Adrian Deckbar. *Streetcar Talk*. Oil, 40″ × 36″. Courtesy of the Hanson Gallery, New Orleans, Louisiana.

Reported advantages of MRI of the breast over conventional imaging techniques include improvements in staging and treatment planning, evaluating the augmented breast, detecting recurrence, and screening high-risk women.

Magnetic Resonance Imaging of the Breast

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Background: *Magnetic resonance imaging (MRI) has the potential to become a useful adjunct in breast imaging. Contrast-enhanced breast MRI has demonstrated a high sensitivity in the detection of invasive breast cancer. In clinical studies, breast MRI has often altered the course of patient care. Although promising results have been generated, MRI of the breast is currently in a development stage.*

Methods: *The authors reviewed the literature on the potential indications, sensitivity, specificity, and limitations of MRI of the breast.*

Results: *Reported advantages of MRI of the breast over conventional imaging techniques include improved staging and treatment planning, enhanced evaluation of the augmented breast, better detection of recurrence, and improved screening of high-risk women. Contrast-enhanced breast MRI is a sensitive modality for detecting breast cancer, but its variable specificity is a major limitation.*

Conclusions: *MRI of the breast is emerging as a valuable adjunct to mammography and sonography for specific clinical indications. Additional clinical studies that define indications, interpretation criteria, imaging parameters, and cost effectiveness are needed. A multi-institutional study designed to address these issues is in progress.*

Introduction

Magnetic resonance imaging (MRI) of the breast is a useful adjunct to mammography and sonography when specific clinical indications exist.[1-3] Potential indications for breast MRI include staging and treatment planning, evaluating palpable masses in the silicone augmented breast, detecting recurrent cancer in the posttreatment breast, identifying a clinically or mammographically occult primary tumor in the patient presenting with axillary breast cancer, evaluating the response to chemotherapy, screening in high-risk women including those who are positive for

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BRCA1 and BRCA2, and evaluating cases of indeterminate mammographic findings including cases obscured by radiographically dense breasts.[1-4] An ongoing international, multi-institutional study may offer standardized clinical indications for MRI of the breast and standardized interpretation criteria for breast MR images.[3] Although there is no evidence to support MRI of the breast as a routine screening tool, published studies have evaluated MRI as a diagnostic tool for certain clinical indications.[3] This article reviews these clinical indications, addresses the sensitivity and specificity of MRI of the breast, and discusses some of the limitations of MRI of the breast.

Staging and Treatment Planning

The American Cancer Society reported that approximately 184,200 new cases of breast cancer were diagnosed and 41,200 individuals died of the disease in the United States in 2000.[5] Properly staging these cancers is essential for appropriate management. Studies have shown that MRI can provide more accurate breast cancer staging than can be provided by conventional imaging techniques.[3] MRI has repeatedly demonstrated unsuspected multifocal or diffuse disease, which is not seen at mammography (Fig 1).

Identification of the extent and potential multifocality of breast cancer is crucial for determining if a patient is a candidate for breast-conserving therapy as opposed to mastectomy.[6] As the National Surgical Adjuvant Breast and Bowel Project (NSABP) trial demonstrated, the extent of breast cancer at lumpectomy is a major issue as nearly 40% of patients suffered a local recurrence with lumpectomy without radiation.[7]

In a study of 64 patients with biopsy-proven or presumed breast cancer, Orel et al[8] identified 13 patients (20%) with mammographically occult multifocal or diffuse disease. In a study of 463 patients and 548 histopathologically correlated lesions, Fischer and colleagues[9] concluded that MRI may reveal occult multifocal, multicentric, or contralateral breast cancer and may result in therapy changes. MRI alone depicted multifocality in 30 patients, multicentricity in 24 patients, and additional contralateral carcinomas in 15 patients. The therapeutic approach was changed in 66 patients (14.3%) because MRI revealed more extensive disease than was noted using conventional imaging techniques along with clinical examination. Harms and associates[10] found additional cancers in 11 (37%) of 30 patients and suggested that MRI could be used to stage candidates for breast-conserving therapy, to more effectively plan lumpectomy, and to reduce repeat excision surgery. Orel et al[11] determined that MRI has a high (82%) positive predictive value for predicting residual disease after initial excisional biopsy. In this study of 47 patients, MRI found 9 instances of multifocal or diffuse disease that were not seen on mammography. In patients with extensive disease as determined by MRI, altering management toward mastectomy may be more cost effective and less morbid than multiple excisions that result in mastectomy.[11] If additional lesions can be ruled out by MRI, small, solitary lesions may be treated by lumpectomy alone, thus sparing patients from the morbidity of radiation therapy.[12,13] Breast MRI may result in improved management and cost effectiveness when deciding between mastectomy and breast conservation with or without radiation therapy.

