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## Breast magnetic resonance imaging for preoperative locoregional staging

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Breast conservation;  
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### Abstract

**BACKGROUND:** Breast magnetic resonance imaging (MRI) has been recommended increasingly in the preoperative setting for patients newly diagnosed with malignancy to evaluate tumor extent, multicentricity, and contralateral disease.

**METHODS:** Results of conventional imaging, breast MRI, and pathology were analyzed from 603 consecutive breast cancer patients who underwent MRI preoperatively. The focus of this retrospective study was imaging-histologic correlation.

**RESULTS:** Reoperation for positive margins after lumpectomy occurred in 8.8% of patients. Multicentricity was identified by MRI alone in 7.7% of patients, whereas 3.7% were found to have contralateral cancer by MRI. The sensitivity of MRI was 93% in detecting multicentric disease and 88% for contralateral disease, whereas sensitivity for conventional imaging was 46% and 19%, respectively. Unsuspected disease was identified by MRI equally for invasive ductal and ductal carcinoma in situ histology, whereas multicentricity was found more frequently with invasive lobular carcinoma.

**CONCLUSIONS:** Breast MRI is recommended for preoperative evaluation of the newly diagnosed breast cancer patient.

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Breast magnetic resonance imaging (MRI) is being used in the preoperative setting for newly diagnosed breast cancer patients, both to define tumor extent and to search for other foci of malignancy. During the development of this modality, preoperative patients were often selected for MRI because conventional imaging was believed inadequate. As a result, the probability of discovering occult multicentricity or bilaterality was possibly magnified, and such results were difficult to extrapolate to the general population of newly diagnosed breast cancer patients.

To assess the impact of breast MRI in the overall population of preoperative patients, we began performing breast MRI on all women newly diagnosed with breast cancer in March 2003, reporting our initial series of 334 sequential patients in which MRI-discovered multicentric disease occurred in 7.7%, whereas contralateral cancers were discovered in 3.6%.<sup>1</sup> The 11.3% total for occult disease discovery by MRI, when coupled with findings at the primary tumor site, impacted surgical therapy in 20% of patients overall.

These findings were comparable with other series reported, such as in a multi-institutional study of 426 patients<sup>2</sup> wherein 10% of women were found to have tumor foci more than 2.0 cm from the index lesion, and an analysis of 103 women in the same collaborative group<sup>3</sup> that revealed a 4% chance of contralateral cancer.

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Recently, the American College of Radiology Imaging Network (ACRIN) Trial 6667 announced multi-institutional results of preoperative staging with MRI in 969 women, reporting a 3.1% probability of discovering occult contralateral cancer missed by mammography and examination.<sup>4</sup> The sensitivity of MRI for detecting contralateral cancer was 91% and the specificity was 88%. Notably, the detection of these cancers was not influenced by breast density, menopausal status, or the histologic features of the primary tumor.

Because the ACRIN study provided further evidence for the routine use of preoperative MRI, the question is raised as to whether or not comparable results can be achieved when breast MRI is used in the community setting. This current series of 603 sequentially diagnosed patients is an update of our earlier review, representing what we believe to be the largest single-site study to date, with the primary intent being that of imaging-histologic correlations.

## Methods

### Patient selection

From March 2003 through December 2006, consecutive patients newly diagnosed with breast cancer underwent breast MRI and were included for study according to an institutional review board-approved protocol. Record review included conventional imaging, MRI, and pathology reports. Histologic confirmation of diagnosis was available before the MRI through image-guided biopsy or surgical biopsy. Because our focus was on imaging-histologic correlations, those patients who received neoadjuvant chemotherapy were excluded from the study because partial and complete pathologic responses would automatically impart discordance to the MRI performed at the time of diagnosis. Other reasons for exclusion were as follows: patients who refused surgical intervention after the MRI or were lost to follow-up evaluation, and patients in whom no residual was found on MRI after definitive surgical excision led directly to radiation therapy rather than more surgery. Thus, all patients included in this study underwent additional surgery shortly after the MRI, providing the basis for correlating histology and MRI findings. In addition, for the purposes of this review, lobular carcinoma in situ was not scored as malignant.

