MRI OF THE BREAST

Department of Radiology, The University of Chicago
Gillian Maclaine Newstead, M.D.

INTRODUCTION

Breast magnetic resonance (MR) imaging has steadily gained acceptance during the last 10 years, as an important complementary diagnostic method for use in the evaluation of breast disease. Conventional mammography and ultrasonography (US) are still the primary imaging methods used for breast cancer screening and diagnosis. Despite significant advances in mammography technique however, limitations in sensitivity and specificity, continue to prompt investigation into new imaging methods. MR imaging has now emerged as a promising new modality for the detection, diagnosis, and staging of breast cancer. The higher soft tissue contrast images and gadolinium-enhanced techniques which are available with MR imaging, allow the detection of clinically, mammographically, and sonographically occult cancers. There are some genuine biological and physical limitations that radiographic imaging of the breast is not likely to overcome. The introduction of intravenous gadolinium contrast agents, dedicated breast RF coils and faster imaging techniques has changed the diagnostic possibilities significantly. Contrast enhanced MRI has been shown to be more sensitive than mammography for breast cancer detection, and enhancement and morphologic characteristics may be used to differentiate benign and malignant lesions. Some investigators have reported a 98.4% sensitivity for detecting breast carcinoma and have stated that the absence of an abnormal finding on MR is a reliable method of excluding carcinoma (1).

Not all breast cancers are found with mammography and ultrasound. Can MR improve upon the sensitivity of mammography and ultrasound? Cancers may be obscured at mammography owing to overlapping fibroglandular tissue in the radiographically dense breast.

The false negative rate has been reported to be 25-29% (2-3). Ultrasonography is currently under evaluation for screening in selected high risk patients (4). Is it possible that MR imaging might improve upon the specificity of mammography and ultrasound? Are there MR characteristics that could reliably discriminate between benign and malignant lesions?

MR imaging is now proving to be clinically useful, and does provide important information unattainable by conventional imaging methods.

TECHNICAL REQUIREMENTS.

Most breast cancers enhance rapidly and profoundly following the intravenous injection of gadolinium contrast agents, and this makes them conspicuous on MR images. These contrast agents are distributed in the extracellular space after intravenous injection and tend to accumulate in tissues with rich vascularity (5). The secretion of tumor angiogenesis factor promotes the recruitment of new blood vessels, resulting in the high vascularity of most breast cancers larger than 1 cm in diameter. It has been reported that the density and distribution of microvessels may be directly associated with the rate of contrast
enhancement (6). Benign lesions may often be relatively poorly vascularized (7). Generally breast cancers enhance rapidly, following bolus injection of paramagnetic agents (8,9). Other factors likely accounting for the enhancement patterns of breast cancers include an increase in capillary permeability, changes in osmolar pressure and expansion of the interstitial space, (5,10)

Whereas there are standard, generally recognized techniques for the performance of the mammographic examinations, there are no universally accepted standards for MR imaging of the breast. There are many different techniques employed, and this may partly explain the variability in findings reported by multiple investigators. Magnet strength varies, (1.5T, 1.0T, 0.5T). Other factors which affect image quality include gadolinium dose and injection rate, coil construction and single slice versus whole breast volume imaging. A dedicated breast coil is needed. Most techniques aim to strike a balance between spatial and temporal resolution, and in the ideal situation, whole breast, high-resolution images would be obtained in a few seconds. It is generally accepted that T1-weighted sequences obtained before and after gadolinium contrast injection are required to detect and characterize lesions. Various gradient-echo and spin-echo techniques have been used (11-14).

High-resolution techniques with rapid acquisition and fat suppression have been advocated by some investigators (15). Fat suppression is needed because enhancing lesions may become isointense to fat. Enhancing lesions therefore may not be discernable from the background fatty tissue. 2D imaging studies with excellent results have been reported, however 3D techniques are probably preferable, as they provide expeditious high signal-to-noise, gapless, high-resolution images. Multiplanar (MPR) reformatted images allow excellent appreciation of spatial relationships (12). MR imaging may be performed without fat suppression using post-processing image subtraction, however patient motion is a potential problem with this technique. Rapid imaging techniques (3D volume in 90 seconds or less) with high spatial resolution are currently under investigation. New techniques such as parallel imaging may allow simultaneous image acquisition of both breasts, at high spatial and temporal resolution.