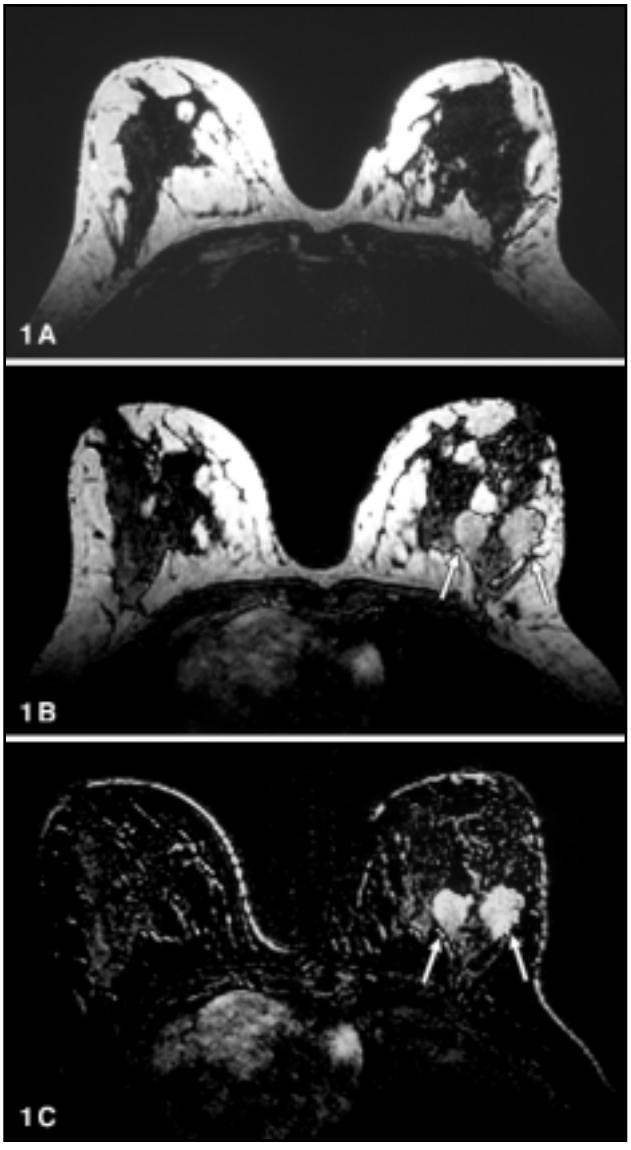


Fig 1. — T1-weighted axial breast MR images. (A) Precontrast, (B) postcontrast, and (C) subtraction images show two lobulated masses in the upper outer quadrant of the right breast (arrows), which revealed invasive ductal cancers on biopsy.

Evaluation of the Augmented Breast

Approximately 2 million American women have silicone breast implants.[14] In a study of 11,676 women with breast implants, Berkel and colleagues[15] demonstrated that women with silicone breast implants do not have a higher risk of breast cancer compared with the general population. However, Silverstein et al[16,17] suggested that breast cancer patients with implants present with more advanced stages of breast cancer and have a higher rate of axillary metastases. Also, standard mammographic views have an increased rate of false-negative diagnoses in patients with implants.[17] In a study of 18 patients with implants and breast cancer, standard mammography demonstrated an abnormality in only one patient.[17] Thus, although breast augmentation is not a risk factor for breast cancer, women with silicone implants are at increased risk for failure to detect cancer at mammography.[2] Silicone implants may obscure mammographic images of the breast tissue and interfere with the interpretation of mammograms, thus hindering detection of breast cancer.[18-20] One study estimated that augmentation mammoplasty obscures 22% to 83% of breast tissue on mammography.[21] MRI has been shown to be more sensitive than mammography for identifying coincidental malignancy in women with breast implants.[22]