### MRI technique

For the first 249 patients in the series, axial and sagittal gradient echo T1 acquisitions were performed for both breasts preceding and after manual infusion of .2 mmol/kg gadolinium followed by a 20-mL saline flush, using an Aurora (North Andover, MA, USA) breast-dedicated .5-Tesla MRI with bilateral breast coil. Subtractions and T2-weighted pulsing sequences also were performed.

For the next 354 patients, high-resolution rotating delivery of excitation off-resonance (RODEO®) axial acquisitions were obtained of both breasts using an Aurora 1.5-Tesla breast-dedicated MRI. Sequences were performed preceding and after the infusion of .2 mmol/kg gadolinium administered as a bolus dose with a power injector followed by a 20-mL saline flush. Subtraction images also were performed.

### Physician participation and source of data

Radiology interpretations for conventional breast imaging were performed primarily by 5 radiologists at Mercy Health Center, and 10 surgeons and 3 pathologists completed the treatment and histologic evaluations, respectively, in the majority of cases. A minority of patients had some portion of their diagnosis, treatment, or pathology performed at outlying facilities, and written reports were relied on in these cases. Tissue processing on all breast specimens was routine, under no special protocol for additional histologic sections. Re-excision rates were compiled through follow-up phone calls to surgeons' offices and hospital medical records departments at delayed intervals, up to 6 months after initial surgery when re-excisions were anticipated by close or positive margins.

MRI results form the crux of this retrospective review, and all MRIs were performed at Mercy Women's Center. MRI interpretations all were performed by 3 of the 5 radiologists who manage conventional breast imaging at this same facility. Written reports for MRI as well as actual images were used in data acquisition, usually presented along with conventional images and pathology slides at a weekly interdisciplinary breast conference.

## Results

From a total of 4,569 patients who underwent breast MRI during the study period, 650 were performed for preoperative locoregional staging. Of these 650 patients, 37 were excluded because of neoadjuvant chemotherapy, 6 patients were excluded when they moved directly to radiation therapy after surgical biopsy, and 4 patients were excluded when they declined any further treatment after the initial biopsy or were lost to follow-up evaluation, leaving 603 patients for inclusion in the study group in which direct histologic correlations to the MRI findings could be made.

Histologic types included 388 invasive ductal carcinomas (and subtypes), 149 patients with ductal carcinoma in situ (DCIS), 65 with invasive lobular carcinoma, and 1 patient with a malignant phyllodes tumor. Diagnosis was made by image-guided biopsy in 547 patients, whereas the remaining 56 patients underwent a surgical biopsy. The term *image-guided biopsy* includes all forms of lesion sampling (core, vacuum-assisted, and so forth) under radiologic guidance, be it radiograph, ultrasound, or MRI. Wire-local-

**Table 1** Surgical approaches used in patients undergoing preoperative MRI

Unilateral lumpectomy	58.5% (353*/603)
Bilateral lumpectomy	1.7% (10/603)
Unilateral mastectomy	28.9% (174/603)
Bilateral mastectomy	10.8% (65/603)
Unilateral mastectomy and contralateral lumpectomy	.2% (1/603)

\*Includes 4 patients who underwent double lumpectomy.

ization procedures before surgical excision were considered as a surgical biopsy.

### Breast conservation

Patients were treated surgically with the approaches as outlined in Table 1. Overall, the breast conservation rate was 60.2%, but this number is skewed lower by the patients who opted for bilateral preventive mastectomy when unilateral lumpectomy would have sufficed for the index lesion. Of the 65 patients who underwent bilateral mastectomy, only 22 had bilateral breast cancer, so 43 opted for a more aggressive prevention strategy against future primaries. If these preventive surgeries are excluded, then 65% (363 of 560) underwent breast conservation.

