

MRI of the breast and emerging technologies

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INTRODUCTION

Magnetic resonance imaging (MRI) of the breast is an important tool for the detection of breast cancer ([image 1](#) and [image 2](#)) and assessment of silicone implant integrity ([image 3](#)). The use of MRI with contrast agents for the detection of breast cancer was first reported in 1986 [1]. The high sensitivity of MRI for breast cancer has led to the increasing use of MRI for breast cancer detection, assessment, and treatment monitoring, although appropriate indications, scanning techniques and interpretations remain variable among facilities.

This topic will review breast MRI techniques, interpretation, and indications as well as emerging tools for breast cancer detection. Issues regarding screening for breast cancer, the role of mammography and ultrasound in women with suspected disease, surveillance for patients with known breast cancer, and the physics of MRI are discussed separately. (See ["Breast imaging for cancer screening: Mammography and ultrasonography"](#) and ["Screening for breast cancer: Strategies and recommendations"](#) and ["Clinical features, diagnosis, and staging of newly diagnosed breast cancer"](#) and ["Principles of magnetic resonance imaging"](#) and ["Approach to the patient following treatment for breast cancer"](#), section on 'Breast MRI'.)

BREAST MRI TECHNIQUE

MRI creates images of the breast by measuring changes in the movement of protons in fat and water with the application of changing magnetic fields. By utilizing the differences in

tissue relaxation characteristics, an image is acquired by processing the signal changes that occur following application of pulses of energy. The physics of MRI is discussed in detail elsewhere. (See "[Principles of magnetic resonance imaging](#)", section on 'Magnetic resonance physics'.)

Breast MRI for the detection of breast cancer requires administration of the contrast agent gadolinium. The use of MRI for breast cancer detection is based on the concept of tumor angiogenesis or neovascularity. Tumor-associated blood vessels have increased permeability, which leads to prompt uptake and release of gadolinium within the first one to two minutes after administration, leading to a pattern of rapid enhancement and washout on MRI ([figure 1](#)). This dynamic rapid enhancement pattern helps to distinguish breast cancers from benign lesions. Breast MRI techniques continue to evolve, but some general recommendations can be made based on minimum standards used by the American College of Radiology Imaging Network (ACRIN) 6667 Trial [\[2\]](#) and the European Society of Breast Imaging [\[3\]](#).

- **Bilateral breast examination** – Both breasts should be evaluated in an MRI study, for comparison purposes, even when concern about possible pathology involves only one breast.
- **Magnet** – The magnet field strength recommended for breast MRI is ≥ 1.5 -Tesla. High-field-strength magnets (3-Tesla and 7-Tesla) provide higher signal-to-noise ratios than conventional breast MRI, performed with 1.5-Tesla-field-strength magnets. The high-field-strength magnets result in higher spatial resolution and improved detection of breast cancers < 5 mm in size compared with conventional techniques [\[4-7\]](#).
- **Coil** – A dedicated breast coil should be used for breast MRI. The breast coil is designed to receive signals generated from breast tissue and permits imaging of both breasts simultaneously. Surface coils are necessary to achieve adequate spatial resolution while maintaining high signal-to-noise levels.
- **Positioning** – Patients are placed in the prone position, over the breast coil, which has openings for the patient's breasts. The coils surround the breasts and detect the magnetic signals from the breast. Some centers image the patient with the breasts in mild compression, which minimizes motion artifact and aids in biopsy planning.
- **Patient comfort** – Patients are given ear plugs before the exam begins to help diminish the loud "knocking" sounds that are typically heard during an MRI exam. Claustrophobia can be diminished with a short-acting anxiolytic prior to the exam.
- **Contrast** – Intravenous gadolinium contrast must be used to maximize cancer detection and is administered before breast MRI to highlight the neovascularity

associated with cancers. Contrast is **not** necessary when the study is performed to evaluate silicone implant integrity.

Allergic and anaphylactoid reactions to gadolinium are rare, but can occur. In addition, in patients with renal failure, gadolinium can cause contrast nephropathy and/or nephrogenic systemic fibrosis. (See "[Patient evaluation before gadolinium contrast administration for magnetic resonance imaging](#)".)

A few studies have also reported gadolinium deposition in the brain from repeated intravenous administration, with the degree of deposition varying based on the specific contrast agent. The clinical significance of this deposition remains unknown, and no data for humans exist to show any adverse effects at this time [8,9].

- **Imaging** – Images are acquired within 45 seconds of contrast injection and then every one to two minutes with completion within four minutes in order to observe the early preferential signal enhancement associated with the hypervascularity of malignant tumors. Slice thickness should be ≤ 3 mm.

After the first few minutes following contrast injection, benign breast tissue may also enhance. This time constraint means that a compromise must be reached between temporal and spatial resolution. Imaging strategies such as high spatial resolution and the use of fat-suppression techniques improve the sensitivity of breast MRI for small or multifocal lesions, but also increase scan times [10,11]. Dynamic techniques, in which images are acquired at intervals of one minute or less, achieve higher temporal resolution and improve specificity by allowing the time course of contrast uptake to be better defined [12-14]. Alternative approaches combine low temporal resolution kinetic information with high spatial resolution anatomic information as a means of achieving high sensitivity and specificity in a single-scan technique [15-18]. Most centers compromise by acquiring temporal resolution at 1 to 1 minute 30 seconds with higher spatial resolution.

MRI INTERPRETATION

Breast MR images are analyzed and reported according to the standardized Breast Imaging Reporting and Data System (BI-RADS) reporting system [19]. The report describes overall breast composition (density and background parenchymal enhancement) and specific lesions.

Breast composition — The breast composition is assessed overall and is categorized by tissue composition (ie, amount of fibroglandular tissue) and by the level of background parenchymal enhancement. Background parenchymal enhancement is the degree to which

normal fibroglandular tissue enhances with contrast, versus breast density, which is not dependent on contrast administration.

Background parenchymal enhancement may be associated with future invasive breast cancer risk [20]. In a multicenter study of 4247 women among whom 176 developed in situ or invasive breast cancer over a median follow-up of 2.8 years, mild, moderate, and marked background parenchymal enhancement was associated with increased cancer risk with hazard ratios (HRs) of 1.8 (95% CI 1.1-2.90), 2.4 (95% CI 1.5-3.9), and 3.4 (95% CI 2.1-5.7), respectively. For the subgroup of invasive cancer, combined mild, moderate, and marked background parenchymal enhancement was again associated with an increased risk (HR 2.7, 95% CI 1.7-4.5). The risk of a future invasive breast cancer diagnosis associated with increased background parenchymal enhancement is independent of breast density.

Lesions — Lesions are categorized as mass or non-mass lesions. The sensitivity of breast MRI is reported as 71 to 100 percent; however, the specificity is less than 65 percent [21,22]. The low specificity is due to the overlap in the enhancement pattern of benign and malignant lesions. Positive findings are more likely to be accurate for mass lesions than non-mass lesions [23]. Breast MRI findings must be correlated with the patient's mammographic and/or sonographic imaging.

- Mass lesions are assessed for shape, margin characteristics, and enhancement patterns. Margin characteristics, such as smooth, irregular, or spiculated margins, are significant predictors of malignant versus benign diagnoses. As with mammography, masses with irregular or spiculated margins are worrisome for malignancy. Rapid uptake and washout of gadolinium is seen more commonly in malignant lesions. Progressive enhancement over time is most often encountered in benign lesions or normal breast tissue. In one study of 266 lesions detected on breast MRI, progressive enhancement was seen with 83 percent of the benign lesions as compared with 9 percent of the malignant lesions [24].
- Non-mass lesions are characterized by spatial distribution and patterns of enhancement within the breast. Spatial distribution can be diffuse, regional, segmental, or linear. A clumped-ring enhancement pattern is a predictor of malignant versus benign diagnoses. The non-mass lesions present substantial diagnostic challenges and account for a high percentage of false positives. As an example, in one study of 132 patients who underwent 151 biopsies for breast lesions detected on breast MRI, non-mass lesions represented only 20 percent of all lesions detected, but accounted for almost half of the false positive interpretations [23].

MRI of high-risk breast lesions identified by core biopsy — Breast MRI is sometimes used as an adjunct to further assess high-risk proliferative breast lesions with or without atypia, including papillomas, radial sclerosing lesions, lobular neoplasias, and atypical

hyperplasias, identified by core needle biopsy [25-27]. In a retrospective review of MRI assessment of 227 high-risk breast lesions, contrast enhancing lesions (n = 155) were significantly more likely to be associated with a breast malignancy (invasive or noninvasive) compared with nonenhancing lesions (18 versus 3 percent) [27]. The diagnosis was confirmed by excision of the lesion. The cancer probability was also greater for non-mass lesions compared with mass lesions (43 versus 14 percent).

However, the negative predictive value (NPV) is low for proliferative lesions with atypia, including lobular neoplasias (NPV 88 percent) and atypical ductal hyperplasia (NPV 90 percent) [26]. These lesions should be excised when identified on a core needle biopsy. In comparison, the NPV for proliferative lesions without atypia (papilloma and radial scar) was 97.4 and 97.6 percent, respectively. Patients with these lesions may be safely observed with repeat annual mammographic, ultrasound or MRI imaging, depending upon patient and clinician preference. (See ["Overview of benign breast diseases", section on 'Proliferative lesions without atypia'](#) and ["Overview of benign breast diseases", section on 'Proliferative lesions with atypia'](#).)

LIMITATIONS OF BREAST MRI

Hormonal changes and cancer treatments can affect the accuracy of breast MRIs and should be taken into account when scheduling and interpreting the study. Although there is variation in the performance of breast MRIs, reporting should follow standard guidelines. Facilities that perform breast MRI should have MRI-biopsy capability.

