

Changes in the Surgical Management of Patients with Breast Carcinoma Based on Preoperative Magnetic Resonance Imaging

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Received January 20, 2003; revision received March 24, 2003; accepted April 8, 2003.

BACKGROUND. Breast magnetic resonance imaging (MRI) is a developing technique for the evaluation of patients with primary breast carcinoma. The authors assessed the impact of preoperative breast MRI on surgical management.

METHODS. The current study was a retrospective review of 267 patients with primary breast tumors who had MRI studies prior to undergoing definitive surgery.

RESULTS. Two hundred sixty-seven patients with invasive breast carcinoma who had preoperative breast MRI studies and had complete clinical, radiologic, and pathologic data available were identified and formed the basis of this analysis. The overall sensitivity of MRI for detecting primary, intact breast tumors was 95%. Planned surgical management was altered in 69 of 267 patients (26%); and, in 49 of those patients (71%), there was pathologic verification of malignancy in the surgical specimen that confirmed the need for wider or separate excision or mastectomy. Forty-four of 267 patients (16.5%) had conversion of planned breast conservation to mastectomy. In a univariate analysis, change in management was associated significantly with histology; management was altered in 11 of 24 lobular tumors (46%) compared with 58 of 243 ductal tumors (24%; $P = 0.02$).

CONCLUSIONS. Breast MRI was very sensitive for the detection of primary, intact, invasive breast carcinoma and improved local staging in almost 20% of patients. Preoperative breast MRI studies may be particularly useful in surgical planning for and management of patients with lobular carcinoma. *Cancer* 2003;98:468-73.

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KEYWORDS: breast carcinoma, magnetic resonance imaging, surgery, staging.

Surgical planning for and treatment of patients with breast carcinoma relies on adequate assessment of the extent of disease present, including the size of the primary tumor and the presence of multiple tumor foci, either within the same quadrant (multifocal) or in different quadrants of the breast (multicentric). Identification of macroscopic multifocal or multicentric disease generally is considered to result in higher rates of local recurrence and, thus, a contraindication to breast conservation.^{1,2} Estimates of the frequency of multifocality and multicentricity in breast carcinoma vary widely and, depending on the specific criteria used, may range from 7% to 63%.³⁻⁶ Nonetheless, with the overall high incidence of breast carcinoma in Western cultures, a significant number of women can be expected to have multifocal or multicentric disease at presentation and, thus, may not be ideal candidates for breast conservation. Preoperative identification of these patients is important for their appropriate surgical management.

It has been shown that magnetic resonance imaging (MRI) of the

breast, as a diagnostic modality in patients with breast carcinoma, has high sensitivity (94–100%).^{7–9} Several small studies have described changes in treatment in 11–20% of their patient cohorts based on MRI findings.^{9–12} In particular, MRI has proven to be important in facilitating breast conservation in patients with unusual presentations, such as nipple discharge and axillary lymph node metastasis.^{13,14}

Although MRI clearly alters the management strategy in a significant percentage of patients with breast carcinoma, the indications for MRI within this large patient group remain unresolved. We undertook the current retrospective study to assess whether the findings on preoperative breast MRI studies had an impact on surgical management in a large patient cohort and to attempt to identify specific subpopulations of patients with breast carcinoma who may be more likely to have their management altered by preoperative MRI staging.

MATERIALS AND METHODS

Patient Population

The current study was a retrospective review of 437 patients with breast carcinoma who had MRI studies prior to undergoing definitive surgical therapy between February 1992 and October 1998. Of 437 patients, 425 patients received their care at the University of Pennsylvania. From this cohort, 53 patients who had only ductal carcinoma in situ were excluded from analysis, in addition to 4 patients who presented with an axillary mass, leaving 368 patients eligible for the review. For 99 patients, records were not available or were incomplete; and, in 2 patients, after obtaining a complete data set, it was not possible to determine whether MRI studies had any impact on the surgical care rendered; these patients also were excluded. In the remaining cohort of 267 patients (72.5% of the patients who were eligible for analysis), radiology and pathology reports were examined in addition to the patient chart, which was reviewed to determine the surgical plan pre-MRI and post-MRI.

Mammographic and Ultrasound Imaging

Seventy-five percent of the patients in the current study had mammography performed at the University of Pennsylvania or had outside images reviewed at our institution. In the remaining 25% of patients in our study group, the reports of outside films were used for this review. Because only 95 patients (36%) had preoperative ultrasound studies, the results of ultrasound were not used in the current retrospective analysis.

