



## Breast MR imaging

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Breast cancer is a significant health care problem in the United States. More than 180,000 American women are diagnosed with breast cancer each year, and approximately 50,000 of these women will die of their disease [1]. Breast cancer is the second leading cause of cancer death among women. Imaging plays a crucial role in all aspects of breast cancer care. This includes early detection through screening, diagnosis and associated image-guided biopsy, treatment planning, and follow-up. The limitations of current x-ray mammography have led to extensive efforts over the past 15 years to develop complimentary imaging techniques to improve breast imaging performance, particularly in the radiographically dense breast. The most accepted adjunct modality is breast sonography, which is now widely used in the diagnostic evaluation of women with abnormal screening mammography or clinical exams. Other techniques that have been proposed that are less widely used include scintigraphy with Tc99 Sestamibi and  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography.

Early in its history, MR imaging was proposed as a technique to assist in the detection and diagnosis of breast cancer. Early reports of breast MR imaging confirmed that high-quality MR images of the breast could be obtained with local surface coils [2,3]. In the absence of exogenously injected contrast agents, however, it was difficult to detect breast cancer. In 1989, Kaiser and Zeitler [4] and Heywang et al [5] independently published on the application of MR imaging contrast agents to detect breast cancer. Their findings—that the use of intravenous gadolinium chelates allow MR imaging to detect and possibly

diagnose breast cancer—were extremely exciting and led to significant follow-up work.

Using a higher resolution, three-dimensional (3D) technique, Harms et al [6] demonstrated the power of MR imaging to detect mammographically and clinically occult breast cancer. They performed careful correlations between examinations performed on women prior to mastectomy and the resultant pathology, and showed that high-resolution MR imaging, performed with a technique pioneered in his laboratory rotating delivery of excitation off resonance (RDEO), was able to detect occult multifocal cancer in up to 40% of women.

Despite the extremely high sensitivity for breast cancer MR imaging demonstrated in these early studies, it was clear that contrast enhancement alone was not specific for breast cancer. This led to intense efforts to identify distinguishing characteristics between benign enhancing lesions and malignant enhancing lesions. The use of information obtained from the architecture of the enhancing lesion and qualitative and quantitative interpretations of the pharmacokinetics of enhancement have been studied extensively for this purpose. Although many different pharmacokinetic imaging approaches have been described, the most commonly adopted method is the qualitative approach to the time signal intensity curve of gadolinium, which was popularized by Kuhl et al [7] and Kaiser et al [4]. Work by Orel et al [8] and Nunes et al [9] clearly demonstrated the importance of lesion architecture for distinguishing between benign and malignant lesions. Today most practitioners agree that a combination of gadolinium pharmacokinetics and lesion architecture is important for proper interpretation of breast MR images.

Recently, breast MR imaging has become more widely used as a supplemental imaging modality in

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the breast. The most common clinical indications for which breast MR imaging is being performed include difficult diagnostic evaluations and the evaluation of extent of disease within a breast affected with breast cancer. This article discusses breast MR imaging techniques, interpretation strategies, and strategies for clinical implementation.

### Breast MR imaging techniques

Breast MR imaging should be performed using a dedicated breast surface coil. There are commercially available unilateral and bilateral breast surface coils. Most currently available surface coils also allow for some access to the breast for image-guided procedures. Similar to mammography of the breast, MR imaging requires breast compression for optimal imaging. The compression also provides stabilization to prevent motion and reduces the breast size in one dimension reducing the requirement for coverage in the medial to lateral dimension.

Almost all reports of breast MR imaging in the literature have been performed at 1.0 or 1.5 T. Although there have been scattered reports of breast MR imaging being performed successfully at 0.5 T [10], there is no scientific literature regarding the performance of breast MR imaging at field strengths less than 0.5 T. Due to the technical demands of breast MR imaging and the physical properties of gadolinium, optimal imaging performance is attained using increased MR field strengths. There is no clinical data, however, that provides a guide to the relative clinical performance of breast MR at different field strengths. Despite this, I would exercise great caution at performing contrast-enhanced breast MR imaging at field strengths less than 0.5 T.