- **Menstrual cycle** – To minimize the effects of physiologic glandular enhancement that accompany the menstrual cycle, premenopausal patients or patients on cyclic hormone replacement therapy can be imaged between days 5 to 15 of their cycle [28-31]. (See ["Normal menstrual cycle"](#).)
- **Lactation** – Breast MRI during lactation is of limited value given the increased breast density and rapid diffuse enhancement that occur as a result of normal hormonal changes and interfere with accurate interpretation [32,33].
- **Cancer treatment** – Surgery and/or radiation therapy within 12 to 18 months before breast MRI can lead to increased gadolinium uptake and false positive studies [34,35]. It is not known how recent chemotherapy impacts gadolinium uptake, although there are reports that selective estrogen receptor modulators (eg, [tamoxifen](#)) and aromatase inhibitors (eg, Arimidex) can cause malignancies to appear smaller or even undetectable on MRI [36,37]. Based upon a prospective study that included 40 women, tamoxifen, and to a lesser extent aromatase inhibitors, substantially suppress

background enhancement, making it challenging to detect even benign breast lesions by MRI imaging [38].

- **MRI reporting** – Breast MRIs are increasingly reported using the Breast Imaging Reporting and Data System (BI-RADS) [19]. The BI-RADS system was originally developed by the American College of Radiology to standardize mammography reporting, but is now also used for breast ultrasound (US) and MRI ([table 1](#)) [39]. However, the probability of malignancy for these assessment codes for US and MRI are not as well established, although it is believed that they are likely similar to that with mammography. (See "[Breast imaging for cancer screening: Mammography and ultrasonography](#)", section on 'BI-RADS final assessment categories'.)
- **Standardization** – The specific sequences acquired during the examination vary between facilities [40]. In addition, the dynamic enhancement data often are not archived with the image files. The lack of standardization in breast MRI impairs the ability to compare studies from different institutions, thus leading to repeat MRIs when patients seek second opinions.
- **Biopsy capability** – Based on current National Comprehensive Cancer Network (NCCN) guidelines, imaging centers that perform MRI should have the ability to perform MRI-guided needle sampling and/or wire localization of MRI detected findings [41]. Almost half of abnormal findings on MRI may not be evident on other imaging studies [42].
- **Cost** – In the United States, MRI of the breast is expensive, costing approximately 10 to 15 times more than mammography or US, and is not uniformly reimbursed by insurance. In addition, for up to 10 percent of all women who undergo MRI, the study results in recommendation for follow up MRI in six months to reassess nonspecific, but probably benign findings.
- **Menopause status** – Postmenopausal patients with breast cancer more commonly exhibit slow initial-phase contrast uptake and persistent enhancement on delayed imaging rather than the classic early rapid contrast uptake with washout on delayed MR sequences. In a retrospective review of 273 patients with breast cancer (153 intraductal cancers, 24 lobular cancers, and 4 mixed histology), typical kinetic findings (rapid contrast uptake) were less likely to be seen in postmenopausal patients (n = 155) compared with premenopausal (n = 110) and postmenopausal patients using hormone replacement therapy (n = 8) (56.8 versus 80.9 versus 50.0 percent) [43]. In addition, postmenopausal women with cancers were more likely to have persistent enhancement on delayed imaging compared with premenopausal women (57 versus 46 percent).

PRECAUTIONS

Contraindications for breast MRI include pregnancy, implanted devices and foreign bodies, and any prior history of gadolinium allergy or diminished renal function. Since no guideline can cover all devices, when the safety of particular devices is being considered, readers are referred to safety information for specific devices which is compiled on dedicated web sites (www.MRIsafety.com) and, when available, manufacturer's product information [44]. The contraindications for MRI are discussed in detail elsewhere. (See "[Patient evaluation for metallic or electrical implants, devices, or foreign bodies before magnetic resonance imaging](#)", section on '[Assessing implants, devices, or foreign bodies for MRI](#)'.)

INDICATIONS FOR BREAST MRI

The appropriate use of breast MRI is established for certain indications, while others are still being investigated. Breast MRI has been used for the assessment of silicone implant integrity, diagnosis of occult primary breast cancers, determination of disease extent in newly diagnosed breast cancer patients (when indicated), documentation of response to neoadjuvant chemotherapy, diagnosis of recurrence, clarification of inconclusive clinical or mammographic findings, and screening of high-risk patients.

Assessment of breast implants — Breast MRI is useful for detection of silicone implant rupture and diagnosis of masses caused by free silicone injections. There is no role for breast MRI in [saline](#) implant assessment.

Silicone implants — Most silicone implants have a shell around the actual implant capsule; hence implant ruptures are described as intracapsular or extracapsular [45]. Intracapsular ruptures are defined as rupture of the silicone shell or envelope around the liquid silicone, with an intact fibrous capsule. Extracapsular ruptures are defined as rupture of both the envelope and fibrous capsule, allowing leakage into the surrounding tissue. Both types of rupture usually require surgical removal of the implant. Surgical excision of an extracapsular rupture is technically more challenging because of the silicone leakage into the surrounding tissue.

Breast MRI is the most useful imaging test for detecting both intracapsular and extracapsular ruptures of a silicone breast implant with a sensitivity and specificity of over 90 percent ([image 4](#)) [45-49]. The most reliable sign of rupture on MRI is the presence of multiple curvilinear lines, which represent the collapsed implant shell floating inside the silicone gel, referred to as the "linguine sign."

The most important risk factor for silicone breast implant rupture is time since placement, since 50 percent of implants rupture after 12 years [50]. The United States Food and Drug

Administration (FDA) recommends that regular MRI screening be performed for asymptomatic women with silicone implants five years after implantation and every two to three years thereafter [51]. However, there is little evidence to support a recommendation for regular MRI screening, which is expensive and may lead to anxiety and false positive results, and result in unnecessary surgery. Therefore, most experts agree that breast MRI should be used as a confirmatory diagnostic test and not be used to screen asymptomatic women for implant rupture [51,52].

Free silicone injections — Direct injection of liquid silicone into the breast tissue for breast augmentation was done in the 1950's [53,54]. This practice led to the development of painful hard silicone masses in the breast, termed silicone granulomas or siliconomas. Although this practice was banned by the FDA in the United States in 1965, free silicone injections are still performed in other countries and women may present with sequelae of this technique [54]. Breast MRI is helpful in differentiating siliconomas from other breast masses because most silicone masses do not enhance with contrast administration.

Saline implants — There is no role for breast MRI imaging to detect rupture of [saline](#) implants, as rupture results in rapid deflation of the implant and is easily detected on physical examination and/or mammography. (See "[Screening for breast cancer: Strategies and recommendations](#)", section on 'Breast augmentation for benign reasons'.)

Detection of occult primary breast cancer in women with axillary metastases — Breast MRI is useful for detection of an occult primary breast cancer when a patient presents with metastatic disease in the axillary lymph nodes with no evident primary breast lesion. Several observational series have demonstrated that breast MRI can detect a primary breast cancer in the majority of women who present with axillary adenocarcinoma ([table 2](#) and [image 3](#)) [22,41,55-66]. The evaluation and treatment of women with occult primary breast cancer is discussed in detail elsewhere. (See "[Axillary node metastases with occult primary breast cancer](#)".)

Preoperative evaluation of newly diagnosed breast cancer patients — Although many invasive breast carcinomas enhance on gadolinium-enhanced breast MRI [1,10,11,15,22,67-76], including occult and contralateral lesions ([image 5](#) and [image 6](#) and [image 7A-B](#)), routine use of preoperative breast MRI has not clearly demonstrated either surgical or outcomes benefits. A preoperative breast MRI for women who carry a deleterious mutation in breast cancer susceptibility gene 1 (*BRCA1*), breast cancer susceptibility gene 2 (*BRCA2*), or other high-risk genetic syndromes may be useful for detection of an ipsilateral or contralateral cancer (see "[Overview of hereditary breast and ovarian cancer syndromes](#)"). Almost half of abnormal findings on MRI may not be evident on other imaging studies.

Based upon a meta-analysis of four studies that included 3180 affected breasts and 3169 patients, there was no difference in the rate of local recurrence at eight years for patients

receiving a preoperative breast MRI compared with those without preoperative imaging (97 versus 95 percent) [77]. In addition, there was no difference in eight-year disease-free survival for those managed with a preoperative MRI (89 versus 93 percent).

By contrast, in a subsequent retrospective review of 2483 patients diagnosed with invasive breast cancer in the Netherlands, on multivariable regression analyses, preoperative MRI was associated with a reduced risk of positive resection margins after breast-conserving surgery (adjusted odds ratio [OR] 0.56, 95% CI 0.33-0.96) [78]. However, based upon a retrospective review of the Surveillance, Epidemiology, and End-Result-Medicare database that included 45,453 women diagnosed with early stage breast cancer, and after adjusting for patient and cancer characteristics, a preoperative breast MRI did not reduce the incidence of multiple breast cancer related operations [79].

Major disadvantages of breast MRI are its limited specificity due to enhancement of benign breast lesions, which can lead to additional and unnecessary biopsies and a slightly higher rate of contralateral mastectomies in some studies [80-82], as well as delays in regional and/or systemic treatment. Other studies have shown an increase in contralateral mastectomy rate independent of the use of preoperative breast MRI [83,84]. (See "[Contralateral prophylactic mastectomy](#)".)

Evaluation of a suspected breast cancer — A breast MRI may be helpful in the clinical setting of a questionable clinical or mammographic/ultrasonic examination in a patient who is not an operative candidate. (See "[Diagnostic evaluation of suspected breast cancer](#)".)

Measurement of response to neoadjuvant chemotherapy — Neoadjuvant systemic therapy, also referred to as primary or preoperative systemic therapy, is the accepted approach for women with locally advanced breast cancer to reduce the size of the cancer and possibly allow for breast conservation. In most cases, response to treatment can be assessed with physical examination, which may be supplemented, in some cases, by the breast imaging technique that most clearly showed the cancer at the time of diagnosis. (See "[General principles of neoadjuvant management of breast cancer](#)", section on '[Clinical assessment and indications for imaging](#)'.)

There is increased interest in using breast MRI for assessment of the response to chemotherapy since decreases in lesion size and changes in enhancement kinetics correlate with pathologic response ([image 8](#)) [85-89]. However, MRI has been shown to both overestimate and underestimate the amount of residual tumor after neoadjuvant chemotherapy [89]. For patients receiving neoadjuvant therapy, assessment of cancer enhancement patterns, tumor distribution patterns, tumor size, and background enhancement may improve the MRI specificity to monitor cancer response to therapy [90].

