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Canadian Association of Radiologists Journal 63 (2012) 192–206

CANADIAN ASSOCIATION OF RADIOLOGISTS JOURNAL

www.carjonline.org

Magnetic Resonance Imaging / Formation image de résonance magnétique

# Management of Breast Magnetic Resonance Imaging-Detected Lesions

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**Abstract**

Breast magnetic resonance imaging (MRI) has become an essential component of breast imaging. Whether it is used as a problem-solving tool or a screening test or for staging patients with breast cancer, it detects many lesions in the breast. The challenge for the radiologist is to distinguish significant from insignificant lesions and to direct their management. A brief summary of the terminology according to the American College of Radiologists lexicon will be provided. This review article will cover the differential diagnosis of enhancing lesions, including masses and nonmass enhancement, from benign and malignant causes. Some of the specific morphologic and kinetic features that help to differentiate benign from malignant lesions will be illustrated, and positive predictive values of these features will be reviewed. The various methods of investigating enhancing lesions of the breast will be discussed, including second-look ultrasound, ultrasound-guided biopsy, stereotactic biopsy, and MRI-guided biopsy. A practical approach to the management of MRI-detected lesions will include timing of follow-up, when to biopsy and when to ignore enhancing lesions in the breast.

**Résumé**

L'imagerie par résonance magnétique (IRM) mammaire est devenue une composante essentielle de la mammographie. Qu'elle serve d'outil de résolution de problèmes, de dépistage ou de stadification du cancer du sein, l'IRM détecte un grand nombre de lésions du sein. Pour les radiologistes, le défi consiste à distinguer les lésions importantes des lésions frustes, et à orienter leur gestion en conséquence. Un sommaire de la terminologie inspirée du lexique du American College of Radiologists est fourni. L'article porte sur le diagnostic différentiel des lésions prenant le contraste, incluant les rehaussements avec et sans masse, de causes bénignes à malignes. L'article présente certaines fonctions morphologiques et cinétiques qui facilitent la différenciation des lésions bénignes et malignes, en plus d'analyser leurs valeurs prédictives positives. Les diverses méthodes d'examen des lésions prenant le contraste sont abordées, notamment l'échographie de second regard, la biopsie guidée par ultrasons, la biopsie stéréotaxique et la biopsie guidée par IRM. Une approche pratique de la gestion des lésions détectées par IRM doit définir quand procéder aux examens de suivi et à une biopsie et quand ne pas tenir compte des lésions prenant le contraste dans le sein.



*Key Words:* Breast magnetic resonance imaging; Magnetic resonance imaging lesions; Breast magnetic resonance management; Magnetic resonance biopsy

The implementation of the widespread clinical use of breast magnetic resonance imaging (MRI) has been impeded by the lack of standardization of breast MRI techniques, lack of availability of breast MRI-guided interventional tools, lack of training in breast MRI, and an apparent low level of specificity. These limitations have dissuaded many radiologists from embracing the technique. However, the sensitivity of breast MRI has proved to be the highest of all imaging tools clinically available for breast imaging. Because of greater standardization provided by the American College of Radiologists (ACR) breast MRI lexicon, increased availability of MRI-guided interventional tools, and increased access to breast MRI training, reporting breast MRIs no longer poses the same challenges. In the past 10 years, breast MRI has been adopted into regular clinical practice in much of North America, Europe, and Asia, and is now an essential component of breast imaging. This increase in clinical use requires that radiologists become more familiar with management of MRI-detected lesions. The purpose of this review article is to provide a practical approach to the management of MRI-detected lesions, with a focus on how to differentiate benign from malignant lesions, when and how to biopsy, and when to follow up or ignore MRI-detected lesions.

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0846-5371/$ - see front matter 
doi:10.1016/j.carj.2010.11.003

For a lesion to be identified on breast MRI, it must enhance. Contrast-enhanced breast MRI relies on tumour neo-angiogenesis, whereby tumours incite the formation of new vessels and proliferation of existing capillaries [1]. This neovascularization is faulty: there is increased capillary leakage because of large endothelial fenestrations, arteriovenous shunting, and perfusion of the capillary bed is poorly controlled by regular physiologic mechanisms. Identification of early enhancement of tumours secondary to their more rapid accumulation of contrast than surrounding tissue is the underlying principle of breast MRI, which allows for highly sensitive detection of invasive tumours. It is what distinguishes tumours from the more gradually enhancing glandular tissue. However, when hormonal stimulation is present, glandular tissue enhances more intensely and rapidly [2]. Therefore, the best method to minimize benign glandular enhancement is to image patients in week 2 (also called the postmenstrual phase) of the menstrual cycle, when hormonal stimulation is lowest. Kuhl et al [2] found a significant reduction in the number of enhancing lesions and the enhancing velocity in the second week of the menstrual cycle compared with the first, third, and fourth weeks ($P > .001$). They also demonstrated that more than 60 enhancing foci were present in 16 or 20 normal volunteers and that 73% of these foci resolved completely during follow-up [2]. The timing of the breast MRI in the second week of the menstrual cycle, therefore, is the single best method to minimize glandular enhancement and maximize detection of truly malignant lesions. The most marked glandular enhancement is seen in lactational women, who have significant hormonal stimulation, which can significantly impair sensitivity of the MRI (Figure 1).

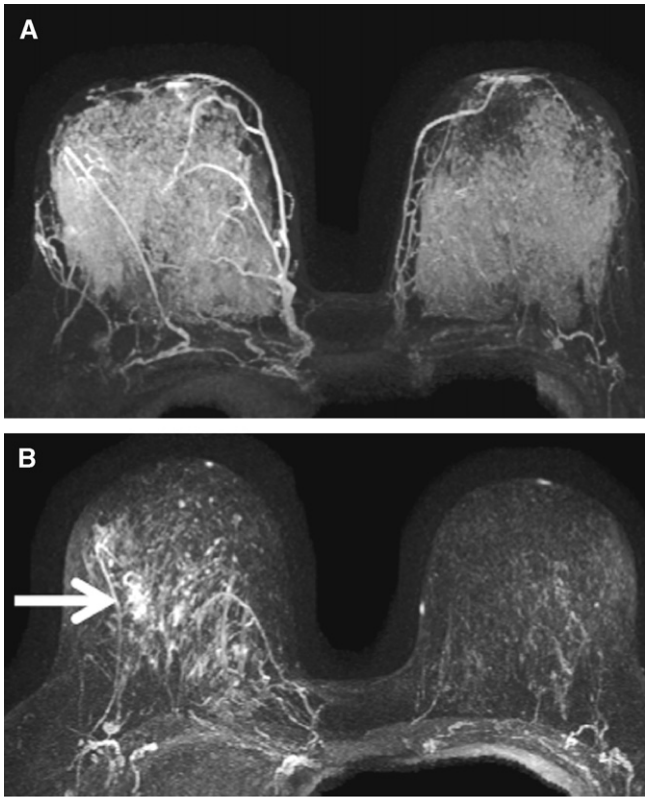


Figure 1. A 33-year-old lactating woman with right breast cancer. (A) Axial maximum intensity projection (MIP) image, demonstrating diffuse glandular enhancement, which obscures the enhancing right breast cancer. (B) Six months later, after 4 cycles of chemotherapy and cessation of lactation, the axial MIP image, showing that the glandular enhancement has all but resolved, which makes the enhancing cancer in the right breast much more conspicuous (arrow).

## Terminology

A standardized terminology was developed through the ACR lexicon [3]. A *focus* is defined as a punctate nonspecific area of enhancement and usually is less than 5 mm, too small to be further characterized (Figure 2). A focus has a small likelihood of malignancy; it was found to be less than 3% in 1 study [4]. A *mass* is a space-occupying lesion, which has a correlate on nonenhanced T1- and T2-weighted (W) images (Figure 3). *Nonmasslike enhancement* (NME) is defined as an area, not a space-occupying mass, whose internal enhancement results in a pattern discrete from the surrounding parenchyma, often interspersed with fat or normal tissue (Figures 4 and 5). No correlate is identified on noncontrast T1- and T2-W sequences. *Kinetics* refers to the plot of signal intensity (SI) of a lesion over time, after contrast injection. This is divided into the *initial phase*, which occurs in the first 2 minutes of the injection, and *delayed phase*, 2-10 minutes, which may be *persistent* (type I): progressive, continued increase in contrast enhancement over time (6% malignant) (Figure 6); *plateau* (type II): the SI does not change over time, (64% malignant); and washout (type III), where SI decreases after peaking (87% malignant) (Figure 3) [5]. When assessing the kinetics of a lesion, only the most suspicious enhancement should be reported, because there may be significant heterogeneity to the enhancement.

