapid and strong. This type of background enhancement is what we propose to call a "dense" breast on MR images. This has important implications for the technique's overall sensitivity

and specificity, as will be explained later. It is important to understand that the degree of background enhancement on MR images and radiographic breast density do not correlate. In other words, a breast that appears very dense on mammograms (ACR mammographic breast density category 4) may not exhibit any background enhancement on breast MR images. In turn, a patient with only scattered fibroglandular tissue (ACR mammographic breast density category 2) on mammograms may exhibit strong and diffuse background enhancement in that residual tissue.

Coding Background Enhancement

It is well accepted that the sensitivity of mammography for breast cancer detection decreases with increasing breast density. To communicate this, it is imperative to include an assessment of mammographic breast density in any mammographic report. It would be important to do the same in breast MR imaging reports. In breast MR, however, it is the degree of background enhancement of the fibroglandular tissue, not the actual amount of residual tissue, that may interfere with breast cancer diagnosis. Accordingly, we propose to rate background enhancement in breast MR reports to communicate the degree of confidence with which a breast cancer can be diagnosed by using a given study (Figs 6–8). We suggest the term *severe background enhancement* to indicate that strong, early-phase, multifocal or diffuse fibroglandular enhancement may mask enhancing breast cancer. The absence of background enhancement would indicate a case of a homogeneously dark background without enhancement in the fibroglandular tissue, including the late postcontrast phase (Fig 6). Mild and moderate background enhancement could be coded accordingly (Fig 7). This concept of coding background enhancement to communicate the interpretability of an MR study will probably be adopted in the new edition of the MR BI-RADS lexicon.

How to Integrate Imaging Findings

It is clear that the more criteria one applies, the less likely it is that a given lesion will behave like a "typical" breast cancer or fibroadenoma in every aspect. The appropriate weighing of the different imaging findings in different constellations and different clinical scenarios is still a matter of research. Moreover, breast MR imaging diagnoses may not be established in a vacuum. In each case, findings on corresponding mammograms and/or US studies, as well as the patient's personal or family history, must be evaluated before a treatment recommendation is given. It should be well understood that the art of differential diagnosis of enhancing lesions on breast MR images requires personal experience and expertise—it requires the reading of many breast MR studies and cannot be acquired from textbooks. In this respect, breast MR imaging does not differ from any other breast imaging techniques, notably including mammography.

Sensitivity and Specificity

Of all breast imaging techniques that are currently available, including mam-

Figure 5

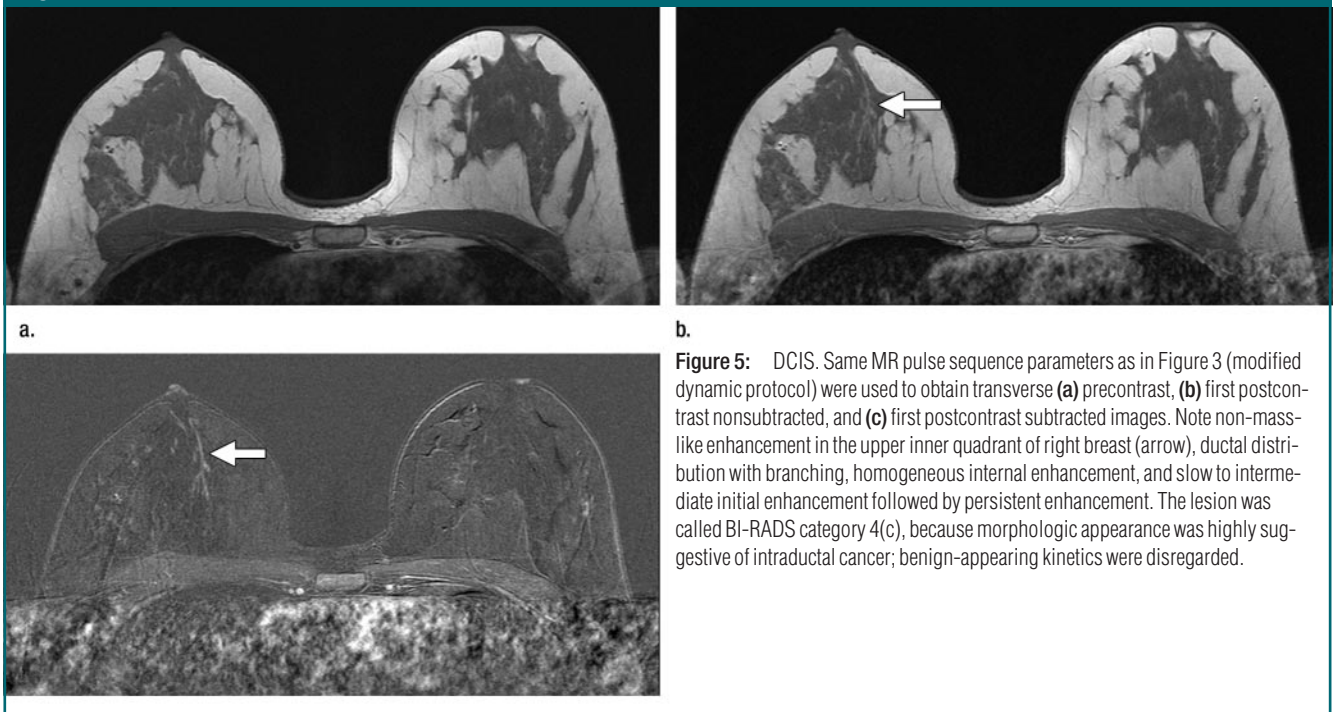


Figure 5: DCIS. Same MR pulse sequence parameters as in Figure 3 (modified dynamic protocol) were used to obtain transverse **(a)** precontrast, **(b)** first postcontrast nonsubtracted, and **(c)** first postcontrast subtracted images. Note non-mass-like enhancement in the upper inner quadrant of right breast (arrow), ductal distribution with branching, homogeneous internal enhancement, and slow to intermediate initial enhancement followed by persistent enhancement. The lesion was called BI-RADS category 4(c), because morphologic appearance was highly suggestive of intraductal cancer; benign-appearing kinetics were disregarded.

mography, high-frequency breast US, fluorodeoxyglucose positron emission tomography, and scintimammography, MR offers the highest sensitivity for invasive breast cancer (50–66). Sensitivity rates are surprisingly concordant and seem to be maintained across all image acquisition strategies—as long as an intravenous contrast agent is used. Published sensitivity levels range between 89% and 100%. In all studies that can be found in the literature, the sensitivity of MR imaging was higher than that of mammography. The degree to which the sensitivities of mammography and breast MR imaging differ in the same patients depends on the mammographic breast density and the type of breast cancer: The difference increases with increasing breast density and for cancers that are difficult to diagnose on the basis of mammographic findings. The latter is the case, for example, in cancers with a diffuse growth pattern, such as invasive lobular cancers (67–71), and in cancers that exhibit benign morphologic features, such as medullary cancer (61). The sensitivity of breast MR imaging is not impaired by the amount or density of the fibroglandular tissue nor by scar tissue (eg, after tumorectomy), radiation therapy, or prosthetic breast implants or other types of breast reconstruction.

Overlooking invasive breast cancer on MR images is rare, but it certainly does happen. Nonenhancing invasive breast cancers are exceedingly rare (72). More often, the reason for failure to diagnose invasive cancer with breast MR imaging is early and strong enhancement in the surrounding normal fibroglandular tissue that may mask the enhancing cancer. In a 2002 publication (32), cancer was missed on 83% of false-negative studies because of strong enhancement in the fibroglandular tissue around the cancer in women with strong background enhancement. The likelihood with which surrounding fibroglandular tissue will mask an enhancing cancer increases with the time needed for image acquisition. This will more often be the case if pulse sequences with long (>2 minutes.) acquisition time are used (73) (Figs 1, 7, 8).

