

Freehand iMRI-Guided Large-Gauge Core Needle Biopsy: A New Minimally Invasive Technique for Diagnosis of Enhancing Breast Lesions

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The lack of reliable methods for minimally invasive biopsy of suspicious enhancing breast lesions has hindered the utilization of contrast-enhanced magnetic resonance imaging (MRI) for the detection and diagnosis of breast cancer. In this study, a freehand method was developed for large-gauge core needle biopsy (LCNB) guided by intraprocedural MRI (iMRI). Twenty-seven lesions in nineteen patients were biopsied using iMRI-guided LCNB without significant complications. Diagnostic tissue was obtained in all cases. Nineteen of the 27 lesions were subsequently surgically excised. Histopathologic analysis confirmed that iMRI-guided LCNB correctly distinguished benign lesions from malignancy in 18 of the 19 lesions. The histology revealed by core biopsy was partially discrepant with surgical biopsy in 2 of the other 19 lesions. Freehand iMRI-guided LCNB of enhancing breast lesions is promising. Larger studies are needed to determine the smallest lesion that can be sampled reliably and to precisely measure the accuracy of iMRI-guided LCNB as a minimally invasive tool to diagnose suspicious lesions found by breast MRI. *J. Magn. Reson. Imaging* 2001;13:896-902. © 2001 Wiley-Liss, Inc.

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THE EMERGENCE OF CONTRAST-ENHANCED BREAST MAGNETIC RESONANCE IMAGING (MRI) as a sensitive means of detecting radiographically occult breast cancer is precipitating an increasing number of breast MRI scans every year. As more scans are performed, more enhancing lesions are being discovered that merit biopsy. The primary method for sampling MRI-detected lesions remains

preoperative MRI-guided needle localization (either stereotaxic (1-3) or freehand (4,5)) and hookwire placement followed by surgical biopsy. Surgical biopsy is costly, invasive, and affects the cosmetic appearance of the breast. The purpose of this study was to develop a nonsurgical method for minimally invasive large-gauge core needle biopsy (LCNB) of enhancing breast lesions using direct, intraprocedural MRI (iMRI) guidance. We report our experience using a freehand iMRI-guided LCNB method that is based on a previously described method for preoperative needle localization and lesion marking (4).

MATERIALS AND METHODS

Patient Population

The study population consisted of 19 patients, ranging from 33 to 67 years old, who underwent iMRI-guided LCNB between May 14, 1998 and November 3, 1999. Two patients had three lesions each, four patients had two lesions each, and 13 patients had one lesion each, for a total of 27 biopsied lesions. Lesion diameter ranged from 0.5 to 4.0 cm (average 1.8 cm) on preliminary diagnostic MRI. Six lesions were 1 cm or less; 12 lesions were 1-2 cm; six lesions were 2-3 cm; three lesions were 3-4 cm. To facilitate rapid recruitment for this feasibility study, any patient with a suspicious lesion visible on previous diagnostic MRI was eligible for the study, regardless of whether the lesion could have been biopsied by other means, such as under mammographic or sonographic guidance. Lesions were considered suspicious if any of the imaging modalities or physical exam indicated biopsy. On MRI, focal lesions with rapid initial enhancement on dynamic imaging or abnormal morphology on high-resolution imaging were considered suspicious. Seven lesions were mammographically visible. Seven lesions were palpable. Fifteen lesions, four of which were sonographically visible, were imaged with ultrasound. All patients gave their signed informed consent in accordance with our institutional panel on human subjects.

