MR Imaging of the Breast with Rotating Delivery of Excitation Off Resonance: Clinical Experience with Pathologic Correlation

An investigative study was undertaken to determine the potential for a new magnetic resonance (MR) imaging technique, RODEO (rotating delivery of excitation off resonance), for use as a diagnostic imaging tool for the breast. The RODEO technique provides fat suppression with T1 weighting and is ideal for gadolinium-enhanced breast imaging. It is a short repetition time, steady-state sequence for high-resolution three-dimensional acquisitions and provides a clinically efficient imaging time of approximately 5 minutes for 128 sections. Imaging findings were correlated with serially sectioned pathologic specimens in 30 breasts with 47 malignant and 27 benign lesions. MR imaging had a sensitivity of 94% and a specificity of 37%. MR imaging depicted additional cancers not seen at mammography in 11 of the 30 patients (37%). The lesions not seen at mammography varied in size from 3 mm to 12 cm. RODEO MR imaging may be used to improve diagnosis of breast cancer in patients with mammographically dense breasts or silicone implants/injections and to stage disease in patients who are candidates for lumpectomy.

Index terms: Breast, diseases, 00.72 • Breast neoplasms, MR, 00.31, 00.32 • Gadolinium • Magnetic resonance (MR), contrast enhancement • Magnetic resonance (MR), pulse sequences


The use of magnetic resonance (MR) imaging for the diagnosis of breast cancer is not new. Images of the breast were some of the first produced of any human anatomic part with MR imaging (1,2). MR imaging of the breast was performed as early as 1978, before head images and 4 years before the first commercial image appeared in 1982 (1). When commercial MR imaging began, early clinical trials predicted the potential for MR imaging in breast cancer diagnosis (3–6). More detailed clinical studies, however, revealed that MR imaging had little to offer over less expensive and more widely available conventional imaging methods (7).

By the late 1980s, MR imaging of the breast was thought by most experts in the field to have little future (7,8). About the same time, gadopentetate dimeglumine was introduced in Europe. Research with this agent revealed that breast cancer consistently enhanced after administration of gadopentetate dimeglumine and that these enhancing cancers could often be differentiated from some benign lesions (9–11). Most tumors demonstrated rapid contrast enhancement within the first 5 minutes. Because of this rapid enhancement, tumors can be differentiated from normal breast parenchyma. Tumor enhancement was substantially greater than that of breast parenchyma within the first 5 minutes and was nearly equal to that of breast parenchyma at 10 minutes after injection. Scars, sometimes thought to represent cancer on mammograms, did not enhance on MR images (9–13).

In Germany, where surgical biopsy is routine and needle biopsy is seldom used for diagnosis, the use of MR imaging was believed to be of value in prebiopsy imaging to reduce the number of biopsies performed for false-positive mammograms. In countries where needle biopsy is more accepted, the use of MR imaging as the only tool for improving specificity was more difficult to justify, since a needle biopsy is less expensive than MR imaging and provides a definitive histologic diagnosis. In centers where needle biopsy is an accepted alternative to surgical biopsy, major problems remain for the application of MR imaging for routine breast diagnostic management in most clinical situations. Even with use of modern MR imaging techniques with contrast enhancement and conventional fat suppression, investigators found in a recent study that lesions were missed at conventional MR imaging that were seen at mammography (14).

For MR imaging to play a major role in breast cancer management, it must meet several major technologic considerations: (a) it must have high resolution (approximately 1-mm resolution in all three planes) for detection of small lesions, (b) it should employ fat suppression for differentiation of enhancing tumors from fat, and (c) acquisition should be rapid (preferably less than 6 minutes) for differentiation of enhancing tumors from breast parenchyma.

Previous studies have indicated that cancers enhance early and can be best differentiated from benign masses and breast parenchyma in the first 6 minutes after injection of contrast material (9–11). These factors were the incentive for our research in creating a new breast MR imaging technique called RODEO (rotating delivery of excitation off resonance). The purpose of our study was to evaluate this new method with rigorous pathologic correlation and compare

Abbreviations: MIP = maximum intensity projection, MT-FATS = magnetization transfer with fast adiabatic trajectory in the steady state, RODEO = rotating delivery of excitation off resonance, TE = echo time, TR = repetition time.
this method with conventional imaging (i.e., mammography, sonography, and galactography).