Figure 6

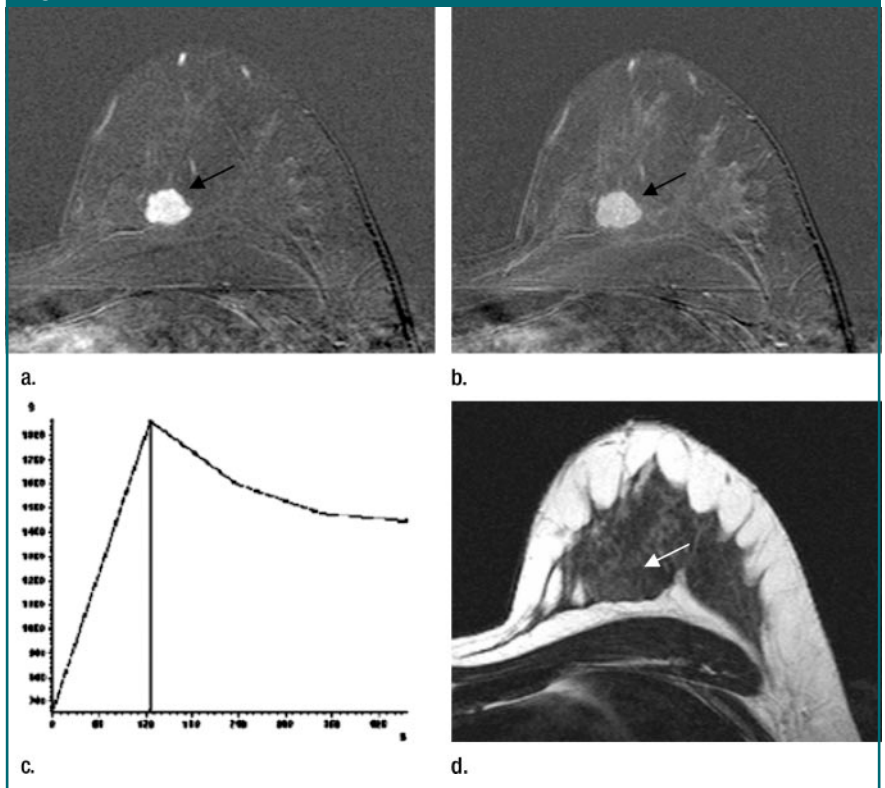


Figure 6: Value of kinetic parameters in well-circumscribed breast cancer in patient with invasive ductal cancer. Same MR pulse sequence parameters as in Figure 3 (modified dynamic protocol). Transverse **(a)** precontrast, **(b)** first postcontrast subtracted, and **(d)** T2-weighted turbo spin-echo (3800/110; turbo factor, 19) images and **(c)** time–signal intensity curve of enhancing mass (arrow). Note very dense fibroglandular tissue in **a** and **d** and enhancing mass in the prepectoral region of left breast, with lobulated shape, smooth borders, homogeneous internal enhancement, and absence of dark internal septations. On **c,** note fast initial enhancement increase followed by strong early washout kinetics. Note low signal intensity in corresponding image **d** (compare with Fig 4e). The mass was called BI-RADS category 4, because kinetic criteria (and signal intensity on **d**) were not typical of fibroadenoma. Benign-appearing morphologic criteria were disregarded. This breast has very dense tissue but an absence of background enhancement in the early and late postcontrast phases. Sensitivity and negative predictive value will be unimpaired.

Therefore, if strong background enhancement is present, it will be as crucial to communicate such an "MR imaging–dense breast" as it is to code a mammogram as ACR category 4, so that referring physicians understand that the high sensitivity that they may expect from a breast MR study may not be available in this particular case.

In fat-saturated (ie, actively fat-suppressed) imaging protocols, small breast cancers may occasionally be difficult to diagnose if they are surrounded by fatty tissue, possibly due to phase cancellation effects that occur if opposed-phase echo times (around 2.3 msec at 1.5 T) are used.

The sensitivity for diagnosing DCIS is lower than that for diagnosing invasive cancers. This is intuitively plausible because DCIS, by definition, is confined to the basal membrane of the ductal epithelium, such that there should be no interaction between the intraductal cancer and the surrounding periductal tissue—a postulate that should exclude any notable angiogenic activity. Surprisingly enough, DCIS is visible on breast MR images, although enhancement kinetics may differ from those observed in

invasive cancers and correspond instead to those of benign lesions. The relatively benign enhancement kinetics of DCIS are probably the reason for the low sensitivity of breast MR imaging for DCIS (74,75) in early publications from the investigators emphasizing enhancement kinetics over lesion morphology (the "kinetic camp," discussed later) for diagnosis. Diagnosis of DCIS requires different criteria than does diagnosis of invasive cancers (Table). If these criteria are used, MR imaging and mammography will be complementary for diagnosing DCIS. According to more recent publications, about 10% of DCIS cases that are diagnosed with the aid of mammography will not be diagnosed with MR owing to absence of enhancement. In turn, today up to 40% of DCIS cases are diagnosed only with breast MR imaging. There is increasing evidence to suggest that, overall, breast MR imaging may be more sensitive specifically for diagnosis of high-grade DCIS (55,57,58, 76–82).

In addition, it has been shown that the breast MR imaging appearance of DCIS correlates with its biologic aggressiveness, as indicated by common histopathologic and immunohistochemical predictors (83,84).

Obstacles and Difficulties in Implementing Breast MR Imaging

Breast MR imaging has been only reluctantly integrated into the routine clinical care of patients. In addition to cost considerations, other important obstacles have impeded the more widespread use of the technique. One important obstacle has been the lack of standardization of acquisition techniques, as well as in interpretation guidelines and terminology for MR imaging findings (85,86). The other major issues were the allegedly low specificity and high false-positive rate of breast MR imaging and the lack of techniques for MR-guided biopsy to manage lesions that are visible on breast MR images alone.

Lack of Standardization: Where We Are Today

Hardly any clinical application of diagnostic radiology is standardized to the extent that holds true for mammography. This is explainable by the fact that if a technique is used for mass screening, maintenance of consistent quality is of quintessential and socioeconomic importance. Another reason why mammography is greatly standardized is because it is easily standardizable, which, in turn, is due to the fact that it is a relatively simple technique. Yet even for mammography, it took many years to establish the level of standardization that is in practice today. Compared with mammography, breast MR imaging is still in its infancy—and MR is a far more difficult and complex imaging technique. However, standardization is necessary for quality assurance. In breast MR imaging, just as in mammography and breast US, an inappropriate or suboptimal imaging technique will result in poor or suboptimal diagnostic perfor-

Figure 7

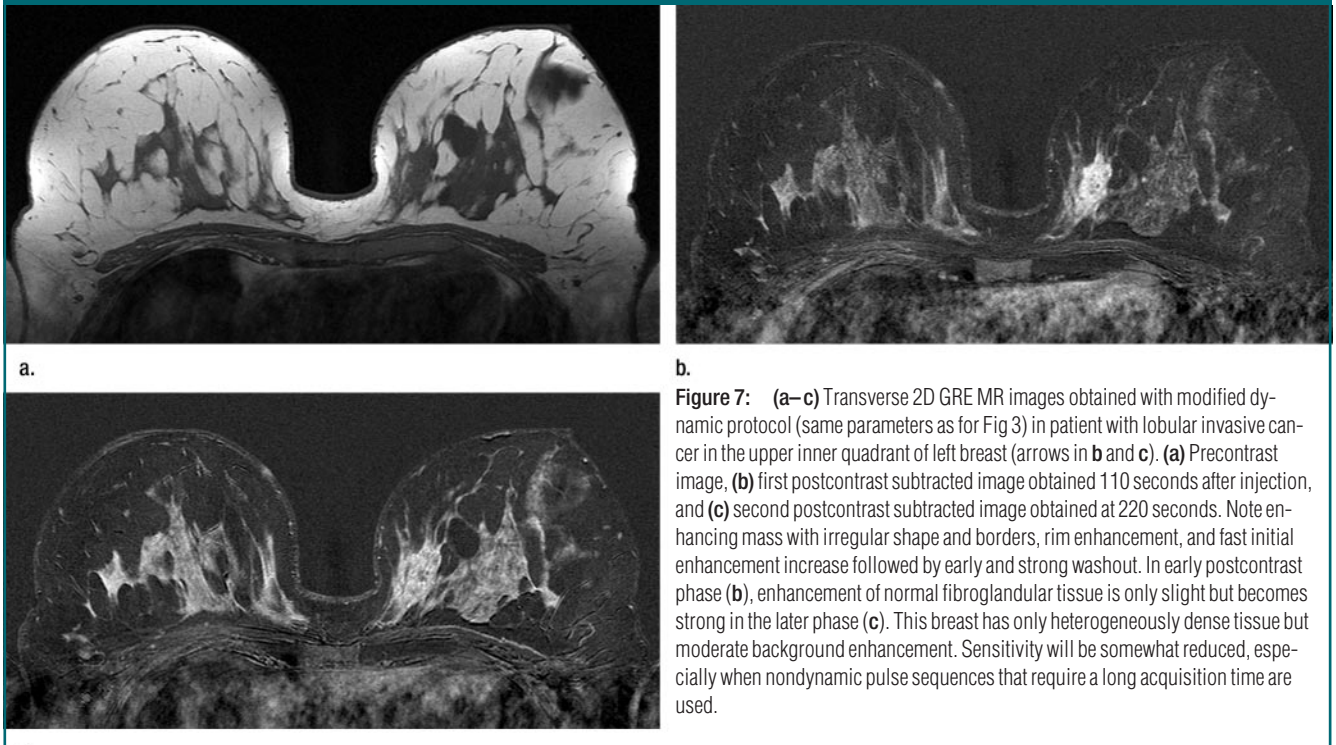


Figure 7: **(a–c)** Transverse 2D GRE MR images obtained with modified dynamic protocol (same parameters as for Fig 3) in patient with lobular invasive cancer in the upper inner quadrant of left breast (arrows in **b** and **c**). **(a)** Precontrast image, **(b)** first postcontrast subtracted image obtained 110 seconds after injection, and **(c)** second postcontrast subtracted image obtained at 220 seconds. Note enhancing mass with irregular shape and borders, rim enhancement, and fast initial enhancement increase followed by early and strong washout. In early postcontrast phase (**b**), enhancement of normal fibroglandular tissue is only slight but becomes strong in the later phase (**c**). This breast has only heterogeneously dense tissue but moderate background enhancement. Sensitivity will be somewhat reduced, especially when nondynamic pulse sequences that require a long acquisition time are used.