A trial sponsored by the American College of Radiology Imaging Network (ACRIN) study 6657 is underway to study the use of MRI for the assessment of response to neoadjuvant chemotherapy [91]. Indications for neoadjuvant chemotherapy and the evaluation of response to treatment are discussed elsewhere.

Differentiating postoperative changes from recurrence — Approximately 10 to 15 percent of patients with breast cancer will develop a locoregional recurrence within 10 years of treatment with breast conserving therapy. Breast MRI can be used to differentiate surgical scarring and radiation changes from breast cancer recurrence in cases where the physical examination and imaging with mammography and/or ultrasound (US) is difficult to interpret ([image 9](#)) [21,92-94]. Enhancement in the prior surgical site is suggestive of recurrence and merits core biopsy, while the absence of enhancement in the biopsy bed suggests fibrosis [95]. However, false positive readings can result from fat necrosis which also can enhance avidly.

The recommendations for post-treatment surveillance and the management of locoregional recurrence after breast conserving therapy are discussed elsewhere. (See "[Surgery and radiation for locoregional recurrences of breast cancer](#)", section on 'Management of in-breast recurrence following BCT' and "[Approach to the patient following treatment for breast cancer](#)", section on 'Breast MRI'.)

Evaluation of inconclusive clinical or imaging findings — Breast MRI can be used for the evaluation of equivocal findings on conventional imaging with mammography and US, such as focal asymmetry or a mammographic abnormality seen on only one view ([image 10](#) and [image 11A-B](#)) [96]. MRI may be helpful as an adjunct study to provide guidance for targeted US or core biopsy when localization would be difficult with conventional imaging alone. However, a negative MRI does not obviate the need for biopsy for suspicious findings on conventional imaging or physical examination [15,97].

There is no data to support the use of breast MRI to evaluate patients with breast pain or patients with palpable lumps who have had normal mammography and sonography. Suspicious palpable breast lumps require biopsy for diagnosis. Conventional breast imaging techniques, the evaluation of breast pain and breast lumps, and the diagnostic approach to women with suspected breast cancer are discussed elsewhere. (See "[Breast imaging for cancer screening: Mammography and ultrasonography](#)" and "[Breast pain](#)" and "[Clinical manifestations, differential diagnosis, and clinical evaluation of a palpable breast mass](#)" and "[Diagnostic evaluation of suspected breast cancer](#)".)

Breast MRI for the evaluation of spontaneous nipple discharge when mammography and US of the periareolar area fail to identify a focal finding [97-102] can sometimes help guide biopsy or surgery, but the gold standard for pathologic nipple discharge remains terminal

duct excision. The evaluation and treatment of nipple discharge is discussed in detail elsewhere. (See "[Nipple discharge](#)".)

Screening high-risk women — MRI has higher sensitivity for the detection of breast cancer in the high-risk population than mammography or US and thus is recommended for screening women who are at significantly high risk (lifetime risk 20 percent or higher) for the development of breast cancer ([image 12](#)) [22,103-112]. However, there is no evidence for a reduction in mortality or improved disease-free survival from screening with MRI, despite evidence that MRI can detect smaller cancers and more node-negative malignancies in high-risk women than other imaging modalities [108].

Guidelines from major groups (including the National Comprehensive Cancer Network [NCCN] [113] and the American Cancer Society [114]) recommend a combination of annual mammography and breast MRI for breast cancer surveillance in women who are *BRCA* mutation carriers or those with significantly elevated risk of developing breast cancer. The optimal screening interval is not determined and while some centers perform annual mammography and breast MRI simultaneously, others alternate the two imaging studies at six month intervals. In high-risk women undergoing MRI screening, two recent studies have questioned the value of routine mammography screening in this cohort as very few additional cancers were detected [110,111].

Despite these results, high-risk women are still offered both mammography and MRI screening annually. These high-risk women include those with any of the following:

- ***BRCA* mutation** – Women who have a proven mutation in one of the major susceptibility genes for breast cancer (*BRCA* mutations) or a family history of *BRCA* mutations are at a high risk of developing breast cancer. The testing for mutations in these genes is commercially available. Genetic testing for *BRCA* mutations is discussed elsewhere. (See "[Genetic testing and management of individuals at risk of hereditary breast and ovarian cancer syndromes](#)".)

Management of those found to have pathogenic variants in *BRCA*, or other genes associated with hereditary breast cancer, is discussed elsewhere. (See "[Cancer risks and management of *BRCA*1/2 carriers without cancer](#)" and "[Overview of hereditary breast and ovarian cancer syndromes](#)".)

- **Strong family history** – Women who have a strong family history with an estimated lifetime risk of breast cancer greater than 20 to 25 percent by BRCAPRO or equivalent risk models are at high risk of developing breast cancer. In a randomized trial of 1355 women with a cumulative lifetime breast cancer risk of at least 20 percent due to familial predisposition, none of whom had a personal history of breast cancer or a mutation in *BRCA 1/2* or tumor protein p53 (*TP53*), more breast cancers were detected

with annual MRI plus every-two-years mammography than with annual mammography (5.9 versus 2.2 percent, at a median follow-up of 5.2 years) [115]. Invasive cancers were smaller and less frequently node positive in the MRI group. However, the incidence of false positives was also higher in the MRI group (16 versus 9 percent, with mammography only).

- **History of chest radiation** – Women who received chest irradiation, such as mantle radiation for Hodgkin lymphoma, are at significantly increased risk of breast cancer. (See "[Second malignancies after treatment of classic Hodgkin lymphoma](#)", section on '[Breast cancer](#)'.)

There is insufficient data to support annual screening with MRI for women who are of lower, but still elevated risk, such as those with a personal history of breast cancer, dense breasts, or a prior benign biopsy revealing atypia. No evidence exists to support screening average-risk women with breast MRI. (See "[Screening for breast cancer: Evidence for effectiveness and harms](#)", section on '[Magnetic resonance imaging](#)'.)

EMERGING IMAGING TECHNOLOGY FOR BREAST CANCER DETECTION

Recognition of the limitations of mammography, ultrasound (US), and breast MRI has led to investigation of other breast imaging techniques including abbreviated breast MRI protocols, contrast-enhanced dual energy digital mammography, high-field strength MRI, magnetic resonance spectroscopy, diffusion weighted imaging, breast-specific gamma imaging, and positron emission mammography.

Abbreviated breast MRI protocols — Abbreviated breast MRI for breast cancer screening consists of a shortened imaging protocol such that patients are on the MRI scanner for no more than 5 to 10 minutes in total, as compared with 15 to 20 minutes for a full diagnostic study. There are a few retrospective studies in women with variable risk profiles and breast density that have shown that the abbreviated MRI protocol has comparable sensitivity with the full diagnostic protocol [116-120]. In addition, one study in women with prior breast surgery showed that when an abbreviated MRI protocol was compared with screening breast US and mammography, the MRI detected all 12 cancers, 7 of which were not detected on the other modalities, suggesting that abbreviated MRI may eventually have a role in screening women at increased risk for breast cancer [121]. In a separate retrospective study, among 475 women of average risk with dense breasts and negative digital breast tomosynthesis, supplemental abbreviated breast MRI resulted in a clinical detection rate of 27.4 per 1000 women [122]. However, at present, despite these promising results, most insurers do not cover supplemental MRI screening for women of average risk with dense breasts.

Contrast-enhanced dual-energy digital mammography — Bilateral dual-energy (DE) contrast-agent-enhanced (CE) digital mammography is a technique for detecting breast cancer that consists of high-energy and low-energy digital mammography following an intravenous injection of an iodinated contrast material [123]. This technology may be a useful adjunct for patients who cannot undergo MRI evaluation (eg, claustrophobic, pacemaker), as studies have shown comparable sensitivity [124].

The following studies illustrate the benefits of contrast-enhanced mammography:

- A prospective study that included 52 patients with a newly diagnosed breast cancer who underwent conventional mammography and an MRI followed by DE CE mammography found that MRI and DE CE mammography detected 50 (96 percent) of the index tumors [125]. Conventional mammography detected 42 cancers (81 percent). MRI detected 22 of 25 (88 percent) additional ipsilateral cancers while DE CE mammography detected 14 cancers (56 percent). An enhancing lesion identified on DE CE mammography was more likely to be malignant compared with enhancing lesions identified by MRI (positive predictive value 97 versus 85 percent).
- A prospective study of 89 women with dense breast tissue that included 72 malignancies and 28 benign lesions found that CE subtracted mammography increased the rate of cancer detection (specificity) compared with conventional mammography (92.7 versus 71.5 percent) [126]. In addition, CE subtracted mammography also improved specificity (67.9 versus 51.8 percent) and accuracy of diagnosis (85.8 versus 65.9 percent).

Magnetic resonance spectroscopy — MR spectroscopy is a specialized MRI sequence that allows assessment of the chemical composition of tissue. Breast MR spectroscopy is designed to detect choline and its derivatives, based on the observation that malignant tumors have elevated choline levels [96,127]. Choline is a molecule required for fatty acid synthesis during cell membrane production.

MR spectroscopy may provide an adjunct to conventional breast MRI, with the potential to increase specificity and avoid benign biopsies in a substantial number of women. MR spectroscopy is also promising for the evaluation of non-mass like suspicious findings on breast MRI [128]. However, MR spectroscopy misses some breast cancers, because not all express choline. In a study of 16 invasive ductal tumors; 88 percent had detectable choline peaks [129]. MR spectroscopy remains investigational, but it may have a future role in predicting outcome and monitoring response of therapy [130,131].

Diffusion weighted imaging — Diffusion weighted imaging is a noninvasive imaging technique that assesses the random motion of the water molecules in tissue, based on the observation that water diffusion is abnormal in breast cancers. The signal strength of water

molecules is proportional to the degree of diffusion. The results of diffusion-weighted imaging are calculated and then reported with a quantitative measure termed the apparent diffusion coefficient (ADC) for the tissue being studied.

Invasive breast cancers demonstrate restricted or less water diffusion than normal breast tissue or benign breast lesions, which results in a lower ADC [96,132-134]. A few observational studies have shown that diffusion-weighted imaging can differentiate benign from malignant breast lesions with equal sensitivity and greater specificity than MRI [135-137].