The breast imaging technique used for breast examinations at our institution, which we find most useful, provides excellent image quality with elimination of fat signal and a useful balance between spatial and temporal resolution. A bilateral fast spin-echo T2-weighted sequence in the axial plane is acquired before administration of contrast. This sequence is valuable for the assessment of scar tissue and post-treatment changes such as postoperative seromata and post surgical breast deformity and volume loss. This sequence also allows assessment of cysts, fibroadenomata and lymph nodes. Bilateral coronal images are then obtained before contrast injection and repeated five times post-contrast with an acquisition matrix of 192 x 256 (in-plane spatial resolution 1.25 x 1.4 x 1.4 mm) using a three-dimensional spoiled gradient echo sequence (Fast low angle shot, repetition time of 14sec, echo time of 7msec, flip angle of 25 degrees and one signal averaged). Each sequence produces a set of sixty 2.5 mm thick slices in less than 58 seconds, with a total imaging time of less than 10 minutes. MIP (maximum intensity projection) images can be performed on the subtracted data sets in order to distinguish enhancing lesions from blood vessels. MPR can also be performed on any of the data sets, to produce three-dimensional images, allowing excellent appreciation of spatial relationships. Sagittal fat suppressed spin echo sequences post contrast is also obtained. Information about the rate and degree of enhancement of a lesion can be measured by
placing an ROI (region-of-interest) on the area of concern and by generating enhancement curves, which graph the signal intensity at five points in time.

CHARACTERIZATION OF BREAST LESIONS

It has been reported that breast cancers enhance consistently with gadolinium contrast agents, and that most benign lesions enhance slowly or not at all (8,16). There is good evidence that breast carcinomas tend to enhance faster and washout earlier, than benign tissues (14,16). Enhancement scan protocols vary widely amongst different investigators. Technical limitations aside, it would be preferable to acquire data with very high temporal resolution, i.e. with 5-10 samples during the first pass of the contrast media bolus. Under these conditions the product of vascular permeability and perfusion rate (F*E), can be accurately measured (17). These parameters are linked to tumor grade and prognosis (18). Interstitial volume can also be measured. A rapid time resolution protocol has been investigated by Boetes et al (19). In this study single slice, non-fat suppressed, gradient echo images were obtained. [2.6x1.3 mm in plane spatial resolution, 10 mm slice thickness, at 2.3 sec. time intervals]. Any lesion exhibiting enhancement within 11.5 sec. of arterial enhancement was considered suspicious for carcinoma. A 95% sensitivity and an 86% specificity for carcinoma were achieved with this technique. Hulka et al using 6 second temporal resolution and echo-planar imaging, initially achieved sensitivity of 86% and specificity of 93%. (20), but later reported sensitivity of 83% and specificity of 79% (18). The authors in these studies conclude that the critical dynamic window for Gd-DTPA uptake in tumors is within the first 120 seconds, and suggest a resolution of 2 or 3 points within the first 60 seconds. Sardenelli et al (21) imaged 63 breast lesions with acquisition every 15 seconds during the first minute after contrast injection. This series was followed by an acquisition every 60 seconds for 8 minutes. Observers demonstrated 100% lesion sensitivity for both the high temporal resolution images (15-60 seconds) and the standard (1-8) minute images, with specificities of 94-97% for the high temporal resolution images, and 83-89% for the standard sequences. Each of these studies shows a gain in specificity for lesion differentiation with the higher temporal resolution techniques. Some of the increased sensitivity is probably accounted for by the more accurate evaluation of perfusion/permeability.

An important benefit of high temporal resolution technique is that the breast parenchyma enhances relatively slowly and therefore the morphology of enhancing structures can be evaluated against a dark background. A report by Kuhl et al (22) proposed that the shape of the time-signal intensity curve was an important factor in the differentiation of benign and malignant lesions. The enhancement curves were classified as: type 1, straight or curved time-signal intensity line with steadily increasing enhancement, type 2, plateau of time-signal intensity line, type 3, time-signal intensity line exhibiting a washout time course. The study group consisted of 230 patients with 266 enhancing lesions. 57% of the malignant lesions demonstrated a washout type of time-signal intensity curve whereas 83% of the benign lesions demonstrated a steady, straight or curved time-signal intensity line. In this study, with the time-signal intensity curve as the only diagnostic criterion, the following results were reported. Positive predictive value 77% (92 of 120), negative predictive value 94% (137 of 146), sensitivity 91% (92 of 101), specificity 83% (137 of 165). A recent study
(23) has shown that time to peak enhancement together with lesion morphologic assessment, are the most reliable diagnostic indicators for breast lesions.