Figure 8

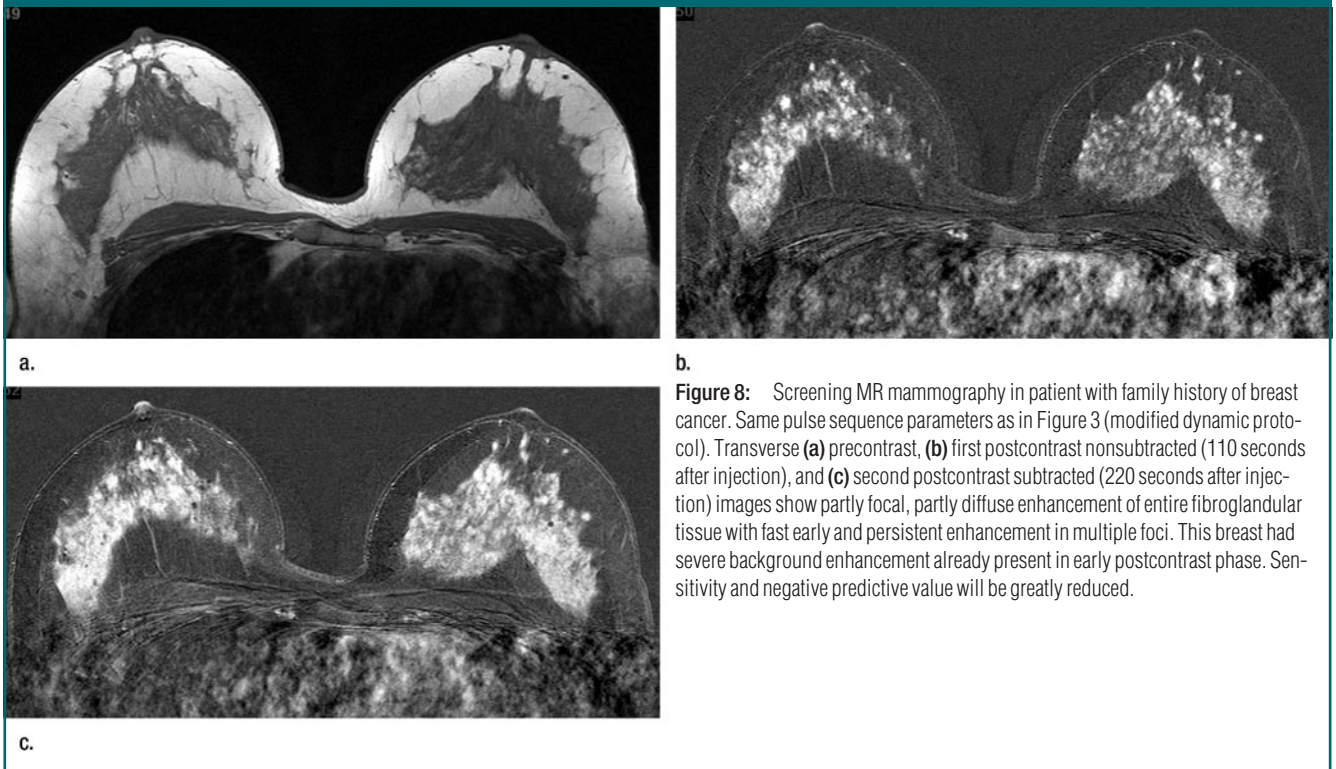


Figure 8: Screening MR mammography in patient with family history of breast cancer. Same pulse sequence parameters as in Figure 3 (modified dynamic protocol). Transverse **(a)** precontrast, **(b)** first postcontrast nonsubtracted (110 seconds after injection), and **(c)** second postcontrast subtracted (220 seconds after injection) images show partly focal, partly diffuse enhancement of entire fibroglandular tissue with fast early and persistent enhancement in multiple foci. This breast had severe background enhancement already present in early postcontrast phase. Sensitivity and negative predictive value will be greatly reduced.

mance. Given the variety of adjustable technical parameters in MR imaging compared with those in mammography or US, quality control may be even more important in MR imaging. In addition, a standardized acquisition technique should help result in similar image contrast and image information—a necessary prerequisite for the definition of diagnostic criteria that should be more or less universally applicable.

Until recently, when searching the published literature for breast MR imaging reports one would be overwhelmed by a myriad of technical approaches and a seemingly unlimited number of diagnostic criteria. The reason for this confusion dates back to the early days of breast MR, a time when MR systems offered only limited technical capacities—and thus limited choices. At that time, the published imaging protocols could be assigned either to the "kinetic camp" (represented mainly in European working groups) or to the "morphology camp" (mainly in U.S. working groups).

The kinetic approach (50,53,87) was based on the observation that enhancement patterns of benign and malignant lesions differ. To observe kinetics, dynamic imaging was advocated. At that time, such "fast" imaging allowed only limited spatial resolution, typically with a reduced 256 × 256 imaging matrix. Since European vendors offered bilateral breast coils, bilateral imaging was used, which, however, was accompanied by a further reduction in spatial resolution. Image subtraction was the only technique that was feasible; owing to the bilateral (ie, large) FOV and the time constraints, active fat suppression was not an option.

In contrast, the morphologic approach (39,52) was based on the well-established fact that malignant lesions exhibit characteristic morphologic features. Since the assessment of enhancement kinetics was not attempted and the issue of the fading contrast between cancers and normal tissue was not well known, image acquisition time was of no concern, such that time-consuming thin-section 3D GRE imaging was performed. With the available equipment, only one breast could be imaged at a time—for the morphologic approach, this was making a virtue out of necessity, since single-breast imaging requires only a small FOV. With the limited acquisition matrix that was available at that time, the small FOV translated into relatively high spatial resolution. Owing to the small FOV and the absence of time constraints, fat saturation with direct (active) techniques was feasible.

Accordingly, at that time, published breast MR protocols would vary considerably, with bilateral dynamic (temporally resolved) subtracted transverse acquisitions with poor spatial resolution in publications from the kinetic camp and unilateral spatially resolved sagittal acquisitions with active fat suppression and without dynamics in publications from the morphology camp. It is important to note that in the early times of breast MR, it was necessary to choose between either temporal or spatial resolution. Accordingly, these seemingly different approaches were, to a large

extent, merely a result of the different technical options (unilateral vs bilateral) that were available for breast imaging with the MR systems of European versus those of U.S. vendors.

Today, mostly owing to the technical progress that has been made, it is possible to better integrate diverging demands rather than compromise on one or another. As a consequence, today, there is considerable agreement that high spatial resolution is indispensable for breast MR imaging—as is fast imaging for optimum arterial phase contrast of enhancing lesions (20,33,34,61,88,89). Depending on the diagnostic criterion that is given priority, the compromise can be set more toward the spatial or the temporal resolution. So even today, pulse sequences may vary with respect to imaging plane, acquisition matrix, acquisition technique, section thickness, and type or mode of fat suppression. Although this can be considered a lack of standardization and be used to corroborate the technique's reputation of being "nonstandardizable," this is debatable. Of course, the more choices a technique offers, the more difficult it will be to obtain consensus on all options. In addition, MR imaging belongs to the most rapidly evolving techniques of contemporary clinical medicine—for good or bad, this jeopardizes attempts to standardize the modality. Accordingly, prescribing a detailed imaging protocol would probably be futile because such a protocol would be outdated the very day of its publication.

Is detailed standardization unattainable? Probably. Does that mean that the technique is not mature for clinical patient care or for clinical multicenter trials? Probably not. Defining standards regarding in- and through-plane resolution, temporal resolution, and type of pulse sequences is possible. These standards will need to give ranges of acceptable parameters, to acknowledge the fact that there may be more than one appropriate parameter setting. This has already been put into practice for several National Cancer Institute (NCI)- and ACR Imaging Network (ACRIN)-sponsored multi-institutional trials on breast MR imaging (NCI trials 6883, 6884; ACRIN trial 6667). In addition, ACR accreditation for breast MR imaging is in preparation. Although it may not be the all-encompassing standardization that works for mammography, it is noteworthy that the entire field of radiology, including cardiac, abdominopelvic, neurologic, and even neurofunctional imaging, has been successfully using MR imaging with its current variety, with no attempt to prescribe details of pulse sequences—and yet without suffering from an alleged lack of standardization. Why should the same not work for breast imaging?

