

Magnetic Resonance Imaging-Guided Biopsy of Mammographically and Clinically Occult Breast Lesions

Isabelle Bedrosian, MD, James Schlencker, MD, Francis R. Spitz, MD, Susan G. Orel, MD, Douglas L. Fraker, MD, Linda S. Callans, MD, Mitchell Schnall, MD, PhD, Carol Reynolds, MD, and Brian J. Czerniecki, MD, PhD

Background: Breast magnetic resonance imaging (MRI) is a very sensitive technique for detection of breast cancer. We report on MRI-guided needle localization for biopsy of abnormalities seen only on MRI.

Methods: A retrospective review was performed of 231 patients with invasive breast cancer or ductal carcinoma-in-situ who had MRI as part of their evaluation and treatment at the University of Pennsylvania between 1992 and 1998. Clinical, radiological, and pathologic data were examined.

Results: MRI needle localization was performed in 41 (18%) patients. MRI needle localization was required for a finding of a mammographically or clinically occult lesion in 31 patients, better MRI definition of tumor in 5 patients, and surgeon's choice in 5 patients. In all cases, MRI localization and excisional biopsy were successfully completed. Nineteen of 31 patients were found to have additional mammographically and clinically occult tumors. There were 12 (29%) false-positive MRI scans.

Conclusions: MRI has a high sensitivity for detection of breast cancer; additional mammographically and clinically occult sites of tumor are detected in approximately 1 (15%) of 7 breast cancer patients. These otherwise occult sites of disease can be appropriately biopsied with MRI needle-localization techniques.

Key Words: Magnetic resonance imaging—Breast cancer—Biopsy—Mammography.

Surgical planning and treatment of breast cancer rely on adequate assessment of the extent of disease, the size of the primary tumor, and the presence of multiple tumor foci. Identification of macroscopic multifocal (multiple foci of tumor within the same quadrant) or multicentric (separate areas of tumor in different quadrants) disease is generally considered to result in higher rates of local recurrence and is, therefore, a contraindication to breast conservation.^{1,2} Estimates of the frequency of multifocality in breast cancer vary widely, and, depending on the specific criteria used, can range from 7% to 63%.³⁻⁶ Nonetheless, with the overall high incidence of breast

cancer in Western cultures, a significant number of women can be expected to have multifocal disease at presentation and therefore can be expected not to be ideal candidates for breast conservation. Preoperative identification of these patients may be important for appropriate surgical management.

As a diagnostic modality in breast cancer patients, magnetic resonance imaging (MRI) of the breast has been shown to have high sensitivity (94%–100%).⁷⁻⁹ In addition, in these highly selected patients, MRI demonstrates other unsuspected areas of cancer in approximately one third of such cohorts.^{8,9} Comparative studies of MRI to mammogram, ultrasound, and clinical assessment consistently show MRI to have higher accuracy for determining the extent of disease, including the presence of multifocal or multicentric disease.¹⁰⁻¹² However, the specificity of breast MRI remains highly variable (37%–100%)^{7,8,13} and overall is lower than would be desired, because of the enhancement of some benign breast lesions with the administration of contrast.^{14,15} Therefore,

Received September 10, 2001; accepted February 9, 2002.

From the Departments of Surgery (IB, JS, FRS, DLF, LSC, BJC) and Radiology (SGO, MS), University of Pennsylvania, Philadelphia; and the Department of Pathology (CR), Mayo Clinic, Rochester, Minnesota.

Address correspondence and reprint requests to: Brian J Czerniecki, MD, PhD, Department of Surgery, 4 Silverstein, HUP, 3400 Spruce St., Philadelphia, PA 19104; Fax: 215-662-7476; E-mail: czerniec@mail.med.upenn.edu.

the optimal management of lesions seen on MRI alone remains to be determined. We undertook this study to determine whether MRI needle localization was feasible for assessing the pathology of lesions observed on breast MRI.

METHODS

Patient Population

From 1992 to 1998, 320 patients with biopsy-proven invasive breast cancer or ductal carcinoma-in-situ (DCIS) were evaluated with MRI before undergoing definitive surgical therapy. Patients who had excisional biopsy for diagnosis were excluded from this analysis, leaving a cohort of 231 patients for this analysis. Clinical, radiological, and pathologic data on this cohort were retrospectively examined.