Other investigators have concentrated on high spatial resolution techniques, using the exquisite soft tissue detail available with MR, to provide detailed morphologic assessment of enhancing lesions (12, 14). For example, a high-resolution 3D image with fat suppression (3D spoiled gradient echo sequence, <20°/4.5; flip angle <45 degrees) could be used for the initial evaluation. Architectural features which are considered suggestive of malignancy include, enhancing mass with irregular or spiculated margins, rim enhancement, intense focal segmental enhancement and enhancement in a ductal distribution. Ductal carcinoma in situ is often imaged as a non-mass enhancement in a ductal distribution. Features suggestive of benign disease include, non-enhancing masses, masses with smooth, rounded or lobulated borders, and masses with nonenhancing internal septations

There is without doubt significant overlap. The problem is that benign and pre-cancerous tissues also enhance. These tissues include fibroadenomata, papillomata, non-proliferative and proliferative fibrocystic changes, inflammatory change, fat necrosis, sclerosing adenosis, lobular carcinoma in situ, and atypical ductal hyperplasia (8, 15). It has also been shown that some cancers enhance slowly or not at all (14, 16, 24). A pattern of rim enhancement has been noted in cancers but not in benign tumors (14, 25). Investigators have shown, in a study designed to use a temporal resolution of 2 seconds that benign lesions enhanced centrally initially, while cancers enhanced from the periphery to the center (26). The evaluation of both lesion kinetics and lesion morphology is likely needed for precise lesion discrimination. The exact protocols used will vary at different institutions. A time-resolved study on all focally enhancing lesions with indeterminate or suspicious morphologic findings is probably necessary. Correlation of the results of both methods may well provide for more precise lesion characterization. The American College of Radiology has provided a lexicon for the description of the morphologic and kinetic characteristics of breast lesions seen at MR imaging (27). At the present time a single optimal method for breast MR has not been uniformly accepted and adopted. It may well be that for some time to come, the best method for a given practice, will depend on the available hardware and software at the site. Ongoing technical improvements, such as parallel imaging, offer the prospect of optimal bilateral MR examinations, with high temporal and spatial resolution. Despite the fact that there are many different approaches and opinions about MR technical and interpretive criteria, it is generally agreed that MR imaging is the most sensitive imaging technique available today, for breast cancer detection.

PRETREATMENT ASSESSMENT OF PATIENTS WITH BREAST CANCER

One of the roles suggested for breast MR is the pretreatment assessment of the breast cancer patient. There are a variety of treatment options for the breast cancer patient. The tumor size, grade, location and breast size/tumor size ratio all impact upon surgical decisions. All patients, those selected for breast conservation, and those for whom other treatment is appropriate, need accurate tumor staging. Is it possible that MR can provide a more accurate assessment of the size, margins, number and location of breast cancers and thus provide a more accurate pre-treatment evaluation? MR imaging allows the detection of multifocal and multicentric breast cancer in many patients when conventional imaging suggests unifocal disease. Several investigators have shown that MR is more sensitive in the detection of
additional lesions in these patients (12, 28). Treatment planning depends on many factors, one of the most important criterions being the extent of tumor within the breast. Most treatment failures occur after 2-3 years and usually in the vicinity of the tumorectomy site. The reported improvement in sensitivity of tumor extent, compared with other methods, may result in a reassessment of therapeutic options. The likelihood of tumor recurrence may be reduced perhaps, by providing the oncologist and surgeon with a more accurate estimation of tumor extent. One study of 18 such patients with breast cancer found that in half, the results of the MR changed the planned treatment. This was necessary because of new information about size, multifocality, multicentricity and chest wall invasion (29). MR provides accurate information about tumor load in lesions that are difficult to evaluate with mammography and ultrasound. Invasive lobular carcinoma and ductal carcinoma in situ may be difficult to excise completely. Mammography may underestimate tumor size in these lesions. Many non-calcified low grade DCIS lesions are not visible mammographically. Several investigators have reported contrast enhancement of DCIS lesions (30, 31). Gilles et al found contrast enhancement to be present in 34 of 36 patients with DCIS, with microinvansion present in 12 cases (30). The most common appearance of DCIS is a focal area of non-mass-like enhancement, in a ductal or segmental distribution. It is important to note however, that unless reliable criteria are developed to distinguish between benign and malignant enhancing lesions, MRI could result in inappropriate treatment.