## Benign Masses

Benign tumours enhance on breast MRI. They tend to enhance in a more gradual and less intense fashion than malignant tumours, but there is considerable overlap. Empiric measurements have been used, including maximum rate of enhancement (slope of enhancement uptake) and increase in signal intensity after contrast agent administration [2, 5–8]. Typically, benign lesions on breast MRI have a gradual enhancement pattern and smooth, well-circumscribed margins [3]. The reader is referred to many comprehensive textbooks on this subject, because this review article cannot encompass the description of all benign lesions shown on MRI. The most common benign neoplasm of the breast is the fibroadenoma, which enhances to a variable extent on breast MRI. The enhancement curves are usually continuous or plateau. On noncontrast T2-W images, SI varies according to fluid content; more cellular and myxomatous lesions often seen in younger patients are high in

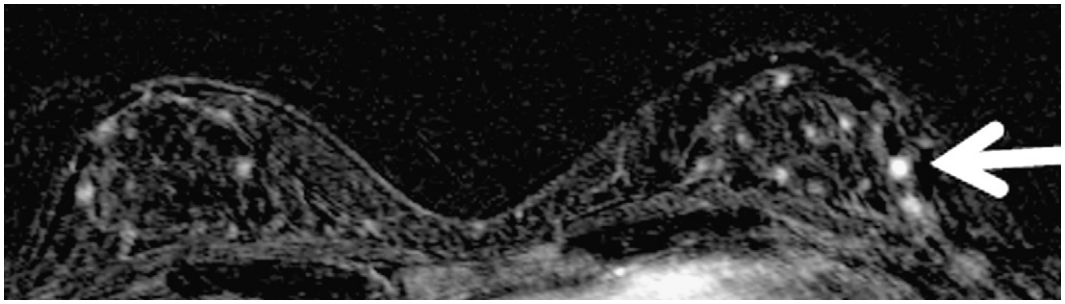

Figure 2. Foci in a high-risk patient on annual screening magnetic resonance imaging (MRI). Axial subtracted gadolinium-enhanced image, demonstrating multiple small enhancing foci in both breasts; the most prominent is seen in the left lateral breast (arrow). All foci remained stable on MRI for several years.

signal, whereas less cellular and sclerotic lesions, seen in older patients, may have low or intermediate SI [9]. On T1 contrast-enhanced images, fibroadenomas are usually round, oval, or lobulated, with smooth, circumscribed margins. Cellular, myxomatous fibroadenomas show uniform and homogenous enhancement. Of enhancing fibroadenomas 40%-60% contain nonenhancing septations, which, if seen, are diagnostic with up to >95% certainty (Figure 6) [10]. When there is no enhancement, there is an almost 100% certainty of benignity [9]. Papillomas are solitary or multiple: when solitary, they are typically located adjacent to the nipple-areolar complex and appear as enhancing, well-circumscribed, subareolar masses, and 50% are associated with duct ectasia [9, 11, 12]; when multiple, they tend to be more peripherally located and bilateral [9, 13]. Their enhancement pattern is usually gradual or plateau. Cysts are the most common lesion seen on MRI. They are well circumscribed, of high SI on T2-W images, low on T1-W images before contrast, unless there is high protein or blood content, when they may be of high SI on T1. Cysts do not enhance; however, when cysts are inflammatory, they will demonstrate rim enhancement of the cyst walls, which may be confused with the rim enhancement of a malignant tumour. A second-look ultrasound (US) will easily confirm their cystic nature. Biopsy cavities have inflammatory changes and may also simulate rim-enhancing lesions, but the history of recent biopsy or surgery is essential to avoid overcalling these lesions (Figure 7).

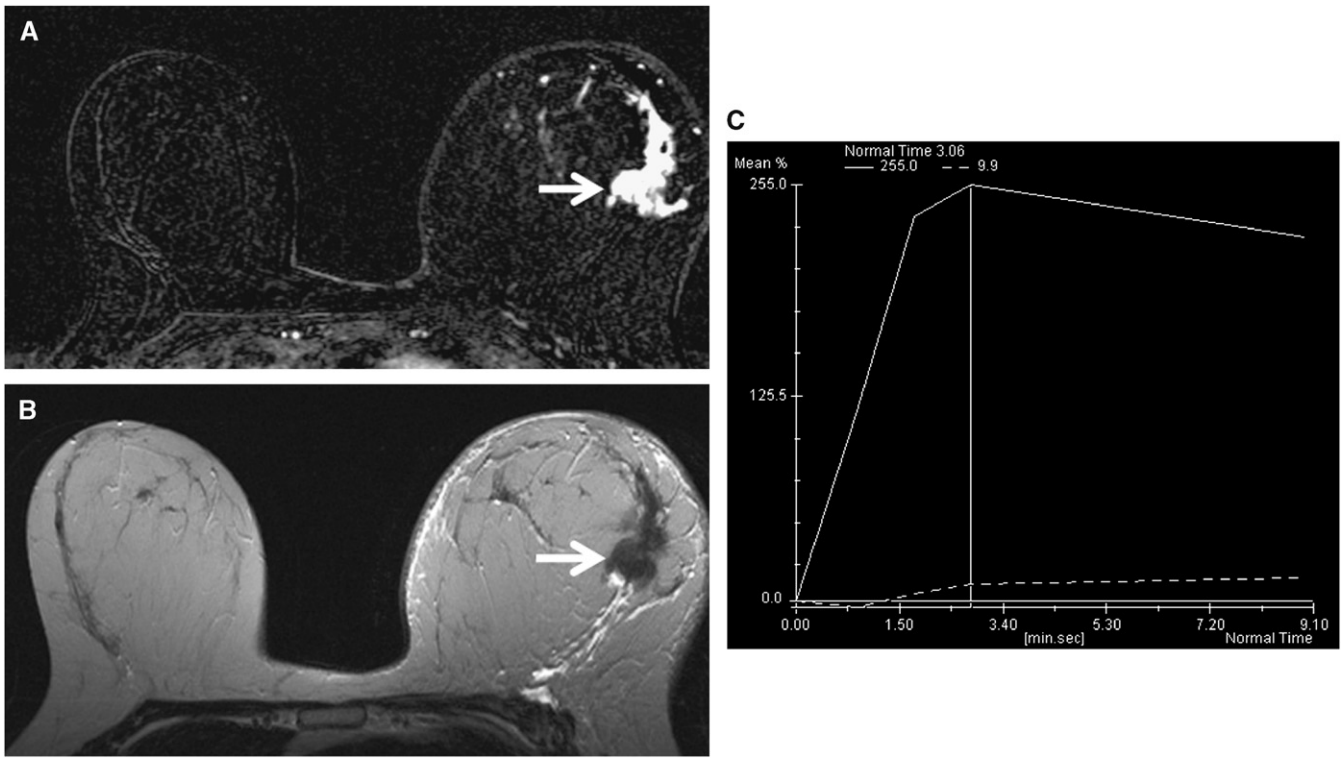


Figure 3. A 56-year-old woman with an enhancing breast mass. (A) Axial gadolinium enhanced subtracted T1 WI at 2 minutes, showing marked enhancement of a mass in the left breast at 3 o'clock (arrow). (B) Axial T2 WI at the same location, showing a low signal intensity space-occupying lesion, with irregular, angular margins. (C) Enhancement curve through the lesion, demonstrating malignant kinetics, with early intense enhancement greater than 250% by 2 minutes and washout after 3 minutes.

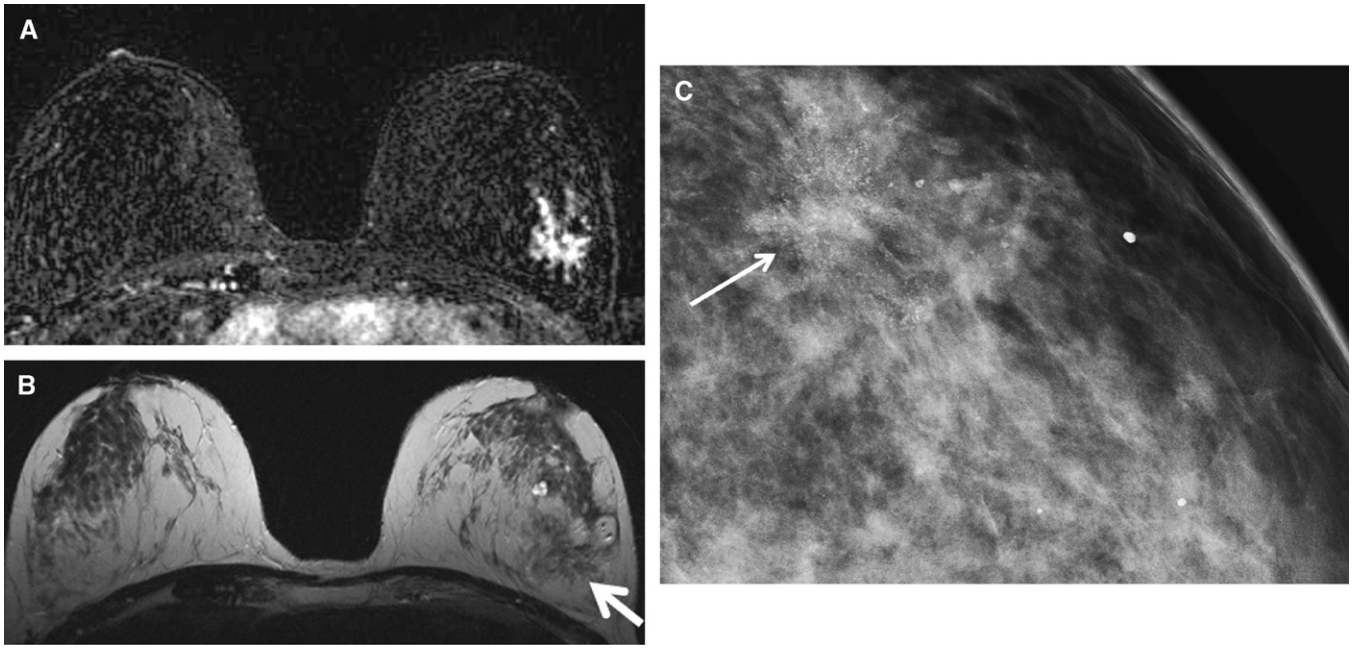


Figure 4. A 58-year-old woman with nonmass enhancement. (A) Axial gadolinium enhanced image with subtraction, 2 minutes after injection, showing an irregular enhancing lesion in the left breast at 3 o'clock. (B) Axial T2 WI, demonstrating no mass-displacing parenchyma at the same site (arrow). (C) Corresponding magnified mammographic image, showing the pleomorphic calcifications at the site of nonmass enhancement (arrow); biopsy of the area yielded intermediate grade ductal carcinoma in situ.

Fat necrosis is a common lesion seen on MRI, which occurs after loss of the vascular supply from surgery or trauma. The MRI appearance of fat necrosis is characteristic; it consists of a mass of low SI on T2-W, high signal on T1-W sequences without fat suppression, and low signal on T1-W with fat suppression. Rim enhancement of the fat is often identified and usually consists of a thin rim of enhancement, which corresponds pathologically to a giant cell granulomatous reaction [14]. The enhancement curves of the lesion may be deceptive and may demonstrate washout but are variable, with plateau and gradual curves also shown. Enhancing septations may also be shown (Figure 8).