In addition to acquisition technique, another area of confusion was the interpretation criteria that were published for differential diagnosis of enhancing lesions. Fortunately, along with the convergence of the acquisition techniques came a convergence of interpretation criteria such that broad agreement exists today regarding the criteria that are useful for differential diagnosis (although there may still exist differences regarding the ranking of the importance of the different criteria). Meanwhile, the first edition of the MR BI-RADS lexicon has been published (35). This lexicon can, in fact, be considered a consensus statement regarding lesion features that are thought to be diagnostically relevant and should be evaluated for the purpose of differential diagnosis. It provides a sound basis for the reporting of a breast MR study and incorporates both morphologic and kinetic criteria. Although the positive (or negative) predictive values of the many different findings are not yet fully investigated, this lexicon will be a step toward not only standardized reporting but also standardized interpretation of breast MR studies.

It is a step backward if reports are being published today in which nonestablished descriptors for nonestablished criteria are used in the attempt to, for example, assess the efficacy of a new contrast agent (90). This is even less acceptable if the study is designed as an interindividual comparison. In interindividual trials, the broad variations in enhancement patterns of benign and malignant breast lesions on MR images will considerably confound the results and probably override other effects which may be the actual subject of investigation.

Low Specificity and Positive Predictive Value: What Are the Facts Today?

Early reports on breast MR imaging (particularly those from the morphology camp) found poor specificity—as low as 30%—for contrast-enhanced breast MR (52). These reports established the technique's reputation for low positive predictive value and specificity. In these early reports, however, no attempt was made to further classify enhancing areas. The mere presence or absence of enhancement was the only criterion that was used to determine whether a breast MR study was positive or negative.

Today, when an enhancing area is identified, this constitutes the start of the process of differential diagnosis, not its end. Determining that a breast MR study is positive as soon as enhancement is seen is about equivalent to recommending biopsy on the basis of every mammogram that shows calcifications, irrespective of the number, size, morphology, density, distribution, and so forth. Today, differential diagnosis with breast MR imaging is based on an entire battery of criteria. The wealth of tissue information provided by breast MR imaging is intriguing and should even help improve differential diagnosis, compared with what is achieved with mammography or breast US. And in fact, more current publications (55,57,58, 61–63) suggest that breast MR imaging does not unduly increase the false-positive biopsy rate and that it provides about the same specificity as mammography and a significantly higher specificity than breast US: Positive predictive values of 35%–64% have been reported for breast MR screening in high-risk women; this is not perfect, but it is acceptable, particularly if one considers the (lower) positive predictive value that is achieved with mammography or US in the same cohorts.

It is important to note that these results have been obtained at centers where a high volume of breast MR studies are performed. This means that these conclusions are valid only as long as a seemingly simple prerequisite is fulfilled: Breast MR studies should be read with sufficient expertise—ideally with the same level of expertise with which the corresponding mammograms or US

studies are interpreted. This, however, is not the case at the majority of institutions. So another factor that maintains the reputation of breast MR imaging as high-sensitivity, low-specificity imaging and that adds to the limitations inherent to the technique (as mentioned earlier) is the different degree of expertise with which conventional, as opposed to MR imaging, studies have been and are read. It is well established that the accuracy of any diagnostic imaging modality depends on the experience of the interpreting radiologist (91–94). This is why national authorities or guidelines require a minimum number of mammograms to be read each year by radiologists who wish to participate in mammographic screening (95,96). There is no reason to assume that this correlation should not apply for the interpretation of breast MR studies. However, while in the United States more than 20 000 000 mammograms are read each year (97), the total volume of breast MR studies has been substantially smaller: Estimates range between 9000 and 20 000 studies per year, or less than 1% of the mammographic case volume. The wide gap between the presumed average expertise in reading mammograms compared with the respective expertise in reading breast MR studies may be another reason for the reported limited specificity of breast MR imaging.

Apart from costs and lack of standardization, the allegedly low specificity is the major reason why the more widespread use of breast MR imaging is discouraged, and it continues to represent one of the major reasons for the decision by some health care insurance providers not to reimburse for breast MR imaging. Without reimbursement, it is unlikely that the technique will be offered on a broader scale. If the technique is not used, however, the average level of practitioner experience will remain low, as will the positive predictive value. Therefore, it seems that the allegedly low positive predictive value of breast MR imaging is simultaneously the cause and the effect of the continued underutilization of this technique, thus perpetuating the current situation.

Another difficulty that complicates the situation is that breast MR imaging is a clinical application that "lies on the border:" Since MR imaging is not a traditional breast imaging modality, it is usually not listed in the curriculum of breast imaging fellowships. In many countries, radiologists may specialize in either (body) MR or in breast imaging, with only limited overlap between the two groups. As a consequence, breast MR is liable to become a victim of turf battles: Breast MR studies have been read by radiologists who were not familiar with other breast imaging techniques, specifically mammography or breast US. Since an in-depth understanding of breast cancer diagnosis and stage-dependent treatment can be considered a prerequisite and since best diagnostic results are only obtainable if breast MR images are interpreted in conjunction with mammograms (notably not by using the written report but by interpreting the images), this may well cause a limited diagnostic performance for breast MR that is entirely unrelated to the technique itself. In turn, if breast MR studies are interpreted by breast radiologists who did not have full training in MR imaging, this may cause avoidable difficulties and diagnostic errors as well, particularly if a suboptimal imaging technique is used.

While the repeated allegations regarding low specificity and positive predictive value can be proved clearly wrong, there is room for improvement. The most important cause of diagnostic difficulties are the many small enhancing foci and areas of non-masslike enhancement that occur, especially (but certainly not exclusively) in premenopausal women. In the majority of cases, these foci will be due to proliferation of the glandular tissue (adenosis) or to hormonal stimulation of normal breast parenchyma. The differentiation from a small breast cancer or (in cases of multiple foci or non–mass-related enhancement) DCIS will, however, be difficult if not impossible. So while remarkable progress has been made, there is still a substantial demand to improve the classification of enhancing areas. Fortunately though, there are a number of candidate technologies and candidate criteria that should further improve the distinction of benign and malignant foci and non–mass-related enhancement (see below).

Lack of Availability of MR-compatible Biopsy Equipment: Where We Are Today

The lack of availability of MR-guided interventions (lesion localization, core biopsy) has been identified as the single major reason for the delayed adoption of breast MR imaging in clinical practice (85,86). It is clear that if one offers breast MR imaging to a patient, this is done with the explicit intention to identify additional breast cancers that are occult at mammography and US. If a suspicious lesion is identified that has no correlate on either mammograms or second-look targeted US studies, MR guidance for biopsy is needed. If MR-guided intervention is offered to obtain histologic proof of such a lesion and no means is offered to enable a safe and tissue-sparing way to remove small additional cancers, then breast MR is a waste of time and effort and serves only to scare and anger patients and referring physicians alike. The availability of MR-guided interventions should be considered a mandatory prerequisite for offering breast MR imaging to a patient, just as is the availability of mammographic or US guidance for biopsies in a conventional breast imaging service.

In the past, MR-guided interventions were cumbersome and time consuming and thus expensive (98–102). There used to be only a limited number of commercially available biopsy devices. MR-compatible needles were virtually blunt—a major hazard to MR-guided core biopsy attempts (102).

With the improved functionality of recent MR-compatible needles, this problem has been greatly alleviated. Meanwhile, many MR-compatible breast biopsy devices are commercially available from a variety of vendors. There is now impressive published evidence regarding the efficiency and safety of MR-guided interventions. MR-guided hook-wire placement for localization of nonpalpable "MR-only" lesions (ie, lesions visible only on MR images) has become an easy, fast, and safe procedure and is fully integrated into clinical routine (Fig 9) (103–113).

MR-compatible vacuum-assisted biopsy has become an effective means to obtain direct histologic proof of lesions with MR imaging guidance, thus obviating surgical biopsy (Fig 10).