When therapeutic choices are broken down by pathology groups, the patients with DCIS had the highest rate of breast conservation at 63%, but they also had the highest rate of bilateral mastectomies (19%), mostly for prevention. When a unilateral approach was chosen for unilateral disease, then the breast conservation rate for DCIS was 77% (91 of 118). Breast conservation for invasive ductal carcinoma was performed in 61% of patients (237 of 388), and for invasive lobular carcinoma, conservation was accomplished in 48% (31 of 65).

### MRI evaluation of the index lesion after image-guided biopsy

Assessment of residual tumor at the site of the index lesion after image-guided biopsy is summarized in Table 2. Because there are limitations to traditional dichotomous reporting in light of the fact that MRI can overestimate (and underestimate) the amount of residual tumor, results are

**Table 2** MRI assessment of residual tumor at site of the index lesion after image-guided biopsy, compared with final pathology measurement

True-positive within 1.0 cm	80% (395/496)
True-positive within 1.0–2.0 cm	10% (49/496)
True-positive, but difference >2.0 cm	6% (30/496)
Overall PPV	96% (474/496)
False-positive result	4% (22/496)

**Table 3** MRI assessment of residual tumor at the site of the index lesion after surgical excision, compared with final pathology measurement

Any microscopic residual as positive		<1.0 cm residual as positive	
Sensitivity	82%	Sensitivity	88%
Specificity	76%	Specificity	80%
PPV	89%	PPV	89%
NPV	65%	NPV	80%
Accuracy	.80	Accuracy	.86

provided in this table that reflect the positive predictive value (PPV) of MRI within different size ranges.

The negative predictive value (NPV) of MRI at the image-guided biopsy site has little clinical significance because surgical excision will be performed regardless of MRI findings. Nevertheless, a negative MRI after a malignant image-guided biopsy correctly predicted no microscopic residual in 29% and minimal microscopic residual in an additional 49%. Thus, in 78% of patients, a negative post-biopsy MRI predicted zero or microscopic residual confined to the biopsy site. The remaining 22%, however, had residual tumor exceeding 1.0 cm, a false-negative rate in excess of what is seen when breast MRI is used to evaluate breast tissue undisturbed by a biopsy.

### MRI evaluation of the index lesion site after surgical excision

For patients undergoing a surgical biopsy before MRI, the estimation of residual disease can have more significant implications because further surgery may or may not be necessary. Two definitions of the PPV of MRI in the detection of residual disease were used, one being strict (zero residual on final pathology, neither in situ nor invasive), the other being minimal residual (<1.0 cm) having uncertain clinical significance. Results are shown in Table 3.

### MRI impact on index lesion management

Preoperative MRI still can impact decisions regarding the index lesion. In an attempt to quantify how often this occurs, a strict definition of a significant find at the biopsy site was used. When the MRI indicated a primary lesion that was more than 2.0 cm larger than the measurement through conventional imaging (and the MRI size was confirmed on final pathology), yet excluding those patients with a pattern such that they were scored as having multicentricity (see later), 4% (25 of 603) of patients had a significant discovery at the site of the index lesion. Despite this larger tumor size, either unifocal or multifocal, 40% of these patients still underwent breast conservation, so the surgeon often was able to plan for a larger segmental resection. Our application of this definition underestimates the benefit of MRI in this

**Table 4** Multicentric cancers as discovered through conventional imaging (mammography and ultrasound) and then additionally through preoperative MRI

Index lesion histology	Conventional imaging	Breast MRI
Invasive ductal carcinoma	7.2%	7.8%
DCIS	8.0%	4.3%
Invasive lobular carcinoma	4.8%	13%
Total	7.1% (43/603)	7.7% (43/560*)

\*560 patients cleared by conventional imaging.

study because we excluded patients having neoadjuvant therapy from review, and this includes patients whose need for preoperative chemotherapy came through MRI findings at the site of the index lesion.

