VOLUME 23 · NUMBER 8 · MARCH 10 2005

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

# Magnetic Resonance Imaging of the Breast: Opportunities to Improve Breast Cancer Management

*Nola Hylton*

*J Clin Oncol 23:1678-1684. © 2005 by American Society of Clinical Oncology*

From the Department of Radiology, University of California San Francisco, San Francisco, CA.

Submitted November 18, 2004; accepted December 6, 2004.

Author's disclosures of potential conflicts of interest are found at the end of this article.

Address reprint requests to Nola Hylton, PhD, Magnetic Resonance Science Center, University of California San Francisco, 1 Irving St, Room AC-109, San Francisco, CA 94143-1290; e-mail: nola.hylton@radiology.ucsf.edu.



0732-183X/05/2308-1678/$20.00

DOI: 10.1200/JCO.2005.12.002

## INTRODUCTION

Magnetic resonance imaging (MRI) is a relatively recent diagnostic tool for the breast, and the role of MRI in breast cancer management is evolving. As an adjunct to mammography and ultrasound, MRI can be a valuable addition to the work-up of a breast abnormality or biopsy-proven cancer. MRI has the advantages of providing a three-dimensional view of the breast, performing with high sensitivity in dense breast tissue and using non-ionizing radiation. MRI has significant disadvantages as well, including its high cost, variability in performance, and moderate specificity that, in combination with high sensitivity, often leads to unnecessary work-up.

As MRI finds wider use, there is concern among clinicians that it may lead to more aggressive treatments for breast cancer without necessarily improving patient outcomes. MRI may be oversensitive, revealing noninvasive disease that may never progress, or residual disease that would be effectively treated by radiation. MRI also adds considerable cost to patient care. However, it is possible that judicious use of MRI could lead to changes in practice patterns that have been adopted based on outcomes using current methods for detecting and staging breast cancer. Many standards of care are applied broadly to groups of patients, although it is known that they benefit only a subset. The high sensitivity of MRI may allow breast cancers to be characterized more precisely such that less invasive and better-tailored treatment options, including watchful waiting, can be used. This review discusses the current clinical applications for breast MRI and emerging areas where MRI has the potential to change and improve breast cancer management.

## MRI VERSUS MAMMOGRAPHY

The different physical bases of mammography and MRI support their complementary use for detecting and diagnosing breast cancer. Mammography has an established role in breast cancer screening and diagnosis. Mammography is an x-ray method optimized for evaluation of breast tissue and the detection of breast cancers while minimizing radiation dosage. Cancers in the breast are detected by mammography on the basis of differences in x-ray attenuation between cancers and noncancerous breast tissue, distortions in tissue architecture, or appearance of certain patterns of microcalcifications. Mammography is relatively quick to perform and inexpensive. Decades of experience with large-scale breast cancer screening programs and the more recent implementation of mammographic quality standards have led to improved performance of mammography equipment and radiologic interpretations in large-volume centers.

The high soft tissue contrast and three-dimensional format of MRI allows anatomic structures of the breast to be viewed in great detail. The anatomic detail alone, however, is not sufficient to make a diagnostic assessment. Malignant lesions are often indistinguishable from normal and benign

structures on standard T1-weighted or T2-weighted MRI. Cancer detection requires the use of an intravenous contrast agent. The increased density and leakiness of microvessels associated with cancer growth is reflected by an early, significant increase in the signal intensity after contrast is injected, the basis of cancer detection using MRI.

An important distinction between mammography and MRI, that again supports their complementary roles, is in their sensitivity to breast microcalcifications that can often signify breast cancer. Mammography is very effective for demonstrating the presence and distribution of microcalcifications. However, while calcium deposits can occasionally be seen on MRI as tiny signal voids, breast MRI is not a reliable detection method for microcalcifications. In several studies, MRI was used to evaluate women with suspicious mammographic microcalcifications with the goal of determining if diagnostic specificity could be improved on the basis of MRI enhancement patterns. Results of these studies have been mixed, with some showing improvements in specificity[1,2] and others concluding that MRI has limited diagnostic accuracy for distinguishing benign from malignant mammographic calcifications.[3,4] Few studies have directly evaluated the MRI characteristics of the signal voids created by microcalcifications.[5,6] One study of excised breast specimens used a high spatial resolution technique to correlate signal voids with microcalcifications on histology; however, clusters of microcalcifications appeared as single signal voids and MRI was not able to further characterize important features such as size, shape, and clustering that are associated with the presence of breast cancer.[5] These considerations imply that MRI should not be a replacement for mammographic screening since microcalcifications can often be an early sign of breast cancer.