The most sensitive study to determine the integrity of silicone breast implants is MRI, followed by ultrasound and then mammography.[23,24] MRI has produced sensitivities and specificities as high as 94% and 97%, respectively, for identifying implant rupture.[25] Implant rupture can be divided into two types — intracapsular or extracapsular. The double-lumen implant has an outer fibrous capsule and an inner elastomer shell. The most reliable sign of intracapsular rupture, which is the most common type of rupture, is the linguine sign, which presents as multiple curvilinear low-signal-intensity lines floating in silicone gel with no extension beyond the fibrous capsule (Fig 2).[26] The linguine sign represents the collapsed elastomer shell.[26] Extracapsular rupture occurs when both the elastomer shell and fibrous capsule rupture. It can present as gross high-signal-intensity silicone gel external to the fibrous capsule.[2] MRI sequences for evaluating implant integrity do not use intravenous contrast material, so a contrast-enhanced sequence must be added to evaluate a palpable mass and exclude malignancy in a woman with silicone breast implants.[1] Although technical imaging parameters are beyond the scope of this article, special imaging sequences may be necessary to evaluate the complications of breast implants. MRI is a valuable option for evaluating a woman with silicone breast implants who presents with a palpable mass that may be related to implant integrity or a parenchymal breast mass.[3]

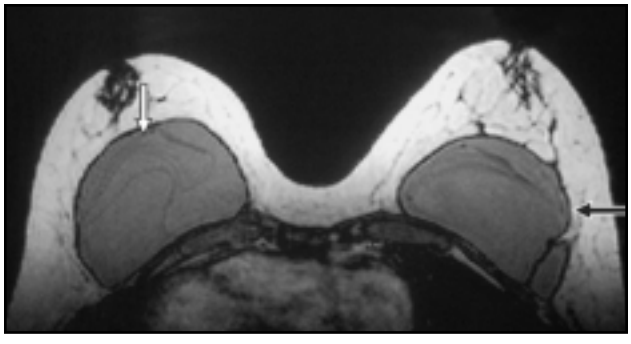


Fig 2. — T1-weighted axial MR image showing capsule herniation of the silicone implant (black arrow) and the linguine sign of intracapsular rupture (white arrow).