**Re-excision rate of index lesion**

A more direct approach to assess impact of MRI on the index lesion is through re-excision rates. In this retrospective study, there were no predefined criteria for re-excision, with the procedure recommended by the individual surgeons on the basis of their discomfort with close or positive margins. Of the 363 patients who underwent unilateral lumpectomy, double lumpectomy, or bilateral lumpectomy, 8.8% (32 of 363) were taken back to the operating room for repeat re-excision (24 patients), mastectomy (3 patients), or bilateral mastectomy (5 patients). In 20 of 32 patients, no residual disease was identified in the re-excision or mastectomy specimen.

**MRI detection of multicentricity**

Multicentric disease was defined as a separate focus of cancer more than 5.0 cm away from the index lesion or tumors that extended to another quadrant through a discontinuous growth pattern, the latter definition being more common with lobular histology. Satellite nodules of multifocality near the index lesion were not included here, but are described earlier.

Although 43 patients were known to have multicentric disease before the preoperative MRI, an additional 43 patients were identified as having multicentric disease on the MRI alone, representing 7.7% (43 of 560) of the patients considered as having a solitary lesion by conventional imaging.

Pathology of the index lesions that eventuated in the discovery of multicentric disease is represented in Table 4. The histology of the MRI-discovered multicentric foci included: 25 patients with invasion (17 ductal and 8 lobular, with 5 of 8 having 3- and 4-quadrant disease) and 18 patients with DCIS, 9 of which were multiquadrant high-grade lesions.

**Table 5** Analysis of 47 false-positive results generated by MRI during the discovery of 43 additional patients with multicentric carcinoma

Overall false-positive rate	8.4% (47/560)
MRI lesions called benign after second-look ultrasound	32% (15/47)
Benign biopsy performed for enhancing lesion on MRI	47% (22/47)
No multicentric foci found in mastectomy specimen	21% (10/47)

In calculating the false-negative rate in the discovery of multicentricity through MRI, only those patients who underwent mastectomy were included whereby histologic evaluation was performed. Of the 239 patients who underwent mastectomy, 7 were found to have multicentric foci for a false-negative rate of 2.9%. These foci included a 1.5-cm area of invasive lobular, a .3-cm invasive ductal, and 5 patients with DCIS, one of which was high-grade and multiquadrant.

To identify the additional 43 patients with multicentricity, 47 false-positive results were generated with outcomes represented in Table 5.

In assessing the impact of false-positivity on patients, it is noteworthy that 70% of these patients (33 of 47) underwent breast conservation despite the concerns raised by MRI, and 86% of those who had a benign biopsy (19 of 22) underwent breast conservation.

The overall performance parameters for MRI in the detection of multicentric (and contralateral) disease are shown in Table 6. By using conventional imaging alone for the detection of multicentricity, sensitivity was 46%.

**MRI detection of contralateral disease**

Contralateral cancers were known to be present through conventional imaging in 6 patients (1%). Preoperative MRI yielded an additional 22 patients with contralateral disease from the remaining 597 (3.7%).

These contralateral cancers were invasive (12 ductal and 3 lobular) in 68% and DCIS in 32%. In 50% (11 of 22) of

**Table 6** MRI performance with regard to the detection of multicentric and contralateral cancers in the entire patient population

	Detection of multicentricity	Detection of contralateral cancer
Sensitivity	93%	88%
Specificity	91%	90%
NPV	99%	99%
PPV	65%	34%
Accuracy	.92	.90



**Table 7** Contralateral cancers discovered through conventional imaging and then-additionally through preoperative MRI

Index lesion histology	Conventional imaging	Breast MRI
Invasive ductal carcinoma	1.0%	3.1%
DCIS	.6%	4.7%
Invasive lobular carcinoma	1.5%	4.7%
Total	1.0% (6/603)	3.7% (22/597*)

\*597 patients cleared by conventional imaging.

contralateral cancers, the unsuspected contralateral disease was the same or worse stage than the ipsilateral cancer.

The probability of discovering contralateral cancer through the use of MRI, as related to histology of the primary, is shown in Table 7.