Fat suppression has a demonstrated value in the identification of contrast-enhancing lesions on T1-weighted images when the surrounding, normally hyperintense fat may obscure the lesion (15–18). Because of the abundance of fat in normal breasts, fat-suppressed imaging is a desirable feature in an imaging protocol designed to detect contrast-enhancing lesions.

A variety of methods are available for producing fat-suppressed images: (a) chemical shift (time domain) imaging with four-dimensional Fourier transform techniques (19), (b) selective saturation or excitation (20–22), (c) phase encoding based on differences in chemical shift evolution between fat and water (23), and (d) methods using relaxation differences between fat and water, such as short inversion time inversion recovery (STIR) (24). These techniques require either a long repetition time (TR) pulse sequence or multiple excitations and are not well suited for steady-state (short TR) three-dimensional applications.

A previously used steady-state fat-suppression sequence, MT-FATS (magnetization transfer with fast adiabatic trajectory in the steady state), employs magnetization transfer contrast to suppress the signal intensity of ductal tissue (17). In comparison to the MT-FATS technique, RODEO provides more T1 weighting, uses a shorter TR for an approximately 50% reduction in imaging time, and has fewer artifacts because of the elimination of the magnetization transfer preparation pulse.

**MATERIALS AND METHODS**

**General Technical Features**

MR imaging was performed with a Signa imager (GE Medical Systems, Milwaukee, Wis) operating with 4X software at 1.5 T. Image reformations and maximum intensity projection (MIP) ray tracings were performed with an independent console (GE Medical Systems).

A prototype linear radio-frequency (RF), transmit-receive breast coil (Medrad, Pittsburgh, Pa) was developed specifically for MR imaging of the breast. For all examinations, the patients were imaged in the prone position without breast compression.

Three-dimensional imaging was performed to improve the image resolution and facilitate image processing methods. The display matrix of 128 × 256 × 256 produces voxel resolution of about 1.4 × 0.7 × 0.7 mm for an 18-cm field of view. The sagittal, coronal, and axial images were reformatted with the same set of image data. The use of the image-processing workstation allows near real-time reformations to facilitate the depiction of oblique imaging planes. The high-signal-intensity breast nodules within the entire volume can be demonstrated with MIP ray tracing.

This method allows considerable flexibility in viewing possible anatomic defects. Multiple-angle, fast reformations allow the reader to follow questionable lesions to determine the identity of the lesion, whether vessel or mass, and the relationship of the defect to other structures. The MIP methods provide a quick survey of disease extent and anatomic relationships.

**Pulse Sequence**

A steady-state fat-suppressed sequence was developed to achieve optimal image contrast for T1-weighted three-dimensional imaging of the breast (Fig 1). RODEO uses a sine excitation on fat resonance followed by a similar sine excitation 180° phase shifted. The second excitation drives fat magnetization back longitudinally (aligned with the applied magnetic field), resulting in suppression of fat on the image. Because water is off resonance for both excitations, both RF pulses are additive for water resonance to result in transverse magnetization that produces MR signals. The RODEO method can be achieved with a very short TR (18.5 msec) and echo time (TE) (3.9 msec) and one excitation for efficient three-dimensional acquisition of approximately 5 minutes.

Fluids with long T2s had high signal intensity, even on T1-weighted images produced with steady-state fast imaging pulse sequences. RF spoiling is a technique that randomizes the phase of the digital RF to reduce the signal intensity resulting from the long T2 steady state. The RF spoiling technique was used to depict lesions with a high fluid content. The precontrast images were obtained without RF spoiling. The RODEO images obtained without RF spoiling demonstrated high-signal-intensity fluid resulting from the steady-state buildup on long T2 spins. The postcontrast images were obtained with RF spoiling to reduce the signal intensity of lesions with a high free fluid content.