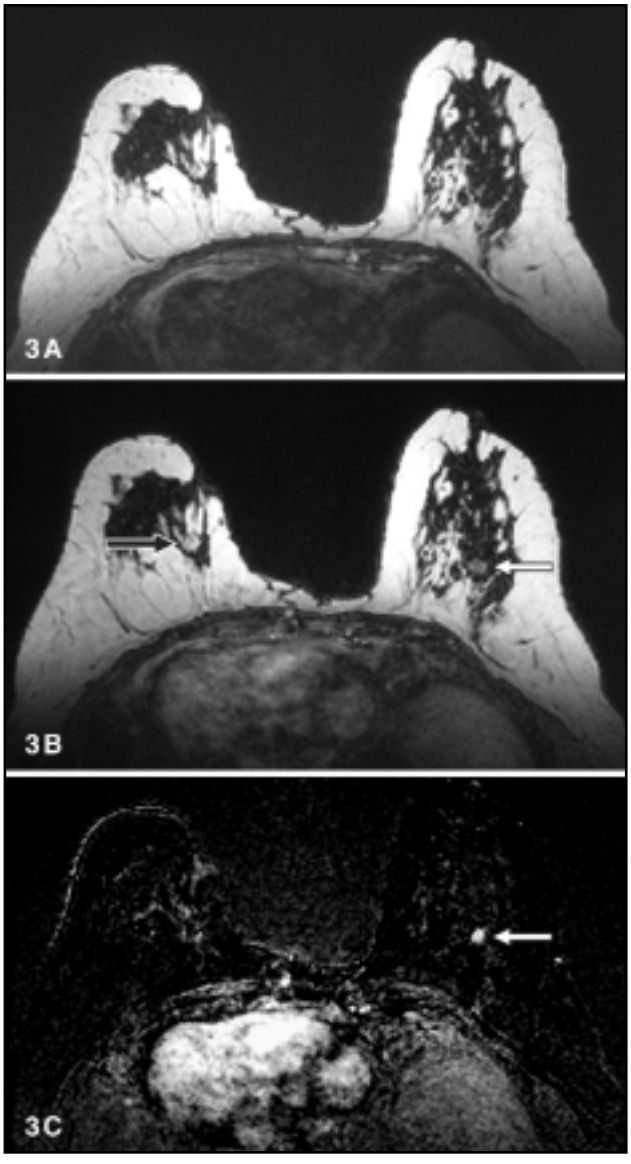


Fig 3. — T1-weighted axial breast MR images. (A) Precontrast, (B) postcontrast, and (C) subtraction images of a young woman status post left lumpectomy show mild distortion at the lumpectomy site (black arrow) and a new cancer in the right breast (white arrows).

Evaluation of the Breast After Conservation Therapy

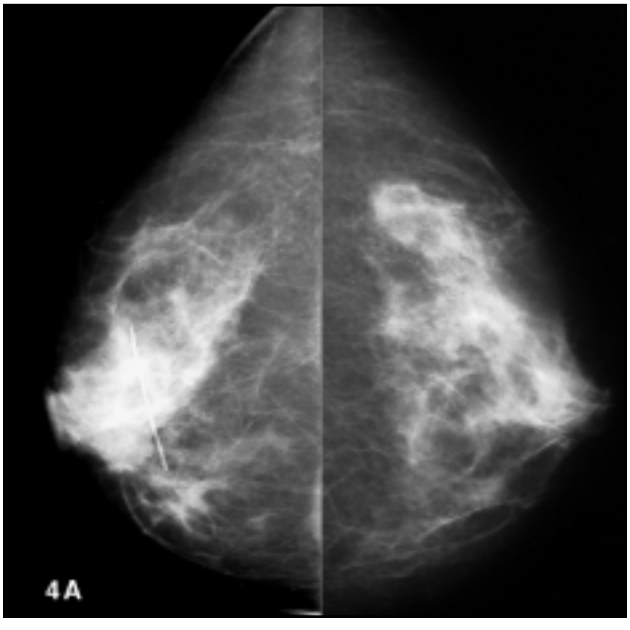
Breast-conserving therapy is increasingly being used in the treatment of breast cancer.[1] Monitoring local recurrence, which occurs in 1%-2% of cases per year, is therefore becoming more important.[1] MRI has proven to be a valuable additional tool for detecting and excluding recurrent tumor 18 months after radiation therapy.[27] After 18 months, enhancement of areas of radiation fibrosis is rare.[27] MRI has proved to be more sensitive than mammography for detecting recurrence in the posttreatment breast, which may obscure conventional images due to scarring, distortion, and density postsurgical changes (Fig 3).[28,29] In a study of 105 patients, the specificity of MRI for detecting recurrence was 93% compared with 67% for clinical examination combined with mammography, and the sensitivity of MRI was 100%, compared with mammography alone.[30] MRI may be helpful for detecting recurrence in the posttreatment breast when conventional imaging is indeterminate or negative or when there is a high clinical suspicion for recurrence.[2]

Search for Occult Breast Cancer With Known Metastases

Breast MRI is effective in localizing the site of primary cancer in patients presenting with axillary metastases and a suspected occult primary breast cancer (Fig 4).[31,32] Breast conservation can be offered to the patient if the occult primary tumor is solitary and well visualized. If MRI cannot identify the occult primary, then breast conservation is not an option.[31] Using MRI, Morris et al[31] identified 9 of 12 occult primary breast tumors. Using MRI, only one of these 12 patients had multiple enhancing lesions that necessitated mastectomy. Two patients had no identifiable tumor on histopathologic analysis at mastectomy, and MRI findings were negative in both cases. Eight patients were candidates for breast conservation therapy. Multiple reports have supported the value of MRI for identifying occult breast cancer in patients with known metastases and negative mammograms and physical examinations.[33-36] Breast MRI in this situation may offer patients the option of breast conservation instead of mastectomy.[31]

Evaluation of the Breast After Chemotherapy

MRI of the breast may be used to evaluate the response of breast cancer to chemotherapy. In one