By using a strict definition of false-negative results, including only those patients who chose a preventive contralateral mastectomy, 4 of 59 patients (6.8%) were found on final pathology to have occult cancer. These included a 1.1-cm invasive lobular carcinoma, a .4-cm tubular carcinoma, a focal area of DCIS, and DCIS in a patient in whom neither the primary nor multicentric foci enhanced on MRI.

False-positive results occurred in 9.2% (55 of 597) of patients without known contralateral disease and these outcomes are reflected in Table 8.

When the entire patient population was considered, the MRI performance parameters for the detection of contralateral cancer were as previously noted in Table 6. Notably, sensitivity for the detection of contralateral disease with mammography was 19%.

## Comments

### Background

When used in the preoperative evaluation of breast cancer patients, breast MRI often identifies more extensive disease than appreciated by conventional imaging. In one of the first large series reported,<sup>5</sup> planned surgical management was altered in 69 of 267 patients (26%) whereas 44 patients (17%) had conversion of planned breast conservation to mastectomy. Because this rate of conversion to mastectomy exceeded the reported local recurrence rates after breast conservation, criticisms arose as to the propriety of MRI-based decision making in the preoperative setting, especially given equal survival with breast conservation or mastectomy in the major clinical trials.<sup>6</sup> In essence, it has been charged that MRI is only confirming in image format what already was known about breast cancer growth patterns established more than 20 years ago through serial subgross sectioning studies.<sup>7</sup> Because the very purpose of radiation therapy is to treat remaining disease not appreciated on

conventional imaging, advocates of breast MRI must address the possibility that high-resolution, high-sensitivity imaging might result in reactionary treatment strategies.

This criticism is partially countered by the rapid acceptance of accelerated partial breast irradiation in the local management of early stage breast cancer,<sup>8</sup> even though it is still investigational and significant questions remain. Accelerated partial breast irradiation at the lumpectomy site offers no coverage for multicentric foci of disease, save for the ameliorating effects of systemic therapy. Thus, secondary sites of cancer within the breast take on renewed importance.

Even with whole-breast radiation, however, the early (5-year) local recurrence rate was 8% in the National Surgical Adjuvant Breast Project B-06 trial.<sup>9</sup> Although the current rates of local recurrence subsequently may have improved at centers of excellence, there could remain widely disparate unpublished results. Even though such local recurrences may or may not directly impact survival, there remains a significant morbidity for recurrence in the irradiated breast. Most notably, mastectomy—the very procedure avoided by the patient's original decision—usually is required. Only now, postradiation, the option of reconstruction with a tissue expander/implant approach carries a complication rate as high as 53%,<sup>10</sup> prompting the usual mandate of an autologous flap.

Furthermore, the psychologic impact of a local parenchymal recurrence in the breast can have a profound negative effect, even when the patient has a good prognosis. It is not unusual for patients to study the published literature, whereupon they will discover diminished survival rates. This can be a disturbing discovery even when arguments are elaborated that such recurrences are only markers of increased risk rather than actual instigators of the reduction in survival.<sup>11</sup> And for those who recur systemically at a later date, there is often a perception by the patient and family that the local recurrence was the causative factor in the development of metastatic disease.

Because there are no survival outcome data available for patients who have undergone preoperative staging with breast MRI, we are left with other end points. Indeed, given presumed survival equivalency, other end points are much more realistic, beginning with local recurrence rates. Because MRI has been introduced only recently, very little has

**Table 8** Analysis of 55 false-positive results generated by MRI during the discovery of 22 additional patients with contralateral cancer

Overall false-positive rate	9.2% (55/597)
MRI lesions called benign after second-look ultrasound	31% (17/55)
Benign biopsy performed for enhancing lesion on MRI	65% (36/55)
No contralateral foci found in mastectomy specimen	4% (2/55)

been published in this regard. One such study of women undergoing breast conservation compared 86 patients who had preoperative MRI versus 122 who did not, with a median follow-up period of 40 months.<sup>12</sup> Both groups were considered equivalent with respect to the type of systemic therapy. For those patients who had preoperative MRI, the local recurrence rate was 1.2% (1 of 86), compared with 6.8% (9 of 133) in the group that did not undergo MRI.