There is no specific patient preparation for breast MR imaging. Patients should undergo standard MR imaging screening procedures. Even though metal objects may be far from the imaging volume, they may affect the ability to fat suppress; thus, all metallic objects should be removed from the patient's body, including zippers and clasps. It is best to place an IV for gadolinium injection prior to the patient entering the magnet suite. An IV line should be established so that the injection of gadolinium can be performed without moving the patient. Gadolinium injection may be performed by a mechanical injector or by hand.

After obtaining pilot images, I routinely perform T2-weighted images. Although in the majority of cases, the T2-weighted images provide no added diagnostic value, they do provide information regarding the characterization of cystic lesions and fibro-

adenomas in some cases. Given the small time commitment necessary to obtain these images, I would advise routinely obtaining T2-weighted images. I obtain T2-weighted images as fat-suppressed, fast spin echo images, using a  $256 \times 192$  matrix over an 18-cm field of view. I use a 3-mm slice thickness. The repetition time (TR)/echo time (TE) of the sequence that I use is approximately 4 seconds per 90 milliseconds.

The most critical part of the breast MR imaging acquisition is the contrast-enhanced T1-weighted acquisition. This consists of contrast-enhanced images performed prior to and after the administration of gadolinium. The precontrast and postcontrast acquisition should adhere to certain principles. There should be sufficient T1 weighting to show differences in contrast enhancement, even at high contrast concentrations. Three-dimensional acquisitions with very short TRs will easily meet this requirement. The same pulse sequence should be used prior to and after the administration of contrast. There should be no change in system operating parameters between precontrast and postcontrast images, so that direct subtractions and quantitative comparisons may be performed. A minimum of two sequential postcontrast acquisitions should be performed. The postcontrast imaging should be initiated dynamically during or after the infusion of contrast agent. Although there is no clear consensus on the required time resolution of postcontrast images, I recommend 3 minutes as an upper limit for the time resolution of the dynamic gadolinium study.

Fat suppression is a valuable aid to improve the conspicuity of contrast enhancement. Most modern scanners can perform fat suppression over a volume that encompasses both breasts. Chemical shift selective inversion performed intermittently during a 3D echo sequence provides a time-efficient method for performing fat suppression. There is relatively little time penalty in obtaining fat suppression in this manner.

During image interpretation, subtraction can further enhance the conspicuity of enhancing lesions. This is considered mandatory if no fat suppression is employed. Even if fat suppression is employed, subtraction can be valuable to offset inhomogeneities in fat suppression or to add further conspicuity to enhancing lesions.

### Quantitative image enhancement and the effect of gadolinium

As discussed in the introduction, there have been many efforts to establish quantitative criteria

based on enhancement profiles to differentiate benign from malignant enhancing lesions. The complex relationship between gadolinium concentration, pulse sequence, and signal intensity makes it extremely difficult for quantitative techniques to be developed that are generalizable across different platforms. To appreciate this issue, it is important to first understand the mechanism by which gadolinium causes enhancement of signal intensity on MR imaging.

The mechanism of action of gadolinium is fundamentally different than what radiologists are accustomed to with iodinated contrast agents. In MR imaging, the gadolinium itself is never actually visualized. Enhancement of the MR signal intensity is derived from the water within the tissue due to the effect of gadolinium interaction with water in tissue. This interaction leads to a shortening of the T1 time and makes water more visible on a T1-weighted image. The resultant increased signal intensity is a complex function of the concentration of the gadolinium delivered to the tissue, the inherent T1 time of the tissue prior to enhancement, and the pulse sequence itself. It is valuable to qualitatively understand how each of these factors affects the enhancement.

As stated above, the mechanism of action of gadolinium is to change the T1 relaxation time of the water within the tissue of the breast. Typical breast tissue and breast lesions have T1 values that vary from 700 to 1000 milliseconds. When the gadolinium is injected, the tissue enhances and the T1 value of that tissue (at 1.5 T) is reduced to approximately 200 milliseconds. Therefore, the signal intensity of breast tissue after contrast enhancement is unrelated to the initial T1 value of the gadolinium concentration. If a signal intensity ratio were to be calculated ( $S_{\text{postcontrast}}/S_{\text{precontrast}}$ ), different values would be obtained for different tissues with different precontrast T1 values, despite the same gadolinium concentration delivered to each tissue. This is because the denominator would be different based on the initial T1. Therefore, it is clear that the precontrast T1 value will influence any signal enhancement ratio that is calculated during a contrast-enhanced breast MR imaging examination.