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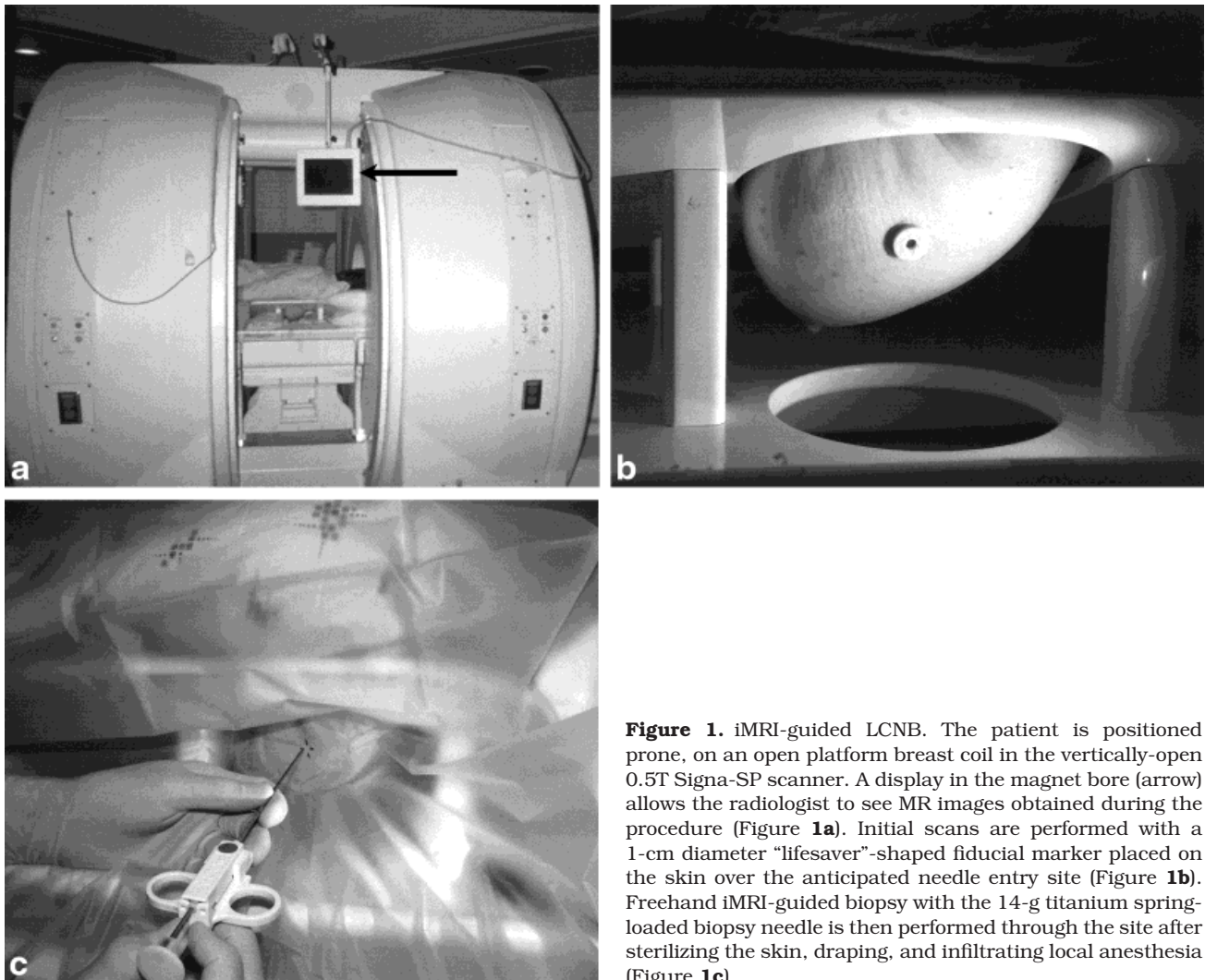


Figure 1. iMRI-guided LCNB. The patient is positioned prone, on an open platform breast coil in the vertically-open 0.5T Signa-SP scanner. A display in the magnet bore (arrow) allows the radiologist to see MR images obtained during the procedure (Figure 1a). Initial scans are performed with a 1-cm diameter “lifesaver”-shaped fiducial marker placed on the skin over the anticipated needle entry site (Figure 1b). Freehand iMRI-guided biopsy with the 14-g titanium spring-loaded biopsy needle is then performed through the site after sterilizing the skin, draping, and infiltrating local anesthesia (Figure 1c).