MRI and Needle-Localization Biopsy

Breast MRI was performed with a 1.5-tesla GE Signa Horizon™ echo speed system (Fairfield, CT) with a compression breast array. Before-and-after intravenous gadolinium MRI scans were performed by using 2-mm slices and $350 \times 700\text{-}\mu\text{m}$ in-plane resolution. Findings of enhancement in a ductal or regional distribution were considered to be in situ carcinoma. Focal mass enhancement was considered to be representative of invasive cancer.

For needle localization, a lateral plate containing a window measuring approximately $6.25 \times 3.75\text{ cm}$ was centered over the area suggestive of malignancy. The location of the lesion was identified on an MRI. The x , y , and z dial positions were calculated with software to accurately position the needle guide. Each of the three dial positioning dials could be moved in intervals of .025 mm. After the dials were appropriately set, the needle was passed into the area of interest. The wire position was subsequently verified for the surgeon by mammography (Fig. 1).

RESULTS

Patient Population

From 1992 to 1998, 320 patients with biopsy-proven invasive breast cancer or DCIS were evaluated with MRI before undergoing definitive surgical therapy. Among this group, 89 patients had already been diagnosed by excisional biopsy and were excluded from this analysis. Of the remaining 231 patients, 41 (18%) were identified as having had MRI-guided needle-localization biopsy (Fig. 2). The reasons for MRI-guided biopsy included 31 patients with an unsuspected lesion detected by MRI and 5 patients with difficult visualization by conventional imaging techniques and conversion to MRI for more accurate localization. In five patients, the choice of MRI

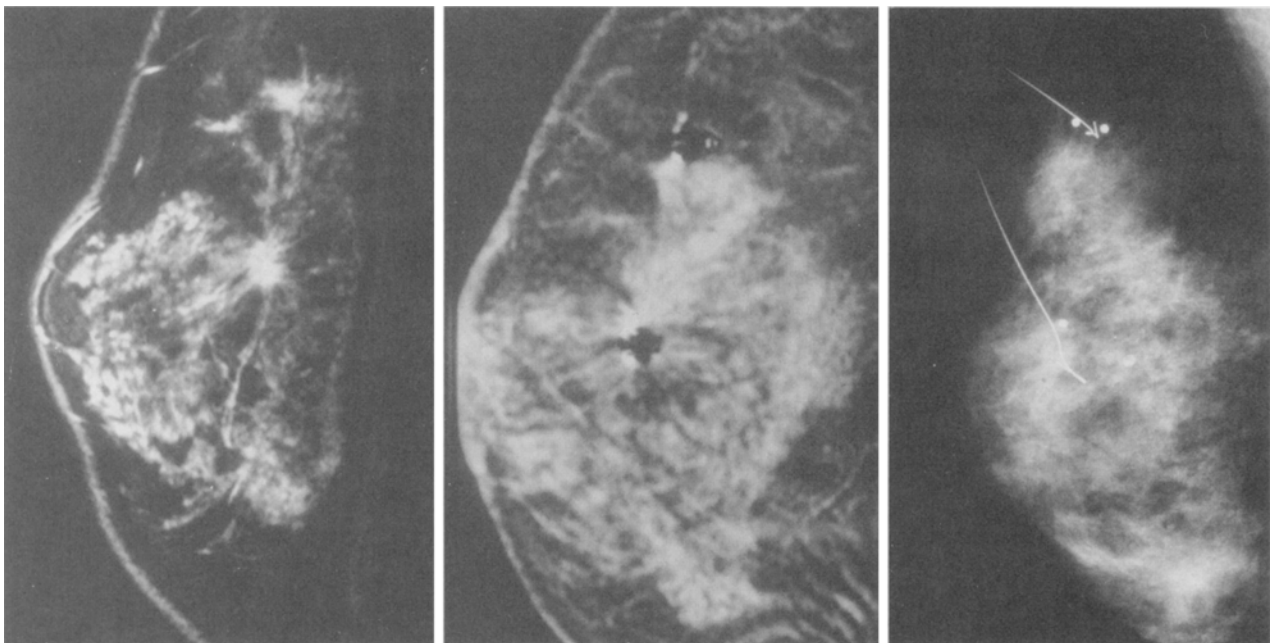


FIG. 1. Magnetic resonance imaging (MRI)-guided needle localization and subsequent mammographic appearance of the wire. (A) Two high-intensity lesions that drop out with MRI localization (B). The wires are then demonstrated on mammography (C).