Lymph nodes are part of the normal anatomy of the breast. They are most commonly seen in the axilla and axillary tail but may be seen in other parts of the breast. Normal lymph nodes are classically identified by their high T2 signal, reniform shape, and well-circumscribed margins, with a fatty hilum (see Table 1). They may enhance markedly with contrast (Figure 9). It is important to confirm that they are lymph nodes, if these features are not present, then

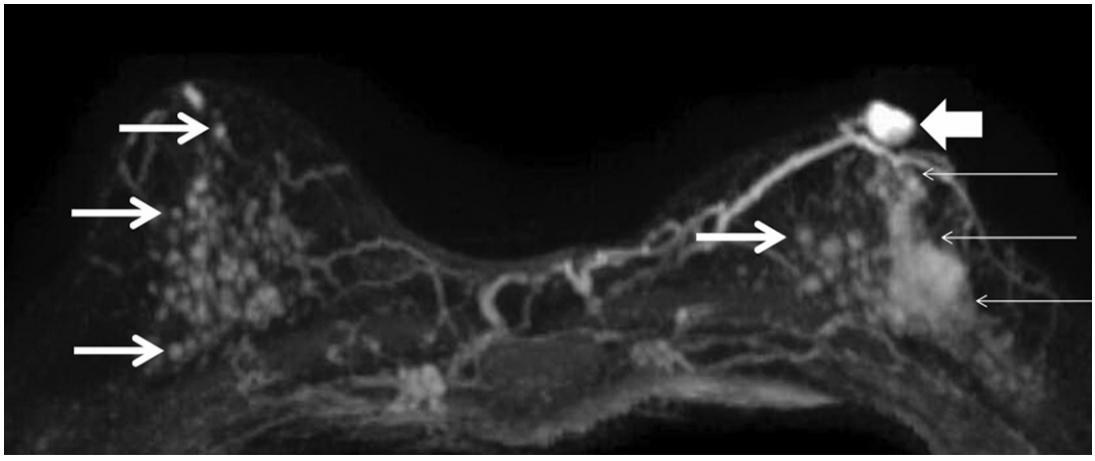

Figure 5. A 54-year-old woman, with biopsy-proven ductal carcinoma in situ (DCIS) in her left breast, who underwent preoperative breast magnetic resonance imaging, demonstrating nonmasslike enhancement in her left breast (long thin arrows) that extended from the chest wall to behind the nipple; a mammographically occult mass in the same breast (short thick arrow) in the retroareolar region; and multiple, enhancing foci in both breasts (white arrows). Left breast ultrasound-guided biopsy confirmed that the retroareolar left breast mass was a 1.2-cm invasive ductal cancer, and the foci in the left breast at mastectomy were benign proliferative changes, the extent of DCIS correlated with the nonmass enhancement.

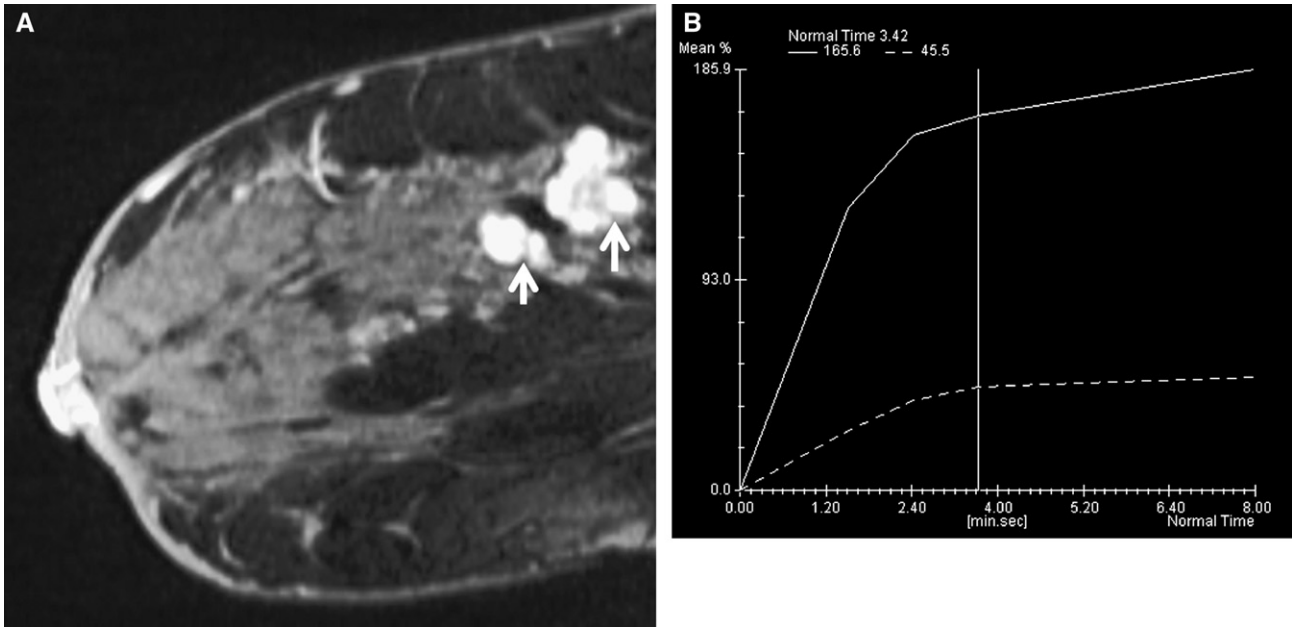


Figure 6. A 50-year-old woman with a lobulated mass with benign enhancement and internal nonenhancing septations on magnetic resonance imaging. (A) Sagittal contrast-enhanced T1 fat-suppressed image of the right breast, showing 2 enhancing masses at 12 o'clock, which contain nonenhancing septations within the lesions (arrows), characteristic for fibroadenomas. (B) Kinetic curve of the larger lesion, demonstrating gradual (type 1) enhancement, consistent with a benign lesion. Ultrasound biopsy confirmed the diagnosis.

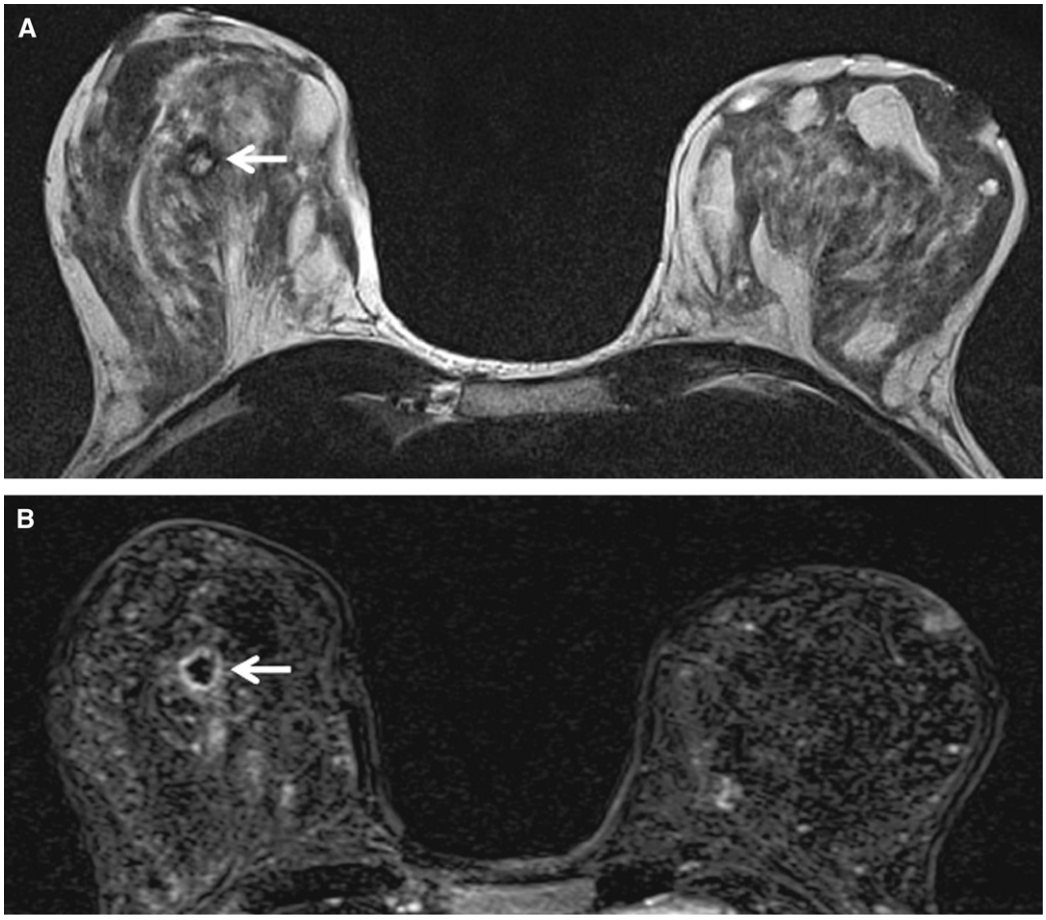


Figure 7. A 42-year-old woman after stereotactic biopsy for ductal carcinoma in situ. (A) Axial T2 image, showing a high signal centre of the right biopsy hematoma at 12 o'clock, with surrounding low signal rim or inflammatory reaction (arrow). (B) Axial subtracted 2-minute enhanced image at the same level, showing the rim of enhancing inflammatory tissue surrounding the biopsy cavity (arrow), which can simulate malignancy.