Preliminary Imaging

All patients underwent unilateral diagnostic breast MRI on a separate day prior to biopsy (1.5T Echospeed Scanner, GE Medical Systems, Milwaukee, Wisconsin; phased array breast coil, MRI Devices, Waukesha, Wisconsin). The protocol included axial unenhanced T1-weighted spin-echo imaging (TR/TE = 500–700/14 msec, 5-mm slice thickness) and rapid dynamic imaging (3D spiral MRI; TR/TE = 38/11.9 msec; water-selective spectral-spatial excitation; 1-2-1 on resonance binomial magnetization transfer pulse; 20 interleaved spirals; 4.5- to 6-mm slice thickness; 20-slice volume per scan using partial Fourier slice encoding, including 10 positive and 4 negative k_z lines; 10.6 seconds per scan repeated for 3.5 minutes during bolus intravenous infusion of 0.1 mmol/kg contrast material; 3-ml-per-second Gd-DTPA, Magnevist, Berlex Laboratories, Wayne, New Jersey; 20-ml saline flush (6)), followed by high spatial resolution 3DSSMT (3D gradient echo imaging, water-selective spectral-spatial excitation, 1-2-1 on resonance binomial magnetization transfer pulse; TR/TE = 33/9 msec; 1.5- to 2.0-mm slice thickness; 64-slice volume; elliptical-centric phase encode ordering; 6:20 minutes (7)), followed by an addi-

tional 4 minutes of dynamic “washout” data (3D spiral MRI using the same parameters as the initial dynamic scan).

Biopsy Technique

iMRI-guided LCNB was performed using a 0.5T vertically open, horizontal field scanner (Signa-SP, General Electric Medical Systems, Milwaukee, Wisconsin) with an elevated platform-type quadrature transmit/receive breast coil (MRI Devices, Waukesha, Wisconsin; $N = 18$ patients) (Fig. 1). In one patient, the lesion could not be accessed using the breast coil because it was high in the axillary tail of the breast; hence, a flexible open-loop surface coil was used, with the patient supine and her arm elevated.

A freehand biopsy technique was used (see Fig. 1 and 2) that is based on previously reported methods for freehand iMRI-guided preoperative needle localization (4,5). This method was chosen because it enables accurate needle placement without need for specialized stereotaxic instrumentation. As with the previous method, all steps up to and including initial needle placement were performed prior to contrast