The pulse sequence also has a large influence on the signal enhancement ratio. All lectures on basic MR imaging physics include a discussion of how short TR times result in T1 weighting. Similarly, for gradient echo images, larger flip angles increase T1 weighting. The ratio of these signals for tissues with different T1 values will vary according to the pulse sequence used. Therefore, a signal enhancement

ratio obtained from one particular pulse sequence will not be directly generalizable to other pulse sequences. Therefore, signal enhancement ratio criteria for diagnosing breast lesions under MR imaging cannot be generalized across institutions and platforms.

A more generalizable solution is to directly calculate the gadolinium concentration delivered to the tumor and use quantitative criteria that rely on the gadolinium concentration itself. This allows for quantitation of each case, independent of the pulse sequence used. This also corrects for the influence of the initial lesion T1 on the signal enhancement ratio.

There are discussions in the literature that use basic physiologic parameters derived from the gadolinium concentration or pharmacokinetic curve to classify breast MR lesions [11,12]. Most of these calculations assume a linear relationship between relaxation time and gadolinium concentration. This would be the case if there were a single compartment within the tissue over which the gadolinium mixed evenly; however, the distribution of gadolinium within a tissue is more complicated. Gadolinium extravasates from blood vessels into the extracellular space, but does not enter cells themselves. Therefore, the water that is inside cells does not have the same access to gadolinium as the water that is outside cells. Thus, tissue is characterized by two separate relaxation times—an intracellular relaxation time and an extracellular relaxation time. If there is rapid exchange of the water across the cell membrane (“rapid” being defined as fast compared with the difference in relaxation rates between the compartments), a linear relationship between gadolinium concentration and average T1 can be assumed, causing no error in the gadolinium concentration calculation. Landis et al [13] recently showed, however, that this is not the case at peak tissue gadolinium concentrations after a dynamic injection of gadolinium. The high concentration of gadolinium in the extracellular space of tumors makes the assumption of rapid exchange invalid. This creates a complicated relationship between the signal intensity ratio and the gadolinium concentration. Correction for this effect is not trivial, but is possible. The point to be understood is that developing quantitative criteria based on signal enhancement characteristics of lesions after dynamic contrast injection that are accurate and reproducible across multiple platforms is extremely difficult. Any recommendation in the literature to apply a quantitative criterion should be reviewed in light of these difficulties.

### Image interpretation

Interpretation of breast MR images is best performed on a computer workstation where reformatting, image processing, image subtraction, and image quantitation is available. Film presentations are difficult, due to the number of images that comprise a breast MR imaging examination. This makes it difficult for patients to have images available for second opinions at other institutions. It is suggested that at least one early phase postcontrast image set that includes the entire breast be available on film at the patient's request. In addition, selected images including reformatting and subtraction through any significant findings should be available. Associated enhancement curves should also be available on film or paper copy if they are felt to be relevant. This is the minimum information needed by a colleague in another institution to assist in the patient's care.

The major task in interpreting breast MR imaging is establishing the likelihood of malignancy for any enhancement observed. There are two major classes of image features that are available to the radiologist

to assist in this interpretation. These are features based on the architecture of the lesion enhancement and features from the times/signal intensity curve of the enhancement.

A structured approach to the use of architectural features in breast MR imaging has been described by Nunes et al [9]. This approach has been refined and some of its aspects are being integrated into a breast MR imaging lexicon being developed under the auspices of the American College of Radiology [14]. These approaches would suggest that the initial approach to enhancement of breast is to make a determination of whether the enhancement represents a focal mass or not a focal mass. An example of focal and nonfocal mass enhancement is shown in Fig. 1. Data from Nunes et al [9] suggests that approximately half of the focal masses identified in a diagnostic population will be cancer. In order to define which of these masses are malignant and which are benign, other architectural features can be utilized. An important feature is the shape and border of the lesion (Fig. 2). The more irregular or spiculated the lesion margin is, the more likely it is to be cancer.