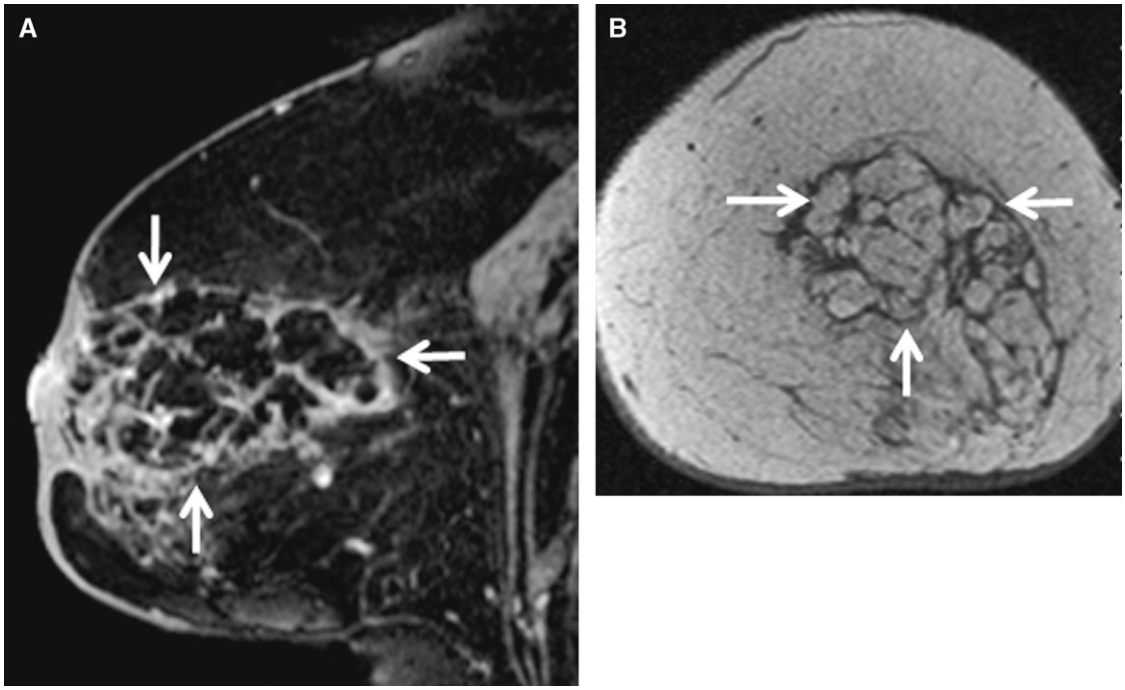


Figure 8. A 64-year-old woman with a history of prior right breast cancer and left reduction mammoplasty with clinically suspicious palpable mass in the left breast. (A) Contrast-enhanced T1 sagittal image with fat suppression, demonstrating a central 5-cm mass with multiple enhancing septations. (B) Coronal T1 image without fat subtraction of the same lesion, showing that the internal signal is isointense to fat, which corresponds to a large area of fat necrosis.

the enhancing lesions should be categorized as BI-RADS 3 (Breast Imaging Reporting and Data System), and followed up with MRI to avoid missing small enhancing cancers (Figure 10). Abscess and mastitis will cause significant inflammation in the breast and enhance markedly with contrast. This may easily be confused with malignancy (Figure 11). Pseudoangiomatous stromal hyperplasia may have a mass appearance and show enhancement on MRI [15, 16].

For lesions with definitely benign features, such as fat necrosis in which the central fat is clearly identified, fibroadenomas with nonenhancing septations, classic lymph nodes, and inflammatory cysts, then the breast MRI can be classified as a BI-RADS 2, as one would for mammography and breast US, and no further follow-up would be required. If some features suggest a benign entity, but a definite benign diagnosis cannot be made, then a BI-RADS 3 classification would be assigned, and a follow-up MRI, usually in 6 months time would be recommended to confirm stability. Typical lesions that are called BI-RADS 3 are well-circumscribed masses with gradual (type 1 curves) enhancement but with no nonenhancing septations, a solitary focus in a high-risk patient, and non-masslike enhancement that is likely glandular but found to be asymmetric. It is helpful to remember to correlate with prior mammograms and a second-look US in determining if the lesion remains BI-RADS 3; for example, a mammogram may demonstrate stable glandular tissue at a site of NME, which confirms that it is benign, and, in fact, BI-RADS 2. The assignment of a BI-RADS 3 lesion should be reserved for lesions with a high likelihood of benignity, with a less than 2% chance of malignancy, as with other breast imaging studies.

Table 1
Benign breast magnetic resonance imaging features

- Fatty hilum or fatty containing lesion
- Nonenhancing internal septations
- Rim-enhancing cyst

## Malignant Masses

The most common invasive cancers manifest on MRI as enhancing masses, with spiculated, irregular, or lobulated margins. The internal enhancement is heterogenous and may demonstrate rim enhancement, a feature highly predictive of malignancy [10]. Cancers tend to have early rapid initial enhancement that peaks by 2-3 minutes and then plateau (type II curve) or washout (type III curve). On non-fat-suppressed T2-W images, breast cancers tend to be hypointense relative to glandular tissue, which may distinguish them from benign lesions that show ‘‘malignant’’ type enhancement, such as lymph nodes, typically high SI on T2-WI (Figure 9) [1].

## Benign Non-masslike Enhancement

Nonproliferative fibrocystic changes, which are not associated with an increased risk of breast cancer, consist of cysts of varying sizes, stromal fibrosis, and apocrine metaplasia. Proliferative fibrocystic changes include hyperplasia without atypia, papillomas, and sclerosing adenosis. Atypical

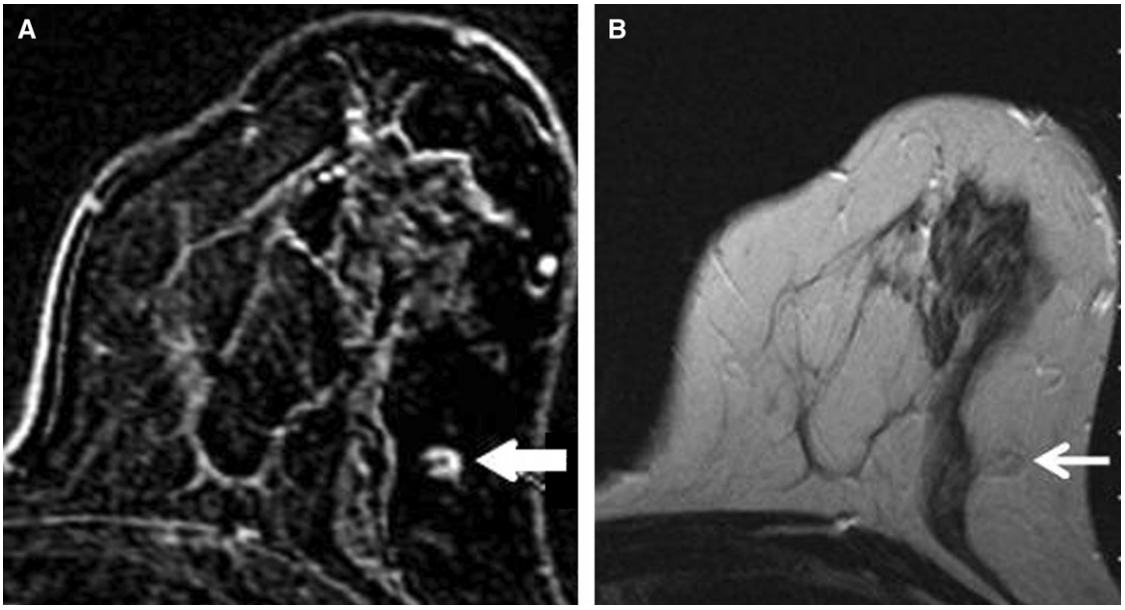


Figure 9. A benign intramammary lymph node. (A) Axial 2-minute enhanced subtracted T1 image, showing an enhancing reniform-shaped lesion at 3 o'clock in the left breast (arrow). (B) Axial T2 sequence at the same level, demonstrating the high-signal fatty hilum and rim (arrow) of intermediate signal intensity, which confirm the typical appearance of a benign lymph node.

hyperplasia (atypical lobular and atypical ductal hyperplasia) included in the spectrum of fibrocystic disease are associated with an increased risk of breast cancer [17]. All of these entities may be identified on MRI, usually as NME, and enhance to a variable extent. Sclerosing adenosis often shows patchy or diffuse NME [18].

## Malignant Non-masslike Enhancement

The 2 malignant diagnoses that may have NME are ductal carcinoma in situ (DCIS) and lobular carcinomas. A recent study demonstrated that DCIS is visualized by direct uptake of gadolinium within neoplastic mammary ducts, collecting within the ducts [19], in comparison with invasive tumours, which depend on tumour angiogenesis. This direct

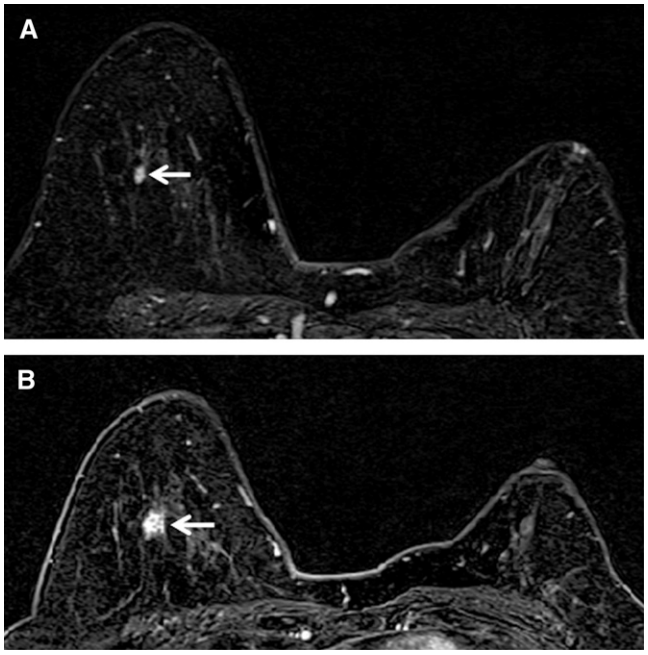


Figure 10. Small invasive carcinoma mistaken for a lymph node. (A) Axial subtracted T1 image of an oval-shaped lesion (arrow), in a high-risk patient, presumed to be a benign lymph node. However, the margins are slightly irregular, and the lesion was not seen on T2 WI, nor was a definite fatty hilum seen. The patient presented 9 months later with a new mammographic finding at the same location. (B) Repeated magnetic resonance imaging, demonstrating enlargement of the lesion with poorly defined margins (arrow); stereotactic biopsy diagnosed a small invasive ductal carcinoma.