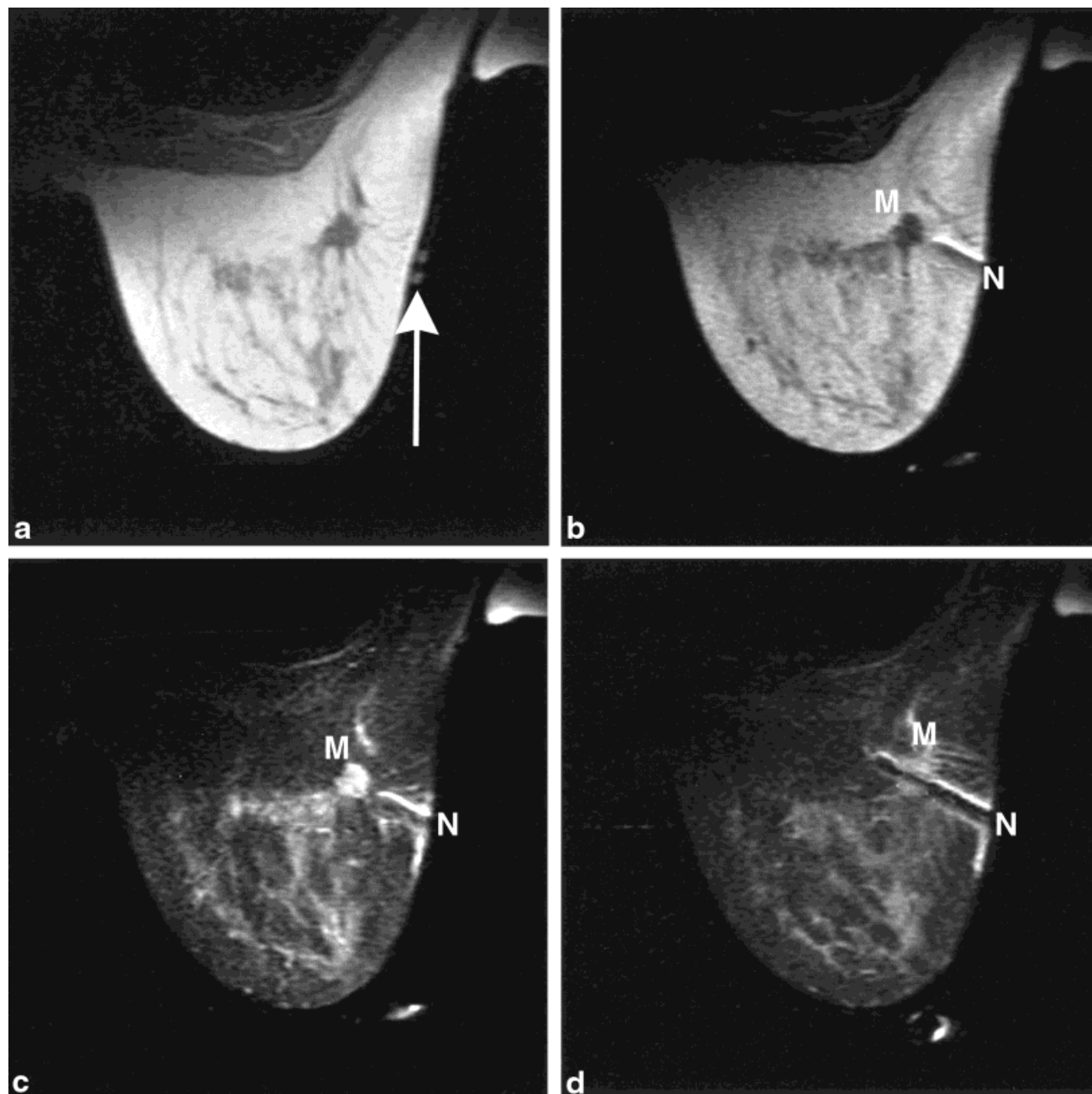


Figure 2. IMRI-guided Breast Biopsy. A T1-weighted FSE image of the breast (Figure 2a) shows the marker on the skin indicating the planned skin entry site (arrow). A fat-specific image from a 3-point Dixon FSE scan (Figure 2b) reveals the needle (N) approaching the mass (M). The corresponding Gd-enhanced water-specific image from the 3-point Dixon scan (Figure 2c) confirms enhancement of the mass beyond the tip of the needle. A water-specific image from the Gd-enhanced 3-point Dixon FSE scan (Figure 2d) performed after advancing the inner stylet of the biopsy needle reveals the suspicious enhancing lesion centered on the biopsy slot of the needle. Histopathology revealed a 1.8 cm invasive ductal carcinoma. See text for scan parameters.

administration because the preferential enhancement of suspicious breast lesions over background breast tissue is brief. Gadolinium-enhanced imaging was reserved for the most crucial portion of the procedure, insertion of the biopsy needle into the enhancing lesion. Because all patients had undergone recent preliminary diagnostic imaging in the same position at our institution (see above), there was no need to confirm the presence of the lesion prior to beginning the biopsy procedure.

Details of the freehand needle placement technique have been reported previously (4). To summarize, a lifesaver-shaped aqueous fiducial marker (Radionics, Z Medical Inc., Baltimore, Maryland) was fixed to the skin of the breast overlying the approximate position of the lesion. The position of the marker relative to the target was determined by comparing unenhanced axial T1 fast spin echo (FSE) images (TR/TE/ETL = 300/13/4, 24 seconds per stack of three 5-mm-thick slices) with axial T1 spin echo and axially reformatted contrast-