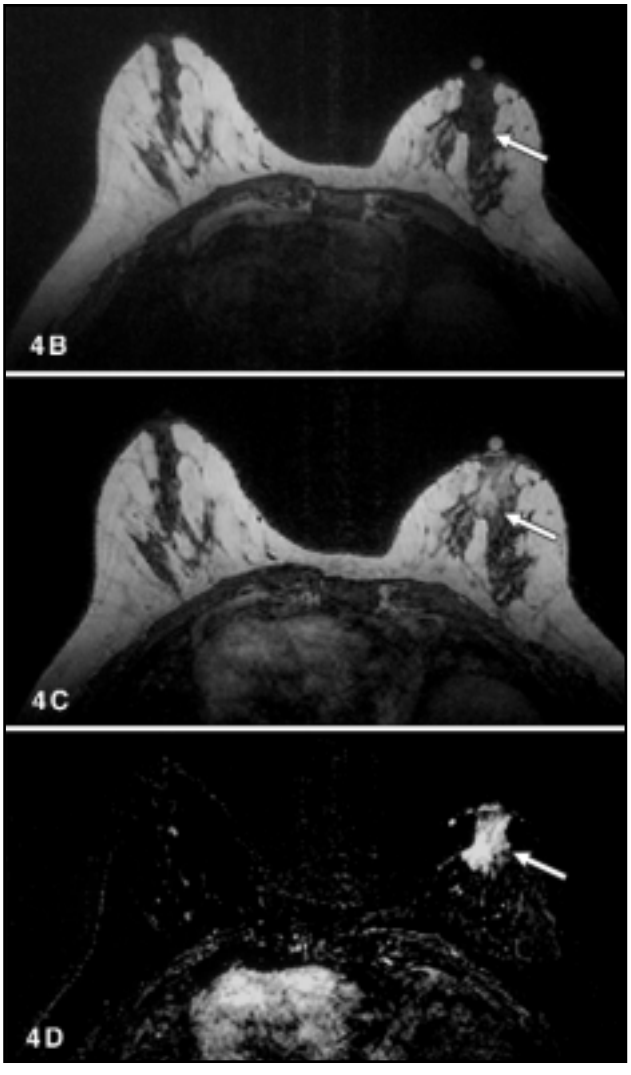


Fig 4. — (A) Unremarkable craniocaudal mammogram. T1-weighted axial (B) precontrast, (C) postcontrast, and (D) subtraction images show an occult invasive breast cancer (white arrows) in the right retroareolar tissue of a patient who presented with right axillary lymph node metastases.

study, MRI demonstrated evidence of therapeutic response after the first or second cycle with a high probability based on contrast uptake curves.[37] In another study, MRI accurately identified residual breast cancer after preoperative chemotherapy.[38] Fields et al[39] demonstrated that decreased contrast uptake of tumors treated with chemotherapy correlated with a reduction in viable tumor on histopathologic examination. MRI may be helpful in determining the response to chemotherapy and in deciding whether to use surgery or irradiation for local tumor control.

Screening in High-Risk Women

Breast cancer is the most common form of cancer in women and the second most common cause of cancer-related deaths.[40] Of more than 184,000 new cases of breast cancer that occurred in 2000, approximately 5%-10% were due to or associated with a genetic predisposition for breast cancer.[2,4,41] Therefore, at least 9,000 new breast cancer cases per year are associated with a genetic predisposition for the disease.

Mutations in BRCA1 and BRCA2 account for approximately 45% and 35%, respectively, of hereditary cases of breast cancer.[2,42] For carriers of BRCA1 and BRCA2, the lifetime risk of developing breast cancer is 56%-87%.[43-45] In contrast, the lifetime risk of the average woman in the United States for developing breast cancer is approximately 10%-12%. Also, if a carrier of BRCA1 or BRCA2 has already had one breast cancer, she then carries a 50%-64% risk of developing a second breast cancer by 70 years of age.[44]