## MRI FOR BREAST CANCER SCREENING

Two areas where the advantages of MRI over conventional breast imaging make it likely to have an impact on care are: (1) early detection in high-risk women; and (2) treatment staging. In the area of early detection, enthusiasm has been fueled by data from many studies showing that virtually all malignancies of the breast enhance following injection of contrast agent, and that small cancers can be detected without adverse impact from dense breast tissue.[7-13] The implementation of MRI as a widespread breast screening practice is not feasible, however, due to a number of factors: most significantly, its high cost, difficulty in standardizing the test, limited specificity, and the complexity of performing biopsies under MRI guidance. More likely and potentially important applications of screening MRI are for women with elevated breast cancer risk or as a secondary screen for women with mammographically dense breast tissue.

A number of ongoing clinical trials are evaluating breast cancer screening by MRI in high-risk populations. Trials underway in the Netherlands, United Kingdom, Canada, Germany, and the United States have reported between 1% and 4% cancer yield on initial screening MRI in high-risk populations.[14-18] One third to one half of screened cancers detected by MRI were not seen on mammography or found at clinical exam. Among *BRCA1* and *BRCA2* mutation carriers, the reported cancer yield is even higher (4% to 9%).[14,16] In the large series of 1,909 patients included in the Netherlands MRI screening trial, a number of differences existed among the tumor characteristics of the 358 mutation carriers and the moderate- (15% to 29% cumulative lifetime) and high-risk (30% to 49% cumulative lifetime) groups, including higher histologic grade and lower hormone positivity in the mutation carriers.[14] Interestingly, of the five interval cancers found on second or third MRI screening exams, four were in mutation carriers, possibly suggesting faster growth rates of these tumors.

The MRI screening trials vary in the imaging protocols employed, risk levels used for study inclusion, and interpretation standards. The true screening performance of MRI in such populations will be difficult to establish. Even more difficult to determine will be the appropriate risk levels at which screening MRI should be recommended. Nonetheless, it is likely that high-risk women and their physicians will continue to pursue screening MRI as an option since so few alternatives are available.

## MRI FOR DIFFERENTIAL DIAGNOSIS

The greatest diagnostic challenge for breast MRI lies in the spectrum of disease from proliferative hyperplasia to noninvasive and low-grade invasive carcinoma. These conditions produce the majority of false positives and false negatives, which have important implications for the use of breast MRI. While false negatives are fairly infrequent, enhancement of benign disease occurs often and can add ambiguity in the diagnostic work-up of a breast abnormality. The limitation of low specificity prevents MRI from playing a major role in the work-up of a specific breast abnormality, with biopsy remaining the recommended procedure for making a definitive diagnosis in most cases. MRI of a suspicious breast lesion can often play a confirmatory role while providing information about the size and multifocality of the lesion.[12,19,20] MRI can also add value for the evaluation of patients with axillary carcinoma and negative mammographic and clinical findings[21-26] and women with questionable mammographic findings and previous breast surgery, to distinguish postsurgical scar from recurrent carcinoma.[27-30]

## MRI FOR BREAST CANCER STAGING

MRI is effective for staging the extent of disease following a biopsy diagnosis of cancer. In numerous studies, MRI has been shown to be superior to mammography and ultrasound for estimating tumor size when compared with

histopathology.[12,31,32] In a comparison of mammography, ultrasound and MRI using concordance with histopathology as the end point, Esserman et al[32] found that MRI showed the greatest improvement over mammography and ultrasound for staging disease extent when multifocal disease or ductal carcinoma-in-situ (DCIS) was present. Information about the extent of disease is useful in determining suitability for breast conservative surgery and can be used to help guide breast conservation.[33] However, in practice, it is difficult to translate the anatomic boundaries of the enhancing lesion seen on MRI to surgical coordinates with enough precision to ensure adequate margins while minimizing the amount of tissue excised. A criticism of MRI is that it is likely to result in more aggressive surgical approaches without necessarily improving outcomes. Occult multifocality suggested by MRI should be verified by biopsy before recommending substantial alteration to the surgical plan.

## MRI FOR STAGING DCIS

A less well-established application for MRI is the characterization of DCIS. DCIS presents challenges for MRI. It is more frequently missed on MRI than invasive disease.[34-37] At the same time, it is unclear how aggressively MRI should be used to detect otherwise occult DCIS. Detection will lead to surgery and treatment that may not be necessary. Nonetheless, MRI can depict the extent and distribution of DCIS more effectively than mammography or ultrasound.[19,38] DCIS is being detected more frequently with the widespread use of screening mammography and there is a great need to find better methods for treating DCIS. DCIS is an early form of breast cancer defined by the confinement of cancer cells within the ducts. DCIS has an excellent prognosis and cures can be achieved with successful local treatment. DCIS is most commonly detected by screening mammography and generally presents with linear, pleomorphic, or clustered calcifications. The increased use of screening mammography over the last several decades has led to greater detection rates for DCIS and, as a result, more is known about DCIS. Like many invasive cancers, once detected, DCIS is treated surgically. However, in the absence of a lump to guide breast-conservation surgery, DCIS is often treated by mastectomy, and attempts at breast conservation often result in positive margins and the need for re-excision.