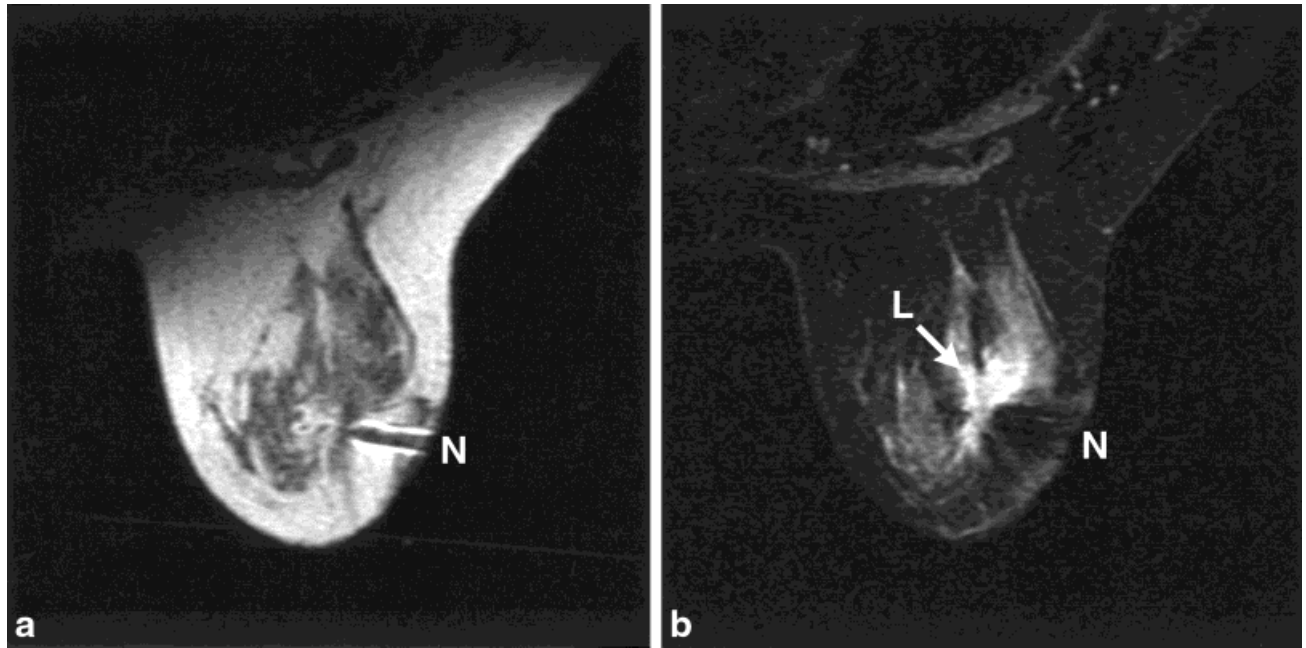


Figure 3. iMRI-guided LCNB of enhancing lesion that was poorly seen on mammography as only vague architectural distortion. Although comparison of the T1-weighted FSE images after initial needle placement (Figure 3a) with diagnostic scans performed prior to biopsy (not shown) suggested that the position of the needle (N) was approaching the suspected location of the suspicious enhancing lesion, the exact location of the target remained unclear. Rapid T1-weighted water-specific image from a Gd-enhanced 3-point Dixon FSE scan (Figure 3b) confirmed the enhancing lesion (L) at the tip of the needle. Histopathology revealed infiltrating lobular carcinoma.

enhanced 3DSSMT images from the preliminary diagnostic MRI. To determine the optimal needle entry site on the skin, the marker was repositioned and reimaged until both the center of the fiducial marker and the center of the suspected target were visualized in the same axial image. The skin entry site was marked with a pen, sterilized with betadine, draped, infiltrated with 1% lidocaine, and nicked with an MRI-compatible disposable scalpel (Microsurgical Techniques, Fort Collins, Colorado). An MR-compatible core biopsy needle (14-g titanium single-action spring-loaded biopsy needle, Daum Corp, Chicago, IL) was inserted, imaged, and interactively repositioned until T1 FSE images revealed the needle tip at the edge of the target. Enhancement of the target was then confirmed using rapid, water-specific imaging (three-point Dixon GRE (4), $N = 5$ patients; or three-point Dixon T1-FSE, $N = 5$ patients) after intravenous infusion of 0.1 mmol/kg contrast material (Gd-DTPA, Magnevist, Berlex, Wayne, New Jersey). Three-point Dixon imaging was used because conventional fat-saturation techniques are unsatisfactory due to the eccentric location of the breast in the magnet bore, the inability to achieve a robust shim in the open MR scanner, and the relatively poor separation between the spectral peaks of fat and water at 0.5T (only 72 Hz). In one patient, contrast-enhanced imaging could not be performed due to inability to secure intravenous access. After any necessary repositioning, the needle was extended into the suspicious lesion and imaged, and biopsy was performed. Multiple-core biopsy samples were removed from the lesion in this fashion (range, 2–8 samples per lesion; average, 4.4 samples per lesion). A single contrast injection was used in all cases.