Magnetic Resonance Imaging and Needle Localization Biopsy

All MRI studies were performed at our institution and were reviewed by one of two radiologists (M.S. and S. G. O.). Breast MRI studies were performed using a 1.5-Tesla Signa Horizon echo speed system (General Electric Medical Systems, Milwaukee, WI) utilizing a compression breast array. Preintravenous and postintravenous gadolinium MR scans were performed using 2 mm slices and 350×700 micron, in-plane resolution. Findings of enhancement in a ductal or regional distribution were considered carcinoma in situ. Focal mass enhancement was considered representative of invasive carcinoma. Detection of residual disease around a biopsy cavity was based on the extent of enhancement of the seroma cavity, as described previously.¹⁵

For needle localization, a lateral plate containing a window measuring approximately $6.25 \text{ cm} \times 3.75 \text{ cm}$ is centered over the area suspicious for carcinoma. The location of a lesion is identified on an MR image. The x, y, and z dial positions are calculated with software to accurately position the needle guide. Each of the 3 dial-positioning dials can be moved in intervals of 0.025 mm. After the dials are set appropriately, the needle is passed into the area of interest. The wire position is verified subsequently for the surgeon by mammography.

Assessment of Change in Surgical Management

Patient charts were reviewed to assess the impact of MRI on surgical management. Change in surgical management was recorded as follow: 1) wider excision to encompass areas of MRI-visualized disease, 2) additional partial mastectomy (separate incision) to encompass areas of MRI-visualized disease, or 3) converted from planned breast conservation to mastectomy. Most patients who underwent wider excision or additional excision for removal of MRI suspicious sites had this area needle localized preoperatively under MRI guidance, as described previously.¹⁶

Statistical Analysis

The sensitivity, specificity, and positive and negative predictive values were calculated using standard definitions. The associations between patient and tumor characteristics and the frequency of change in patient management were assessed with the chi-square test. A P value ≤ 0.05 was considered statistically significant. Statistical analysis was performed using StatXact 3 software (Cytel Software Corp., Cambridge, MA).

TABLE 1
Patient Characteristics^a

Characteristic	No. of patients
Clinical presentation ^b	
Breast mass	104
None (abnormal mammogram)	65
Axillary mass	10
Nipple discharge	6
Breast pain	4
Dimpling	1
Nipple retraction	1
Peau d'orange	1
No data	5
Tumor size ^b	
T1	132
T2	45
T3	19
T4	1
Lymph node disease	
Yes	104
No	142
N/A	21

N/A: not available.

^a Tumor size and lymph node status were based on final pathologic assessment.^b Excludes patients who presented after undergoing initial excisional biopsy.

RESULTS

Patient Population

Complete clinical, radiologic, and pathologic data were available for 267 of 368 patients (72.5%). One hundred ninety-seven patients (74%) had MRI studies prior to undergoing any excisional biopsy. The remaining 70 patients presented to the University of Pennsylvania after undergoing a margin positive excision of the primary tumor and were referred for further evaluation with MRI studies prior to undergoing reexcision. Patient characteristics are outlined in Table 1.

Detection of Residual Disease on Magnetic Resonance Images

Among 197 patients with breast carcinoma who had MRI studies prior to any surgical intervention, MRI had high sensitivity and identified the primary tumor in all but 9 patients (95%). Five of these nine patients had abnormalities detected on mammogram, and the rest had clinical findings. Histologically, one of those nine patients had a colloid tumor, and the remaining patients had invasive ductal carcinoma.

In contrast, in the remaining 70 of 267 patients who were had imaging studies after undergoing excision of the primary tumor, the sensitivity of MRI was diminished markedly for the detection of residual disease around the biopsy cavity. Sixty of 70 patients had residual disease present around the biopsy cavity on

TABLE 2
Detection of Residual Disease around the Biopsy Cavity in Patients Undergoing Magnetic Resonance Imaging after an Initial Excisional Biopsy^a

MRI result	No. of patients		
	Pathology positive	Pathology negative	Total
Positive	34	4	38
Negative	26	6	32
Total	60	10	70

MRI: magnetic resonance imaging.

^a The sensitivity of MRI in this cohort was 57% (34 of 60 patients), with a specificity of 60% (6 of 10 patients) and with positive and negative predictive values of 89.5% (34 of 38 patients) and 19% (6 of 32 patients), respectively.

final pathology, with foci of residual disease ranging from microscopic to 8 cm. Overall, the sensitivity of MRI in this subgroup was 57% (34 of 60 patients), and the specificity was 60% (6 of 10 patients) (Table 2). Thirty-two patients who underwent prior biopsy had no MRI evidence of malignant disease; of these, 26 patients (81%) had residual disease confirmed on pathologic examination (negative predictive value 19%). In contrast, in 38 patients there was MRI evidence of residual disease around the previous biopsy site that was confirmed pathologically in 34 patients (positive predictive value, 89.5%).