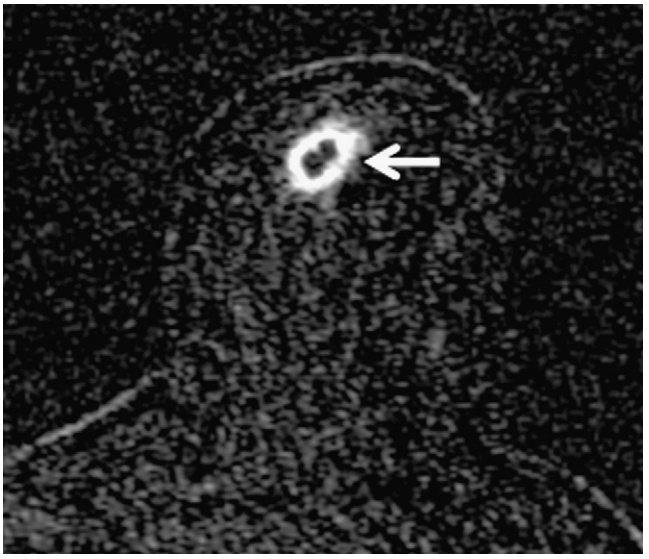

Figure 11. Mastitis in a high-risk patient. Axial T1 2-minute enhanced subtracted image of the left breast, demonstrating a rim-enhancing lesion adjacent to the nipple, suspicious for cancer; biopsy diagnosed mastitis.

visualization allows for good demonstration of the extent of DCIS. It has been shown that higher-grade DCIS is more likely to enhance on MRI, whereas lower-grade DCIS is not always visualized [20]. Results of several studies demonstrated an increased sensitivity of MRI when compared with mammography for detection of DCIS [20–23]. In 1 study, of 167 women with a final surgical pathology diagnosis of pure DCIS, who had undergone both MRI and mammography, 93 of these cases (56%) were diagnosed by mammography and 153 by MRI (92%) ($P < .0001$). Of the 89 high-grade DCIS, 43 (48%) were missed by mammography but were diagnosed by MRI alone; all 43 cases missed by mammography were detected by MRI [20].

Lobular cancers grow by a diffuse growth pattern (linear infiltrating pattern of growth) and may not have a mass appearance. These infiltrating cells may be fed by means of diffusion of pre-existing fibroglandular capillaries, which is why they may demonstrate weak angiogenic activity and may show a more ''benign'' enhancement pattern (Figure 12). One should not rely on kinetics for nonmass enhancement: although some malignant lesions will demonstrate type II and III curves, many will not.

The distribution of NME is important and can be compared with the distribution of calcifications in mammography. A segmental or regional distribution of NME should raise suspicions for malignancy, just as it would with this pattern with calcifications. Similarly, linear or ductal enhancement is concerning for DCIS. In this regard, sagittal images and reconstructed maximum intensity projection images are very helpful to assess the extent of enhancement. Any asymmetric pattern of enhancement should be considered worthy of investigation (Figure 12), first by correlating with the mammogram, because it may correspond to a new cluster of calcifications, or an asymmetric density. If a mammographic correlate is identified, then a stereotactic biopsy should be performed. If no mammographic correlate is found, then a second-look US should be obtained. If a sonographic correlate is identified, then an US-guided biopsy should be done. If there is no sonographic correlate found, then an MRI-guided breast biopsy must be performed.

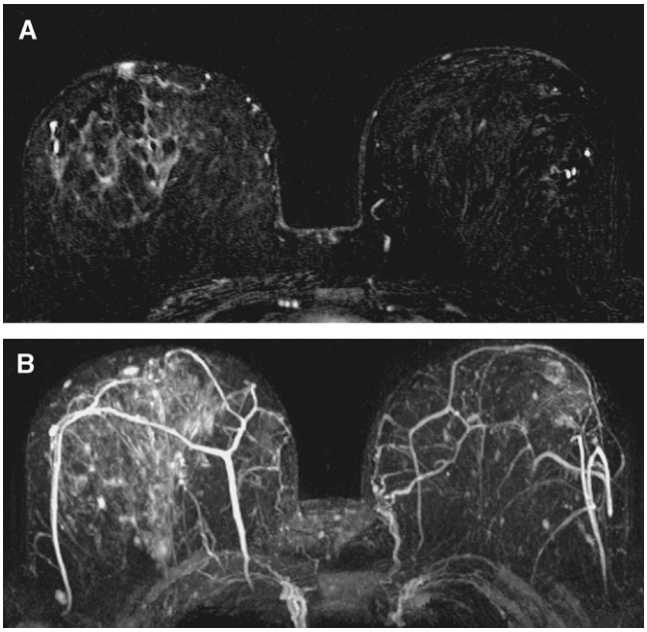


Figure 12. A 54-year-old woman with right invasive lobular cancer. (A) Axial T1 2-minute enhanced subtracted image, showing mild non-mass-enhancement in the right lateral and central breast with no mass. (B) Axial maximum intensity projection at 9 minutes, showing more diffuse gradual enhancement of the right breast. The asymmetric enhancement is helpful in making the diagnosis; the kinetic pattern is not helpful. The diagnosis was confirmed on ultrasound-guided breast biopsy (not shown).

## Computer-Aided Detection

Computer-aided detection (CAD) programs have been introduced into clinical practice to help discriminate between benign and malignant lesions, and help improve specificity of breast MRI. They are being increasingly used in clinical practice [24, 25]. CAD programs for breast MRI provide automated lesion kinetic information. In 1 study, of 154 consecutive lesions (41 malignant, 113 benign) in 125 women, false-positive rates were reduced by 23.0% at the 100% enhancement threshold ($P = .02$) when compared with the initial interpretation of radiologists [25]. In another study, of 125 lesions (42 malignant and 83 benign), no significant differences in the initial phase of enhancement were detected, but a significant difference in delayed kinetics categorized by most suspicious enhancement types was found ($P = .0005$) [26]. The best CAD parameters to distinguish benign from malignant lesions have not yet been established, but these studies point to the improved specificity of breast MRI with the use of CAD. Practically, CAD provides a visual map to demonstrate the most suspicious enhancement and may be particularly helpful in a patient with multiple enhancing lesions. With 1 image, the most suspicious lesions may be clearly identified, which permits easier determination of the need for subsequent management (Figure 13). This will usually include further evaluation with MRI-directed US and biopsy. The use of CAD, therefore, may improve efficiency of reading breast MRIs and reduce the number of false-positive results.

## Overall Assessment

The positive predictive values (PPV) for MRI-detected lesions are reported in the order of 25%, with a range of 15%-40% [27, 28]. A recent meta-analysis of 19 studies showed that PPV ranged from 19%-100% for detection of multifocal and multicentric disease [29]. For evaluation of contralateral disease in patients with recently diagnosed breast cancer, the PPV of MRI is 25% [30]. In women who are at high risk, the PPVs are higher: 35%-64% [31, 32].

In multivariate analysis of combinations of features, masses of 1 cm or larger with heterogeneous enhancement and irregular margins had a 68% probability of malignancy [33]. Masses of 1 cm or larger, with smooth margins and homogeneous enhancement, had the lowest predicted