A significant feature of hereditary breast cancer is the patient's relatively early onset of disease. By 50 years of age, approximately 50% of BRCA1 and BRCA2 carriers will develop breast cancer.[46,47] Due to the high lifetime risk of developing breast cancer and the early onset of disease, screening examinations of high-risk women should begin at a younger age, which may be 25 to 30 years of age, than is recommended for the general population.[48-50] The appropriate screening modality to be used for high-risk women is uncertain. Mammography can be less sensitive in younger, premenopausal women due to the dense breast tissue in this age group.[51-57] Also, in vitro evidence suggests that breast tissue containing a BRCA mutation may be more vulnerable to the ionizing radiation from mammography than normal breast tissue.[58-64] The high sensitivity of MRI is not limited by dense breast tissue, and MRI does not use ionizing radiation. When the alternative to screening high-risk women with MRI is prophylactic mastectomy, the value of MRI as a sensitive, cost-effective screening tool is significant.

In a study that included 192 asymptomatic women with a family or genetic history of breast cancer, Kuhl and colleagues[65] found that the accuracy of MRI is significantly higher than that of conventional imaging in screening high-risk women. Mammography found only 3 (33% sensitivity) of 9 breast cancers, while MRI correctly classified and locally staged all nine cancers (100% sensitivity). The positive predictive values were 30% for mammography and 64% for MRI. Therefore, MRI was more effective than mammography in detecting breast cancer in high-risk women, and MRI reduced the number of false-positive results as evidenced by its higher positive predictive value. A second study, which screened 109 high-risk women with MRI, reported the detection of three breast cancers that were occult at mammography.[66] MRI detected all three cancers in an early (T1 N0) stage. By analyzing a retrospective cohort of 179 high-risk women for over 6 years, Stoutjesdijk et al[67] detected 13 cancers with screening examinations. Seven of these cancers were not detected by mammography, but all 13 were revealed by MRI. In a prospective study of 196 women at high risk for hereditary breast cancer, Warner et al[68] performed a single round of screening with MRI, mammography, and ultrasound. The three modalities were performed on the same day to allow for comparison. Six invasive breast cancers were detected in the round of screening. Breast MRI detected all six invasive cancers and demonstrated a sensitivity of 100% in the cohort. Mammography detected only two of six invasive cancers, and ultrasound detected three of six invasive cancers. Interestingly, all four cancers missed by mammography were located in relatively dense breasts as determined by quantitative mammographic density analysis. The two cancers detected by mammography were surrounded by adipose tissue and were located in low-density breasts. These findings support the possibility of an MRI breast cancer surveillance program in high-risk women.

To date, no MRI screening studies have been published from institutions in the United States. Feasibility studies are needed to warrant the design of a larger, multiple-year, multicenter trial of MRI as a screening tool in high-risk women. Orel and Schnall[42] concluded that MRI as a high-risk screening tool should be investigated within the context of a clinical trial.

Evaluation of the Indeterminate Mammogram

In patients with one or more risk factors and with an indeterminate screening mammogram, MRI may be a useful diagnostic option for some of these patients (Fig 4). Radiographically dense breasts may compromise the interpretation of mammograms.[4] Dense breasts are more

common in premenopausal women, but they can occur in postmenopausal women who use hormone replacement therapy.[4] Harms and associates[4] found that magnetization transfer contrast is an essential component of MRI for accurately imaging dense breast parenchyma. As previously noted, silicone breast implants may degrade mammographic images by impairing the transmission of radiation and may limit the interpretation of breast masses or implant integrity. Women with old scars in their breast tissue resulting from surgery or trauma may demonstrate lesions on mammography that are difficult to differentiate from cancer.[4] Since old scars do not enhance, contrast-enhanced MRI can differentiate old scars from any lesions suspicious for cancer. MRI of the breast may be useful when a problematic histologic type of cancer, such as ductal carcinoma in situ (DCIS) or lobular carcinoma, is suspected. The presence of DCIS may be effectively identified with mammography, but MRI may be needed to determine the extent of DCIS and the possible coexistence of infiltrating carcinoma.[4,69] Lobular carcinoma, which accounts for 10% of all breast cancers but 30% of malpractice lawsuits for failure to diagnose cancer on mammography, may be effectively diagnosed using rotating delivery of excitation off resonance (RODEO) MRI.[4] MRI may be useful for patients with a compromised mammogram.