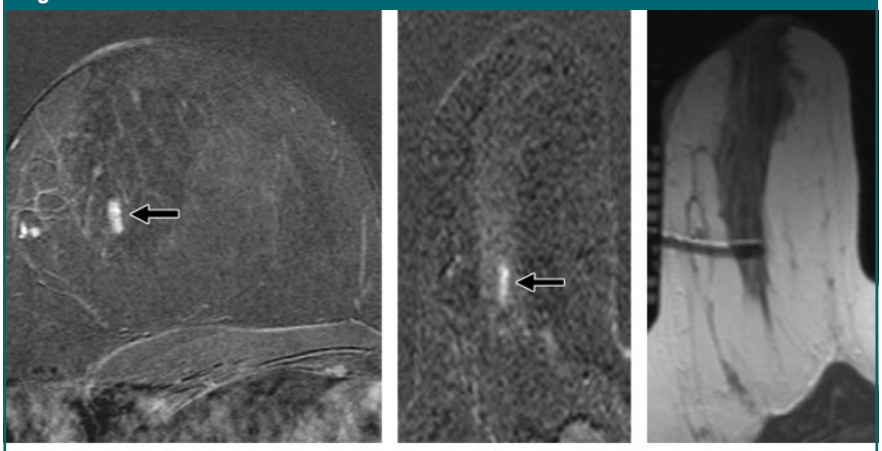
All in all, the table is set—what lacks are the people: The number of institutions that offer breast MR imaging has been increasing exponentially over the past years, whereas the number of institutions that offer MR-guided interventions is still small. It has been shown that second-look US can help identify up to 60% of seemingly MR-only lesions (114,115); therefore, targeted US should be the first step in the work-up if a suspicious finding is visible on MR images. This strategy requires close cooperation between the interpreter of the MR study and the interpreter of the US study (in the ideal case, it should be the same person). Yet even after second-look US, at least about 40% of all MR-only lesions will have no detectable correlate, and an MR-guided intervention will be required. Even if a correlate is identified at second-look US, it is sometimes difficult (or impossible) to definitely determine whether it is in fact the lesion that was seen on MR images—and if any doubt persists, MR-guided interventions will be inevitable. The necessity to be able to confidently correlate MR with US findings is another reason why breast MR imaging should be embraced by breast radiologists.

In view of the availability of MR-guided localization and biopsy procedures it is unacceptable and against standards of care to operate on an MR-only lesion without localization. It is even less acceptable and clear medical misconduct if therapeutic decisions are based only on images (eg, if mastectomy is performed instead of breast conservation for an additional focus detected only on MR images and without histologic proof of the imaging findings).

If an institution decides that the volume of breast MR studies is too low for dedicated MR biopsy equipment to be a financially sound investment, it should not offer this technique in the first place. The second best solution is to identify a cooperating center that offers these interventions. In this latter case, the referring institutions should, however, be obliged to keep track of the biopsy results in order to establish a learning curve and to perform a minimum number of breast MR studies in patients per year to develop an appropriate standard of expertise. This is necessary to ensure that the referring institution establishes the indication for biopsy with an adequately high positive predictive value. If this is not done and the referring institution fails to maintain a high level of expertise, the center that receives these patients will end up dealing with a large number of women who are referred because of false-positive diagnoses. In such a situation, the radiologists who offer the MR-guided intervention will find themselves in a quandary: Either they perform an MR-guided biopsy for a lesion that, to them, seems benign—which will probably result in a waste of time and money (not to mention unnecessary patient distress and anxiety)—or they decide against a biopsy and recommend follow-up instead—which, however, can place them in a difficult medicolegal situation.

The problem is aggravated by the fact that it is far more difficult to read an MR study from another institution than a study that has been acquired at one's own institution with familiar equipment and acquisition strategies. Unlike mammography, where image contrast is predictable and will be constant irrespective of the type of equipment used and the country of origin, this is not the case with MR imaging. For MR, image contrast and overall image impression varies substantially across different pulse sequence protocols, and, even if all acquisition parameters are kept constant, different window settings can have a considerable effect on the detectability of lesions and the appearance of their margins and internal enhancement architecture. The change of image contrast and overall image appearance between different types of MR protocols is at least as important as the difference between, for example, screen-film and digital mammography. Accordingly, it can be very difficult to give a second opinion for an MR study from another institution, and it will be even more difficult to check the indication for biopsy.

Figure 9



a. b. c.

Figure 9: MR-guided localization of 10-mm atypical papilloma in patient with right breast nipple discharge. **(a)** Transverse dynamic subtracted GRE breast MR image (300/4.6; flip angle, 90°) and **(b, c)** images obtained during MR-guided intervention with dedicated biopsy device. Note ductal enhancement in **a**, suggestive of DCIS or papilloma (arrow). **(b)** Visualization of target lesion (arrow) and biopsy device. **(c)** Position control after hook-wire release, with guidewire tip in the targeted position.

Conclusions and Further Objectives

There is broad consensus regarding the necessity of fast high-spatial-resolution imaging. Owing to the technical advances that have been made over recent

years, it is now possible to integrate both morphologic and functional criteria for detection and differential diagnosis of lesions by using breast MR images. The first issue of the MR BI-RADS lexicon has been an initial and important step toward a standardized interpretation of breast MR studies; the establishment of an ACR breast MR imaging accreditation program will be the next step. It is important to enforce the consistent use the proposed terminology for image interpretation, particularly in scientific studies and, thus, the published literature. This will be crucial in the collection of data regarding the respective positive and negative predictive values of the different MR imaging findings. Quality assurance is at least as important for breast MR as it is for diagnostic mammography; it will be important to define guidelines that set standards for minimum technical requirements. A lot of progress has been made regarding the availability of MR-compatible biopsy equipment, including guidewires and materials for direct vacuum-assisted core biopsy of lesions.

To further promote the technique's use in clinical practice, it will be important to better integrate MR imaging into breast imaging fellowship programs. Breast radiologists should gain direct access to MR systems to understand the immediate effect of different pulse sequence parameters on image contrast, signal-to-noise ratio, spatial resolution, and artifacts. Breast imaging fellowship programs should embrace MR as a natural component of the contemporary breast imaging armamentarium and train breast radiologists to become competent MR users—only as far as breast imaging is concerned, but in the broadest sense of the word. Breast radiologists do not need to receive in-depth training on pulse sequence design, but they do have to become familiar with some important basic principles such as *(a)* T1 contrast (and pulse sequence parameters that influence it), *(b)* the parameters that determine spatial resolution and the effects of those parameters on signal-to-noise ratio, *(c)* the interrelation of temporal and spatial resolution, *(d)* the factors that influence the effectiveness of fat saturation, and *(e)* the appearance of different types of artifacts.

Figure 10

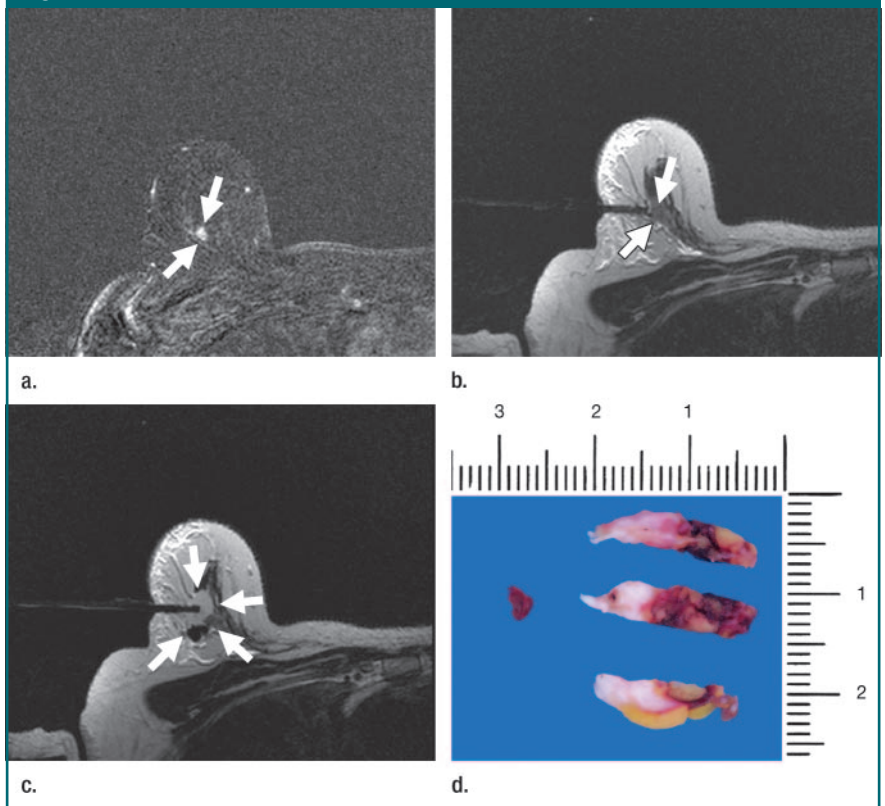


Figure 10: MR-guided 9-gauge vacuum-assisted core biopsy (ATEC; Suros, Indianapolis, Ind) in 42-year-old patient; the final diagnosis was cancer. Diagnostic breast MR study (not shown) revealed enhancing mass with suspicious morphology and enhancement kinetics. No correlate was seen at mammography or targeted breast US. **(a)** Contrast-enhanced subtracted MR image shows biopsy device and oval enhancing mass with irregular margins (arrows). **(b)** Corresponding T2-weighted MR image shows mass with intermediate signal intensity. Note coaxial needle sheath in place, with needle tip in front of the mass (arrows). **(c)** Repeat T2-weighted turbo spin-echo MR image after completion of vacuum biopsy shows biopsy cavity with air-fluid level (arrows). **(d)** The mass was entirely removed. Histologic examination confirmed grade 3 (pT1b N0 M0) 6-mm ductal invasive cancer. Subsequent surgery after MR-guided localization did not reveal residual breast cancer.