MRI is also useful in the assessment of patients treated with preoperative chemotherapy. Three-dimensional volumetric measurements, possible with MR imaging, allow more accurate estimation of tumor volume, than linear measurements obtained with mammography or ultrasound. Pre-treatment and post-treatment images are compared, in order to determine response to treatment more accurately (32).

THE PATIENT WITH POSITIVE MARGINS FOLLOWING TUMOR EXCISION

Rates of positive margins following tumor excision vary widely, but may approach 70 % (33). There are many false positive histologic assessments, and exact information regarding the precise location of the positive margin within the breast, is often difficult to obtain. Mammographic and ultrasonographic imaging in these patients is often compromised by post surgical distortion. Standard breast compression is usually not possible. MR imaging may predict and localize residual disease within a week or two of surgery. The postoperative seroma/hematoma is seen as low signal with an enhancing rim. The normal seroma rim usually exhibits smooth enhancement with a maximum thickness of 2-3mm. Areas of residual tumor may present as nodular masses adjacent to, or remote from the seroma cavity. When residual tumor is found, Needle localization using MR Guidance may be useful prior to re-excision surgery.

POST TREATMENT ASSESSMENT OF PATIENTS WITH BREAST CANCER

Early detection of local recurrence improves long-term survival but mammographic and ultrasonographic evaluation of these patients is often limited. This is particularly true in those patients with dense fibroglandular tissue and significant post surgical and post radiation fibrosis. Residual or recurrent tumor exhibits early enhancement whereas sterile fibrosis shows no substantial enhancement. Several investigators have demonstrated that it is possible to detect recurrent tumor with MR (34-37). Breast recurrence must be differentiated from acute and subacute posttreatment changes. MR can be used to
detect or exclude recurrent tumor. Most true recurrent tumors, unlike unrecognized residual tumor, usually presents after two years. In one series there was no significant enhancement of scar tissue after eighteen months in 30 of 32 cases, whereas diffuse enhancement was noted in all recurrent tumor (34, 35). Normal parenchymal enhancement is usually diminished following breast irradiation, therefore enhancing tumor is readily visible, and easily distinguished from unenhancing scar, in the post-irradiated breast. Initial encouraging results suggest therefore that MR will likely provide an important additional adjunctive diagnostic method for the evaluation of the post-treatment breast.

THE PATIENT WITH POSITIVE AXILLARY NODES, NO KNOWN PRIMARY

MRI is useful and should be performed for the evaluation of those patients who present with enlarged palpable axillary nodes, positive for adenocarcinoma, and no known primary lesion (28, 29). These patients present with axillary adenopathy, without detectable abnormality within the breast or elsewhere. Physical examination of the breast, mammography and ultrasound are normal. The incidence of this presentation is approximately 0.4% of all patients presenting with breast cancer. The treatment of these patients is still controversial, and most investigators in the past have recommended mastectomy as the treatment of choice. The sensitivity of MR for the detection of invasive cancer approaches 100%

Identification of the primary lesion with MR imaging might allow for a more limited surgical procedure, and provide important histological information for therapy planning.

MR IMAGING-GUIDED BIOPSY

MR imaging-guided biopsy systems are needed when a suspicious lesion is visible on MR images alone. Although freehand needle localizations can be performed, more accurate needle placement with a guidance system is preferable. MR guidance devices for use with needle localization and percutaneous biopsy techniques have been developed (38-41). Most systems employ a unilateral radio-frequency coil with perforated compression plates. The breast is imaged and the coordinates of the lesion are calculated from the images. Mild breast compression is used, and the needle is inserted through the appropriate aperture in the compression plate. The patient is then re-imaged to confirm accurate needle placement. Gadolinium injection for lesion visualization is often necessary. Contrast agents with longer half lives would be useful. Contrast may wash out of small enhancing cancers, thus the lesion undergoing biopsy may no longer be visible, by the time the needle placement images are obtained. There are two commercially available localization and biopsy devices manufactured by MRI devices (Waukesha, WI) and USA Instruments (Aurora, OH). The current systems appear adequate for most needle localization procedures performed prior to excisional biopsy. Further improvements are needed in order to facilitate the reliable performance of fine needle aspiration and core biopsy procedures. Improvement in the design of the biopsy coils, in order to provide access to the posterior breast and axillary tail, is of the utmost importance. A greater variety of non-ferromagnetic needles and guns are also needed.