While diffusion weighted imaging is promising for use in preoperative assessment of disease extent in breast cancer patients, the available data is limited and this technique cannot be used for screening asymptomatic women or to exclude breast cancer in patients with suspicious breast masses or abnormal mammography [138,139]. However, a retrospective review of 101 women (20 malignant, 84 benign breast lesions) undergoing additional DWI found that DWI at the time of breast MRI can reduce the number of MRI-guided false positive or benign biopsies by 34.5 percent without false-negative findings [140].

Nuclear breast imaging — Nuclear breast imaging techniques include breast-specific gamma imaging (BSGI), positron emission tomography (PET) scanning, and positron emission mammography (PEM). These techniques provide a functional assessment of breast lesions at the cellular and the metabolic levels. Nuclear imaging techniques are limited by suboptimal spatial resolution of whole body cameras, hindering detection of small lesions. However, with the development of dedicated breast units, nuclear breast imaging has the potential to detect lesions less than 1 cm in size.

Nuclear breast imaging techniques are promising for indications similar to those of breast MRI, including determination of disease extent, high-risk screening, and monitoring response to therapy. However, there are limited data to justify the use of nuclear breast imaging techniques and they should be considered investigational. In addition, unlike MRI, nuclear breast imaging requires radiation exposure and radiation-related risks should be taken into consideration and discussed with the patient. (See "[Radiation-related risks of imaging](#)".)

Breast-specific gamma imaging — BSGI is a nuclear medicine imaging technique, using gamma cameras with 2 to 3 mm in-plane resolution in a mammographic configuration to provide images of the breast [141,142]. BSGI is based on the observation that breast cancers accumulate technetium-99m sestamibi in intracellular mitochondria. Intracellular mitochondria are present in greater numbers in breast cancer cells as compared to normal cells.

BSGI is performed after intravenous injection of 25 mCi of technetium-99m sestamibi. The patient is imaged approximately 5 to 10 minutes following the injection of the radioisotope. Two scans are performed of each breast using mild compression for craniocaudal and mediolateral oblique views. Images should be correlated with the patient's mammograms, breast US and clinical breast examination. If a biopsy is necessary for a lesion not seen on other imaging modalities, a BSGI-compatible biopsy system is used to direct tissue sampling.

In several observational studies, BSGI demonstrated equal sensitivity and greater specificity than MRI for the detection of breast cancer [143-148]. While BSGI is promising for use in the preoperative assessment of disease extent in breast cancer patients, the available data are limited and we do not use this technique for screening or to exclude breast cancer in patients with suspicious breast masses or abnormal mammography. We note, however, that it is used for screening at some centers.

Positron emission tomography scanning — PET scanning is a nuclear medicine imaging technique which produces a three-dimensional image.

- **Fluorine-18-labeled deoxyglucose PET** – PET scanning for breast cancer detection is based on increased glucose metabolism in cancer cells as compared with normal tissue; hence, malignancies can be detected with a radioactive tracer that reflects the process of increased glycolysis. A sugar, fluorine-18-labeled deoxyglucose (FDG), is used as the radioactive tracer for PET scanning because it is actively transported across the cell membrane, undergoes phosphorylation to FDG-6-phosphate, and is trapped within the cells. Tumor cells accumulate higher concentrations of the tracer than normal cells and are seen on the imaging scan as an area of enhancement.

Because glucose is used as the radioactive tracer, patients must fast for four to six hours prior to injection to minimize cardiac uptake, and avoid strenuous activity for 24 hours prior to the study to minimize skeletal muscle uptake. A high-protein, low carbohydrate diet for 24 to 48 hours prior to imaging is also recommended, in an effort to minimize myocardial uptake of glucose. The patient's serum glucose should be less than 200 mg/dL for optimal results.

To prepare for the scan, the patient is injected intravenously with 10 to 15mCi of the isotope FDG, and allowed to rest quietly in a warm room. After the isotope circulates for 60 to 90 minutes, the imaging can be performed. Although malignancies take up the agent, false positives can result from any metabolically active process such as acute infection, radiation treatment, or trauma.

A conventional positron emission tomography (PET) device does not have the spatial resolution to reliably detect primary breast malignancies less than 1 cm in size. PET scanning, with or without computed tomography (CT) image fusion, has been utilized in

selected cases for staging of breast cancer for axillary and distant metastatic disease, evaluating patients with recurrence, and monitoring response to chemotherapy [149-153]. Routine post-treatment surveillance with PET in women treated for breast cancer is not recommended. (See "[Approach to the patient following treatment for breast cancer](#)", section on '[Role of laboratory evaluation and other imaging](#)'.)

- **Fluoroestradiol F-18 PET** – A novel methodology, using fluoroestradiol F-18 as the radioactive diagnostic agent, is approved by the US Food and Drug Administration for the detection of estrogen receptor (ER)-positive lesions, as an adjunct to biopsy, in patients with recurrent or metastatic breast cancer [154]. However, drugs such as [tamoxifen](#) and [fulvestrant](#) block the ER and reduce the uptake of fluoroestradiol F-18. Therefore, for patients receiving this type of imaging, it should be performed prior to starting such systemic therapies. Given that aromatase inhibitors (AIs) act by impeding the production of estrogen, concurrent use of AIs during fluoroestradiol F-18 imaging is permitted.

In a study involving 200 patients with newly diagnosed metastatic breast cancer, [fluoroestradiol F-18](#) PET had a sensitivity of 95 percent and a specificity of 80 percent for ER positive lesions [155].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "[Society guideline links: Screening for breast cancer](#)" and "[Society guideline links: Breast cancer](#)".)

SUMMARY AND RECOMMENDATIONS

- Magnetic resonance imaging (MRI) may be used in select circumstances for breast cancer detection, assessment, and treatment monitoring, although appropriate indications, standardization of techniques, and interpretation remain variable among facilities. MRI of the breast is also an important tool for the assessment of silicone implant integrity. (See '[Introduction](#)' above.)
- The use of MRI for breast cancer detection is based on the concept of tumor angiogenesis or neovascularity. Tumor associated blood vessels have increased permeability, which leads to prompt take up and release of the contrast agent and helps to distinguish breast cancers from benign growths. (See '[Breast MRI technique](#)' above.)

- A dedicated breast coil should be used for breast MRI. The breast coil is designed to receive signals generated from breast tissue and permits imaging of both breasts simultaneously. (See '[Breast MRI technique](#)' above.)
- Intravenous gadolinium contrast must be used to maximize cancer detection and is administered during breast MRI to highlight neovascularity associated with cancers. Contrast is **not** necessary when the study is performed to evaluate silicone implant integrity. Gadolinium is contraindicated in patients with compromised renal function. (See '[Breast MRI technique](#)' above.)
- Breast MRI images are analyzed for morphology and initial and delayed contrast enhancement. Lesions are categorized as mass or non-mass lesions. The sensitivity of breast MRI is high, but the specificity is lower due to the overlap in the enhancement patterns of benign and malignant lesions. (See '[MRI interpretation](#)' above.)
- Hormonal changes and cancer treatments can affect the accuracy of breast MRIs. Although there is variation in the performance of breast MRIs, reporting should follow standard guidelines. Facilities that perform breast MRI should have MRI-biopsy capability. (See '[Limitations of breast MRI](#)' above.)
- Contraindications for breast MRI include pregnancy, implanted devices and foreign bodies, and any prior history of gadolinium allergy or diminished renal function. (See '[Precautions](#)' above.)
- The appropriate use of breast MRI is evolving and some indications remain controversial. Breast MRI has been used for the assessment of silicone implant integrity, the diagnosis of occult primary breast cancers, the determination of disease extent in newly diagnosed breast cancer patients (when indicated), documentation of response to neoadjuvant chemotherapy, diagnosis of recurrence, clarification of inconclusive clinical or imaging findings, and screening of high-risk patients. (See '[Indications for breast MRI](#)' above.)
- Recognition of the limitations of mammography, ultrasound, and breast MRI has led to investigation of other promising breast imaging techniques including high-field strength MRI, magnetic resonance spectroscopy, diffusion weighted imaging, and breast-specific gamma imaging. (See '[Emerging imaging technology for breast cancer detection](#)' above.)

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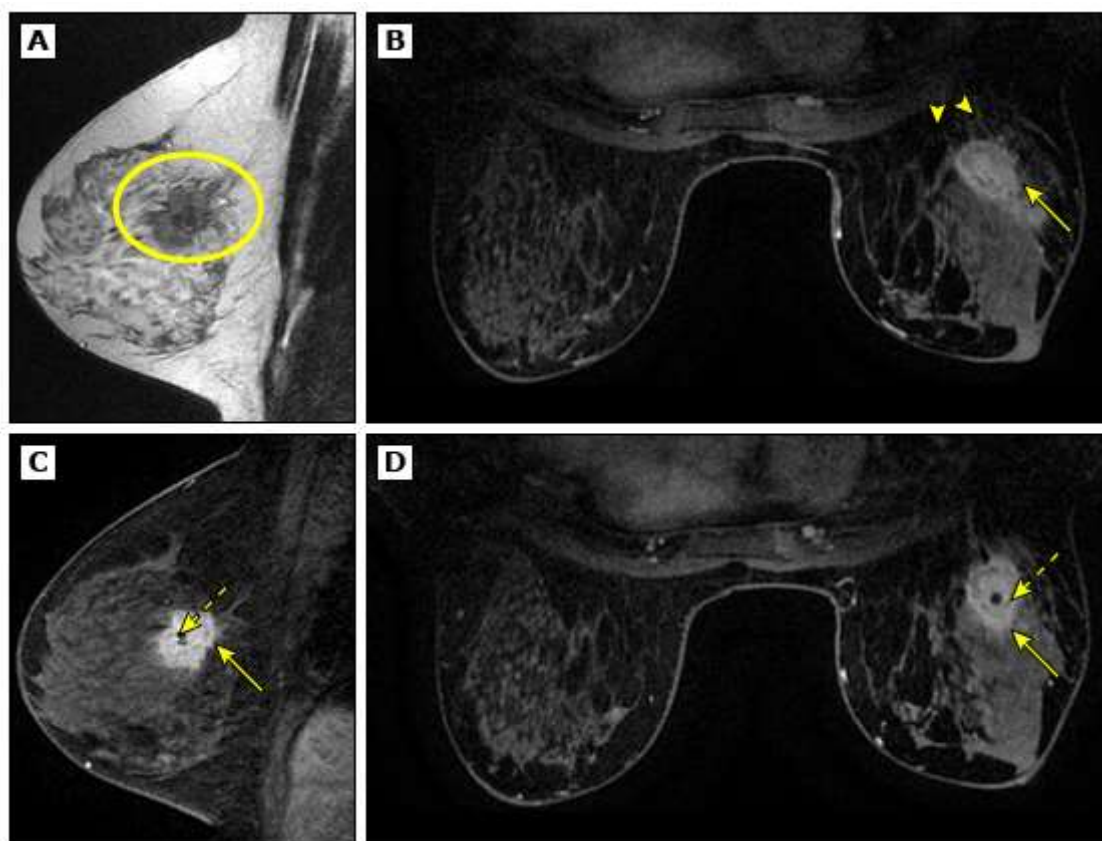
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Topic 14972 Version 42.0