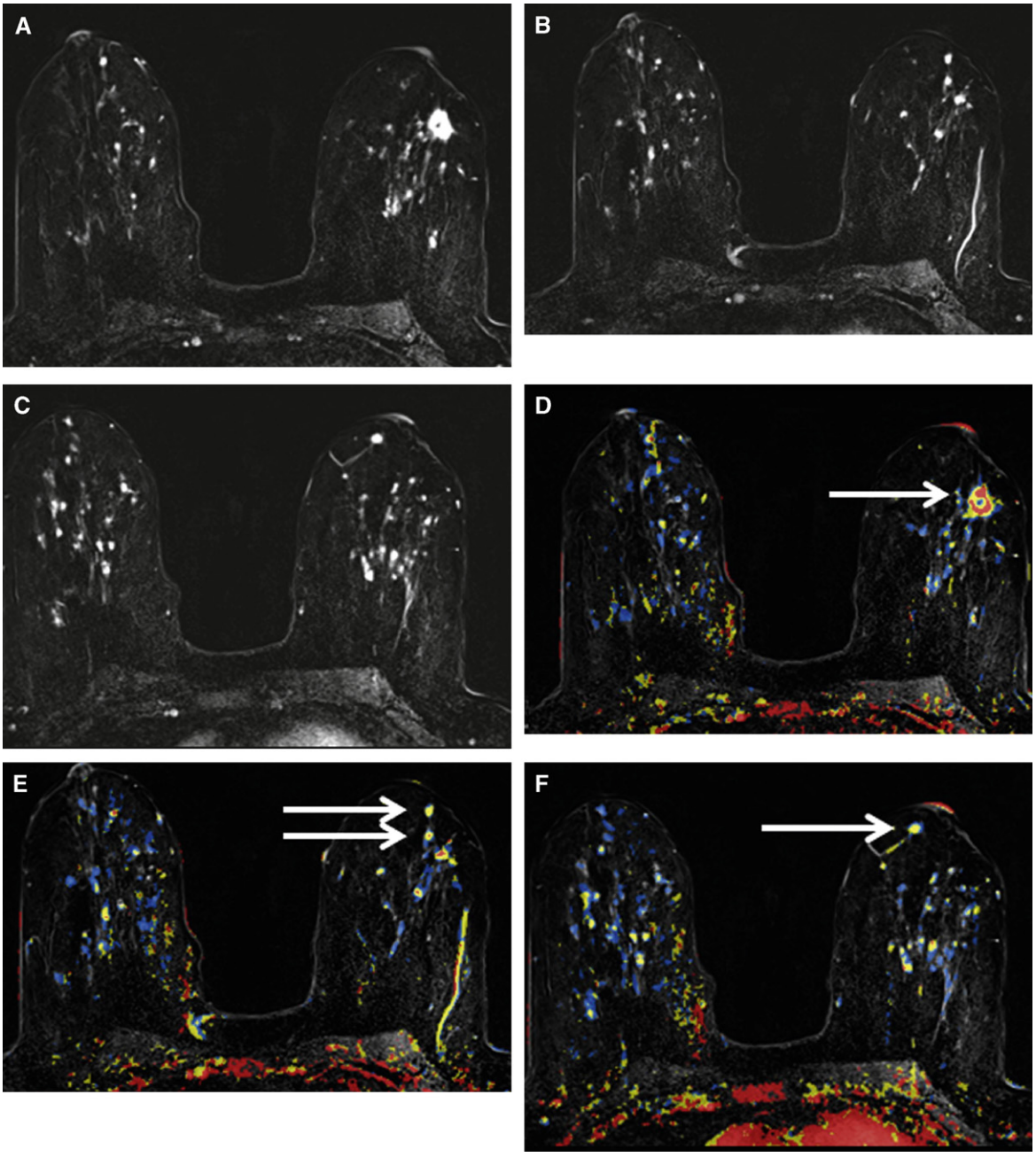


Figure 13. A 52-year-old patient with left invasive ductal cancer and preoperative staging breast magnetic resonance imaging, where computer-aided detection (CAD) permits a quick visual map of lesions, which warrants further workup. (A) Axial T1 2-minute enhanced subtracted image, demonstrating a spiculated enhancing lesion in the left breast at 3 o'clock, which corresponds to the known cancer. (B, C) Axial slices in the same sequence, showing multiple enhancing lesions in both breasts as well as several adjacent to the biopsy proven cancer, difficult to assess on a per lesion basis. (D) Axial enhanced image with CAD software, showing the rim enhancing cancer, which is red with CAD, in keeping with the most suspicious enhancement curve of cancer. The other enhancing lesions in both breasts are blue, in keeping with benign enhancing foci. (E) CAD image of 2 adjacent enhancing lesions that are yellow, in keeping with plateau (type II) curves, which merit further evaluation with second-look ultrasound (US). (F) A third CAD image, demonstrating another yellow lesion at 9 o'clock in the retroareolar location, is concerning for multicentric disease. Second-look US and biopsy of all 3 lesions were diagnostic for benign papilloma and fibroadenomas, which allows breast conservation surgery. This figure is available in colour online at http://carjonline.org/.

probability of malignancy, of 3% [33]. In a study of 100 consecutive patients with MRI-guided biopsy, overall PPV for MRI-detected lesions was 25%, with carcinoma found in 15 of 60 masses (25%) vs 10 of 40 nonmass lesions (25%); most malignant masses (73%) were infiltrating carcinoma, whereas most malignant nonmass lesions (90%) were DCIS [34]. The features with the highest PPV were spiculated margin (80% carcinoma), rim enhancement (40%), and irregular shape (32%) for mass lesions and segmental (67%) or clumped linear and ductal enhancement (31%) for nonmass lesions (see Table 2) [34]. In this same study, visually assessed kinetic patterns were not significant predictors of

Table 2
Suspicious breast magnetic resonance imaging features

- Spiculated margin
- Rim enhancement
- Irregular shape for mass lesions
- Segmental or clumped linear and ductal enhancement for nonmass lesions

carcinoma, but washout was present in 70% of infiltrating carcinomas vs 9% of DCIS lesions ($P < .01$) [34]. Carcinoma was present in 17 of 88 lesions (19%) classified as suspicious vs 8 of 12 lesions (67%) classified as highly suggestive of malignancy ($P = .001$) [34]. In another study, ductal enhancement accounted for 21% of MRI-detected lesions that had biopsy and had a PPV of 26% [18]. Combinations of BI-RADS lesion descriptors can predict the probability of malignancy for breast MRI masses but not for NME. A study of 258 lesions in 196 women showed that BI-RADS descriptors and size were not predictors of malignancy in NME [33]. Further research focused on predictive features of NME is needed.

## Biopsy of MRI-Detected Lesions

When an enhancing lesion is identified on the MRI, the first job of the radiologist is to determine if it looks benign. If no definite features of a benign lesion are present, then a definite diagnosis must be obtained, usually with image-guided biopsy. Once a lesion is identified as suspicious or not definitely benign, the radiologist must investigate further, with the help of other breast imaging. The first step is to correlate with the most recent mammograms, preferably within the past 6 months of the breast MRI. If the enhancing MRI lesion is identified on the mammogram and appears definitely benign, for example, lymph node or fat necrosis, then no further investigation is required. If the lesion is seen on the mammogram and is not definitely benign, then a stereotactic biopsy may be performed. In some cases, MRI lesions may correspond to asymmetric densities or masses on the mammogram and can be successfully targeted for stereotactic biopsy (Figure 14).

All patients should have a recent mammogram available to correlate with the breast MRI. In the high-risk screening population, annual breast MRIs are obtained at the same time as an annual mammogram or are staggered at 6-month intervals. The mammograms should be available at the time of the breast MRI reporting to allow for immediate correlation of the MRI with the mammogram, which is useful to demonstrate a benign intramammary lymph node or to show a stable enhancing mass on serial mammograms of a benign lesion. Having the mammogram available also allows for correlation in case of biopsy; if the enhancing lesion corresponds to a mammographic finding it allows for stereotactic guidance (Figure 14).

If the lesion is not seen on the mammogram, then the next step is to perform a ''second-look'' US. The term second-look US is commonly used, but other terms that may be more appropriate are ''targeted ultrasound,'' or MRI-directed

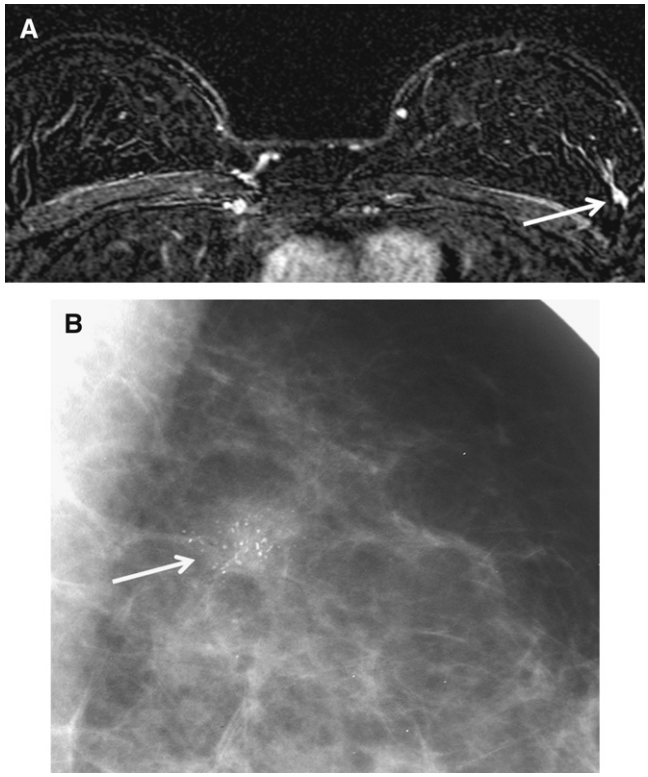


Figure 14. A 34-year-old high-risk patient with a mammographic abnormality that corresponded to the magnetic resonance imaging lesion. (A) Axial contrast enhanced subtracted T1 WI at 2 minutes, showing a linear, irregular area of nonmass enhancement at 2 o'clock in the left breast (arrow). (B) Magnified mediolateral oblique view of the left breast, demonstrating suspicious microcalcifications at the same site (arrow), which permitted a diagnosis of ductal carcinoma in situ with stereotactic biopsy. A mammogram 8 months earlier had been normal at that site.

ultrasound.'' An MRI-directed US allows greater characterization of the lesion and may diagnose a definitely benign lesion, such as a benign intramammary lymph node, inflammatory cyst, or fibroadenoma, or may serve to identify the suspicious lesion and provide the target for US-guided biopsy. It is always easier, cheaper, and more comfortable for the patient to perform an US-guided biopsy if a sonographic correlate is identified. More than 50% of suspicious enhancing lesions on MRI are seen with targeted ''second-look'' US [35, 36]. It is important to emphasize to referring physicians and patients that a ''second-look'' US is a targeted breast US directed to the MRI abnormality and may yield new findings, regardless of whether the patient underwent a breast US before the MRI was performed, because this area may not have been imaged on the first breast US. If the enhancing lesion is a mass, then the likelihood of it being detected is about 65% and is even higher (85%) if the lesion is malignant [35, 36]. Even a 6-mm mass may be clearly identified with targeted US (Figure 15). Conversely, if the lesion consists of NME, then the likelihood of it being identified with US is much lower, in the range of 11%-31% [35–37]. Size matters, and the larger the lesions, the more likely they are to be seen at ''second-look'' US. In 1 study, of 202 lesions, 63% of masses 5-10 mm, 71% of masses 11-20 mm, and 88% of