Current devices allow for performance of standard core biopsy and vacuum-assisted core biopsy. A major problem with MR-guided needle localization procedures, is the inability to confirm lesion removal with specimen imaging. Careful correlation with histology
results and MR imaging follow up if appropriate, is needed. MR biopsy capability is a critical component of any breast MR imaging program. Therapeutic ablative procedures using MR guidance are in the developmental phase.

MR IMAGING SCREENING FOR BREAST CANCER

Does MR have the potential to replace mammography as a screening test for breast cancer? The World Health Organization defines the criteria needed for a population based screening program. The program must use an adequately sensitive and specific test, with reproducible results. The test must identify previously undiagnosed disease, and be affordable and acceptable to the public. Follow-up services must also be available. Does MR meet these criteria? MR imaging has been shown to be a highly sensitive and specific imaging modality, for the detection of breast cancer. MR imaging does not require the use of ionizing radiation, however it is more expensive than mammography and there is limited availability. Studies are reported from the United States, Germany, the United Kingdom, Canada and the Netherlands, demonstrating the value of MR screening in high-risk women. Detection of differences in mortality however, will require large study populations and long term follow up.

At the present time there is insufficient data available to evaluate the efficacy of MR screening in the general population. Even if low-cost, technologically capable, dedicated breast systems were to be produced, the total costs, including the cost of gadolinium, would prohibit the examination of even a fraction of the female population at this time.

CONCLUSIONS

Breast MR imaging is emerging today, as a promising adjunctive imaging modality. The advantages of this technique include the absence of ionizing radiation, and the ability to detect cancers, which are not visible by other imaging methods. It is generally agreed that MR is probably the study of choice for the evaluation of implant integrity. Breast MR is now used with increasing frequency for the evaluation of the breast cancer patient before and after treatment. Investigators have shown that MR can detect invasive breast cancer with a high sensitivity. The true sensitivity of MR is not known yet however, as large clinical trials would be needed to establish the sensitivity of MR for cancer detection at screening. MR imaging examinations of the breast are currently performed with a wide variety of techniques, coils and field strengths. Imaging protocols, post-processing techniques and biopsy systems are currently under evaluation. The cost-effectiveness of MR imaging needs further study, and a cost-benefit analysis will be necessary before breast MR imaging examinations become uniformly reimbursable.

There are several questions which remain to be answered. What technique is optimal? Should both breasts be imaged? Should only the breast with the suspected abnormality be imaged? What is the significance of MR detected, otherwise occult, cancers? Do we have thresholds to suggest biopsy in such cases? Should we screen women at higher risk for developing breast cancer? Controlled studies with the purpose of comparing conventional breast imaging with MR imaging, and subsequent patient outcome, are currently underway. These studies may yield the additional information needed. The promise that MR imaging will provide an improved method for the detection and characterization of breast cancer, and assume an important role in patient management, may soon be realized.
REFERENCES
4. American College of Radiology Imaging Network Clinical Trial ACRIN 6666 “Screening Breast Ultrasound for High-risk Women”


画像分科会からのご案内（テーマ：乳房画像）

日時：2006年4月8日（土曜日）午後13時15分-16時15分
会場：パシフィコ横浜会議センター（304室）

第59回画像分科会は、乳房画像に関して世界的に著名な二人の放射線科と、藤田広志先生に講演をお願いしています。ディジタルマンモグラフィや乳房のMRに興味を持つ方々など、この機会を逃さず多数お集まりください。

プログラム

教育講演 Digital Mammography and computer-aided diagnosis
Robert A. Schmidt, MD, Professor, The University of Chicago

講演1 ディジタルマンモグラフィ研究への期待と課題
岐阜大学大学院 藤田広志

講演2 Clinical applications of breast MR for the cancer patient
Gillian M. Newstead, MD, Associate Professor, The University of Chicago

講演終了後にパネルディスカッション

以上