Sensitivity and Specificity

Contrast-enhanced breast MRI has demonstrated a sensitivity of 94%-100% in the detection of breast cancer.[70] However, specificity has generally been lower and more variable and ranges from 37% to 97%.[3] In a study based on 519 histopathologically correlated lesions, Heywang-Köbrunner and colleagues[71] illustrate the relatively high sensitivity and relatively low specificity of MRI of the breast. Although the multicenter study was aimed at improving standardization of imaging parameters and interpretation guidelines, the elegant design of the study demonstrated the relatively low specificity of MRI of the breast and the tradeoff between specificity and sensitivity. If specificity levels were set at 30%, 50%, and 64%-71%, then the respective sensitivity levels were 98%, 97%, and 96% at a magnetic field strength of 1.0T.

Accurate differentiation of benign lesions from malignant lesions serves to increase the specificity of breast MRI.[70] The two major means to differentiate benign from malignant are enhancement kinetics and lesion morphology.[72] Studies of enhancement kinetics suggest that rapid and strong enhancement within the first 2 minutes and washout of signal intensity as demonstrated by a time-signal intensity curve are sensitive indicators of malignancy.[73,74] Benign enhancement kinetics would be slow early-phase enhancement rate or velocity and a pattern of steady enhancement, as demonstrated by a time-signal intensity curve.[73,74] Lesion morphologies that suggest malignancy include spiculated or irregular borders, peripheral enhancement, and ductal enhancement.[72] Lesion morphologies that suggest a benign lesion include smooth or lobulated borders, nonenhancing internal septations (fibroadenoma), patchy parenchymal enhancement, and no enhancement.[72] The integration of both enhancement kinetics and lesion morphology may result in optimal discrimination between benign and malignant lesions.[72] An ongoing multi-institutional study will be helpful in defining standardized interpretation criteria.[3]

Limitations

A major limitation of contrast-enhanced breast MRI is its relatively low specificity.[71] False-positive enhancement has reduced specificity and cost effectiveness. To increase specificity, premenopausal patients should undergo contrast-enhanced breast MRI between days 7 and 14 of the menstrual cycle, which have the least amount of false-positive enhancement.[1,75,76] Studies have shown that healthy premenopausal breast tissue can demonstrate both diffuse and nodular enhancement during all phases of the menstrual cycle, especially in weeks 1 and 4.[75,76] Specificity is a major issue that is preventing MRI from potentially obviating some of the "unnecessary" biopsies, which are performed on the basis of suspicious mammographic findings.[2] Since only 25%-29% of the open surgical biopsies are positive and since surgical biopsies are the largest cost component of screening costs, MRI could be more cost effective and less invasive than biopsy if MRI could identify the 70%+ cases that are benign.[2] Breast MRI must become more specific to assume this role. Fibroadenomas, especially the myxoid type, and fibrocystic changes including sclerosing adenosis may demonstrate false-positive enhancement.[1-3] Other entities that may produce false-positive enhancement include fat necrosis, radial scars, mastitis, and atypical hyperplasia.[3] To increase specificity in general, MRI should not be used in populations with a low prevalence of breast cancer, including young patients with no risk factors for cancer.[1]

The need for accurate and commercially available MR-guided localization biopsy systems is a current limitation of breast MRI. Accurate MR-guided localization systems to evaluate suspicious lesions that are mammographically and clinically occult have been developed.[77-79] When mammography is able to detect a suspicious lesion, core biopsy would be less costly, more specific, and equally sensitive compared with a diagnostic MRI study.[1] Clinicians should be cognizant of the

limitations of breast MRI in order to maximize the accuracy of this valuable adjunct to conventional imaging.

Conclusions

MRI of the breast is a valuable adjunct to mammography and sonography for specific clinical indications. Notable advantages of MRI compared with conventional imaging techniques include superior evaluation of the extent and multifocality of cancer when staging patients, enhanced detection of recurrence, better evaluation of lesions in the augmented breast, and improved screening of high-risk women. Contrast-enhanced MRI of the breast is a sensitive method for detecting breast cancer, but its variable specificity is a major limitation. An international multi-institutional study currently in progress has been designed not only to define clinical indications, interpretation criteria, and technical requirements for imaging, but also to develop accurate biopsy systems and address cost effectiveness.

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