With the variable use of RF spoiling, cysts and masses had the opposite appearance on the pre- and postcontrast images. On precontrast images, cysts had high signal intensity and masses had low signal intensity. On postcontrast images, masses had high signal intensity and fluid-filled lesions had low signal intensity as a result of RF spoiling.

**Patient Studies**

Eighty-eight breasts were imaged at our institution with RODEO MR imaging and mammography. Patients entering the study had a high suspicion for breast cancer on the basis of clinical findings or conventional imaging studies. Other imaging studies, such as galactography and sonography, were performed as clinically warranted. The patients ranged in age from 32 to 87 years (mean, 56 years). Of the patients who underwent RODEO MR imaging, 30 underwent mastectomy with pathologic analysis of serial sections.

To visualize the early-enhancement features of cancer, MR images were obtained immediately after intravenous injection of 0.1 mmol/kg (usually 8–16 mL) of gadopentetate dimeglumine. To ensure consistent contrast timing, gadopentetate dimeglumine was given at the manufacturer-recommended maximum rate of 10 mL/min beginning at the start of tuning and ending during the initial image data collection.

**Pathologic Analysis**

To accurately correlate the MR imaging and pathologic findings, the patient's skin was marked for longitudinal axis before MR imaging. Images were reformatted along the marked axis at 5-mm intervals and were analyzed with the workstation for comparison with the pathologic specimen. The mastectomy specimens were frozen and sectioned along the marked...
Infiltrating mixed carcinoma (1/44-2%)
Ductal carcinoma in situ (7/44-16%)
Infiltrating lobular carcinoma (7/44-16%)
Benign changes seen only at pathologic examination were noted but were not considered a true-negative finding. Nonproliferative fibrocystic change encountered only with histologic sectioning without identification at MR imaging or mammography were not considered a true-negative finding. If proliferative fibrocystic change corresponded to an area of high signal intensity on MR images and was not seen at mammography, it was considered a false-positive finding for MR imaging and a true-negative finding for mammography.

RESULTS
The clinical and diagnostic imaging data from the 30 breasts with pathologic correlation are summarized in Table 1. Seventy-four lesions were detected: 47 were malignant and 27 were benign. There was no disagreement in the MR imaging observations of all 47 histologically positive lesions (44 true-positive cases and three false-negative cases). Reviewers disagreed in four cases. All of the discrepant lesions were false-positive, and the larger number of lesions (either reviewer) was used for statistical analysis in all cases.

The histologic characteristics of the true-positive and false-positive lesions are summarized in Figures 2 and 3. Focal cancers (n = 47) ranged from 3 mm to 12 cm in diameter, with a mean of 2.6 cm and a median of 2 cm. Lesions missed with mammography ranged from 3 mm to 12 cm in diameter, with a mean of 2.5 cm and a median of 1.4 cm.

Of the 30 breasts examined pathologically, 29 had evidence of cancer. The one case with no evidence of cancer (false-positive finding at MR imaging and mammography) had a fibroadenoma and atypical ductal hyperplasia. The distribution of cancers in the 29 positive breasts at pathologic examination is summarized in Table 2. Diffuse enhancement was identified at MR imaging in six breasts. Of those six breasts, four cases corresponded pathologically to diffuse carcinoma, while the other two cases were focal carcinomas. Mammography was positive in only three of those six cases.

Mammography combined with sonography depicted no cancers that were not also depicted with MR imaging. MR imaging depicted cancers not seen at mammography (solitary and multicentric disease) in 11 of the 30 serially sectioned breast specimens (37%). Two false-negative MR findings occurred with nipple involvement that was interpreted on MR images as normal nipple enhancement.

In these cases, positive MR findings were present elsewhere in the breast and, in retrospect, nipple involvement was also present on the MR image (Fig 4). The other false-negative MR finding was malignant involvement of an intramammary lymph node that did not substantially enhance with contrast material, possibly because of microscopic tumor that did not result in substantial enhancement relative to normal components of the lymph node.