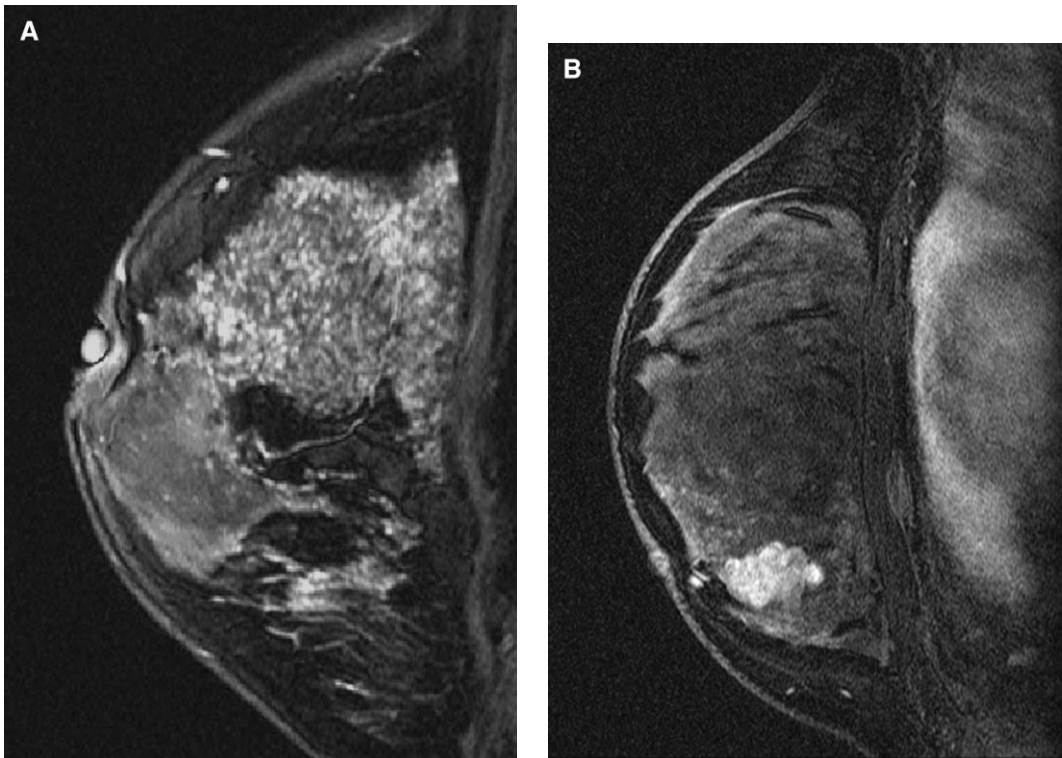


Fig. 1. (A) Example of stippled regional enhancement from benign hyperplasia. (B) Lobulated focal mass, representing a fibroadenoma.

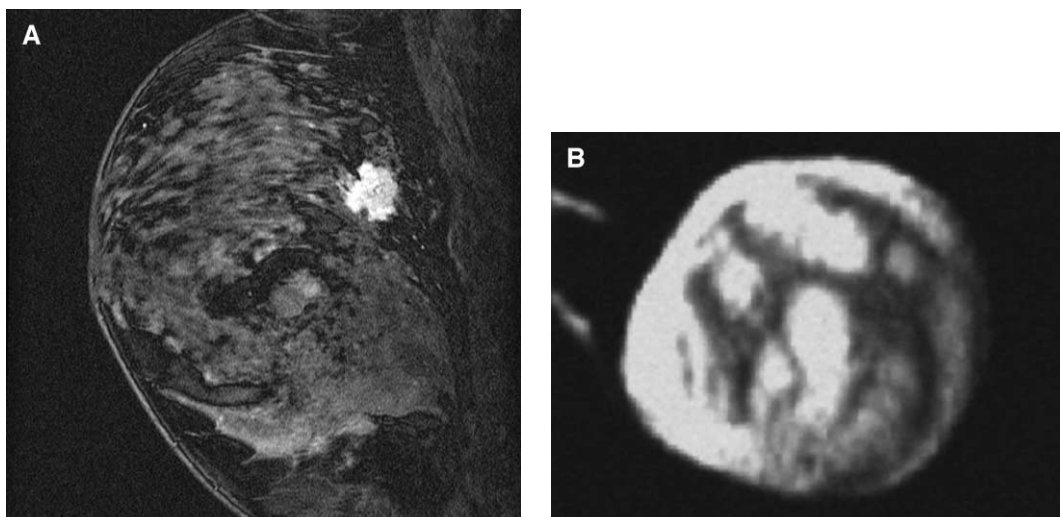


Fig. 2. (A) Irregular-bordered enhancing mass secondary to invasive cancer. (B) Smooth-bordered enhancing mass, representing a fibroadenoma.