Another end point favoring preoperative breast MRI is a reduction in re-excisions after lumpectomy. The 8.8% re-excision rate in this series is well below accepted re-operation rates, which have been reported as high as 27% after the initial attempt at breast conservation.<sup>13</sup> This attractive outcome measure needs to be considered as a major end point in all studies evaluating the cost effectiveness of MRI because fewer re-operations counterbalance the increased costs associated with the use of MRI.

Such end points seem preferable to the attempts at quantifying how often MRI impacts the decision regarding lumpectomy versus mastectomy. It is not always clear in the published literature how this impact is even defined. Short of interviewing each patient and her surgeon as to the influence of MRI on the choices made, one can only make raw assumptions about impact from available data. The decision on the approach to local management is already a complex interplay of physician presentation and patient perceptions,<sup>14</sup> so defining the contribution of MRI is difficult. In reviewing our data, patients sometimes opted for mastectomy even after the MRI indicated excellent candidacy for breast conservation, whereas other patients requested conservation when MRI suggested that mastectomy or neoadjuvant chemotherapy might be more appropriate.

### Evaluation of the index lesion

MRI interpretations at the biopsy site of the index lesion can be a challenge because of clip artifact, rim enhancement, hemorrhage, or a background of severe proliferative change. These can lead both to false-negative and false-positive results. Although the surgeon sometimes is guided by the advance knowledge of satellite nodules and in situ extensions, the impact of MRI on the index lesion is best documented through lower re-excision rates and lower recurrence rates at the lumpectomy site, rather than presumptions as to how often the MRI changes a therapeutic approach.

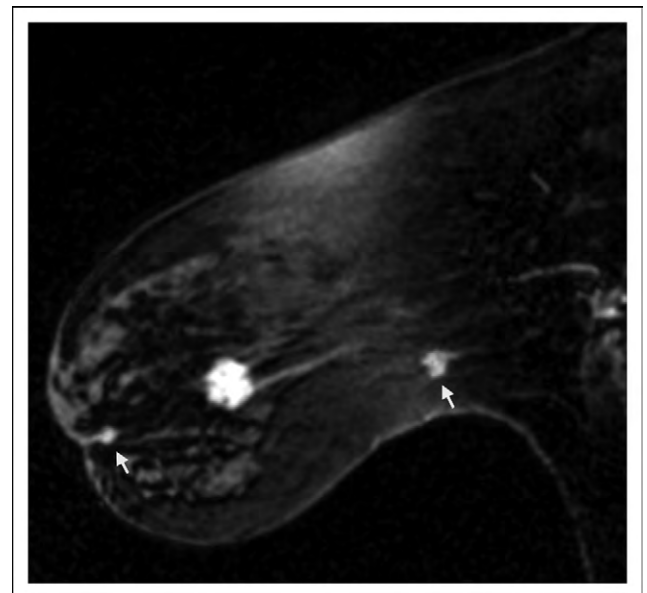
With regard to postlumpectomy MRI, rim enhancement of the cavity prevents MRI from being as accurate as it is in the detection of multicentric and contralateral lesions. The reason for ordering MRI in this instance has been expressed as a means to determine the need for re-excision; however, the NPV of only 65% with regard to any residual after excisional biopsy (and still only 80% with minimal residual) as noted in Table 3 is inadequate to make this determination. Re-excision after lumpectomy should be based on the standard practices using judgment from preoperative conventional imaging and margin assessment, rather than

postlumpectomy MRI. Benefit with regard to the detection of multicentricity and contralateral disease, however, still can be justified.