Impact of Preoperative Magnetic Resonance Imaging on Surgical Management

Among 267 patients who were evaluated in the current review, MRI studies did not alter management in 198 patients (74%). However, in 69 patients, additional abnormalities were identified on MRI studies that led to either an additional biopsy or a more extensive surgical excision. Overall, 44 of 267 patients (16.5%) who were identified initially as suitable for breast conservation by conventional imaging studies and clinical examinations had suspicious findings identified only by MRI that eventually led to mastectomy. Eleven patients (4%) underwent a wider surgical excision than was planned initially; and 14 patients (5%) underwent an additional, separate excisional biopsy to evaluate the area of MRI-detected abnormality. Of 69 patients who underwent these additional procedures to evaluate MRI abnormalities, there was pathologic verification of malignancy in the surgical specimen in 49 patients (71%), confirming the MRI indication for wider or separate excision or mastectomy. The sizes of these MRI-detected lesions ranged from 4 mm to several centimeters. However, in 20 of 69 patients, it was determined on final pathologic examination that ad-

ditional suspicious areas seen on MRI studies were benign. The changes in surgical management among these 20 patients included a wider excision than was planned to encompass the area of MRI-detected abnormality ($n = 10$), a second, separate excisional biopsy to remove an area of MRI-detected abnormality ($n = 8$), and conversion to mastectomy based on MRI suspicion of malignancy ($n = 2$).

Clinical and Histopathologic Correlations to Change in Management

Clinical and histopathologic features of tumors were compared between patients who had a change in management based on MRI and those with no impact from the MRI evaluation. We were interested in determining whether we could identify a group of patients who were likely to benefit from preoperative MRI studies. Therefore, we chose to look at criteria like age, menopausal status, family history, exogenous hormone use, tumor histology, and ER/PR and her-2/*neu* status, which frequently are available to the clinician before definitive surgical excision of the tumor. (Table 3). On univariate analysis of these variables, no statistically significant differences were seen between patients who had a change in their surgical management based on MRI studies and patients who derived no benefit from additional preoperative MRI staging. It is noteworthy that there was a weak association between tumor histology and frequency of change in management ($P = 0.09$). When lobular carcinoma was compared with all other histologic subtypes, patients with lobular carcinoma were twice as likely to have had their surgical plan altered based on new findings on MRI ($P = 0.02$). Overall, it was found that approximately 50% of patients with lobular tumors had a change in their surgical management based on additional MRI findings. It is noteworthy that, among 11 patients with lobular carcinoma who had a change in surgical management based on MRI studies, MR suspicion of malignancy was validated pathologically in 9 patients (82%).

DISCUSSION

It has been demonstrated repeatedly that breast MRI, as a diagnostic modality in patients with breast carcinoma, has high sensitivity.⁷⁻⁹ The current study confirmed this finding. Ninety-five percent of patients who presented with a diagnosis of breast carcinoma imaged with MRI prior to any surgical intervention had a positive MR scan. In contrast, the specificity of breast MRI remains highly variable (37–100%)^{7,8,17} and, overall, is lower than desired, because many benign breast lesions also are enhanced with the administration of contrast.^{18,19} In the current study cohort,

TABLE 3
Univariate Analysis of Menopausal Status, Family History, Exogenous Hormone Use, Histology, Estrogen and Progesterone Receptor Status, and Her-2/*neu* Staining Showing a Trend towards Significance in the Comparison of Tumor Histology Profiles between Patient Management Groups

Characteristic	Change in management ($n = 69$)	No change in management ($n = 198$)	Chi-square <i>P</i> value
Age (yrs)			
Mean	51.14	53.94	—
SD	11.64	12.37	0.11
Menopausal status			
Premenopausal	28	65	—
Postmenopausal	25	78	—
Perimenopausal	2	14	—
Hysterectomy	14	40 (+ 1 male)	0.48
Family history			
Positive	13	43	—
Negative	16	154	0.06
Excluded (no information)	—	1	—
Exogenous hormone use			
Yes	35	101	—
No	23	72	0.79
Excluded (no information)	11	25	—
Histology			
Ductal	56	172	—
Lobular	11	13	—
Mixed	1	6	—
Others	1	7	0.09
Estrogen receptor status			
Positive	43	111	—
Negative	22	76	0.33
Excluded (no information)	3	4	—
Progesterone receptor status			
Positive	42	97	—
Negative	23	90	0.08
Excluded (no information)	3	4	—
Her-2/ <i>neu</i> status			
Positive	21	49	—
Negative	36	113	0.36
Excluded (no information)	11	29	—

SD: standard deviation.

the specificity of MRI appeared to be especially limited (60%; 6 of 10 patients) when imaging patients after an initial diagnostic excisional biopsy. Therefore, in patients with breast carcinoma who present after undergoing excisional biopsy with positive or close margins, the results of MRI studies should not be used to determine whether the patient should undergo re-excision for positive margins.