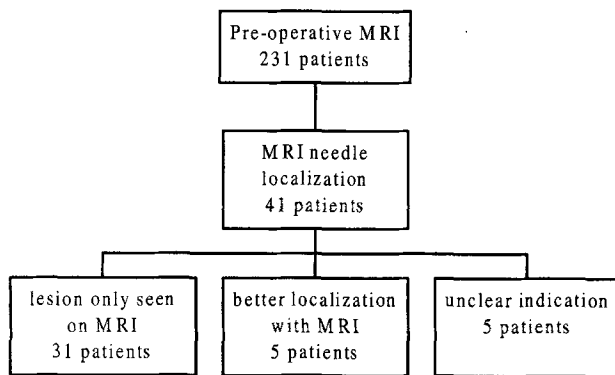


FIG. 2. Patient population. MRI, magnetic resonance imaging.

rather than conventional imaging for needle localization was not readily apparent.

Sites of MRI-Localized Disease

Thirty-one patients had suspicious lesions identified by MRI alone. In the majority (17 of 31) of these patients, the additional site of disease was in a different quadrant from the index lesion (multicentric). Four patients presenting with an axillary mass and a negative mammogram, and two patients with nipple discharge and a negative mammogram, had a mass localized by MRI. In the remaining eight patients, a separate focus of tumor was identified within the index quadrant (multifocal).

Results of Biopsy

All patients undergoing MRI needle-localization biopsy were successfully localized, and excisional biopsy was performed. Biopsy results for the 31 cases of MRI-localized lesions are diagrammed in Fig. 3. Of the 31 previously unsuspected sites suggestive of disease detected by MRI only, 19 (62%) were confirmed as malig-

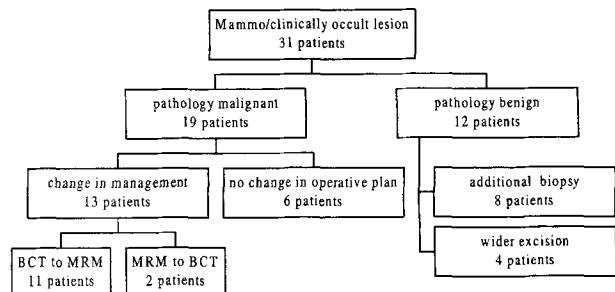


FIG. 3. Change in patient treatment on the basis of preoperative magnetic resonance imaging (MRI). Thirty-one patients were found to have additional, unsuspected disease on preoperative MRI. Of this cohort, 19 patients had malignancy confirmed at biopsy and had a subsequent change in surgical management. BCT, breast-conserving therapy; MRM, modified radical mastectomy.

nant at biopsy. The sizes of these MRI-detected lesions ranged from 4 mm to several centimeters. The histology of these additional sites of disease was predominantly invasive; two patients had pure DCIS lesions picked up by MRI alone.

Table 1 outlines the results of biopsy by quadrant. Additional malignancy in the index quadrant was present in 6 (75%) of 8 patients. In contrast, 8 (47%) of 17 patients with additional sites suggestive of disease that were localized by MRI alone had a confirmed second malignant focus in a different quadrant from the index lesion. MRI identified tumors correctly in 5 (83%) of 6 patients presenting with either an axillary mass or nipple discharge and a negative mammogram.

The 12 false-positive MRI scans were equally distributed throughout the study period. There was no predominant enhancement pattern. The histological findings in these 12 patients included fibrocystic disease, hyperplasia, and atypical ductal hyperplasia.

Change in Treatment on the Basis of Preoperative MRI

All 31 patients with unsuspected disease seen on preoperative MRI had biopsy of these areas suggestive of disease (Fig. 3). Among the 19 patients with additional tumor foci confirmed at biopsy, the preoperative plan was altered in 13, with 11 patients previously believed to be breast-conservation therapy candidates converted to mastectomy. In addition, two patients with axillary masses were able to undergo breast-conservation therapy rather than the planned modified radical mastectomy.

Twelve patients had a negative biopsy at sites of MRI-suspected tumor; eight of these patients had an additional biopsy through a separate incision. In the remaining four patients, a wider excision was performed to incorporate the area of MRI abnormality.