Better treatment approaches for DCIS are needed. MRI is effective for demonstrating the presence and extent of DCIS following a biopsy diagnosis of cancer and can be helpful in the planning for breast-conservation surgery. A substantial number of DCIS patients have been found to have multifocal disease on MRI even when mammography suggests unifocal disease.[39] MRI has also proven to be a good detector of cancers that are occult on mammography.[18,40-42] Since occult microinvasion is most common in DCIS lesions greater than 2.5cm, as well as for high-grade comedo DCIS,[43] MRI may be a useful complementary modality for studying which DCIS lesions have the potential to become invasive lesions. Conversely, MRI might suggest DCIS lesions for which radiation treatment is not required. MRI is also a more reliable modality for women with dense or nodular breasts for whom mammography or clinical examination performs poorly.[41] Morris et al,[18] in a study of 367 high-risk women, found that more than half of the 14 MRI-detected cancers occult on mammography and physical examination were DCIS lesions.

In addition, MRI could be developed to characterize DCIS noninvasively, to assess aggressiveness and likelihood of an associated invasive component, and suitability for nonsurgical treatment approaches.[44] In a study of 51 patients with biopsy-proven DCIS, Hwang et al[41] looked at the performance of MRI for assessment of residual disease, occult invasion, and multicentric disease in order to determine the clinical role of MRI in the management of preinvasive breast cancers. All patients underwent high spatial resolution contrast-enhanced MRI before surgery. MRI findings were correlated with mammography and histopathology. Histopathology demonstrated the presence of residual disease in 39 patients. Invasive cancer was associated with DCIS in seven patients; 16 patients had multicentric disease. The accuracy of MRI was 88% in predicting residual disease, 82% in predicting invasive disease, and 90% in predicting multicentricity. Subgroup analysis demonstrated higher performance of MRI when the diagnosis of DCIS was made by core biopsy rather than surgical biopsy. When compared to mammography, the accuracy of MRI was statistically equivalent for the diagnosis of occult invasion. However, for the diagnosis of residual disease and multicentricity, MRI was more sensitive and had a higher negative predictive value than mammography ($P < .05$).[41] While MRI cannot be used to rule out the presence of residual disease post-lumpectomy, it can provide information regarding the extent of residual disease and can be useful for determining whether re-excision or mastectomy is most appropriate.

DCIS is known to have a heterogeneous histopathology and certain features; grade and presence of comedo necrosis are associated with a higher risk of recurrence. DCIS also demonstrates a wide range of imaging features on MRI.[35-37,40] A significant percentage of mammographically detected DCIS lesions exhibit contrast enhancement on MRI. These findings indicate increased density or permeability of the local microvasculature associated with these lesions that are still confined to the ducts.[45] DCIS associated with invasive cancer is also frequently observed as contrast-enhancing on MRI. DCIS can appear as linear, branching structures, heterogeneously clumped enhancement, and as focal masses (Fig 1).