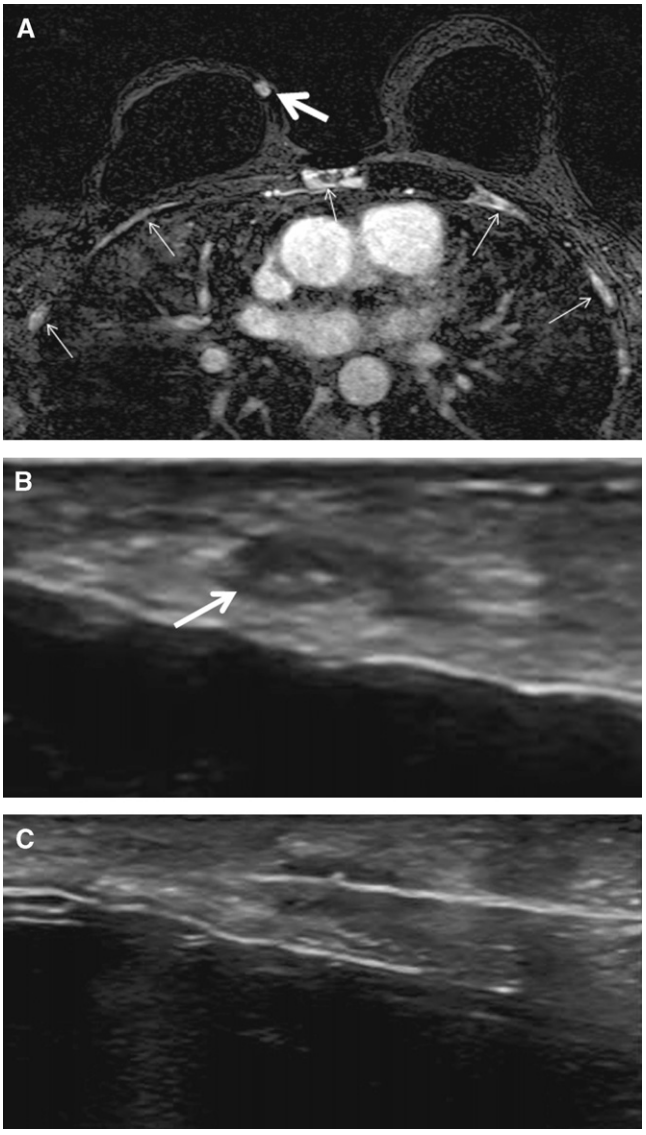


Figure 15. A 65-year-old woman with a primary carcinoma of unknown origin. (A) Magnetic resonance imaging, demonstrating a 6-mm enhancing mass in the right breast (thick arrow) on axial T1 subtracted image. Numerous bony metastases are evident in the thorax (thin arrows). (B) A second-look ultrasound (US) showed a small heterogenous lesion (arrow) overlying the right breast implant. There were minimal suspicious features. (C) A 14-gauge US-guided biopsy provided the diagnosis of invasive lobular carcinoma.

masses larger than 21 mm had sonographic correlates; for nonmass lesions, no cases of NME smaller than 20 mm were found sonographically, whereas 22% of NME $>$ 21 mm had an US correlate [35]. In another recent study, of 519 suspicious MRI-detected lesions in 361 women, 13% of NME 6-10 mm in size, 25% of 11-15 mm NME lesions, and 42% NME $>$15 mm were seen with second-look US [36]. Interestingly, in this study, BI-RADS 5 lesions were much more likely to be seen with US than BI-RADS 4 lesions: for NME, 75% BI-RADS 5 vs 26% BI-RADS 4 lesions were identified with US, whereas for masses 81% vs 59% were seen [36]. For clumped NME, 84% had a sonographic correlate, compared with only 16% of nonclumped NME [36]. Thus, increasing size of the lesion, increased level of suspicion, and clumped NME are all features that help predict whether the second-look US will be positive.

The malignant lesions with successful sonographic correlation tend to present with subtle sonographic findings [35]. The second-look US should use landmarks to identify the area, such as the distance from the nipple, distance from the chest wall, location, that is, for example, o'clock or quadrant. A careful second-look US by a radiologist familiar with breast MRI is critical to the success of the study. A feature of malignant-enhancing masses on second-look US is that the masses may often not demonstrate suspicious or typical malignant features, as defined by the Stavros criteria [38]. For example, in a recent study, of 158 consecutive patients with 202 suspicious enhancing breast lesions, 33% of lesions seen sonographically did not demonstrate any suspicious features [35]. The only findings were poorly circumscribed margins and increased vascularity, secondary

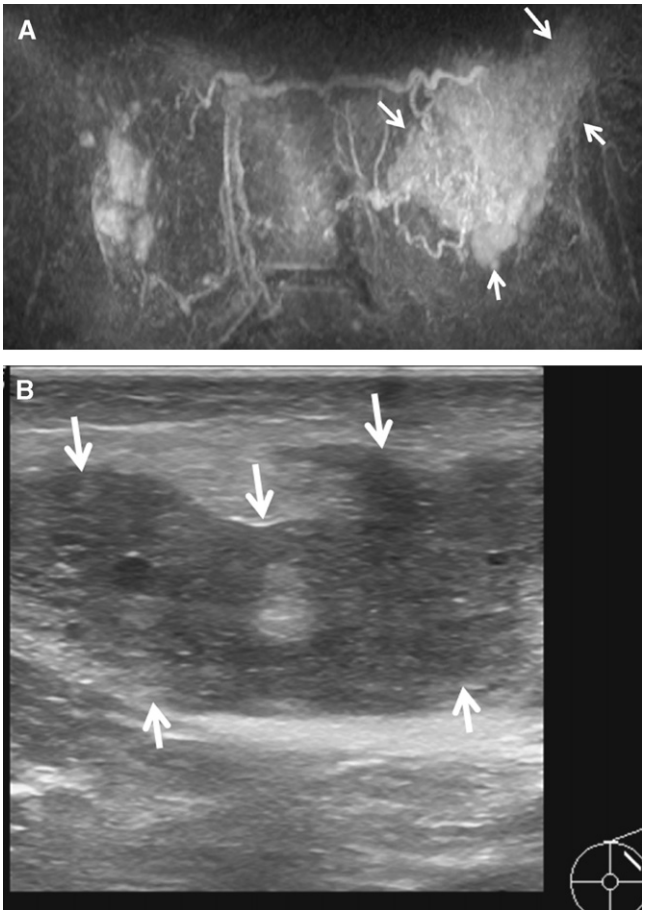


Figure 16. A 37-year-old lactating woman who presented with a palpable mass in left axillary tail. Ultrasound (US) was initially called normal. (A) Coronal 3-dimensional maximum intensity projection image of her breast magnetic resonance imaging, showing asymmetric enhancement in the entire left upper outer quadrant (arrows), which corresponded to the palpable mass. (B) Second-look US, demonstrating a large hypoechoic area (arrows) that is distinct from the normal hyperechoic glandular tissue. US-guided biopsy of the abnormal area yielded the diagnosis of high-grade ductal carcinoma in situ, which was confirmed at mastectomy.

features of malignancy. The radiologist performing the second-look US, therefore, must have a high level of suspicion when evaluating US of an enhancing mass and should proceed to biopsy even when definite suspicious features are not present (Figure 15).

Any suspicious mass seen on US requires further evaluation with US-guided biopsy to confirm malignancy and avoid overcalling cancer. NME that is seen on US also requires US-guided biopsy to confirm or exclude malignancy, with US-guided biopsy (Figure 16). When assessing the breast MRI, to avoid unnecessary delay in surgery, only lesions likely to be seen on second-look US should be targeted. In our experience and as supported by the literature, NME lesions smaller than 10 mm have a low likelihood of sonographic correlate (0%-13%) [35, 36] and may not warrant the time or expense of looking. If the small NME lesions are still suspicious, then it is probably advisable to proceed directly to MRI-guided breast biopsy (Figure 17).

## US-Guided Breast Biopsy

If a suspicious enhancing lesion is identified with targeted US, every attempt should be made to proceed immediately with biopsy. It is inadvisable to have the patient return for a third visit, where another radiologist may not identify the same lesion or have the same level of suspicion as the original reporting radiologist. At our institution, we allow for extra time to perform the US-guided biopsy at the time of the second-look US, if needed. This is most efficient and accurate, and most convenient for the patient. When the lesion is larger than 5 mm, a 14-gauge biopsy needle is used to obtain the tissue with a minimum of 3 cores. However, if the lesion is smaller than 5 mm or consists of a very subtle hypoechoic area, then it may be advisable to proceed to vacuum-assisted biopsy, to avoid underestimation of the lesion [39]. At our institution, we use 14-gauge needles for most sonographic findings and reserve the vacuum-assisted biopsies for those lesions smaller than 5 mm, when the lesion may be completely removed by the biopsy and requires clip placement for localization. A clip should also be placed if there is any uncertainty about the accuracy of the sonographic correlate, and allows for correlation with the MRI after the procedure [36].

## MRI-Guided Breast Biopsy

Results of several studies have shown that masses that are seen on second-look US are more likely to be malignant than masses that are not seen with US. In 1 study, of 64 patients with 93 suspicious, nonpalpable, mammographically occult lesions evident on MRIs and recommended for biopsy, for which directed US assessment was performed, the likelihood of carcinoma was significantly higher among lesions with an US correlate (43% carcinomas) than lesions without an US correlate (14% carcinomas) ($P = .01$) [37] . However, this study highlights that, even when a lesion is not seen with second-look US, there is still a significant chance that it could be malignant. Results of other studies have shown that the incidence of breast cancer in sonographically occult enhancing MRI lesions is in the range of 25% in MRI biopsy series [27, 28]. To perform an MRI breast biopsy, the reader is referred to another recent article in *CARJ* by Price and Morris [40]. The main risk of breast MRI is of overcalling enhancing lesions. Simply recommending surgery for enhancing lesions may lead to unnecessary surgery, such as mastectomy. It is imperative that a tissue diagnosis be obtained when leading to a change in surgical management.