Lesion borders that are smooth or demonstrate gentle lobulations are more likely to be benign. This distinction is still not 100% accurate. There are lobulated-bordered cancers; for example, colloid, tubular, and medullary cancers can have well-defined lobulated borders. In addition, benign lesions such as radial scars can demonstrate spiculation. Other features can be valuable in further distinguishing between benign and malignant enhancing focal masses. Rim enhancement of the lesion is highly suggestive of malignancy (Fig. 3). Note that this is only the case for solid lesions. Cystic lesions in the breast will typically have an enhancing rim. The smooth enhancing rim of a cystic lesion does not suggest any evidence of malignancy. It is noted that enhancing rims in solid lesions can occur not only at the periphery of the lesion, but occasionally can be seen entering the internal portion of a lesion.

There are features that are most suggestive of benignity. Fibroadenomas tend to grow in several adjacent lobulas. They respect the demarcation of these lobulas and develop a fibrous septum between the various lobules. The septum can be seen as a low-signal nonenhancing internal septation within a lesion. This finding is seen on postcontrast images. In addition, fibroadenomas may be edematous and extremely bright on T2-weighted images, particularly in young women. Thus, the fibrous septum can also be seen on T2-weighted images. The finding of septations within a lobulated or smooth-bordered lesion should be considered as good evidence of benignity (Fig. 4). Although fibroadenomas in young women may be

edematous and bright on T2-weighted images, they hyalinize over time. Hyalinized fibroadenomas tend to be low signal on T2-weighted images. Although cancers can occasionally be low signal, this is usually due to extensive desmoplastic reaction and is associated with a spiculated lesion. A smooth border or lobulated lesion that is low signal on T2 will almost certainly represent a hyalinized fibroadenoma. These hyalinized fibroadenomas may enhance or may eventually lose their blood supply and stop enhancing.

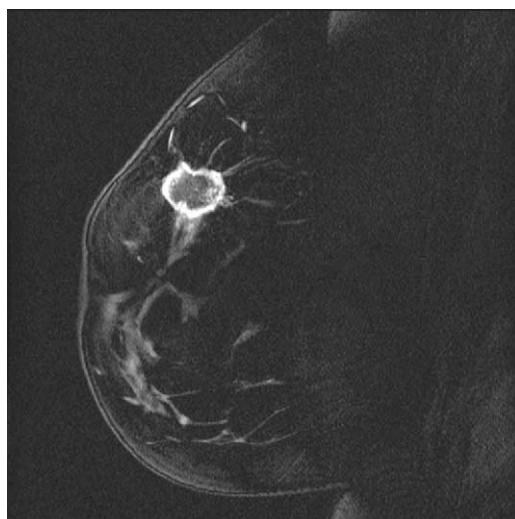


Fig. 3. Rim-enhancing mass, representing an invasive carcinoma.

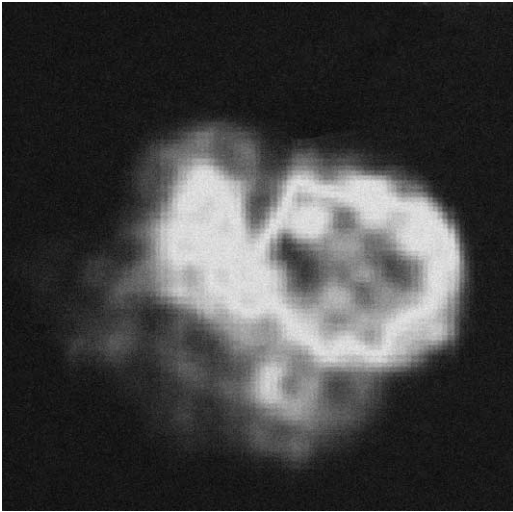


Fig. 4. Lobulated focal mass with internal septations, representing a fibroadenoma.