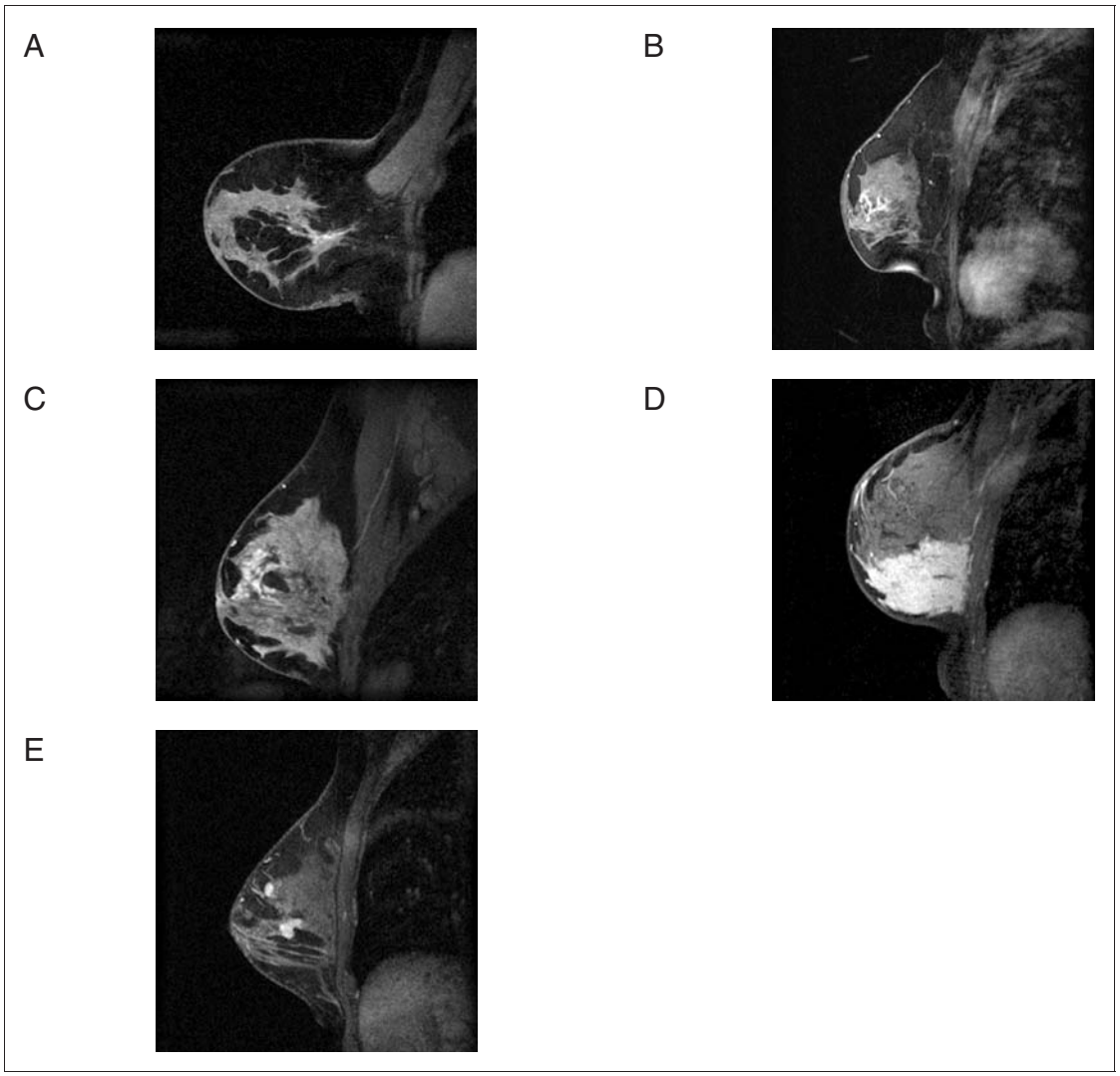


**Fig 1.** Ductal carcinoma-in-situ demonstrates heterogenous patterns of enhancement including (A) linear enhancement with irregular borders; (B) branching ductal enhancement with smooth borders; (C) segmental clumped enhancement; (D) regional homogenous enhancement; and (E) focal mass enhancement.

Mammography remains the primary method for detecting DCIS; however, MRI shows usefulness for determining the extent of disease following a biopsy diagnosis of DCIS and for depicting intraductal extension associated with a primary invasive cancer. In both of these roles, MRI may contribute to better surgical management for patients with breast carcinoma.

## ASSESSMENT OF NEOADJUVANT TREATMENT

As new therapeutic options for breast cancer continue to become available, there is a great need for methods that can be used to rapidly and reliably compare the efficacy of different therapies and treatment strategies. This need has fueled the search for biomarkers that can be assessed for individual patients before or early in their treatment. An acceptable biomarker must show a strong association with survival outcomes in order to be relied upon as a surrogate end point. Imaging has the potential to provide such a biomarker. The appeal of an imaging biomarker is that it can be measured in vivo, repeatedly over time, and represents the entire tumor. MRI has the added benefit over x-ray and nuclear medicine techniques of not using ionizing radiation and can therefore be used safely in serial studies.

Imaging biomarkers are being pursued in the context of preoperative chemotherapy of breast cancer. Systemic chemotherapy is known to improve survival for patients with invasive breast cancer and is considered the standard of care for node-positive patients with large primary tumors and for many patients with high-risk, node-negative disease. A number of trials have compared preoperative chemotherapy with postoperative chemotherapy.