GRAPHICS

Breast MRI invasive cancer

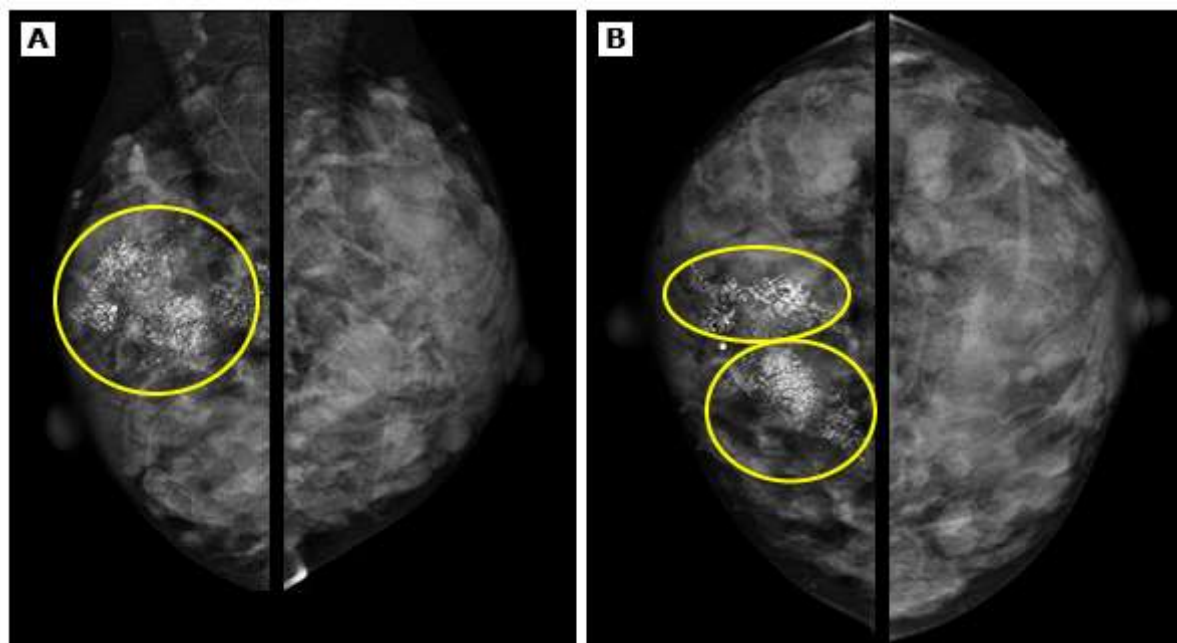


The MRI reveals an invasive ductal cancer of the breast characterized as a dark mass on T2 (ringed by the circle) and as an enhancing mass on the post contrast T1-weighted images (arrow) in the axial (B and D) and sagittal projections (C). The spiculations emanating from the mass (arrowheads) and heterogeneous enhancement are well demonstrated. The signal void (dashed arrow) represents a clip placed at time of ultrasound-guided biopsy.

MRI: magnetic resonance imaging.

Courtesy of Priscilla J Slanetz, MD, MPH, FACR.

Breast mammogram extensive noninvasive cancer



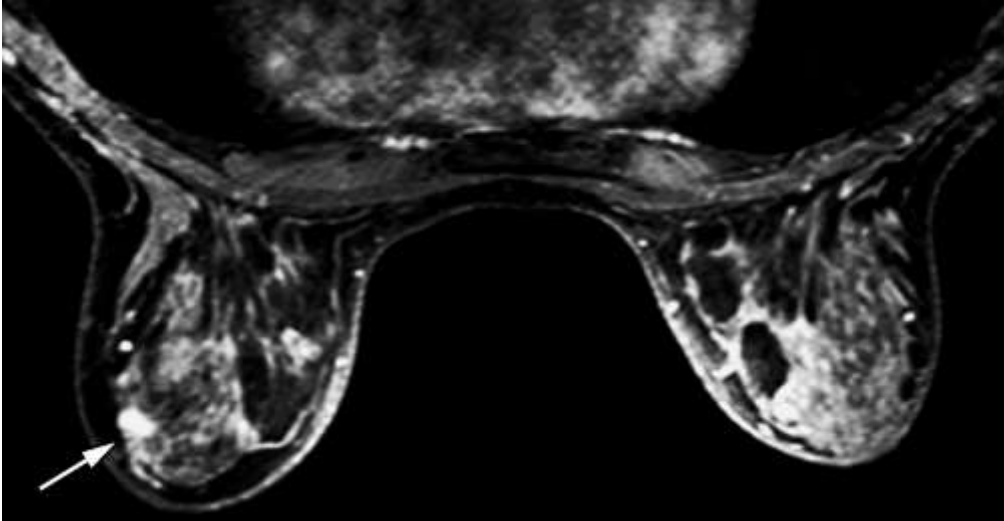
The screening mammogram of the breasts in the MLO (A) and CC views (B) reveal concerning extensive pleomorphic calcifications in the upper inner central right breast.

MLO: mediolateral oblique; CC: craniocaudal.

Courtesy of Priscilla J Slanetz, MD, MPH, FACR.

Graphic 86203 Version 4.0

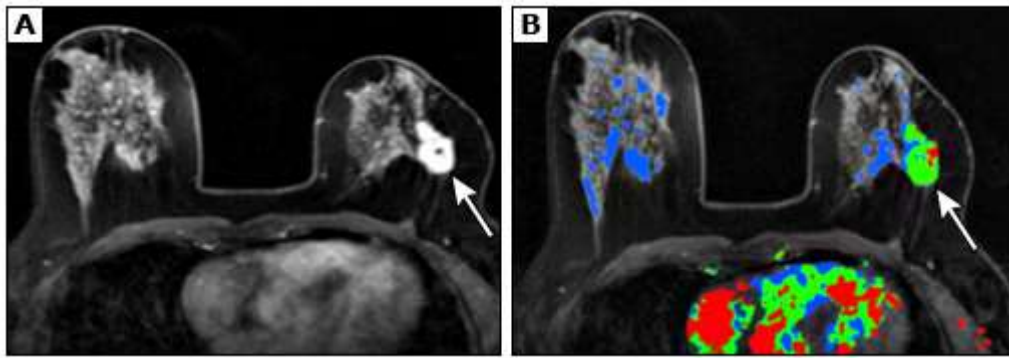
Breast MRI of occult primary breast cancer



Breast MRI can be useful for identifying an occult primary breast cancer when a patient presents with an unknown primary cancer. This MRI depicts a patient who presented with an axillary lymph node metastasis with an unremarkable clinical breast examination and a negative mammogram. The MRI detected a 6 mm suspiciously enhancing irregular mass in the outer inferior right breast (arrow). Biopsy revealed an invasive lobular carcinoma.

MRI: magnetic resonance imaging.

Breast MRI of invasive ductal cancer kinetic color map



The figure shows a breast MRI of a patient with biopsy proven invasive ductal cancer in the left breast.

(A) The T1-weighted fat-suppressed contrast-enhanced axial image shows an irregular lobulated enhancing mass with central signal void (arrow) corresponding to the clip that was placed at time of core biopsy.

(B) The corresponding kinetic color map demonstrates predominantly washout kinetics highly suspicious for malignancy.

BI-RADS assessment categories

Assessment	Management	Likelihood of cancer
Category 0: Incomplete – Need additional imaging evaluation and/or prior mammograms for comparison	Recall for additional imaging and/or comparison with prior examination(s)	N/A
Category 1: Negative	Routine mammography screening	Essentially 0% likelihood of malignancy
Category 2: Benign	Routine mammography screening	Essentially 0% likelihood of malignancy
Category 3: Probably benign	Short-interval (6-month) follow-up or continued surveillance mammography	>0 but ≤2% likelihood of malignancy
Category 4: Suspicious	Tissue diagnosis*	>2 but <95% likelihood of malignancy
Category 4A: Low suspicion for malignancy		>2 to ≤10% likelihood of malignancy
Category 4B: Moderate suspicion for malignancy		>10 to ≤50% likelihood of malignancy
Category 4C: High suspicion for malignancy		>50 to <95% likelihood of malignancy
Category 5: Highly suggestive of malignancy	Tissue diagnosis*	≥95% likelihood of malignancy
Category 6: Known biopsy-proven malignancy	Surgical excision when clinically appropriate	N/A

BI-RADS: Breast Imaging-Reporting and Data System.

* Practice guidelines recommend biopsy for all BI-RADS 4 and 5 lesions. If there are clinical factors (eg, age, comorbidities, etc) for which the patient, in consultation with the clinician, chooses to defer biopsy, the reasoning should be documented in the medical record.

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Breast MRI of silicone implant



Breast MRI is useful for the assessment of silicone implant integrity.

(A) Axial image of an intact subglandular silicone implant with radial folds (normal infolding of the implant envelope). Arrows point to radial folds.

(B) Axial image of a subglandular silicone implant shows curvilinear low signal within the silicone corresponding to a collapsed envelope, called the "linguine sign" (arrow), consistent with an intracapsular rupture.