It is highly desirable to have medical imaging physicists specialize in (breast) MR to help radiologists keep abreast of—and thus fully benefit from—the technical progress that is continuously made. In turn, a direct interaction between imaging physicists and radiologists is also necessary to help the physicist understand possible difficulties encountered during interpretation of images of a given pulse sequence. This is important because what seems appropriate on physical grounds does not always turn out to be useful in clinical practice. In other words, there have been many technical approaches to breast MR imaging that, according to imaging physics theory, should be well suited for breast MR but that, for one reason or another, did not prove suitable for clinical use.

Breast imaging fellowship programs should incorporate performance of MR-guided interventions and core biopsy into their curriculum. Only if breast radiologists embrace these relatively easy interventions during their fellowships will it be possible to overcome existing reservations and thus increase the number of sites that offer MR-guided interventions in the long run. All this is more likely to occur if the reimbursement pol-

icy for breast MR is changed to better reflect the actual clinical value of this technique.

Current Status of Breast MR Imaging: Part II

The second part of this two-part series will provide an overview on the current clinical indications for breast MR imaging. This includes its use as a second-line imaging modality in patients with equivocal mammographic and/or US findings and in patients with clinical signs or symptoms of breast cancer but with negative or benign mammographic or US results. It will also include a survey on the use of breast MR imaging for monitoring response to and delineating residual disease after neoadjuvant chemotherapy. We will discuss the benefits and possible hazards of preoperative breast MR for staging in patients with breast cancer. We will summarize the current level of evidence on the use of breast MR as a primary imaging modality (ie, in screening for breast cancer).

References

1. Folkman J, Klagsbrun M. Angiogenic factors. Science 1987;235:442–447.
2. Folkman J, Watson K, Ingbr D, Hanahan D. Induction of angiogenesis during the transition from hyperplasia to neoplasia. Nature 1989;339:58–61.
3. Schneider BP, Miller KD. Angiogenesis of breast cancer. J Clin Oncol 2005;23:1782–1790.
4. Pham CD, Roberts TP, van Bruggen N, et al. Magnetic resonance imaging detects suppression of tumor vascular permeability after administration of antibody to vascular endothelial growth factor. Cancer Invest 1998;16:225–230.
5. Buadu LD, Murakami J, Murayama S, et al. Breast lesions: correlation of contrast medium enhancement patterns on MR images with histopathologic findings and tumor angiogenesis. Radiology 1996;200:639–649.
6. Aref M, Brechbiel M, Wiener EC. Identifying tumor vascular permeability heterogeneity with magnetic resonance imaging contrast agents. Invest Radiol 2002;37:178–192.
7. Degani H, Gusis V, Weinstein D, Fields S, Strano S. Mapping pathophysiological features of breast tumors by MRI at high spatial resolution. Nat Med 1997;3:780–782.
8. Cohen FM, Kuwatsuru R, Shames DM, et al. Contrast-enhanced magnetic resonance imaging estimation of altered capillary permeability in experimental mammary carcinomas after X-irradiation. Invest Radiol 1994;29(11):970–977.
9. Boné B, Wiberg MK, Parrado C, Falkmer U, Aspelin P, Gad A. Mechanism of contrast enhancement in breast lesions at MR imaging. Acta Radiol 1998;39(5):494–500.
10. Frouge C, Guinebretiere JM, Contesso G, Di Paola R, Blery M. Correlation between contrast enhancement in dynamic magnetic resonance imaging of the breast and tumor angiogenesis. Invest Radiol 1994;29(12):1043–1049.
11. Su MY, Cheung YC, Fruehauf JP, et al. Correlation of dynamic contrast enhancement MRI parameters with microvessel density and VEGF for assessment of angiogenesis in breast cancer. J Magn Reson Imaging 2003;18:467–477.
12. Lewin M, Bredow S, Sergeyev N, Marecos E, Bogdanov A Jr, Weissleder R. In vivo assessment of vascular endothelial growth factor-induced angiogenesis. Int J Cancer 1999;83(6):798–802.
13. Hulka CA, Edmister WB, Smith BL, et al. Dynamic echo-planar imaging of the breast: experience in diagnosing breast carcinoma and correlation with tumor angiogenesis. Radiology 1997;205(3):837–842.
14. Buckley DL, Drew PJ, Mussurakis S, Monson JR, Horsman A. Microvessel density of invasive breast cancer assessed by dynamic Gd-DTPA enhanced MRI. J Magn Reson Imaging 1997;7(3):461–446.
15. Knopp MV, Weiss E, Sinn HP, et al. Pathophysiologic basis of contrast enhancement in breast tumors. J Magn Reson Imaging 1999;10:260–266.
16. Stomper PC, Winston JS, Herman S, Klippenstein DL, Arredondo MA, Blumenson LE. Angiogenesis and dynamic MR imaging gadolinium enhancement of malignant and benign breast lesions. Breast Cancer Res Treat 1997;45:39–46.
17. Kuhl CK, Bieling H, Gieseke J, et al. Breast neoplasms: T2* susceptibility-contrast, first-pass perfusion MR imaging. Radiology 1997;202:87–95.
18. Kuhl CK, Bieling HB, Gieseke J, et al. Healthy premenopausal breast parenchyma in dynamic contrast-enhanced MR imaging of the breast: normal contrast medium enhancement and cyclical-phase dependency. Radiology 1997;203:137–144.
19. Müller-Schimpfle M, Ohmenhauser K, Stoll P, Dietz K, Claussen CD. Menstrual cycle and age: influence on parenchymal contrast medium enhancement in MR imaging of the breast. Radiology 1997;203:145–149.
20. Kuhl CK, Schild HH, Morakkabati N. Dynamic bilateral contrast-enhanced MR imaging of the breast: trade-off between spatial and temporal resolution. Radiology 2005;236(3):789–800.
21. Boetes C, Barentsz JO, Mus RD, et al. MR characterization of suspicious breast lesions with a gadolinium-enhanced TurboFLASH subtraction technique. Radiology 1994;193:777–781.
22. Schorn C, Fischer U, Luftner-Nagel S, Grabbe E. Diagnostic potential of ultrafast contrast-enhanced MRI of the breast in hypervascularized lesions: are there advantages in comparison with standard dynamic MRI? J Comput Assist Tomogr 1999;23(1):118–122.
23. Choyke PL, Dwyer AJ, Knopp MV. Functional tumor imaging with dynamic contrast-enhanced magnetic resonance imaging. J Magn Reson Imaging 2003;17:509–520.
24. Taylor JS, Tofts PS, Port R, et al. MR imaging of tumor microcirculation: promise for the new millennium. J Magn Reson Imaging 1999;10:903–907.
25. Tofts PS, Berkowitz B, Schnall MD. Quantitative analysis of dynamic Gd-DTPA enhancement in breast tumors using a permeability model. Magn Reson Med 1995;33:564–568.
26. Tofts PS, Brix G, Buckley DL, et al. Estimating kinetic parameters from dynamic contrast-enhanced T(1)-weighted MRI of a diffusable tracer: standardized quantities and symbols. J Magn Reson Imaging 1999;10:223–232.
27. Hochman MG, Orel SG, Powell CM, Schnall MD, Reynolds CA, White LN. Fibroadenomas: MR imaging appearances with radiologic-histopathologic correlation. Radiology 1997;204:123–129.
28. Nunes LW, Schnall MD, Orel SG. Update of breast MR imaging architectural interpretation model. Radiology 2001;219:484–494.
29. Kuhl CK, Leutner C, Mielcarek P, Gieseke J, Schild HH. Breast compression interferes with lesion enhancement in contrast-enhanced breast MRI [abstr]. Radiology 1997;205(P):538.
30. Heywang-Kobrunner SH, Haustein J, Pohl C, et al. Contrast-enhanced MR imaging of the breast: comparison of two different

doses of gadopentetate dimeglumine. Radiology 1994;191:639–646.

31. Berg WA, Gutierrez L, NessAiver MS, et al. Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. Radiology 2004;233(3):830–849.

32. Teifke A, Hlawatsch A, Beier T, et al. Undetected malignancies of the breast: dynamic contrast-enhanced MR imaging at 1.0 T. Radiology 2002;224:881–888.