The histologic characteristics of lesions that were false-positive at MR imaging are summarized in Figure 3.

Although these lesions are not considered neoplastic, some are associated with a higher frequency of malignancy.

All forms of breast carcinoma consistently enhanced with contrast material. The fat-suppressed threedimensional imaging method demonstrated previously unidentified lesions in two women with mammographically dense breasts. MR imaging demonstrated cancer in the breast of a postmenopausal woman with a positive axillary lymph node but negative findings at mammography (Fig 5). MR imaging showed abnormal en-
enhancement representing carcinoma in two patients with palpable masses but negative findings at mammography. MR imaging depicted a focus of enhancement in three patients in whom the only mammographic finding was an asymmetric opacity.

In 33 of 47 histologically confirmed carcinomas, the MR imaging–determined tumor size correlated more closely with the pathologically determined tumor size than did the mammographically determined size (Fig 6). In 11 malignancies, MR imaging and mammography were similar in the evaluation of tumor size. In no case was mammography more accurate in the determination of tumor size than MR imaging.

In three of the 47 malignancies determined pathologically, all imaging techniques failed to depict the lesion. Two of five cases of lobular carcinoma were negative at mammography. In the other three cases, the abnormalities were underestimated at mammography. All lobular carcinomas were well demonstrated on MR images, with accurate depiction of lesion extent.

Multicentric disease was defined as multiple true-positive lesions in the same breast. MR imaging and pathologic analysis demonstrated multicentric disease in 12 breasts in 11 patients (Fig 7; Table 2). In patients with multicentric disease, results of mammography were negative in three of 12 breasts, solitary lesions were diagnosed in seven, and diffuse disease was diagnosed in two. In the two patients with evidence of diffuse disease at mammography, RODEO MR imaging showed diffuse enhancement, which was confirmed as diffuse carcinoma at pathologic examination.

In the 10 breasts with discrepant findings at MR imaging and mammography and pathologic evidence of multicentric disease, cancer was identified with MR imaging in the same quadrant in three of the 10 breasts, in two quadrants in four breasts, and in more than two quadrants in three breasts. In one case, infiltrating lobular and infiltrating ductal carcinoma occurred in the same breast. The size of the additional foci not seen at mammography varied from 3 mm to 12 cm. In the multifocal disease not categorized as diffuse, the average size of the lesions missed at mammography was 20 mm.

In five cases, MR imaging was performed before and after a preoperative course of chemotherapy. MR imaging accurately depicted the cancers on all image sets. The postchemotherapy images demonstrated reduction in the enhancing parenchyma that was correlated with the extent of disease by means of pathologic analysis of serial sections in one case. A reduction of mass at MR imaging documented a response to chemotherapy that was confirmed with lumpectomy in four cases. These studies demonstrated the potential of MR imaging to define chemotherapeutic response.

Benign lesions, such as fibroadenoma and sclerosing adenosis (Fig 8), may be difficult to distinguish from malignancies on the basis of enhancement alone. Although areas of fibrocystic change usually do not enhance with contrast material, enhancement did occur in one case. However, areas of proliferative fibrocystic change had abnormal enhancement in three cases.

Many benign lesions that were only seen at pathologic analysis did not enhance with contrast material. These lesions consisted of fibroadenoma, areas of nonproliferative fibrocystic change, and areas of proliferative fibrocystic change.

Among the patients who did not undergo analysis of serially sectioned mastectomy specimens, histopatho-
logic findings were not available in 12, and four were lost to follow-up. A statistical summary of the histopathologic characteristics of breasts not subjected to pathologic analysis is given in Table 3. Review of the biopsy results was useful for demonstrating the ability of MR imaging to exclude malignancy. There were no biopsy-confirmed cases of nonenhancing lesions on MR images that were histologically positive (false-negative cases). Biopsy-confirmed lesions that were positive at mammography and did not enhance at MR imaging included postoperative scar (n = 1), radial scar (n = 1), fat necrosis (n = 1), and silicone leak (n = 2).