Histopathologic Analysis

A pathologist (K.W.N.) independently reviewed the samples obtained by iMRI-guided LCNB. The maximum size of the largest core sample was measured. Adequacy of sample size for diagnosis, as well as presence or absence of significant crush artifact, was determined. Histopathologic diagnoses from the core biopsy samples were then compared with subsequent surgical specimens in the 19 lesions for which surgical specimens were available.

RESULTS

All patients tolerated LCNB well; there were no immediate complications of iMRI-guided LCNB. Representative images from iMRI-guided LCNB are presented in Figures 2 and 3. The time for each LCNB averaged 70 minutes per case, from the start of initial imaging on arrival of the patient in the iMRI suite to the end of final imaging following removal of the last sample. The duration averaged 55 minutes for the cases with a single lesion and 90 minutes for the cases with multiple lesions. Substantial force was required to penetrate some lesions using the 14-g titanium needle. In one case, the tough schirrous nature of the breast bent the inner trocar of the 14-g titanium needle as it was extended. Although no patient injury resulted, the needle had to be removed and discarded before obtaining a sample with a new needle.

All LCNB samples were sufficient for histopathologic analysis. The maximum size of the samples ranged from 3 to 22 mm (average, 10 mm).

Nineteen lesions were sampled after iMRI-guided LCNB by surgical biopsy, including 12 that were localized preoperatively using a technique for freehand iMRI-guided needle localization and hookwire placement that was previously reported for a different set of patients (4). Four lesions were palpable and thus removed without need for iMRI-guided needle localization, and three were removed at mastectomy. No surgical correlation was available for the remaining eight lesions. Samples from the iMRI-guided LCNB's that were attempted on these eight lesions all revealed benign histopathology. Seven of the eight were residual foci of nonspecific enhancement in patients with previously treated tumors; clinical follow-up is pending in these patients. One lesion was in a previously asymptomatic, high-risk patient; imaging and clinical follow-up is pending in this patient as well.

Histopathology of the 19 excised lesions revealed nine malignancies and 10 benign lesions. The malignancies included invasive ductal carcinoma ($N = 4$), infiltrating lobular carcinoma ($N = 3$), mixed invasive ductal/lobular carcinoma ($N = 1$), and patchy involvement by intermediate-grade ductal carcinoma in situ (DCIS) ($N = 1$). The benign lesions included fibrocystic change ($N = 7$), intraductal papilloma ($N = 1$), foreign-body giant cell reaction due to prior biopsy ($N = 1$), and benign breast parenchyma ($N = 1$). iMRI-guided LCNB correctly diagnosed the presence or absence of malignancy in 18 of 19 lesions. The exception was a 3.3-cm enhancing region containing patchy DCIS in a patient whose iMRI-guided LCNB revealed only stromal fibrosis. This patient had previously completed neoadjuvant chemotherapy 5 months before the MRI, with a near complete response. The failure of iMRI-guided LCNB was likely due to sampling error, as the residual DCIS was only intermittently dispersed within more extensive fibrosis. Histopathology of the excised specimens and the corresponding iMRI-guided LCNB specimens was partially discrepant in two other lesions, even though the presence or absence of malignancy was correctly established. iMRI-guided LCNB revealed only high-grade DCIS in a patient who had both DCIS and a 6-mm invasive ductal carcinoma. iMRI-guided LCNB revealed atypical ductal hyperplasia in a patient with a 2.5-cm enhancing region in whom the subsequent surgical biopsy revealed only proliferative fibrocystic change. This LCNB sample had a significant crush artifact, which may have contributed to the false suspicion of atypia.