DISCUSSION

Breast MRI for diagnosis of breast cancer has been repeatedly demonstrated to have high sensitivity,⁷⁻⁹ and we confirm this finding. Similar to previous reports,

TABLE 1. Location and biopsy results of magnetic resonance imaging-identified lesions relative to the location of the index tumor

Location relative to index lesion	No. Patients	No. with malignant disease
Same quadrant (multifocal)	8	6 (75%)
Different quadrant (multicentric)	17	8 (47%)
Axillary mass	4	3 (75%)
Nipple discharge	2	2 (100%)

approximately 1 (15%) in 7 patients evaluated in this study had areas suggestive of malignancy detected by MRI but not clearly visualized by current conventional imaging techniques or clinical examination.¹⁰⁻¹² The detection of potential areas of tumor identified by MRI alone raises the difficult question of how best to address these areas of MRI abnormality.

At the University of Pennsylvania, we have pursued attempts at biopsy of MRI abnormalities before definitive surgery. In this study, 31 patients were identified for MRI needle-localization biopsy. Because the current ability to core biopsy under MRI guidance remains limited, these patients underwent needle localization by MRI followed by excisional biopsy. Biopsy was successfully completed in all 31 patients. Nineteen of these patients had additional sites of malignancy identified by MRI. It is important to note that eight of these patients had multicentric disease that probably would have been missed if the patient had opted for treatment of the index lesion with breast conservation. Whether these MRI-detected, but mammographically and clinically occult, tumors can be appropriately treated with radiotherapy remains controversial. The addition of radiotherapy reduces the risk of ipsilateral tumor recurrence; however, long-term recurrence rates remain at approximately 10% to 20%.¹⁶⁻¹⁸ It remains unclear whether such recurrences are due to inadequate excision of the primary tumor or to unsuspected multifocal or multicentric disease.^{3,16,19,20} Prospective studies using MRI for more accurate staging will be required to assess the long-term effect of the preoperative use of this new staging modality on ipsilateral breast tumor recurrence.

Our study identified MRI as a useful tool for further evaluation of a certain subpopulation of patients—specifically, patients with inadequately visualized or indeterminate lesions on mammography or patients with atypical presentations. In all five patients in our study population with suspicious but poorly defined lesions on mammogram, the tumor was well localized for biopsy by MRI. In five of six patients with carcinoma presenting with an axillary mass or nipple discharge and a negative mammogram, MRI was able to localize the primary tumor. In a review from our institution of 22 patients presenting with axillary node metastasis and unknown primary malignancy, MRI successfully identified a primary breast cancer in 19 patients (86%).²¹ Similarly, the recently published experience from Memorial Sloan-Kettering Cancer Center further supports the use of MRI for localizing and thereby facilitating breast conservation in this patient population.²² Therefore, we believe that MRI should be considered in all patients presenting with

axillary disease and with no primary tumor identified in the breast on clinical examination or mammography.

Although breast MRI seems to identify otherwise occult tumors and consequently to affect surgical management, caution needs to be exercised in using this modality. At present, the specificity of this imaging modality is lower than would be desired, and, as seen in our study, a significant number of patients undergo biopsy with benign findings. Although MRI as a single-step staging tool may be cost-effective,²³ we believe that until the specificity of this tool is significantly and reliably improved, MRI findings should be confirmed by biopsy before definitive surgery. Needle-localization biopsy is clearly feasible; however, it is expensive and time consuming, and it adds a small but definite risk of morbidity. Development of core biopsy techniques that are MRI compatible will be important in advancing this area of patient care.

Additionally, although all patients to date have been successfully localized by MRI for biopsy, a number of technical difficulties have become obvious. First, unlike needle localization under mammography, the specimen removed after MRI localization cannot be imaged to confirm that the area suggestive of disease has in fact been removed. Although we did not in this study consistently reimagine the patients with MRI after biopsy to verify that the suspicious lesion identified on MRI had in fact been removed, we have had many instances of interval postbiopsy MRI evaluations that confirm the success of the MRI-guided needle-localization biopsy. Second, all lesions in the breast localized by MRI are approached laterally, therefore making it somewhat more challenging for the surgeon to access and remove a medial lesion.

CONCLUSIONS

In summary, MRI for preoperative evaluation of breast cancer patients will detect occult tumor and alter treatment in a small but substantial number of patients. MRI-guided needle localization of these otherwise occult sites of disease is clearly feasible. The effect of this approach on locoregional recurrence and long-term survival remains to be determined. Additionally, technical considerations, together with the low specificity of this technique, suggest that this imaging modality, although promising, should for now be further studied within the context of clinical protocols.