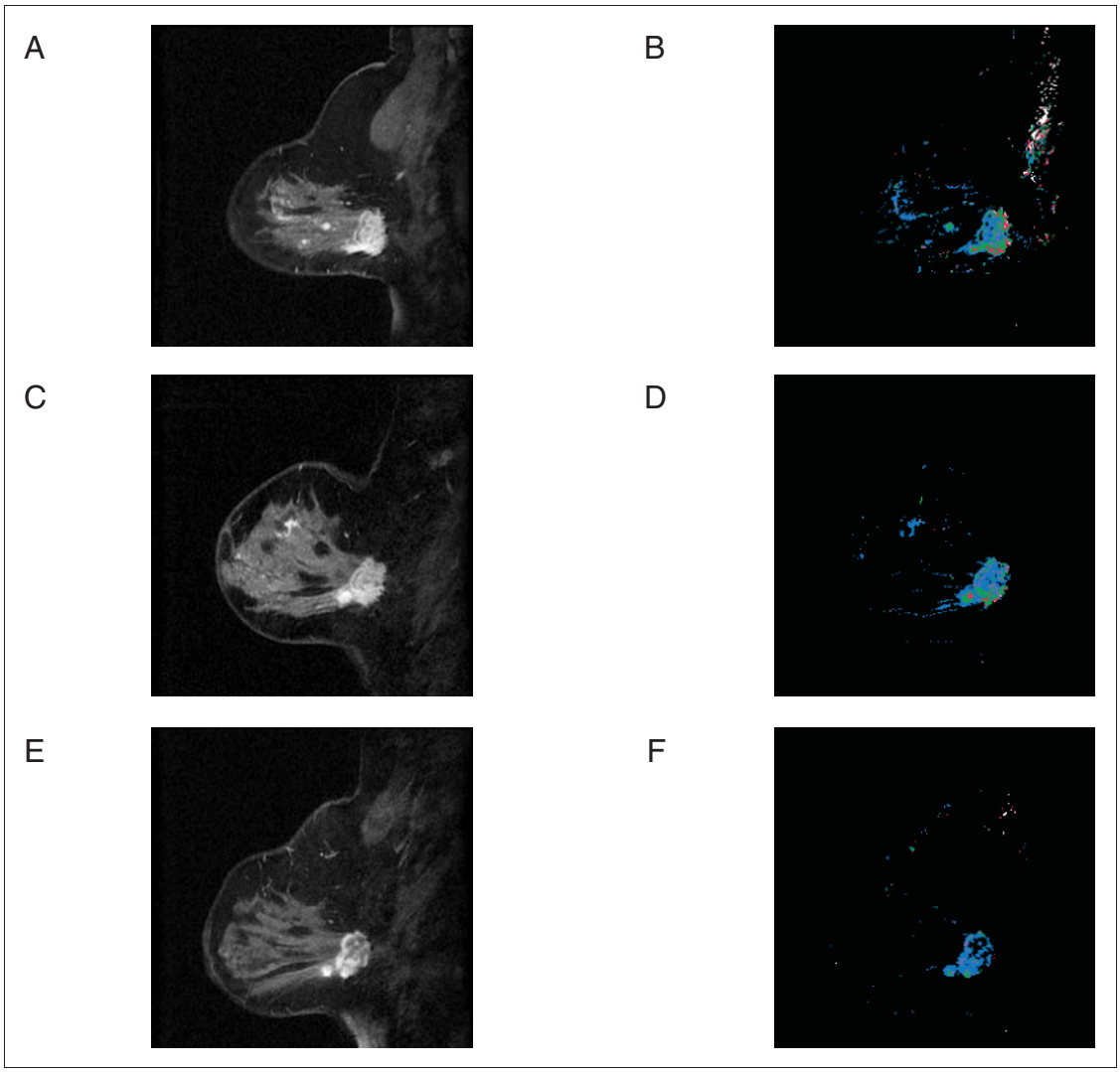


**Fig 2.** Contrast-enhanced magnetic resonance images (A, C, E) and signal enhancement ratio (B, D, F) parametric maps for a patient with locally advanced breast cancer. Central slice images through the tumor are shown pretreatment (A,B), following one cycle of adriamycin-cytoxan (C,D), and following four cycles of adriamycin-cytoxan (E,F). Tumor volume decreased over treatment from 7.4 cc at baseline to 6.5 cc after one cycle of treatment, and to 3.9 at the end of four cycles of adriamycin-cytoxan.

Although, there was no difference in disease-free survival and overall survival, more women receiving preoperative chemotherapy were able to undergo breast conservation. These findings have led to the increased use of preoperative, or neoadjuvant, chemotherapy. Further findings from the National Surgical Adjuvant Breast and Bowel Project B-18 and other studies have demonstrated that response of the primary tumor to treatment, as measured clinically or by histopathology, is associated with both disease-free and overall survival.[46,47] Thus, an additional advantage to preoperative chemotherapy is that it affords the opportunity to monitor the primary tumor response.