(C) Axial image shows rupture of the envelope and capsule with extrusion of silicone into the surrounding breast tissue consistent with an extracapsular rupture. Arrow points to silicone within an intramammary lymph node.

MRI: magnetic resonance imaging.

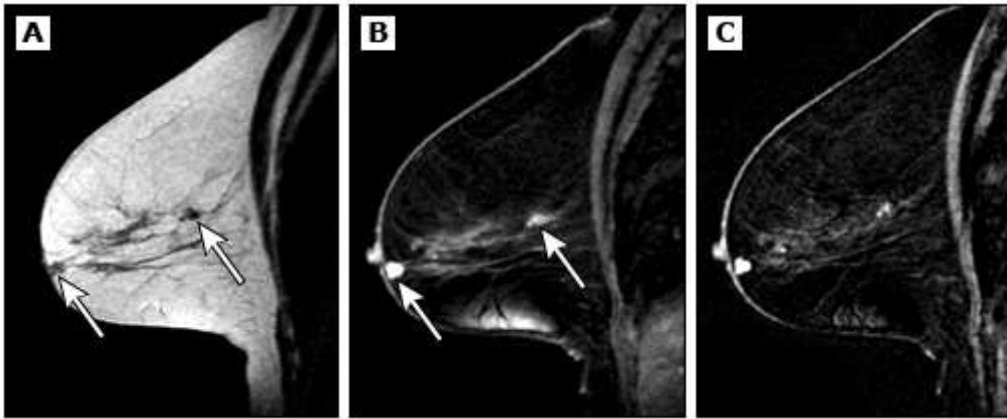
Utility of breast MRI for mammographically-occult breast cancer in patients presenting with metastatic axillary lymphadenopathy

Author, year	n	MRI-positive, percent	Histologic diagnosis of breast cancer
Morris, E; 1997	12	9 (75)	8
Brenner, R; 1997	4	4 (100)	4
Tilanus-Linthorst, M; 1997	4	4 (100)	4
Schorn, C; 1999	14¶	9 (64)	6/9
Henry-Tillman, R; 1999	10	8 (80)	8
Olson, J; 2000	40	28 (70)	21/22*
Obdeijn, I; 2000	20	8 (40)	8
Fourquet, A; 2004	15	14 (93)	9/11
Buchanan, C; 2005	69	42 (76)	26/42 MRI+
			4/12 MRI-

* Number of patients with confirmed MRI findings at the time of surgery.

¶ Included six axillary nodal metastases, one supraclavicular nodal metastases, three bone metastases, three liver metastases, and one lung metastases with an unknown primary.

Breast MRI of multifocal breast cancer



Breast MRI can be useful for determining disease extent in newly diagnosed cancer patients. These images show the MRI of a patient with a palpable retroareolar mass.

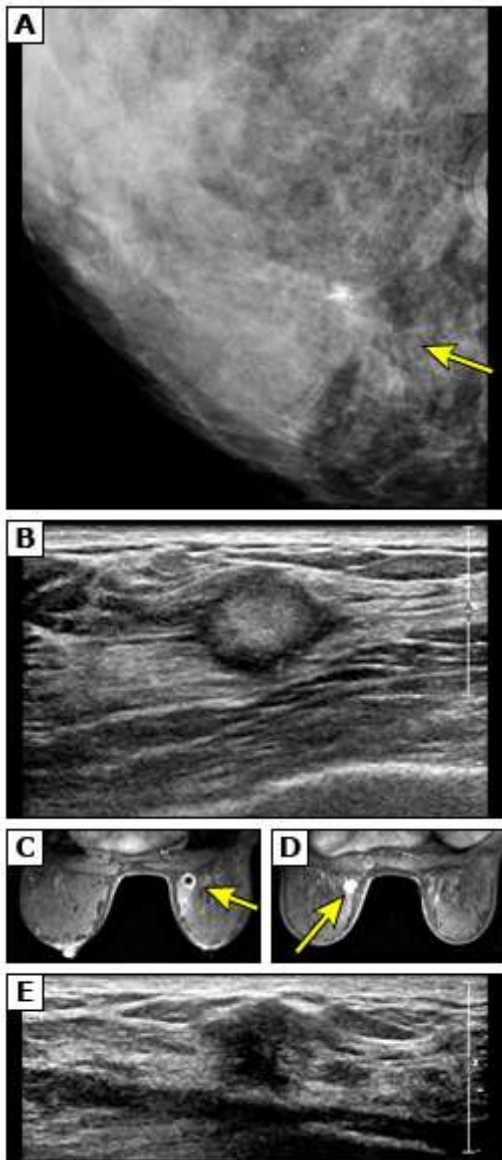
(A) T2-weighted imaging demonstrates an intermediate signal irregular mass just beneath the nipple as well as a T2-hypointense area posteriorly (arrows).

(B) Post contrast T1-weighted sagittal image demonstrates a suspiciously enhancing lesion in the inferior subareolar breast as well as an ill-defined area of non-mass enhancement posteriorly within the same ductal unit (arrows).

(C) Subtraction of pre- and post-contrast images confirm the two separate lesions with the posterior lesion being occult to both mammography and ultrasound. Biopsy of both areas was performed, revealing invasive ductal carcinoma anteriorly and ductal carcinoma in situ posteriorly.

MRI: magnetic resonance imaging.

Breast MRI of contralateral breast cancer



Breast MRI can be used to diagnose contralateral disease in newly diagnosed breast cancer patients. This series depicts a patient with right breast cancer detected on mammography.

(A) Architectural distortion (arrow) was detected in the right breast on screening mammography.

(B) Ultrasound demonstrated a solid mass on the right and biopsy under ultrasound-guidance confirmed invasive ductal carcinoma.

(C) Preoperative MRI confirmed the biopsy clip within the proven cancer in the right breast.

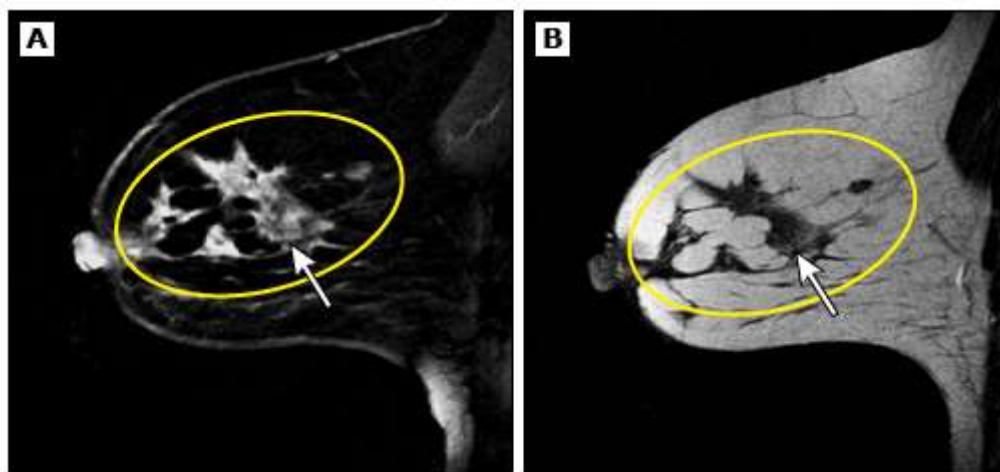
(D) MRI also showed a suspicious lesion in the left breast that was not seen on mammography.

(E) Second look ultrasound revealed an irregular solid mass on the left and subsequent biopsy showed an invasive ductal cancer, confirming contralateral disease.

MRI: magnetic resonance imaging.

Graphic 76575 Version 8.0

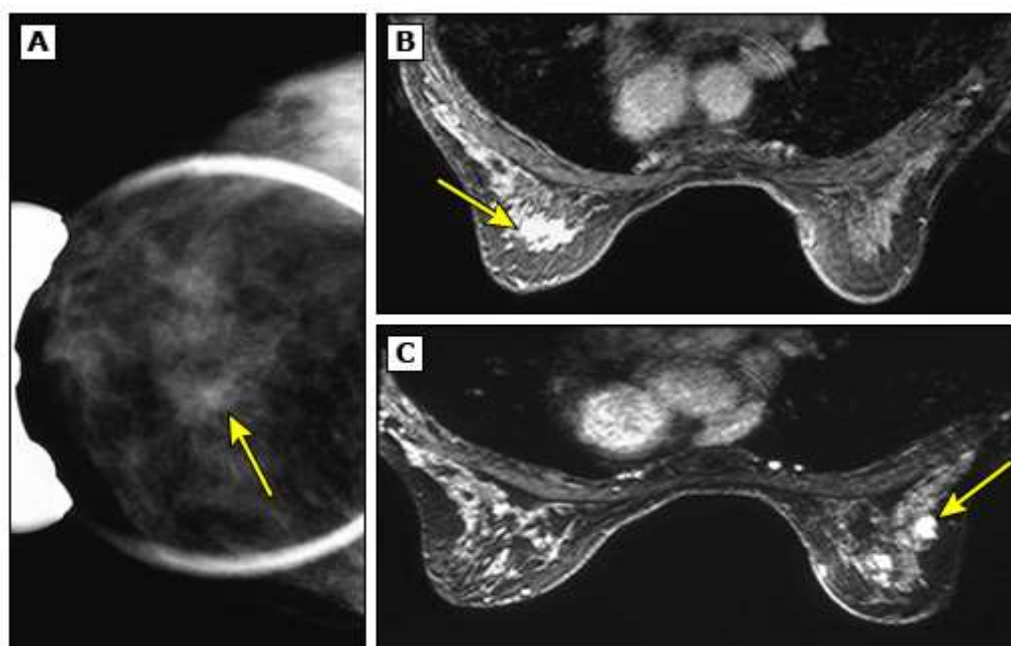
Breast MRI for evaluating extent of disease - case 1



Breast MRI can be used to determine the extent of disease in newly diagnosed cancer patient. The figure depicts the breast MRI of a patient with a palpable mass. Core biopsy revealed invasive lobular carcinoma. Preoperative MRI revealed extensive disease spanning over 7 cm with multiple irregular areas of enhancement (oval; arrows) on T1-weighted post contrast fat suppression imaging (A) with intermediate signal on T2-weighted non-fat suppressed sequences (B).