33. Ikeda DM, Hylton NM, Kinkel K, et al. Development, standardization, and testing of a lexicon for reporting contrast-enhanced breast magnetic resonance imaging studies. J Magn Reson Imaging 2001;13:889–895.

34. Ikeda DM. Progress report from the American College of Radiology Breast MR Imaging Lexicon Committee. Magn Reson Imaging Clin N Am 2001;9:295–302.

35. American College of Radiology. ACR breast imaging reporting and data system (BI-RADS): breast imaging atlas. Reston, Va: American College of Radiology, 2003.

36. Liberman L, Mason G, Morris EA, Dershaw DD. Does size matter? positive predictive value of MRI-detected breast lesions as a function of lesion size. AJR Am J Roentgenol 2006;186:426–430.

37. Kuhl CK, Mielcarek P, Klaschik S, et al. Dynamic breast MR imaging: are signal intensity time course data useful for differential diagnosis of enhancing lesions? Radiology 1999;211:101–110.

38. Kuhl CK. MRI of breast tumors. Eur Radiol 2000;10:46–58.

39. Nunes LW, Schnall MD, Siegelman ES, et al. Diagnostic performance characteristics of architectural features revealed by high spatial-resolution MR imaging of the breast. AJR Am J Roentgenol 1997;169:409–415.

40. Schnall MD, Rosten S, Englander S, Orel SG, Nunes LW. A combined architectural and kinetic interpretation model for breast MR images. Acad Radiol 2001;8:591–597.

41. Baum F, Fischer U, Vosshenrich R, Grabbe E. Classification of hypervascularized lesions in CE MR imaging of the breast. Eur Radiol 2002;12:1087–1092.

42. Kinkel K, Helbich TH, Esserman LJ, et al. Dynamic high-spatial-resolution MR imaging of suspicious breast lesions: diagnostic criteria and interobserver variability. AJR Am J Roentgenol 2000;175:35–43.

43. Leong CS, Daniel BL, Herfkens RJ, et al. Characterization of breast lesion morphology with delayed 3DSSMT: an adjunct to dynamic breast MRI. J Magn Reson Imaging 2000;11:87–96.

44. Kuhl CK, Mielcarek P, Klaschik S, Leutner C, Pakos E, Schild HH. Do T2-weighted TSE pulse sequences help with the differential diagnosis of enhancing lesions in dynamic breast MRI? J Magn Reson Imaging 1999;9:187–196.

45. Qayyum A, Birdwell RL, Daniel BL, et al. MR imaging features of infiltrating lobular carcinoma of the breast: histopathologic correlation. AJR Am J Roentgenol 2002; 178:1227–1232.

46. Szabo BK, Aspelin P, Wiberg MK, Bone B. Dynamic MR imaging of the breast. Analysis of kinetic and morphologic diagnostic criteria. Acta Radiol 2003;44:379–386.

47. Kuhl CK; Mielcarek P, Leutner C, Schild HH. Diagnostic criteria of ductal carcinoma in-situ (DCIS) in dynamic contrast-enhanced breast MRI: comparison with invasive breast cancer (IBC) and benign lesions [abstr]. In: Proceedings of the sixth meeting of the International Society for Magnetic Resonance in Medicine. Berkeley, Calif: International Society for Magnetic Resonance in Medicine, 1998; 931.

48. Liberman L, Morris EA, Dershaw DD, Abramson AF, Tan LK. Ductal enhancement on MR imaging of the breast. AJR Am J Roentgenol 2003;181:519–525.

49. Morakkabati-Spitz N, Leutner C, Schild H, Traeber F, Kuhl C. Diagnostic usefulness of segmental and linear enhancement in dynamic breast MRI. Eur Radiol 2005;15(9): 2010–2017.

50. Heywang-Köbrunner SH, Schlegel A, Beck R, et al. Contrast-enhanced MRI of the breast after limited surgery and radiation therapy. J Comput Assist Tomogr 1993; 17(6):891–900.

51. Heywang-Köbrunner SH, Viehweg P, Heinig A, Kuchler C. Contrast enhanced MRI of the breast: accuracy, value, controversies, solutions. Eur J Radiol 1997;24:94–108.

52. Harms SE, Flamig DP, Hesley KL, et al. MR imaging of the breast with rotating delivery of excitation off resonance: clinical experience with pathologic correlation. Radiology 1993;187:493–501.

53. Gilles R, Guinebretiere JM, Lucidarme O, et al. Nonpalpable breast tumors: diagnosis with contrast-enhanced subtraction dynamic MR imaging. Radiology 1994;191(3): 625–631.[Published correction appears in Radiology 1994;193(1):285.]

54. Gilles R, Guinebretiere JM, Shapeero LG, et al. Assessment of breast cancer recurrence with contrast-enhanced subtraction MR imaging: preliminary results in 26 patients. Radiology 1993;188(2):473–478.

55. Fischer U, Kopka L, Grabbe E. Breast carcinoma: effect of preoperative contrast-enhanced MR imaging on the therapeutic approach. Radiology 1999;213:881–888.

56. Yeh ED, Slanetz PJ, Edmister WB, Talele A, Monticciolo D, Kopans DB. Invasive lobular carcinoma: spectrum of enhancement and morphology on magnetic resonance imaging. Breast J 2003;9:13–18.

57. Liberman L, Morris EA, Dershaw DD, Abramson AF, Tan LK. MR imaging of the ipsilateral breast in women with percutaneously proven breast cancer. AJR Am J Roentgenol 2003;180:901–910.

58. Morris EA, Liberman L, Ballon DJ, et al. MRI of occult breast carcinoma in a high-risk population. AJR Am J Roentgenol 2003;181:619–626.

59. Lee SG, Orel SG, Woo IJ, et al. MR imaging screening of the contralateral breast in patients with newly diagnosed breast cancer: preliminary results. Radiology 2003;226: 773–778.

60. Bedrosian I, Mick R, Orel SG, et al. Changes in the surgical management of patients with breast carcinoma based on preoperative magnetic resonance imaging. Cancer 2003;98:468–473.

61. Kuhl CK, Schmutzler RK, Leutner CC, et al. Breast MR imaging screening in 192 women proved or suspected to be carriers of a breast cancer susceptibility gene: preliminary results. Radiology 2000;215(1): 267–279.

62. Warner E, Plewes DB, Shumak RS, et al. Comparison of breast magnetic resonance imaging, mammography, and ultrasound for surveillance of women at high risk for hereditary breast cancer. J Clin Oncol 2001;19:3524–3531.

63. Stoutjesdijk MJ, Boetes C, Jager GJ, et al. Magnetic resonance imaging and mammography in women with a hereditary risk of breast cancer. J Natl Cancer Inst 2001;93: 1095–1102.

64. Smyczek-Gargya B, Fersis N, Dittmann H, et al. PET with [18F]fluorothymidine for imaging of primary breast cancer: a pilot study. Eur J Nucl Med Mol Imaging 2004; 31:720–724.

65. Samson DJ, Flamm CR, Pisano ED, Aronson N. Should FDG PET be used to decide whether a patient with an abnormal mammogram or breast finding at physical examination should undergo biopsy? Acad Radiol 2002;9:773–783.

66. Avril N, Rose CA, Schelling M, et al. Breast imaging with positron emission tomography and fluorine-18 fluorodeoxyglucose: use and limitations. J Clin Oncol 2000;18:3495–3502.

67. Quan ML, Sclafani L, Heerdt AS, Fey JV, Morris EA, Borgen PI. Magnetic resonance imaging detects unsuspected disease in patients with invasive lobular cancer. Ann Surg Oncol 2003;10:1048–1053.

68. Kneeshaw PJ, Turnbull LW, Smith A, Drew PJ. Dynamic contrast enhanced magnetic resonance imaging aids the surgical management of invasive lobular breast cancer. Eur J Surg Oncol 2003;29:32–37.

69. Kneeshaw PJ, Turnbull LW, Drew PJ. Role of magnetic resonance imaging in the diagnosis and single-stage surgical resection of invasive lobular carcinoma of the breast Br J Surg 2002;89:1296–1301.

70. Weinstein SP, Orel SG, Heller R, et al. MR imaging of the breast in patients with invasive lobular carcinoma. AJR Am J Roentgenol 2001;176:399–406.

71. Munot K, Dall B, Achuthan R, Parkin G, Lane S, Horgan K. Role of magnetic resonance imaging in the diagnosis and single-stage surgical resection of invasive lobular carcinoma of the breast. Br J Surg 2002;89:1296–1301.

72. Fischer U, Kopka L, Grabbe E. Invasive mucinous carcinoma of the breast missed by contrast-enhancing MR imaging of the breast. Eur Radiol 1996;6:929–931.