### Multicentricity

Multicentricity, however, has a more significant role in decisions about local management. When a separate cancer is present in the same breast, a successful lumpectomy with clear margins can be achieved, leaving untreated disease behind (Fig. 1). In our series, 7.7% of patients were found to have occult disease in other quadrants, and although the clinical significance of these additional sites may be unknown for patients undergoing whole-breast radiation, it is likely that most, if not all, of these discoveries are significant for patients considering accelerated partial breast irradiation. As concerning as this 7.7% may be, it is actually lower than what is described elsewhere<sup>5</sup> and may reflect a stricter definition of multicentricity. Another explanation lies in the fact that some patients with multiquadrant disease were steered toward neoadjuvant chemotherapy as a result of MRI findings, yet were excluded from this study.

Although criticisms are warranted if preoperative breast MRI is promoting “more mastectomies” in the face of what we know about survival in clinical trials, it has been postulated that a counterbalance is at work with MRI, allowing women greater confidence in choosing breast conservation



**Figure 1** In this patient, only the largest focus of invasive ductal carcinoma was evident on conventional imaging. The multicentric foci of biopsy-proven invasive disease discovered on MRI (arrows) are so far away from the index lesion that a routine lumpectomy could easily yield clear margins. Without MRI, if lumpectomy were performed, there is a chance that the multicentric foci would be managed adequately with whole-breast radiation and systemic therapy. However, it is unlikely that the patient would receive proper therapy if accelerated partial-breast irradiation were to be used at the lumpectomy site.

by “clearing” the remaining breast tissue as disease-free through the strong negative predictive value of MRI.<sup>15</sup> To date, no detailed study incorporating the nuances of the decision-making process after breast MRI has addressed this potential.

However, in support of this phenomenon, the breast-conservation rate of 60% reported herein (65% if patients who opted for bilateral preventive mastectomy are excluded) compares favorably with the 58% rate of conservation for early breast cancer seen in the National Cancer Data Base.<sup>16</sup> In the year before instituting our breast MRI program (2002), the tumor registry at our facility recorded breast conservation was performed in 48% of patients, and 1 year later, with MRI being performed routinely, this rate was 58%, comparable with the overall rate of conservation in this study of 60%. Analysis of local recurrences before and after institution of breast MRI are planned as the data mature. Nevertheless, it appears that although MRI is selecting 7.7% of patients for mastectomy because of multicentricity (albeit 4 patients chose double lumpectomy), this is likely being countered by an increased acceptance of breast conservation after MRI clearance.

In assessing the impact of false-positive results on this decision-making process, it is noted that 70% of patients with false-positive results on the ipsilateral side underwent breast conservation, and 86% continued with conservation after a benign biopsy for suspected multicentric disease. Although this latter group enjoys a significant selection bias in that the biopsy is being performed because of a pre-existing commitment to breast conservation, the 70% conservation rate after false-positive results in the general group speaks against a strong negative impact of false-positive results.

### Contralateral cancer

Controversy will persist over MRI findings at the site of the index lesion as well as the discovery of occult multicentric disease, but the issues surrounding the contralateral breast assume greater significance because this breast will be treated inadequately if the patient receives a unilateral approach. Although it has become a truism that the index lesion dictates prognosis, especially when metachronous disease is included in the study of bilaterality, decreased survival in patients with bilateral synchronous cancer has been reported,<sup>17</sup> as well as a 3.9-fold increased risk of breast cancer mortality in women who developed bilateral breast cancer within 5 years and at an age younger than 50 years.<sup>18</sup>

It is difficult to relegate these discoveries in our series to subclinical status when the stage of the occult contralateral cancer was equal to, or greater than, the stage of the primary in 50% of the cases. Notably, in 3 patients diagnosed with DCIS, the contralateral cancer was stage I invasive in 1 patient, and stage IIA in 2 patients. Our 3.7% discovery of occult contralateral cancer is similar to the 3.1% described in the aforementioned ACRIN study,<sup>4</sup> as is our distribution

of invasive cancer (68%) to in situ discoveries (32%), these values being 60% and 40%, respectively, in the ACRIN study. In addition, our rate of contralateral cancer discovery is identical (3.7%) to that reported in one of the largest series on preoperative staging that included 405 newly diagnosed patients.<sup>19</sup>

Although the percentage of patients with contralateral occult cancer may seem small, it translates through disease prevalence to a large number of women who currently are receiving unilateral treatment for bilateral disease, and therefore seems to warrant routine preoperative MRI for newly diagnosed breast cancer patients.