MRI: magnetic resonance imaging.

Breast MRI for evaluating extent of disease - case 2



Breast MRI can be used to determine the extent of disease in newly diagnosed cancer patient.

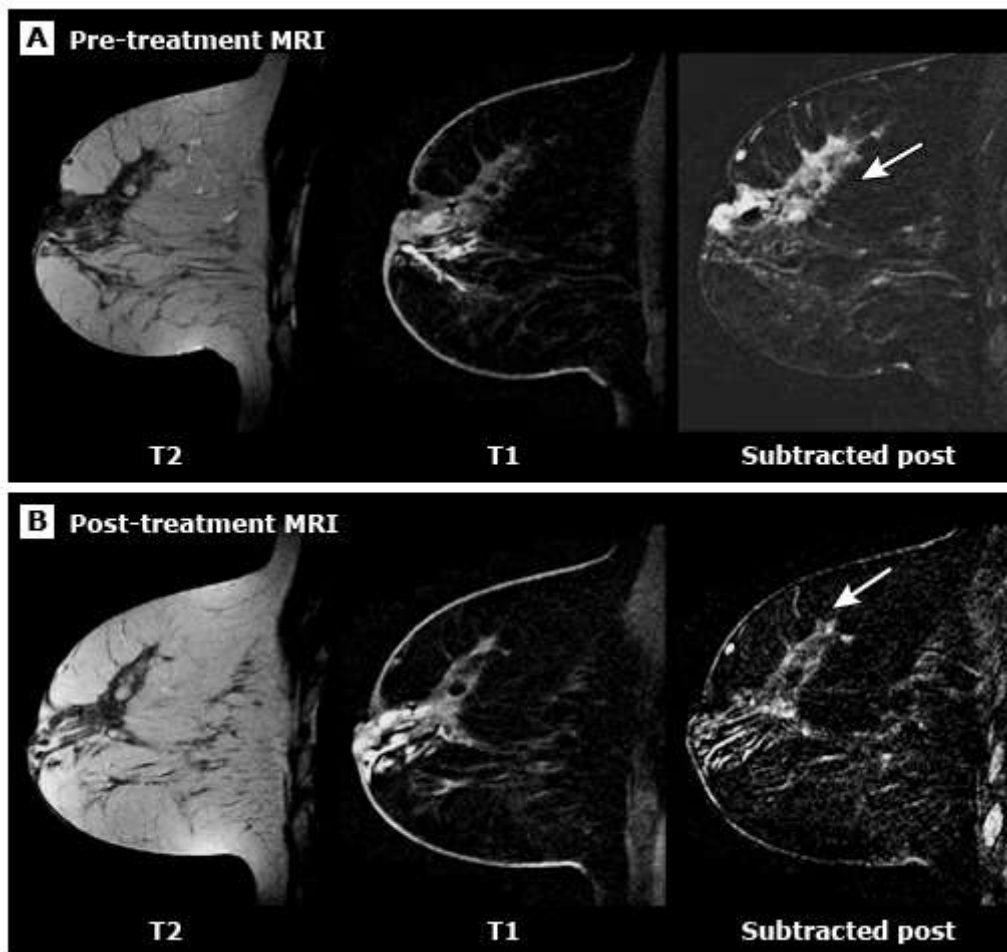
(A) Architectural distortion was detected in the central left breast on screening mammography. Diagnostic mammography confirmed persistence of the abnormality (arrow).

(B) Biopsy under ultrasound guidance confirmed invasive ductal carcinoma. Preoperative MRI confirmed the large invasive cancer (arrow) in the left breast.

(C) A second suspiciously enhancing lesion in the outer right breast (arrow). Subsequent biopsy of the right breast finding revealed an invasive ductal cancer, confirming contralateral disease.

MRI: magnetic resonance imaging.

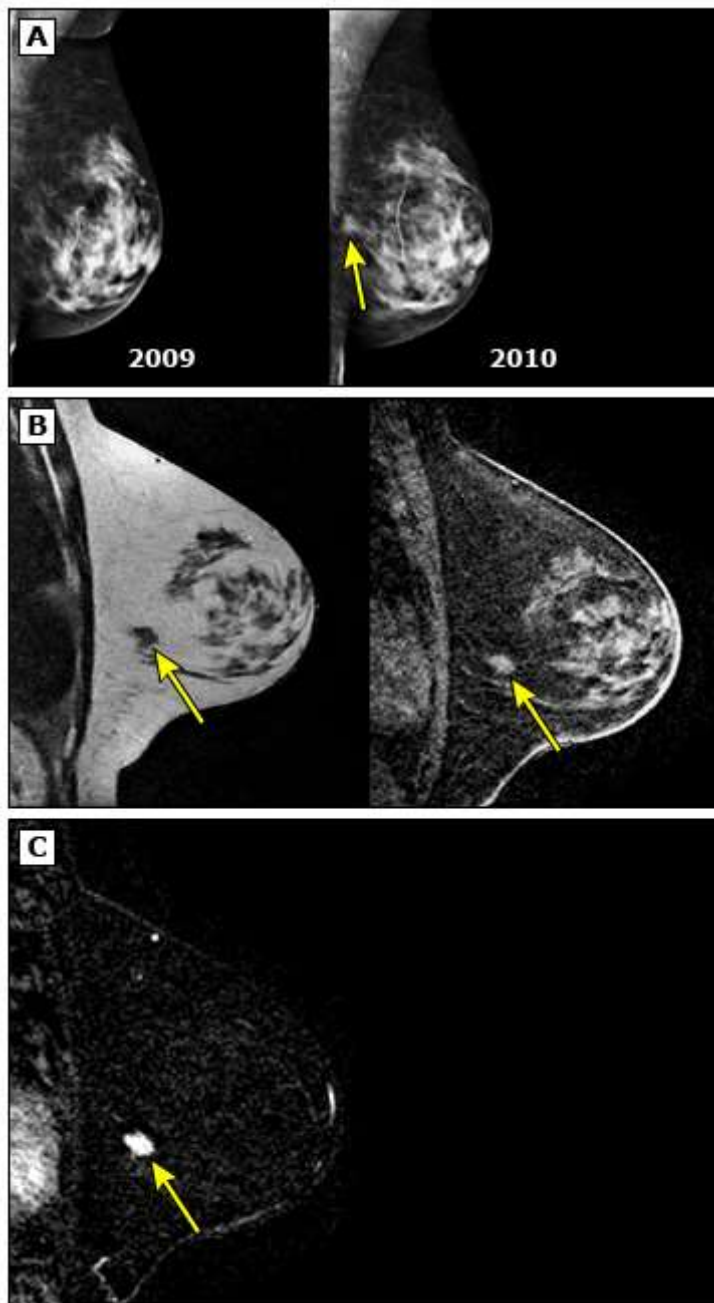
Breast MRI documenting response to neoadjuvant chemotherapy



Breast MRI can be used to document the response to neoadjuvant chemotherapy. This series illustrates the response to chemotherapy in a patient with a palpable right breast mass and nipple inversion. Mammography and ultrasound confirmed a large irregular mass and biopsy showed invasive lobular carcinoma. The patient was treated with neoadjuvant chemotherapy. MRI prior to therapy showed a large irregular mass extending from the nipple and involving the upper and central breast (A, arrow). Post-treatment MRI showed a partial response and scattered foci suggestive of residual disease (B, arrow). Subtraction of imaging prior to and after contrast administration highlights enhancing tissue which has been labeled as subtracted post.

MRI: magnetic resonance imaging.

Breast MRI of breast cancer recurrence



Breast MRI can be used to differentiate postoperative scarring from breast cancer recurrence. This series depicts a patient with a prior history of right lumpectomy for invasive carcinoma who presented for annual mammography.

(A) The mammogram shows a new irregular mass posterior to the lumpectomy bed in the posterior central right breast (arrow). Mediolateral oblique view.

(B) Sagittal MRI images demonstrate a low signal mass (arrow) in the posterior inferior right breast on the pre-gadolinium enhanced T2-weighted image (left) and on the T1-weighted MRI image (right).

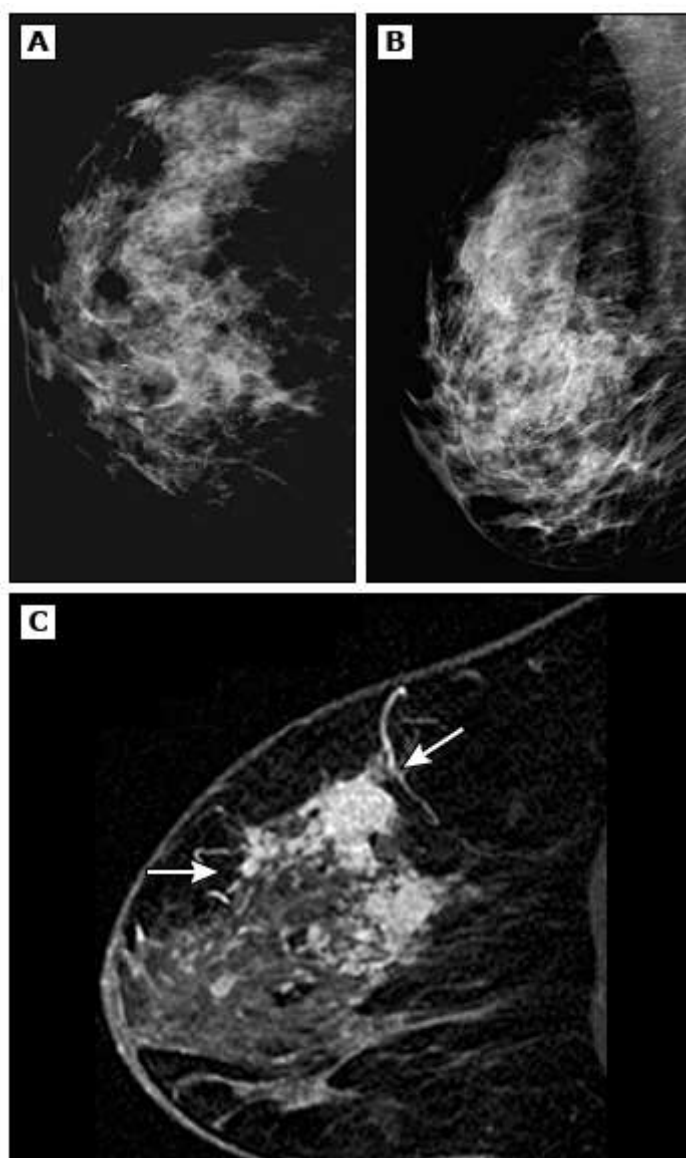
(C) Subtraction of the pre and post contrast sagittal T1-weighted images of the right breast shows an enhancing mass (arrow) in the

posterior central right breast confirming suspicion for recurrence.
Biopsy revealed recurrent invasive ductal carcinoma.