REFERENCES

1. Kurtz J, Jacquemier J, Amalric R, et al. Breast-conserving therapy for macroscopically multiple cancers. *Ann Surg* 1990;212:38-44.
2. Kurtz J. Factors influencing the risk of local recurrence in the breast. *Eur J Cancer* 1992;28:660-6.
3. Holland R, Veling S, Mravunac M, Hendriks J. Histologic multifocality of Tis, T1-2 breast carcinomas. Implications for clinical trials of breast-conserving surgery. *Cancer* 1985;56:979-90.
4. Anastassiades O, Iakovou E, Stavridou N, Gogas J, Karameris A. Multicentricity in breast cancer. A study of 366 cases. *Am J Clin Pathol* 1993;99:238-43.
5. Schwartz G, Patchesfsky A, Feig S, Shaber G, Schwartz A. Multicentricity of non-palpable breast cancer. *Cancer* 1980;45:2913-6.
6. Vaidya J, Vyas J, Chinoy R, Merchant N, Sharma O, Mitra I. Multicentricity of breast cancer: whole-organ analysis and clinical implications. *Br J Cancer* 1996;74:820-4.
7. Gilles R, Guinebretiere J, Lucidarme O, et al. Nonpalpable breast tumors: diagnosis with contrast-enhanced subtraction dynamic MR imaging. *Radiology* 1994;191:625-31.
8. Harms S, Flaming D, Hesley K, et al. MR imaging of the breast with rotating delivery of excitation off resonance: clinical experience with pathologic correlation. *Radiology* 1993;187:493-501.
9. Orel S, Schnall M, Powell C, et al. Staging of suspected breast cancer: effect of MR imaging and MR-guided biopsy. *Radiology* 1995;196:115-22.
10. Fischer U, Kopka L, Grabbe E. Breast carcinoma: effect of pre-operative contrast-enhanced MR imaging on the therapeutic approach. *Radiology* 1999;213:881-8.
11. Drew P, Chatterjee S, Turnbull L, et al. Dynamic contrast enhanced magnetic resonance imaging of the breast is superior to triple assessment for the pre-operative detection of multifocal breast cancer. *Ann Surg Oncol* 1999;6:599-603.
12. Boetes C, Mus R, Holland R, et al. Breast tumors: comparative accuracy of MR imaging relative to mammography and US for demonstrating extent. *Radiology* 1995;197:743-7.
13. Kuhl C, Elevelt A, Leutner C, Gieseke J, Pakos E, Schild H. Interventional breast MR imaging: clinical use of a stereotatic localization and biopsy device. *Radiology* 1997;204:667-75.
14. Orel S, Schnall M, LiVolsi V, Troupin R. Suspicious breast lesions: MR imaging with radiologic-pathologic correlation. *Radiology* 1994;190:485-93.
15. Piccoli CW. Contrast enhanced breast MRI: factors affecting sensitivity and specificity. *Eur Radiol* 1997;7(Suppl 5):281-8.
16. Park C, Mitsumori M, Nixon A, et al. Outcome at 8 years after breast-conserving surgery and radiation therapy for invasive breast cancer: influence of margin status and systemic therapy on local recurrence. *J Clin Oncol* 2000;18:1668-75.
17. Harris J, Recht A, Amalric R, et al. Time course and prognosis of local recurrence following primary radiation therapy for early breast cancer. *J Clin Oncol* 1984;2:37-41.
18. Fowble B, Solin L, Schultz D, Goodman R. Ten year results of conservative surgery and irradiation for stage I and II breast cancer. *Int J Radiat Oncol Biol Phys* 1991;21:269-77.
19. Fisher E, Sass R, Fisher B, Gregorio R, Brown R, Wicherham L. Pathologic findings from the National Surgical Adjuvant Breast Project (protocol 6). II. Relation of local breast recurrence to multicentricity. *Cancer* 1986;57:1717-24.
20. Lagios M, Richards V, Rose M, Yee E. Segmental mastectomy without radiotherapy. Short-term follow-up. *Cancer* 1983;52:2173-9.
21. Orel S, Weinstein S, Schnall M, et al. Breast MR imaging in patients with axillary node metastases and unknown primary malignancy. *Radiology* 1999;212:543-9.
22. Olson J, Morris E, Van Zee K, Linehan D, Borgen P. Magnetic resonance imaging facilitates breast conservation for occult breast cancer. *Ann Surg Oncol* 2000;7:411-5.
23. Esserman L, Hylton N, Yassa L, Barclay J, Frankel S, Sickles E. Utility of magnetic resonance imaging in the management of breast cancer: evidence for improved preoperative staging. *J Clin Oncol* 1999;17:110-9.