## When to Follow up or Ignore MRI-Detected Lesions

Not all MRI lesions can be classified as definitely benign or malignant. A small percentage of these lesions are classified as ‘‘probably benign,’’ or BI-RADS 3. The reported range is 10%-24% of breast MRIs [41−45]. Although accumulated experience with mammography has resulted in a goal of <2% cancer for mammographic lesions classified as BI-RADS 3, the rate of malignancy for MRI-equivalent BI-RADS 3 lesions has yet to be established [46]. A study in 2005 evaluated 79 of 473 women (17%) with probably benign MRI lesions in whom 2-year radiographic and clinical follow-up was available. In this group, 4 women (6%)

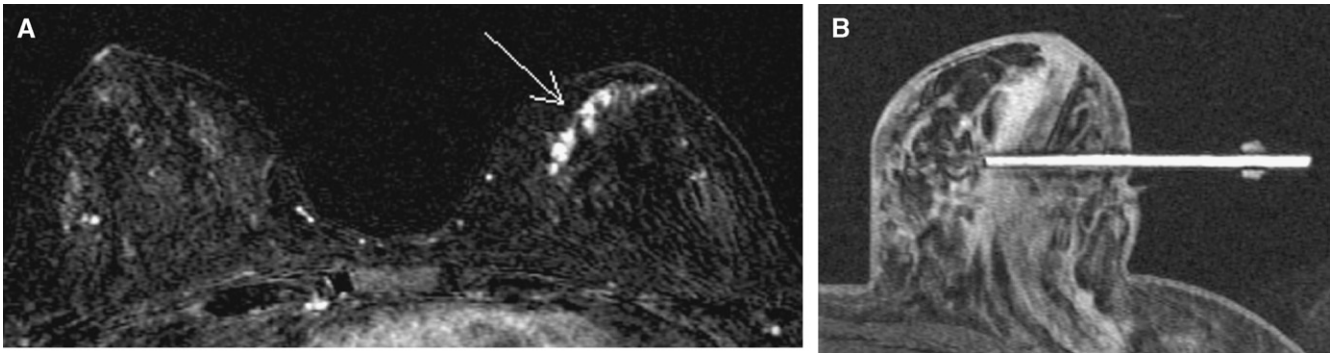


Figure 17. A 37-year-old woman with bloody left nipple discharge. (A) Axial contrast enhanced subtracted 2-minute T1 WI, demonstrating a linear region of nonmass enhancement at the 9-o'clock position in the left breast (arrow), suspicious for ductal carcinoma in situ (DCIS). Second-look ultrasound (not shown) only identified dilated lactiferous ducts. (B) A 10-gauge vacuum-assisted magnetic resonance imaging-guided breast biopsy at the posterior edge of the enhancement was diagnostic for intermediate grade DCIS.

Table 3
Principles of breast MRI reporting

- Be specific, if the lesion looks typically benign, BI-RADS 2
- If the lesion is probably benign but not confirmed on second-look US, then the follow-up with breast MRI in 6 months, BI-RADS 3. If the lesion disappears on follow-up, then return to normal. If the lesion persists, unchanged, then it is unclear for how long it should be followed up, probably for 2 years.
- If the lesion is suspicious, recommend biopsy, directed by correlation with mammogram and second-look US; perform MRI-guided biopsy if no correlate is found, BI-RADS 4 or 5
- Have the mammogram available at the time of the breast MRI reporting and correlate with MRI findings
- Expedite the "second-look" US and biopsy: no more than 7 days after the MRI if possible
- Communicate the findings to the referring surgeon effectively, eg, level of confidence, next step in management

BI-RADS = Breast Imaging Reporting and Data System; MRI = magnetic resonance imaging; US = ultrasound.

were diagnosed with breast cancer between 14 and 18 months after the initial MRI [41]. Liberman et al [43] published their experience of 89 patients with BI-RADS 3 lesions of a total of 367 patients (24%). They found malignancies in 9 women, 5 with DCIS and 4 with invasive cancer, for a total of 10% with malignancy. In their study, the median follow-up was 9 months (range, 1-18 months), and biopsy was precipitated mainly by progression on follow-up MRI [43]. In this study, a large number (24%) were classified as BI-RADS 3, and very likely the BI-RADS 3 rate of malignancy was high given that the population studied was predominantly high risk. Two more recent studies have shown that less common use of BI-RADS 3 (10%) resulted in a much lower rate of malignancy, of 0.9% [44, 45]. Careful use of BI-RADS 3, therefore, is strongly recommended, particularly in high-risk patients, in whom any enhancing lesion should be treated with suspicion.

The criteria for probably benign mammographic lesions may not apply to MRI. In patients with solitary, smooth, MRI-detected masses referred for biopsy in prior studies, the frequency of malignancy was 17%-44% [34, 47]. To date, a subset of MRI-detected lesions that have less than a 2% chance of being malignant have not been identified [43]. However, foci with 100% persistent enhancement have all been shown to be benign on follow-up [44]. Probably, in patients undergoing staging MRI with known cancer, an ipsilateral enhancing lesion smaller than 4 mm will likely be treated by breast radiation and can be safely ignored [48]. Conversely, a 4-mm focus in a high-risk patient undergoing screening should be followed up, particularly when it is the only lesion in the breast, because it may prove significant (Figure 9).

## Pitfalls in Analysis of Breast MRIs

Probably the greatest concern of referring physicians is the false-positive rate of breast MRIs. Overcalling a false positive on a breast MRI may lead to unnecessary surgery, such as mastectomy, when a simple lumpectomy would

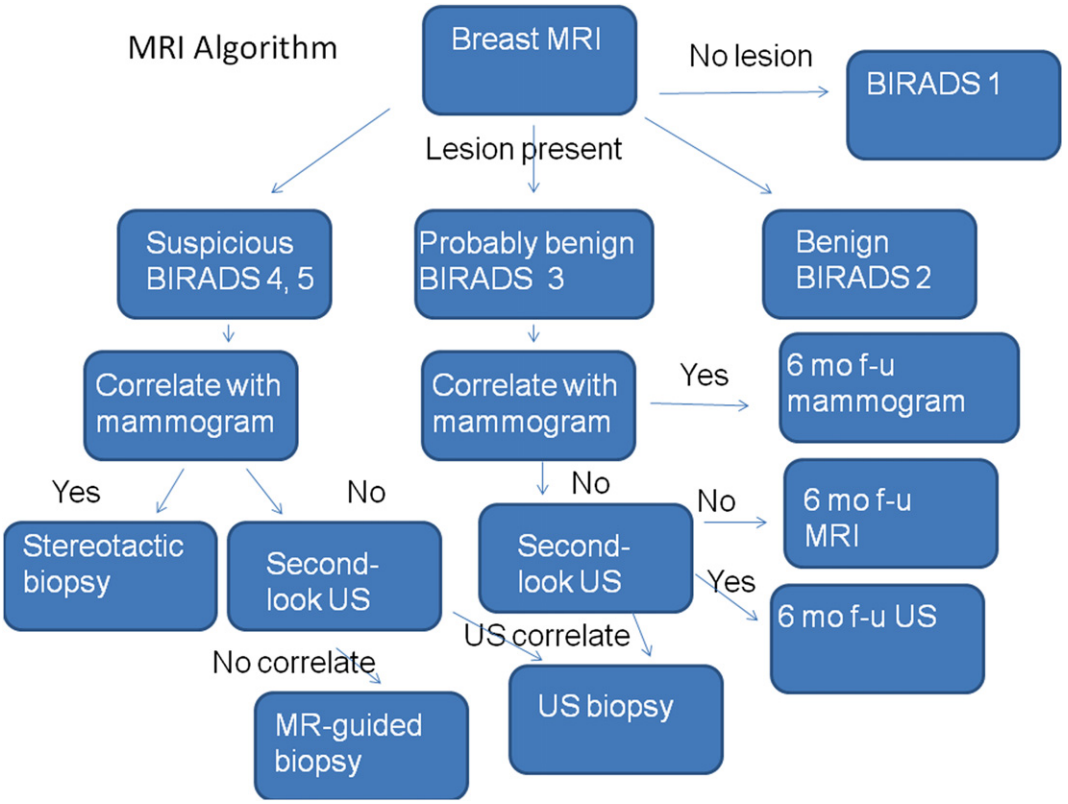


Figure 18. Algorithm for management of a breast magnetic resonance imaging (MRI)-detected lesion. BIRADS = Breast Imaging Reporting and Data System; f-u = follow-up; MR = magnetic resonance; US = ultrasound.

suffice, or surgery for a benign lesion. The simplest way to have the referring physician lose confidence in breast MRI is to have a patient undergo unnecessary surgery. It, therefore, is imperative to confirm with biopsy that disease is present, whenever possible. In our practice, we routinely obtain an MRI biopsy when a positive result will cause a change in patient management. Our practice audit indicates that approximately 7% of all breast MRIs result in an MRI biopsy.

Some principles in the management of breast MRI lesions are: (1) be as definite and specific as possible; (2) for definitely benign lesions, avoid biopsy or follow-up; (3) do not assume a suspicious enhancing lesion is malignant; if it will result in a change in surgical management, then biopsy is required for confirmation; and (4) avoid delays in surgery as much as possible (see Table 3). It is important that reporting radiologists are familiar with the next step of management: breast MRIs should be read by radiologists who are comfortable with recommendations for breast biopsies. As with other breast imaging, a BI-RADS category should be assigned to every breast MRI report. This allows for standardization of the reporting and effective communication of the degree of suspicion of the MRI findings, with a recommendation for further management. BI-RADS provides a standard language that can be used to compare findings across multiple scientific studies and enables all radiologists to describe mammographic findings in a consistent manner [3]. If a lesion is suspicious on MRI, a BI-RADS category 4 or 5 should be assigned, because a biopsy will be performed. Further imaging with a second-look US or mammogram is simply obtained to determine the best technique for image-guided biopsy (Figure 18).

In summary, there are some practical approaches to the management of MRI-detected lesions, which can be followed by most radiologists. Use of the ACR MRI lexicon and BI-RADS categories standardizes reports and directs management that is consistent and easy to communicate. Approximately 25% of breast MRI lesions are positive for cancer, at least 50% of suspicious enhancing lesions are identified on second-look US and mammograms, whereas about 20% lesions require follow-up. A small number of patients, less than 10%, will require MRI breast biopsy for diagnosis.

## Acknowledgement

Special thanks to Dr Susan Peddle for editorial assistance with the manuscript.

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