MRI: magnetic resonance imaging.

Graphic 74918 Version 5.0

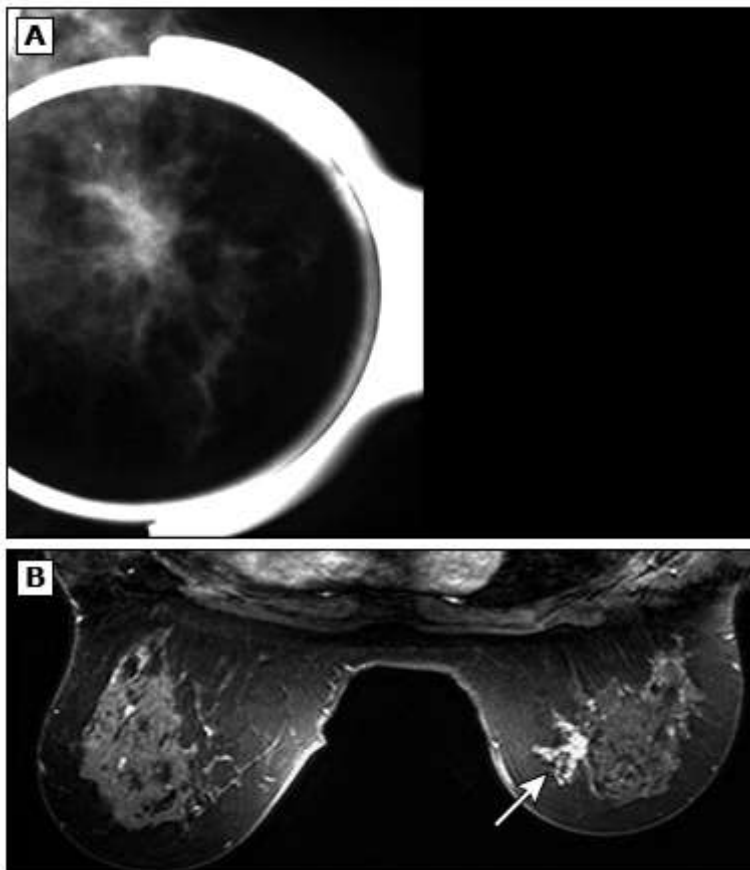
Mammographically occult breast cancer



A dense breast can obscure a cancer. CC and MLO views (panels A and B) in a woman with a palpable breast lump show dense breast parenchyma. No discrete mass or calcifications are seen. A sagittal post contrast MR image (panel C) in the same breast shows multiple enhancing masses (arrows) involving the upper half of the breast worrisome for malignancy. Ultrasound-guided biopsy revealed invasive ductal cancer. If there is a clinical suspicion for cancer, a negative mammogram should not stop further intervention.

CC: craniocaudal; MLO: mediolateral oblique; MR: magnetic resonance.

Breast MRI of inconclusive mammographic findings - case 1



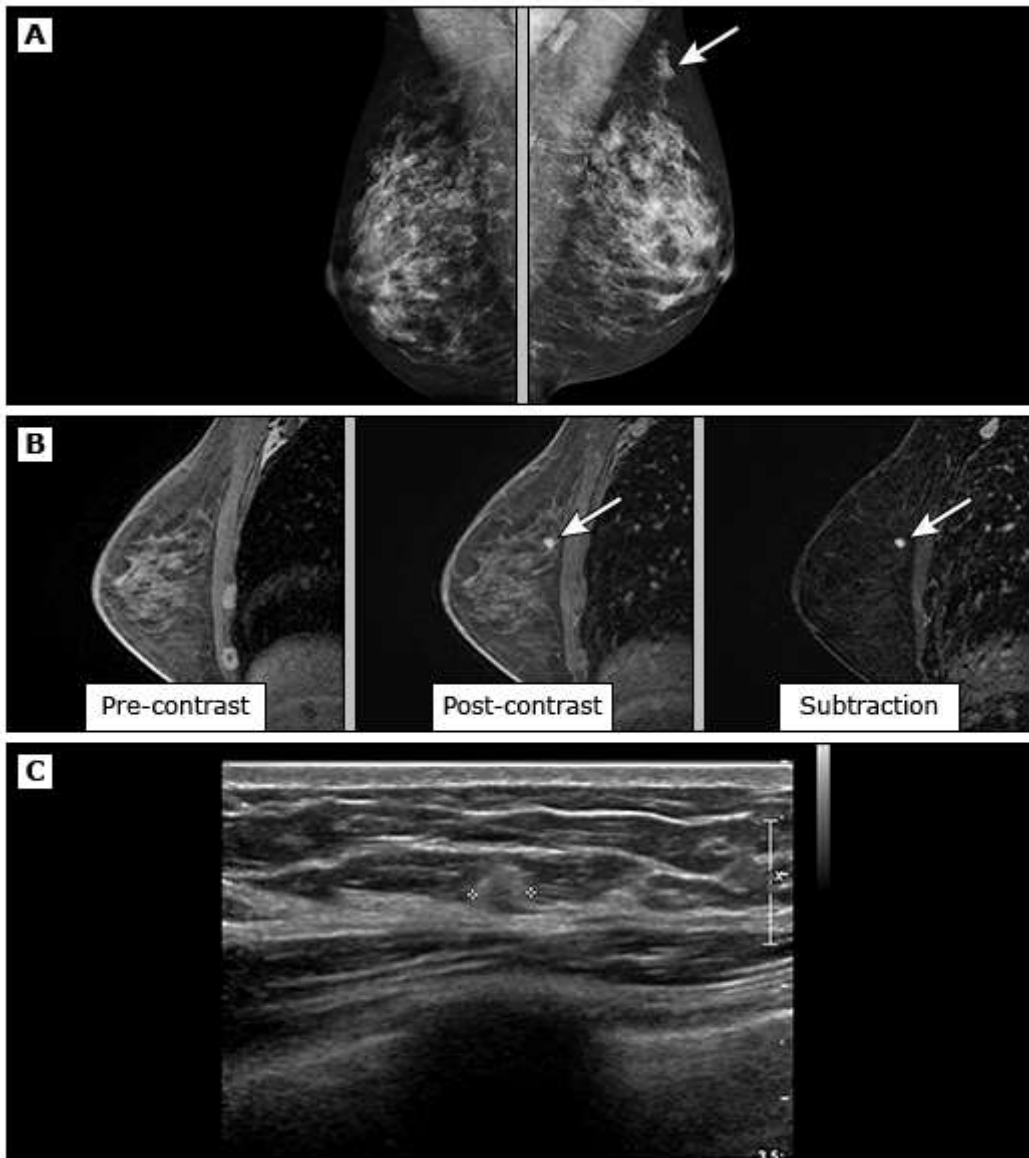
Breast MRI can be useful for problem solving in cases with inconclusive clinical or imaging findings.

(A) The mammogram shows distortion in the medial right breast, visible only on the CC projection.

(B) Breast MRI revealed a suspicious irregular enhancing mass in the medial superior breast (arrow). Biopsy confirmed invasive lobular carcinoma.

MRI: magnetic resonance imaging; CC: craniocaudal.

Breast MRI of inconclusive mammographic findings - case 2



Breast MRI can be useful for problem solving in cases with inconclusive clinical or imaging findings.

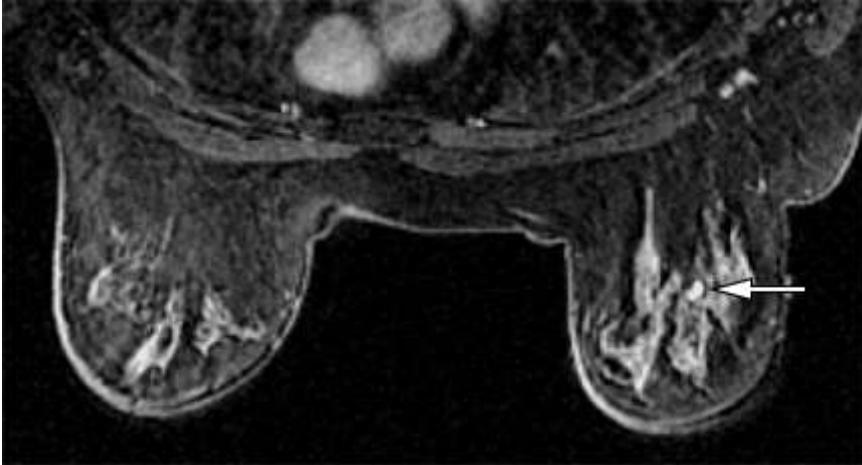
(A) Routine bilateral mediolateral oblique screening mammographic views revealed left breast asymmetry (arrow). No abnormality was seen in the right breast.

(B) Breast sagittal T1-weighted pre-contrast, post-contrast, and subtraction MR images showed a contralateral enhancing mass (arrow).

(C) Targeted transverse ultrasound image revealed an echogenic, heterogeneous mass (outlined by the calipers) which was biopsied and showed invasive ductal carcinoma on pathology.

MRI: magnetic resonance imaging.

Breast MRI screening of BRCA carrier



Breast MRI is useful for screening women with genetic mutations that confer a very high risk for breast cancer. The figure depicts a breast MRI that was performed on a BRCA-1 gene carrier, revealing a focal circumscribed mass in left breast not visible on mammography (arrow). MRI-guided core biopsy confirmed an invasive ductal carcinoma.

MRI: magnetic resonance imaging; BRCA: breast cancer susceptibility gene

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