Because fibroadenomas develop multiple lobules, different lobulations in the fibroadenomas may have different characteristics. Some are edematous whereas others are hyalinized. This may lead to heterogeneous appearances on both postcontrast and T2-weighted images. Applying the principles above to each lobule will allow for a diagnosis to be established.

There are two important characteristics of non-focal mass enhancement that need to be determined. The two main important factors to be determined are the distribution of the enhancement and the form of the enhancement. If the distribution resembles the distribution of breast ducts, it is more likely to be cancer. Distributions can be described as ductal, segmental, regional, or diffuse. Descriptions will also refer to the size of the foci that make up the area of enhancement. These descriptions will include stippled, clumped, inhomogeneous, and confluent. Therefore, using these characteristics, stippled enhancement in a regional or diffuse distribution most likely will be benign (Fig. 5), and confluent or clumped enhancement in a segmental distribution most likely will be malignant. Lesions identified as nonfocal mass enhancement most often will include a significant fraction of in situ cancer; however, there may be associated invasion.

In addition to the architectural information described above, there are features related to the time course of enhancement that are predictive of cancer. As described earlier, the most robust and reproducible features relate to the qualitative assessment of the enhancement curve. The enhancement curve is

not measured as the average enhancement curve over the lesion. Rather, the enhancement curve should be sampled from multiple locations in the lesion, and the most suspicious enhancement curve in the lesion should be assigned to the lesion. Enhancement curves can be divided into three major types: persistent, plateau, and washout. Persistent enhancing curves demonstrate continued enhancement beyond the first 2 minutes of acquisition. Plateau curves will plateau and level off after 2 minutes of contrast injection. Washout curves will reach a peak after 2 minutes of contrast injection and new signal intensity (Fig. 6). Washout is felt to be a feature suspicious for cancer, plateau is felt to be indeterminate, and persistent enhancement is reported to be a feature most consistent with benignity. These features are not 100% accurate in these determinations, and reported accuracies have varied. This is particularly true in nonfocal mass enhancement in which persistent enhancement does not exclude malignancy. Similarly, classic fibroadenomas can

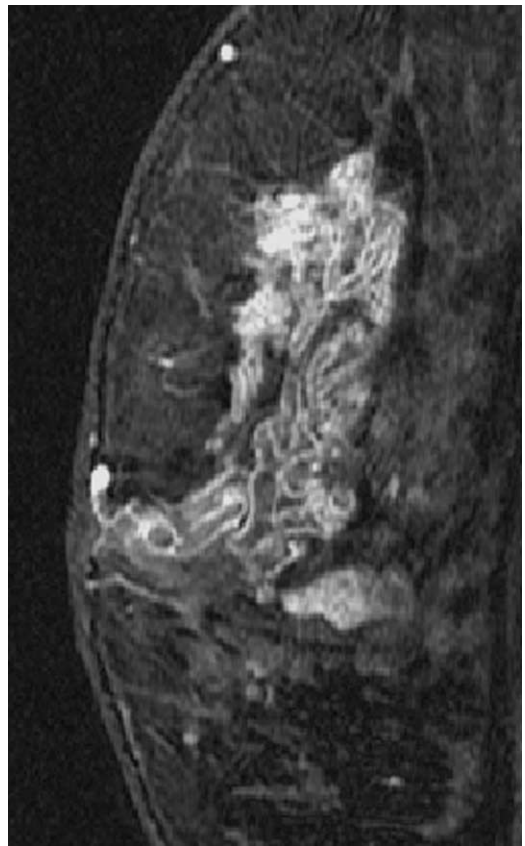


Fig. 5. Clumped enhancement in a segmental or ductal distribution, representing ductal carcinoma in situ.