In several cases, the target was difficult to visualize with iMRI because the degree of enhancement was relatively slight. One was in the patient who had recently completed neoadjuvant chemotherapy, in whom subsequent surgical biopsy revealed residual patchy intermediate-grade DCIS. In a second patient, surgical biopsy revealed foreign-body giant cell reaction due to a previous biopsy and nonproliferative fibrocystic change, but no tumor. The development of a small hematoma made iMRI-guided LCNB progressively more difficult in another case. Since the hematoma was high in signal due to the circulating intravenous contrast material, it was difficult to distinguish from the enhancing target tumor. In one obese patient, biopsy was more difficult

because the patient could only enter the magnet via the side. Thus biopsy had to be performed through the end hole of the magnet. As a result, the biopsy needle was parallel to B_0 and cast only a very small artifact that was difficult to visualize with FSE sequences. Changing to gradient echo images and, in particular, using the three-point Dixon gradient echo sequence enabled this biopsy to proceed without complication.

In order to determine whether sonography would have been an adequate imaging modality for guiding biopsy in lieu of MRI, results of the 15 corroborating sonographic examinations performed prior to biopsy were retrospectively reviewed. Among the five invasive tumors imaged with sonography, a 1.2-cm mixed infiltrating lobular and invasive ductal tumor in one patient and a 3.0-cm infiltrating lobular carcinoma in another patient could not be detected by sonography. Furthermore, among the four sonographically evident solid lesions, one was a benign intraductal papilloma.

DISCUSSION

Our results indicate that direct iMRI-guided 14-gauge LCNB is possible and can provide a nonsurgical pathologic diagnosis of enhancing breast lesions. Previously, Kuhl et al and Fischer et al reported successful MRI-guided core needle biopsy of five lesions and four lesions, respectively (3,8); however, these small studies were not performed with large-gauge (14 g) needles, which are known to be more accurate for breast biopsy (9). The recently available MRI-compatible 14-g titanium spring-loaded needles enabled our study to be performed with larger caliber needles than were previously available. In our experience, however, sample yield from the titanium MRI-compatible 14-g needles still remains slightly worse than the yield from non-MRI-compatible steel 14-g needles of identical design used for freehand ultrasound-guided LCNB.

Successful biopsy mandates adequate visualization of both the target and the biopsy needle. Magnetic susceptibility artifacts from biopsy needles present a potential challenge to biopsy because they are larger than the needle itself and can obscure small breast lesions. While the artifacts cast by the new 14-g titanium spring-loaded needle are no larger than the artifacts from previous smaller-gauge needles, they are still at least 6–7 mm in diameter. Thus during initial needle placement, it remains prudent to stop just short of placing the needle in the lesion, because of the potential for the needle artifact to obscure a small target lesion. Pending future studies to determine the smallest lesion that can be reliably sampled with iMRI-guided LCNB, we feel that lesions should be at least 1 cm before considering iMRI-guided LCNB using current needle technology. Needle artifacts on 3-point Dixon images can be reduced somewhat by using FSE three-point Dixon imaging in lieu of gradient echo three-point Dixon imaging. Continued research into imaging techniques for artifact management may also reduce the diameter of the needle artifact, thereby facilitating biopsy of smaller lesions in the future (10).

The interactive, freehand, direct iMRI-guided LCNB technique has several potential advantages over other

biopsy methods for lesions detected on breast MRI. Fine-needle aspiration has been performed under MRI guidance, but it is difficult and can only provide a cytological diagnosis that does not distinguish invasive from noninvasive carcinoma (11). LCNB has been performed just outside the bore of the magnet using non-MRI-compatible needles inserted via an MR-compatible needle or sheath placed under MRI guidance (12). However, due to the malleable nature of breast parenchyma, even if the breast is compressed and a guiding canula has been perfectly positioned to abut a suspicious lesion, the target may move out of the way under the force of an advancing biopsy needle. Since the non-MR-compatible biopsy needle is never visualized within the lesion, it is impossible to determine whether such errors have occurred. Similarly, when the core biopsy is performed using biopsy-assist devices that use MRI data to facilitate a stereotaxic biopsy needle placement, there is no guarantee that the target remains fixed as the biopsy needle is inserted. Using our freehand iMRI-guided LCNB method (4,5), interactive adjustment of the needle trajectory can compensate for motion of the target. Furthermore, the biopsy needle is visualized within the target lesion, increasing the confidence that the biopsy specimen is representative of the suspicious enhancing lesion.