The high staging accuracy of breast MRI makes it an attractive method for assessing tumor response to preoperative chemotherapy. MRI can contribute in several ways to the management of patients receiving preoperative chemotherapy, including the initial determination of extent of disease for proper staging, early identification of poor responders, and identification of the presence and extent of residual disease for surgical planning. MRI measurements of tumor response may have predictive value for disease recurrence and responsiveness to novel therapeutics. This potential is being explored in a number of clinical studies. MRI can accurately demonstrate the extent of residual disease after neoadjuvant therapy if appropriate adjustments are made to detection thresholds to allow for reduced contrast enhancement after chemotherapy.[48] MRI also has the capability to measure functional properties of the tumor. Measurements of the tumor microvasculature can be derived from the contrast-enhancement kinetics observed

during the first several minutes following the injection of contrast. The multiparametric measurements obtainable from MRI, combining both anatomy and function, have the capacity to predict who will respond to therapy.

A number of MRI parameters have been investigated for their ability to predict response. The morphologic pattern that the tumor forms in the breast can be quite variable, and appears to be predictive of response to therapy.[49] Several studies have looked at the ability of pharmacokinetic parameters ($k_{trans}$, the transfer constant for gadolinium contrast agent between the intravascular and extravascular/extracellular space, and fBV, the fractional blood volume) to predict tumor response.[50-53] Others have used empirically derived parameters such as the signal-enhancement ratio to compare contrast wash-in and wash-out at high spatial resolution. Partridge et al[54] found that tumor volume based on signal-enhancement ratio was most predictive of time-to-disease recurrence (Fig 2). A large multicenter trial sponsored jointly by the American College of Radiology Imaging Network, the Cancer and Leukemia Group B, and the National Cancer institute is integrating serial MRI tumor measurements with serial collection of tissue for biomarkers (expression, genomic, protein arrays, as well as specific immunohistochemical markers and fluorescence in situ hybridization). The goal of such studies is to identify robust combinations of markers, including imaging, to identify early on those women who will have excellent responses to chemotherapy, and those whose tumors have a marginal or modest response. This would allow the early introduction of novel therapeutics that could be assessed using the optimal combination of biomarkers.

## FUTURE DEVELOPMENTS IN BREAST IMAGING

Imaging technologies continue to advance and many powerful new methods for in vivo cellular and molecular imaging are emerging. Multimodal methods that combine anatomic imaging with functional measurements may provide imaging assays that can be used noninvasively to assess the effects of treatment dynamically and over the whole tumor. MRI is intrinsically multiparametric, with anatomic and functional parameters measurable during a single patient exam. Combined measurements of tumor vascularity, water diffusion (reflective of tissue cellularity), and proton-containing metabolite concentrations could add specificity to MRI of breast disease. Tumor-targeted contrast agents for MRI that are under development could also improve the specificity of breast MRI substantially. Higher field strength 3.0 Tesla scanners are now commercially available, bringing improvements in image resolution and signal-to-noise over the current standard 1.5 to 2.0 Tesla systems. The greater signal-to-noise and spectral separation available with the higher field systems should lead to improved ability to sensitively measure metabolites such as choline with in vivo breast MRI spectroscopy methods. Coupled with these advances are the computer workstations and image analysis capabilities to support multimodality image fusion, functional analysis, and visualization tools. Development of integrated imaging systems is moving at a rapid pace and will be important for facilitating the use of advanced imaging technologies for patient care. As the search for better cancer treatments progresses, imaging will undoubtedly play a role in their evaluation and the improved delivery of care to patients.

### *Author's Disclosures of Potential Conflicts of Interest*

The author indicated no potential conflicts of interest.

## REFERENCES


**1.** Nakahara H, Namba K, Fukami A, et al: Three-dimensional MR imaging of mammographically detected suspicious microcalcifications. Breast Cancer 8:116-124, 2001

**2.** Trecate G, Tess JD, Vergnaghi D, et al: Breast microcalcifications studied with 3D contrast-enhanced high-field magnetic resonance imaging: More accuracy in the diagnosis of breast cancer. Tumori 88:224-233, 2002

**3.** Gilles R, Meunier M, Lucidarme O, et al: Clustered breast microcalcifications: Evaluation by dynamic contrast-enhanced subtraction MRI. J Comput Assist Tomogr 20:9-14, 1996

**4.** Westerhof JP, Fischer U, Moritz JD, et al: MR imaging of mammographically detected clustered microcalcifications: is there any value? Radiology 207:675-681, 1998

**5.** Holland AE, Hendrick RE, Jin H, et al: Correlation of high-resolution breast MR imaging with histopathology: Validation of a technique. J Magn Reson Imaging 11:601-606, 2000

**6.** James D, Clymer BD, Schmalbrock P: Texture detection of simulated microcalcification susceptibility effects in magnetic resonance imaging of breasts. J Magn Reson Imaging 13:876-881, 2001