**DISCUSSION**

With advances in the early detection of breast cancer comes the potential for breast-conserving surgery. The selection of candidates for breast-conserving surgery is dependent on the determination of disease extent with clinical and imaging studies (25–28). A highly sensitive imaging tool should play an important role in the staging of candidates for breast-conserving surgery.

In patients with clinically occult, nonpalpable breast cancers detected at mammography, the frequency rate of multicentric disease varies from 44% to 60% (29–32). The potential for failure of breast conservation treatment because of marked "subclinical" disease has been demonstrated (33–34). The evaluation of patients with an imaging method that is sensitive to undetected multicentric disease could have a major effect on breast cancer treatment.

The RODEO method helped detect additional cancers in 37% of the patients and had a sensitivity for cancer detection of 94%. The improved sensitivity of this method could be used to define marked multifocal disease in patients who are candidates for lumpectomy. The major drawback of MR imaging in this role was the inability to accurately distinguish normal nipple enhancement from nipple involvement by carcinoma in two patients. The presence of tumor in the nipple usually eliminates the opportunity for breast-conserving surgery.

Because of its ability to more accurately depict tumor margins, RODEO MR imaging could be used to more effectively plan lumpectomy surgery. Tumor may extend to the margin of...
the excised tissue, which would require repeat surgery to excise the remaining tumor. The use of the RODEO technique may reduce the need for repeat excision surgery for tumor extending to the margin of the lumpectomy site.

Perhaps the greatest dilemma encountered with high-resolution MR imaging of the breast is the lack of specificity (37%). The false-positive studies consisted of lesions associated with an increased risk of malignancy, such as lobular carcinoma in situ, atypical hyperplasia, and areas of fibrocystic change. These lesions composed 53% of the false-positive MR imaging diagnoses.

Other clearly benign conditions that enhanced at MR imaging were sclerosing adenosis and fibroadenoma. All cases of sclerosing adenosis that were identified pathologically were identified at MR imaging as enhancing lesions. Many fibroadenomas that did not enhance at MR imaging were found at pathologic analysis of serial sections. To our knowledge, the lack of enhancement of fibroadenomas has not previously been reported. The discovery of nonenhancing fibroadenomas is a direct result of the rigorous pathologic analysis performed in this study.

Previous studies used pathologic correlation of surgical biopsies and lumpectomies (9-14,17). That correlation was limited to lesions that could be seen with mammography or felt by the surgeon and also excluded the possibility of pathologically detecting lesions not seen at mammography. The results of such analyses led to a low number of false-negative cases and misrepresentation of the sensitivity of the examination.

The application of MR imaging in the clinical management of breast cancer will require a more accurate determination of the histologic characteristics of the lesions than is provided with the current methods. The MR imaging determination of the rate of contrast enhancement of a lesion after injection of a bolus of contrast material has been proposed as a method for differentiating between fibroadenoma and cancer. Cancers were shown to have an early enhancement pattern, whereas fibroadenomas enhanced later (9-11). It is likely that overlap in patterns will exist between the early- and late-enhancing groups. As can be seen in this study, some fibroadenomas enhance early. It is questionable whether this method can help differentiate between sclerosing adenosis, which consistently enhances early, and invasive carcinoma.

In our study, a positive lesion was defined as one that enhanced at imaging. There was no attempt to further categorize lesions on the basis of morphologic characteristics. The specificity of MR imaging probably could be increased if the morphologic features of the lesions, such as well-defined or spiculated configurations (similar to the categorization used in mammography), were considered. The specificity of mammography defined in this study does not correlate with the specificity reported in larger, less biased studies (35,36). The high specificity of conventional imaging was at-

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**Table 2**

<table>
<thead>
<tr>
<th>No. of Cancers Detected per Breast</th>
<th>Pathologic Examination</th>
<th>Mammography</th>
<th>MR Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>17</td>
<td>24</td>
<td>17</td>
</tr>
<tr>
<td>2 in the same quadrant</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>2 in multiple quadrants</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>More than 2 in same quadrant</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>More than 2 in multiple quadrants</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Diffuse</td>
<td>4</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>29</td>
<td>29</td>
</tr>
</tbody>
</table>

Note.—Data are numbers of breasts.