LCNB of MRI-detected lesions has been performed using sonography or CT (13), but not all lesions detected by MRI are visible on sonography or CT. Two of five invasive tumors detected on MRI in our study, both infiltrating lobular carcinomas, were sonographically occult. In addition, there is no guarantee that the target seen on CT or ultrasound corresponds precisely to the lesion identified by MRI. iMRI-guided LCNB enables biopsy of a lesion using the same imaging modality that detected it. Finally, surgical biopsy can be performed following MRI-guided needle localization and hookwire placement (1–5). However, surgical biopsy is invasive, costly, and affects the cosmetic appearance of the breast. Furthermore, the lack of Gd-enhanced specimen MRI techniques makes it difficult to prove that the surgically excised specimen contained the target lesion.

One promising technique that may improve the accuracy of iMRI-guided fine needle aspiration (FNA), iMRI-guided LCNB, and iMRI-guided surgical biopsy is MR spectroscopy of the biopsy specimen (14). When coupled with future developments in diagnostic spectroscopic imaging, this innovation has the potential to corroborate correct sampling of the suspicious target lesion. This is analogous to specimen radiography which confirms that mammographically detected calcifications have been appropriately sampled.

The ability to simultaneously visualize the enhancing target and the core biopsy needle was particularly useful for patients whose lesions were confined within glandular parenchyma and hence difficult to define on unenhanced T1-weighted FSE, as in Fig. 3. Unfortunately, the preferential enhancement of some breast lesions, compared to the surrounding breast parenchyma, may be brief (15 minutes or less in some patients). To best utilize this time window, all steps preceding initial needle placement were performed prior to the intravenous contrast injection. This requires some

experience, as architectural landmarks of breast anatomy on unenhanced T1-weighted images become the primary tools for directing the initial needle placement. In our experience, because the preliminary diagnostic scans were performed with the breast in the same configuration, these landmarks remained constant enough to enable initial biopsy needle placement in close proximity to the target in all cases. Any small errors were then corrected on the immediate postcontrast images, when the target was most conspicuous.

A significant limitation of the current iMRI-guided LCNB method is the speed of water-specific three-point Dixon imaging available. These images, whether gradient echo or FSE, require approximately 3 minutes, including the necessary off-line reconstruction. As breast lesions may become less visible after only a few minutes, this limits the number of interactive manipulations and needle passes that can be performed in some cases. Patients with multiple lesions are more difficult to biopsy because needles must be placed simultaneously at several locations, requiring lengthier three-point Dixon iMRI. This limitation, combined with the smaller sample yield and potential for crush artifact with the titanium needles, may have contributed to the missed diagnosis in one case and the partially discrepant results in two other cases. Biopsy was also more difficult in two of these cases because the target lesion was not very avidly enhancing with contrast material, hence difficult to define at the time of biopsy. It is possible that repeated injections of contrast material could facilitate more lengthy biopsy procedures, although the progressive enhancement of surrounding normal glandular tissue may limit the benefit of multiple injections. Tumor-specific contrast agents that prolong tumor visualization (15) may make iMRI-guided biopsies easier in the future. MR-compatible stereotaxic positioning equipment, or biopsy assist devices, may facilitate iMRI-guided LCNB, particularly when using a conventional closed-bore scanner, by reducing the number of times the needle must be repositioned to reach the target.

One limitation of this study is the lack of long-term follow-up of the histologically benign lesions to ensure that there was no evidence of malignancy. We cannot exclude the presence of tumors that were missed by both the iMRI-guided LCNB and subsequent MRI-localized surgical biopsy.

We anticipate that minimally invasive iMRI-guided LCNB, when mature, will be an essential technology which, by reducing the substantial cost and morbidity associated with biopsy of incidentally discovered lesions, will enable greater utilization of diagnostic breast MRI compared to surgical biopsy. Before implementing iMRI-guided LCNB in lieu of iMRI-guided surgical biopsy, its accuracy as a function of target lesion size must be measured more precisely in larger studies. Criteria must also be established for deciding which borderline pathologic lesions found on iMRI-guided LCNB merit follow-up imaging and which should be surgically excised.

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