Comparative studies of MRI and mammogram, ultrasound, and clinical assessment also show consistently that MRI has higher accuracy for determining extent of disease.^{10,20,21} Recent reports have demonstrated that MRI detects additional, unsuspected areas of tumor in approximately 33% of patients with breast

carcinoma,^{8,9} and changes in treatment based on MRI findings are reported in 11–20% of patient cohorts.^{9,10,12} In the current series, approximately 25% of patients had unsuspected abnormalities identified on MRI, and nearly 1 in 5 patients had a pathologically validated change in operative management. Although breast ultrasound was not used routinely in the current study population (and, thus, its potential impact on the management of our patient population cannot be ascertained), the finding that our observations were consistent with reports in the literature suggests that breast ultrasound may not alter substantially the impact of MRI on clinical management.

In a univariate analysis of clinical and histopathologic characteristics, we found that MRI of the breast was significantly more likely to alter management in patients with invasive lobular histologic subtypes. Patients in the current series with lobular histology were twice as likely to experience a change in therapy based on improved MRI staging compared with patients who had all other histologic subtypes. Among the 24 patients with lobular carcinoma in our series, 11 had a change in management based on more extensive MRI staging; the majority of these patients (8 of 11) were converted to mastectomy. These data are consistent with previous reports demonstrating improved staging of patients with lobular carcinoma using MRI studies.^{22,23}

Invasive lobular tumors account for approximately 5–10% of breast carcinomas;^{24,25} however, they remain a challenge both diagnostically and therapeutically. Mammographic detection of infiltrating lobular carcinoma reportedly has a higher false-negative incidence compared with detection of invasive ductal carcinoma,^{26–27} in part due to the lower rate of suspicious calcifications found with lobular carcinoma and the lower opacity on imaging of this histologic subtype. Even in retrospect, almost 50% of patients with lobular carcinoma who had initial false-negative mammograms may have no evidence of malignancy.²⁶ The sensitivity of ultrasound also is fairly low, ranging from 68% to 87%.^{28,29} In addition, lobular histology reportedly has higher rates of multicentricity compared with ductal carcinoma,³⁰ which may account for the higher rates of mastectomy reported in some series.³¹ Reports of local recurrence rates after breast conservation for invasive lobular carcinoma are few and variable in their findings.^{24,31–32} These reports also were retrospective and, in general, had small patient cohorts,^{33,32} lacked direct comparisons with matched populations of patients who had invasive ductal carcinoma,^{32–34} or involved inadequately staged patients^{24,34} or patients with biologically disparate lobular and ductal carcinoma.²⁴ Because adequate data are

lacking on the risk of locoregional recurrence in invasive lobular carcinoma, proper assessment of the extent of disease is particularly important in patients with invasive lobular carcinoma to ensure that all areas of occult disease are detected. MRI, with its high sensitivity for detection of breast carcinoma, seems uniquely suited for preoperative imaging and staging of these patients.

Whether these additional sites of breast carcinoma, identified only by MRI, can be treated adequately with radiotherapy remains controversial. It is noteworthy that our 16% conversion rate to mastectomy falls within range of the 10–20% long-term local recurrence rates.^{35,36} Currently, the majority of patients who develop locally recurrent disease after initial breast-conservation therapy require salvage mastectomy. We hypothesize that MR evaluation probably will not change the overall mastectomy rate; instead, by using MRI, we believe that we will be able to select patients who are likely to fail breast-conservation therapy. These patients may be offered mastectomy at the time of presentation rather than at the time of local recurrence. It is important to emphasize that, given the high sensitivity but generally lower specificity of MRI, validation of MRI-identified suspicious lesions by core or excisional biopsy is necessary before a recommendation for mastectomy is made.

It is clear from previous reports in the literature, as well as from the current study, that MRI studies for the preoperative evaluation of patients with breast carcinoma can detect occult tumor and may alter management in a substantial number of patients. Criteria for the selection of patients for breast MRI remain indeterminate. Subgroup analysis from our series suggested that patients with invasive lobular histology may benefit from preoperative staging with breast MRI studies. Careful prospective studies comparing clinical examination, mammography, ultrasound, MRI, and pathology are required to clarify the role of MRI in patients with breast carcinoma. We currently are conducting such a study.

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