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**Figure 8.** False-positive diagnosis at MR imaging. Reformatted sagittal RODEO MR images obtained before (a) and after (b) administration of gadopentetate dimeglumine demonstrate an irregularly marginated area of contrast enhancement, which was found to represent sclerosing adenosis at histologic examination. Although most cases of enhancement in sclerosing adenosis and fibroadenoma were well-defined lesions, irregular enhancement occurs and cannot be distinguished from carcinoma.
towed to the study design, in which candidates were selected for MR imaging on the basis of a likelihood of mastectomy determined by means of clinical or mammographic findings. The use of morphologic criteria considerably improves the specificity of mammographic interpretation. However, as demonstrated in Figure 8, absolute differentiation between benign and malignant disease at MR imaging is unlikely, even when using morphologic criteria.

Histologic diagnosis is usually established with biopsy. Core needle biopsies have become a recognized tool for establishing the histologic diagnosis. In centers where core needle biopsy is not performed and surgical biopsy is the only recognized method for biopsy, MR imaging has been proposed as a useful method for reducing the number of surgical biopsies with negative findings that result from the large number of false-positive mammograms (9–12). Surgical biopsies are expensive, require an incision resulting in scar, and have an associated complication risk. Because MR imaging can help differentiate certain benign lesions such as postoperative scar and fat necrosis from cancer on the basis of enhancement, it may play an important role and can effectively reduce the number of surgical biopsies performed.

The major competition for MR imaging in the role of improving the specificity of mammography is needle biopsy. Positive findings at mammography can be investigated with core needle biopsy, which provides histologic information at a fraction of the cost of MR imaging. It is unlikely that MR imaging will play a major role in cancer diagnosis if improved specificity is the only objective. For MR imaging to be successful, it must be used to improve the sensitivity for detecting lesions that cannot be visualized at mammography.

The combination of a dedicated transmit-receive volume coil with the three-dimensional RODEO pulse sequence gives the maximum efficiency for fat suppression and high-resolution, high signal-to-noise ratio, three-dimensional imaging of the breast. Multicoil arrays have been proposed as a method of increasing image quality. The multicoil arrays are receive-only and require the use of slab selection to limit the field of view to avoid aliasing effects. Slab selection limits the excited volume, requires a longer TE and TR, and increases the total imaging time. Because the RODEO technique cannot be used with receive-only coils, other less efficient methods outlined previously would be the only options for multicoil arrays. A transmit-receive volume coil can be made quadrature, which could increase the signal-to-noise ratio. Currently, the coils in a multicoil array are linear, with no prospect for being made quadrature. The signal-to-noise ratio and homogeneity of multiple coils only approaches that of a true volume coil and can never be better. Finally, all current MR systems can use volume coils, whereas multicoil array technology requires the expense of considerable hardware improvements.

The establishment of histologic characteristics of lesions in abnormalities depicted on MR images but not on mammograms will require the use of MR imaging–directed biopsy. Unfortunately, a device for stereotactic biopsy with MR imaging guidance is not commercially available. Because of the critical timing issues in lesion enhancement, pliability of the breast, and lack of inherent fixed references, freehand needle guidance has little chance of success. The greatest problem with the clinical application of MR imaging for improving the sensitivity of the imaging diagnosis of breast cancer is the presence of abnormal enhancement in areas that cannot be detected with conventional methods of diagnosis (mammography and clinical examination). Because of the high rate of false-positive findings with MR imaging, the improvement in sensitivity will be difficult to realize clinically until the advent of MR imaging–guided stereotactic biopsy. Stereotactic biopsy will be necessary to differentiate between false-positive enhancement and cancer. Because of this dilemma, MR imaging will play a limited role in breast cancer staging until MR imaging–directed stereotactic biopsy is available.

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References