**7.** Heywang SH, Wolf A, Pruss E, et al: MR imaging of the breast with Gd-DTPA: Use and limitations. Radiology 171:95-103, 1989

**8.** Kaiser WA, Zeitler E: MR imaging of the breast: Fast imaging sequences with and without Gd-DTPA. Preliminary observations. Radiology 170:681-686, 1989

**9.** Orel SG, Schnall MD, Powell CM, et al: Staging of suspected breast cancer: Effect of MR imaging and MR-guided biopsy. Radiology 196:115-122, 1995

**10.** Stomper PC, Herman S, Klippenstein DL, et al: Suspect breast lesions: Findings at dynamic gadolinium-enhanced MR imaging correlated with mammographic and pathologic features. Radiology 197:387-395, 1995

**11.** Gilles R, Guinebretiere JM, Lucidarme O, et al: Nonpalpable breast tumors: Diagnosis with contrast-enhanced subtraction dynamic MR imaging. Radiology 191:625-631, 1994

**12.** Boetes C, Mus RD, Holland R, et al: Breast tumors: Comparative accuracy of MR imaging relative to mammography and US for demonstrating extent. Radiology 197:743-747, 1995

**13.** Harms SE, Flamig DP, Hesley KL, et al: MR imaging of the breast with rotating delivery of excitation off resonance: Clinical experience with pathologic correlation. Radiology 187:493-501, 1993

**14.** Kriege M, Brekelmans CT, Boetes C, et al: Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. N Engl J Med 351:427-437, 2004

**15.** Leach MO, Eeles RA, Turnbull LW, et al: The UK national study of magnetic resonance

imaging as a method of screening for breast cancer (MARIBS). J Exp Clin Cancer Res 21:107-114, 2002 (suppl 3)

**16.** Warner E, Plewes DB, Hill KA, et al: Surveillance of BRCA1 and BRCA2 mutation carriers with magnetic resonance imaging, ultrasound, mammography, and clinical breast examination. JAMA 292:1317-1325, 2004

**17.** Kuhl CK, Schmutzler RK, Leutner CC, et al: Breast MR imaging screening in 192 women proved or suspected to be carriers of a breast cancer susceptibility gene: Preliminary results. Radiology 215:267-279, 2000

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

**19.** Mumtaz H, Hall-Craggs MA, Davidson T, et al: Staging of symptomatic primary breast cancer with MR imaging. AJR Am J Roentgenol 169:417-424, 1997

**20.** Van Goethem M, Schelfout K, Dijckmans L, et al: MR mammography in the pre-operative staging of breast cancer in patients with dense breast tissue: Comparison with mammography and ultrasound. Eur Radiol 14:809-816, 2004

**21.** Henry-Tillman RS, Harms SE, Westbrook KC, et al: Role of breast magnetic resonance imaging in determining breast as a source of unknown metastatic lymphadenopathy. Am J Surg 178:496-500, 1999

**22.** Orel SG, Weinstein SP, Schnall MP, et al: Breast MR imaging in patients with axillary node metastases and unknown primary malignancy. Radiology 212:543-549, 1999

**23.** Schorn C, Fischer U, Luftner-Nagel S, et al: MRI of the breast in patients with metastatic disease of unknown primary. Eur Radiol 9:470-473, 1999

**24.** Tilanus-Linthorst MM, Obdeijn AI, Bontenbal M, et al: MRI in patients with axillary metastases of occult breast carcinoma. Breast Cancer Res Treat 44:179-182, 1997

**25.** Schelfout K, Kersschot E, Van Goethem M, et al: Breast MR imaging in a patient with unilateral axillary lymphadenopathy and unknown primary malignancy. Eur Radiol 13:2128-2132, 2003

**26.** Chen C, Orel SG, Harris E, et al: Outcome after treatment of patients with mammographically occult, magnetic resonance imaging-detected breast cancer presenting with axillary lymphadenopathy. Clin Breast Cancer 5:72-77, 2004

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

**28.** Melani E, Sardanelli F, Ottonello C, et al: Magnetic resonance mammography in suspected tumor recurrences. Radiol Med (Torino) 89:219-224, 1995

**29.** Muuller RD, Barkhausen J, Sauerwein W, et al: Assessment of local recurrence after breast-conserving therapy with MRI. J Comput Assist Tomogr 22:408-412, 1998

**30.** Whitehouse GH, Moore NR: MR imaging of the breast after surgery for breast cancer. Magn Reson Imaging Clin N Am 2:591-603, 1994

**31.** Soderstrom CE, Harms SE, Copit DS, et al: Three-dimensional RODEO breast MR imaging of lesions containing ductal carcinoma in situ. Radiology 201:427-432, 1996