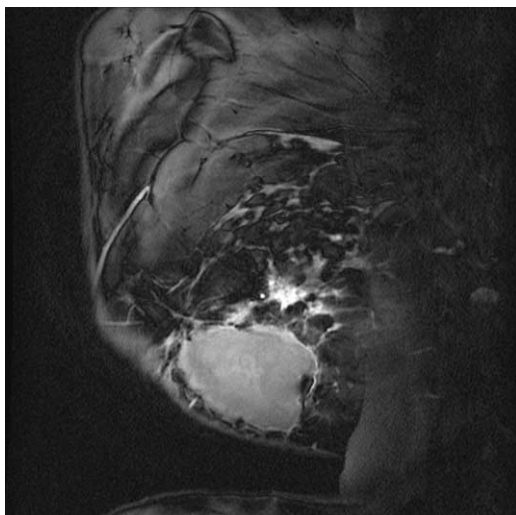


Fig. 6. Patient who has had a primary resection for invasive cancer demonstrating irregular enhancing mass adjacent to the resection cavity, representing additional foci of cancer.

demonstrate washout and this should not be used as evidence of malignancy. My approach is to initially apply an architectural analysis, and then use the time-course kinetics to either confirm a diagnosis or assist interpretation in borderline cases.

#### **Breast MR imaging evaluation of the extent of breast cancer within an affected breast**

One of the major clinical indications for breast MR imaging is to determine the extent of cancer within an affected breast. This use of MR imaging was pioneered by Harms et al [6], who demonstrated additional foci of cancer that were mammographically occult in up to 40% of women undergoing mastectomy for breast cancer. Although this population was biased toward more advanced lesions by virtue of the fact that these women were undergoing mastectomy, this work highlighted a role for MR imaging in the detection of more extensive disease. There are multiple reports in the literature that suggest that breast MR imaging will effect the management of between 10% and 20% of women with newly diagnosed breast cancer [15,16].

There are still many unanswered questions regarding the use of breast MR imaging in the evaluation of the extent of breast cancer. Although it is clear that MR imaging can detect additional foci of disease, it has never been determined that MR imaging has an effect on the recurrence rate of patients undergoing

breast conservation therapy. There is a concern that breast MR imaging will lead to more extensive surgery for breast cancer without a significant effect on the recurrence rate or long-term survival. In effect, MR imaging may be guiding the excision of foci of tumor that could be treated with radiation therapy. This issue needs to be studied in a prospective, well-controlled trial. In addition, the evaluation of the contralateral breast is another significant issue that needs to be studied. Reports in the literature suggest a 5% to 10% detection rate of cancer in the contralateral breast, using breast MR imaging at the time of presentation of the initial cancer. The determination of contralateral breast cancer has an affect on management strategy and is best determined at the time of presentation rather than in subsequent years. Only small, single-institution studies have been performed to date. A larger, multi-institutional trial is needed to clearly establish the role of breast MR imaging in evaluating the contralateral breast.

#### **Breast cancer screening**

The expense and technical resources required by breast MR imaging in its current form makes it difficult to think of this technique as a general screening technique. There has been tremendous progress in quantifying an individual women's risk for breast cancer [17,18], however. In high-risk patients, the enhanced sensitivity of MR imaging may offer an important adjunct to their screening regiment. Several small pilot studies [19–22] have concluded that breast MR imaging has the potential to detect mammographically and clinically occult breast cancer in high-risk women. The reported yields for the MR imaging detection of otherwise occult breast cancer in high-risk women is in the 1% to 3% range. These results obviously would be highly dependent on patient population and length of time over which the screening intervention is employed. Studies that have included sonography in addition to mammography and MR imaging also have shown that MR imaging had a similar high yield relative to US in detecting breast cancer in this population [7,20]. Although there are many unanswered questions, a consensus is forming that MR imaging may indeed have a role in screening high-risk women for breast cancer. The performance of breast MR imaging in a screening role (receiver operating characteristic curve) has not been well established. In addition, the manner in which high-risk patients are likely to benefit from MR screening also has not been answered. Other questions such as the timing between MR scans and

at what age MR screens should be initiated remain unanswered. Perhaps the most critical unanswered question is the overall health impact of MR imaging screening in this population. A large-scale screening study involving high-risk women needs to be undertaken to answer these important questions.

## Summary

Contrast-enhanced breast MR imaging has made significant progress since its introduction into the radiological literature in 1989. The techniques and technology continue to be refined, and understanding of the interpretation strategies has improved dramatically. Clinical applications in difficult diagnostic cases and the evaluation of the extent of breast cancer are now being practiced in many centers worldwide. There is great excitement over the potential for breast MR imaging to address the problem of screening high-risk women. Despite all of the progress made over the past years, however, there is still a significant amount of work ahead before a clear understanding of how this technique will affect the health care of women is obtained.

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