73. Bluemke DA, Gatsonis CA, Chen MH, et al. MR imaging prior to breast biopsy: results of the International Breast Magnetic Resonance Consortium (IBMC) trial. JAMA 2004;292:2735–2742.

74. Fischer U, Westerhof JP, Brinck U, Korabiowska M, Schauer A, Grabbe E. Das duktale in-situ-karzinom in der dynamischen MR-mammographie bei 1,5 T. Rofo 1996;164:290–294.

75. Westerhof JP, Fischer U, Moritz JD, Oestmann JW. MR imaging of mammographically detected clustered microcalcifications: is there any value? Radiology 1998;207:675–681.

76. Ikeda O, Nishimura R, Miyayama H, et al. Magnetic resonance evaluation of the presence of an extensive intraductal component in breast cancer. Acta Radiol 2004;45:721–725.

77. Van Goethem M, Schelfout K, Kersschot E, et al. Enhancing area surrounding breast carcinoma on MR mammography: comparison with pathological examination. Eur Radiol 2004;14:1363–1370.

78. Hartman AR, Daniel BL, Kurian AW, et al. Breast magnetic resonance image screening and ductal lavage in women at high genetic risk for breast carcinoma. Cancer 2004;100:479–489.

79. Hwang ES, Kinkel K, Esserman LJ, Lu Y, Weidner N, Hylton NM. Magnetic resonance imaging in patients diagnosed with ductal carcinoma-in-situ: value in the diagnosis of residual disease, occult invasion, and multicentricity. Ann Surg Oncol 2003;10:381–388.

80. Neubauer H, Li M, Kuehne-Heid R, Schneider A, Kaiser WA. High grade and non-high grade ductal carcinoma in situ on dynamic MR mammography: characteristic findings for signal increase and morphological pattern of enhancement. Br J Radiol 2003;76:3–12.

81. Kuhl CK, Schrading S, Schild HH. MRI versus mammography for diagnosing pure ductal carcinoma in situ (DCIS): a prospective observational cohort study [abstr]. In: Radiological Society of North America Scientific Assembly and Annual Meeting Program. Oak Brook, Ill: Radiological Society of North America, 2006; 303.

82. Menell JH, Morris EA, Dershaw DD, Abramson AF, Brogi E, Liberman L. Determination of the presence and extent of pure ductal carcinoma in situ by mammography and magnetic resonance imaging. Breast J 2005;11(6):382–390.

83. Esserman LJ, Kumar AS, Herrera AF, et al. Magnetic resonance imaging captures the biology of ductal carcinoma in situ. J Clin Oncol 2006;24(28):4603–4610.

84. Morrow M. The certainties and the uncertainties of ductal carcinoma in situ. J Natl Cancer Inst 2004;96(6):424–425.

85. Orel SG, Schnall MD. MR imaging of the breast for the detection, diagnosis, and staging of breast cancer. Radiology 2001;220:13–30.

86. Orel SG. MR imaging of the breast. Magn Reson Imaging Clin N Am 2001;9:273–288.

87. Kaiser WA, Zeitler E. MR imaging of the breast: fast imaging sequences with and without Gd-DTPA: preliminary observations. Radiology 1989;170(3 pt 1):681–686.

88. Liu PF, Debatin JF, Caduff RF, Kacl G, Garzoli E, Krestin GP. Improved diagnostic accuracy in dynamic contrast enhanced MRI of the breast by combined quantitative and qualitative analysis. Br J Radiol 1998;71(845):501–509.

89. Schnall MD, Ikeda DM. Lesion diagnosis working group report. J Magn Reson Imaging 1999;10(6):982–990.

90. Sardanelli F, Iozzelli A, Fausto A, Carriero A, Kirchin MA. Gadobenate dimeglumine–enhanced MR imaging breast vascular maps: association between invasive cancer and ipsilateral increased vascularity. Radiology 2005;235:791–797.

91. Esserman L, Cowley H, Eberle C, et al. Improving the accuracy of mammography: volume and outcome relationships. J Natl Cancer Inst 2002;94:369–375.

92. Beam CA, Conant EF, Sickles EA. Factors affecting radiologist inconsistency in screening mammography. Acad Radiol 2002;9:531–540.

93. Beam CA, Conant EF, Sickles EA. Association of volume and volume-independent factors with accuracy in screening mammogram interpretation. J Natl Cancer Inst 2003;95:282–290.

94. Nodine CF, Kundel HL, Mello-Thoms C, et al. How experience and training influence mammography expertise. Acad Radiol 1999;6:575–585.

95. Mammography Quality Standards Act (MQSA) (as amended by MQSRA of 1998 and 2004) Title 42 USC §6a(2f) (1992).

96. Expertengruppe S3 Leitlinie der Deutschen Krebsgesellschaft. Nationale S3-leitlinie zu diagnostik, therapie und nachsorge des mammakarzinoms der frau. Deutsche Krebsgesellschaft Juli 2004.

97. U.S. General Accounting Office. Mammography: capacity generally exists to deliver services—report to the chairman, special committee on aging, U.S. Senate, GAO-02-532. Washington, DC: U.S. General Accounting Office, 2002.

98. Heywang-Köbrunner SH, Huynh AT, Viehweg P, Hanke W, Requardt H, Paprosch I. Prototype breast coil for MR guided needle localization. J Comput Assist Tomogr 1994;18:876–881.

99. Fischer U, Vosshenrich R, Keating D, et al. MR-guided biopsy of suspect breast lesions with a stereotaxic add-on device for surface coils. Radiology 1994;192:272–273.

100. Orel SG, Schnall MD, Newman RW, Powell CM, Torosian MH, Rosario EF. MR imaging–guided localization and biopsy of breast lesions: initial experience. Radiology 1994;193(1):97–102.

101. Kuhl CK, Elevelt A, Leutner C, Gieseke J, Pakos E, Schild HH. Interventional breast MR imaging: clinical use of a stereotactic localization and biopsy device. Radiology 1997;204(3):667–675.

102. Kuhl CK, Morakkabati N, Leutner CC, Schmiedel A, Wardelmann E, Schild HH. MR imaging–guided large-core (14-gauge) needle biopsy of small lesions visible at breast MR imaging alone. Radiology 2001; 220(1):31–39.

103. Fischer U, Kopka L, Grabbe E. Magnetic resonance guided localization and biopsy of suspicious breast lesions. Top Magn Reson Imaging 1998;9:44–59.

104. Kuhl CK. Interventional breast MRI: needle localisation and core biopsies. J Exp Clin Cancer Res 2002;21:65–68.

105. Lampe D, Hefler L, Alberich T, et al. The clinical value of preoperative wire localization of breast lesions by magnetic resonance imaging: a multicenter study. Breast Cancer Res Treat 2002;75:175–179.

106. Perlet C, Heinig A, Prat X, et al. Multicenter study for the evaluation of a dedicated biopsy device for MR-guided vacuum biopsy of the breast. Eur Radiol 2002;12: 1463–1470.

107. Perlet C, Schneider P, Amaya B, et al. MR-guided vacuum biopsy of 206 contrast-enhancing breast lesions. Rofo 2002;174:88–95.

108. Prat X, Sittek H, Grosse A, et al. European quadricentric evaluation of a breast MR biopsy and localization device: technical improvements based on phase-I evaluation. Eur Radiol 2002;12:1720–1727.

109. Lehman CD, Eby PR, Chen X, Dee KE, Thursten B, McCloskey J. MR imaging-guided breast biopsy using a coaxial technique with a 14-gauge stainless steel core biopsy needle and a titanium sheath. AJR Am J Roentgenol 2003;181:183–185.

110. Hrung JM, Langlotz CP, Orel SG, Fox KR, Schnall MD, Schwartz JS. Cost-effectiveness of MR imaging and core-needle biopsy in the preoperative work-up of suspicious breast lesions. Radiology 1999;213:39–49.

111. Liberman L, Bracero N, Morris E, Thornton C, Dershaw DD. MRI-guided 9-gauge vacuum-assisted breast biopsy: initial clinical experience. AJR Am J Roentgenol 2005; 185:183–193.

112. Lehman CD, Deperi ER, Peacock S, McDonough MD, Demartini WB, Shook J. Clinical experience with MRI-guided vacuum-assisted breast biopsy. AJR Am J Roentgenol 2005;184:1782–1787.

113. Daniel BL, Freeman LJ, Pyzoha JM, et al. An MRI-compatible semiautomated vacuum-assisted breast biopsy system: initial feasibility study. J Magn Reson Imaging 2005;21:637–644.

114. Berg WA. Image-guided breast biopsy and management of high-risk lesions. Radiol Clin North Am 2004;42:935–946, vii.

115. LaTrenta LR, Menell JH, Morris EA, Abramson AF, Dershaw DD, Liberman L. Breast lesions detected with MR imaging: utility and histopathologic importance of identification with US. Radiology 2003;227: 856–861.