**32.** Esserman L, Hylton N, Yassa L, et al: Utility of magnetic resonance imaging in the management of breast cancer: Evidence for improved preoperative staging. J Clin Oncol 17: 110-119, 1999

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

**34.** Boetes C, Strijk SP, Holland R, et al: False-negative MR imaging of malignant breast tumors. Eur Radiol 7:1231-1234, 1997

**35.** Orel SG, Mendonca MH, Reynolds C, et al: MR imaging of ductal carcinoma in situ. Radiology 202:413-420, 1997

**36.** Sittek H, Kessler M, Heuch AF, et al: Morphology and contrast enhancement of ductal carcinoma in situ in dynamic 1.0 T MR mammography. Rofo 167:247-251, 1997

**37.** Zuiani C, Francescutti GE, Londero V, et al: Ductal carcinoma in situ: Is there a role for MRI? J Exp Clin Cancer Res 21:89-95, 2002 (suppl 3)

**38.** Hata T, Takahashi H, Wanatabe K, et al: Magnetic resonance imaging for preoperative evaluation of breast cancer: A comparative study with mammography and ultrasonography. J Am Coll Surg 198:190-197, 2004

**39.** Harms SE, Flamig DP: MR imaging of the breast: Technical approach and clinical experience. Radiographics 13:905-912, 1993

**40.** Liberman L, Morris EA, Lee MJ, et al: Breast lesions detected on MR imaging: Features and positive predictive value. AJR Am J Roentgenol 179:171-178, 2002

**41.** Hwang ES, Kinkel K, Esserman LJ, et al: Magnetic resonance imaging in patients diagnosed with ductal carcinoma-in-situ: Value in the diagnosis of residual disease, occult invasion, and multicentricity. Ann Surg Oncol 10:381-388, 2003

**42.** Esserman L, Wolverton D, Hylton N: Magnetic resonance imaging for primary breast cancer management: Current role and new applications. Endocr Relat Cancer 9:141-153, 2002

**43.** Burstein HJ, Polyak K, Wong JS, et al: Ductal carcinoma in situ of the breast. N Engl J Med 350:1430-1441, 2004

**44.** Esserman L, Sepucha K, Ozanne E, et al: Applying the neoadjuvant paradigm to ductal carcinoma in situ. Ann Surg Oncol 11:28S-36S, 2004 (suppl 1)

**45.** Gilles R, Zafrani B, Guinebretiere JM, et al: Ductal carcinoma in situ: MR imaging-histopathologic correlation. Radiology 196:415-419, 1995

**46.** Fisher B, Bryant J, Wolmark N, et al: Effect of preoperative chemotherapy on the outcome of women with operable breast cancer. J Clin Oncol 16:2672-2685, 1998

**47.** Wolmark N, Wang J, Mamounas E, et al: Preoperative chemotherapy in patients with operable breast cancer: Nine-year results from National Surgical Adjuvant Breast and Bowel Project B-18. J Natl Cancer Inst Monogr:96-102, 2001

**48.** Partridge SC, Gibbs JE, Lu Y, et al: Accuracy of MR imaging for revealing residual breast cancer in patients who have undergone neoadjuvant chemotherapy. AJR Am J Roentgenol 179:1193-1199, 2002

**49.** Esserman L, Kaplan E, Partridge S, et al: MRI phenotype is associated with response to doxorubicin and cyclophosphamide neoadjuvant chemotherapy in stage III breast cancer. Ann Surg Oncol 8:549-559, 2001

**50.** Wasser K, Klein SK, Fink C, et al: Evaluation of neoadjuvant chemotherapeutic response of breast cancer using dynamic MRI with high temporal resolution. Eur Radiol 13:80-87, 2003

**51.** Knopp MV, Brix G, Junkermann HJ, et al: MR mammography with pharmacokinetic mapping for monitoring of breast cancer treatment during neoadjuvant therapy. Magn Reson Imaging Clin N Am 2:633-658, 1994

**52.** Hayes C, Padhani AR, Leach MO: Assessing changes in tumour vascular function using dynamic contrast-enhanced magnetic resonance imaging. NMR Biomed 15:154-163, 2002

**53.** Martincich L, Montemurro F, De Rosa G, et al: Monitoring response to primary chemotherapy in breast cancer using dynamic contrast-enhanced magnetic resonance imaging. Breast Cancer Res Treat 83:67-76, 2004

**54.** Partridge SC, Gibbs JE, Lu Y, et al: MRI measurements of breast tumor volume predict response to neoadjuvant chemotherapy and recurrence-free survival. AJR Am J Roentgenol: in press