### Preoperative MRI findings as a whole

Even when one excludes the influence of MRI on the evaluation of the index lesion, the most valuable benefits remain—the discovery of occult multicentricity and bilaterality. In this series, the addition of these 2 findings, 7.7% for the former and 3.7% for the latter, provides an 11.4% probability that a major discovery will occur through preoperative MRI staging, above a reasonable threshold for routine use, especially in a program that offers accelerated partial-breast irradiation.

The discovery of these additional findings in the routine use of preoperative breast MRI, however, comes at the cost of the associated anxiety with false-positive biopsy results. Unlike false-positive results that occur with mammography and ultrasound before a diagnosis of cancer, MRI-generated false-positive results occurred in our series after the diagnosis, conceivably a more anxiety-provoking sequence.

Although it was beyond the scope of this review, in comparing current results with those we previously reported,<sup>1</sup> wherein 81% of the patients were studied with a .5-Tesla magnet, the results then were remarkably similar: 7.7% for multicentricity and 3.6% for occult contralateral disease discovered by MRI. To the original 334 patients, an additional 271 are added herein, all of the latter being studied on a 1.5-Tesla magnet, with almost identical outcomes.

Specificity for multicentric disease was 91% and for contralateral disease was 90%, comparable with the 88% specificity for contralateral disease in the ACRIN trial,<sup>4</sup> all of which contrasts to reports claiming that specificity with breast MRI is lower than mammography.<sup>19,20</sup>

### Preoperative staging versus mapping

The term *preoperative staging* is somewhat misleading in that it addresses a different clinical issue than stage as outlined by the American Joint Committee on Cancer. A more accurate term would be *preoperative mapping*. Breast MRI cannot always distinguish invasive from in situ disease,<sup>21</sup> but this is not the surgeon's primary concern in surgical planning. The surgeon needs to know the 3-dimen-

sional configuration of the tumor, be it invasive or in situ. In fact, the International Consensus Conference II<sup>22</sup> recommended an all-inclusive size of a lesion—in situ and invasion—to be termed *overall size*, whereas the invasive component be reported as *prognostic size*, the latter being the only consideration in American Joint Committee on Cancer staging if both in situ and invasive disease are present. Overall size is mapping as it pertains to local recurrence rates, whereas prognostic size relates to stage and systemic recurrence rates.

### Limitations of pathology

Any study relating MRI to the findings on pathology suffers from limitations inherent in routine tissue processing and the difficulties encountered in tumor measurement. Although these measurements may be considered the gold standard by clinicians, such measurements can be quite subjective, or even erroneous, because of a wide variety of factors. Pathology can overestimate and underestimate sizes “dramatically,”<sup>23</sup> and depending on the plane of section, as much as a 3-fold difference in recorded size can result. It is not only likely, but highly probable, that in some cases of invasive lobular, extensive DCIS, and discontinuous growth patterns, the MRI measurement is more accurate than those made in the pathology laboratory. Thus, MRI data as frequently reported in the literature underestimates accuracy with regard not only to the index lesion, but in reference to the detection of multicentric and contralateral disease. Unless a research protocol is in place within the pathology department, such that surgical specimens are analyzed in great detail with multiple sections, paying close attention to all areas of MRI enhancement, deficiencies in reporting will occur in the pathology laboratory but be reflected in the MRI data instead.

### Conclusions

Preoperative breast MRI can be considered appropriate for all newly diagnosed breast cancer patients by virtue of an 11.4% probability of detecting mammographically occult multicentric disease (7.7%) or occult contralateral disease (3.7%). An additional benefit comes through the 3-dimensional mapping of the index lesion, although quantification of this benefit is best achieved through the outcome measures of local recurrence rates or re-excision rates. Although this study did not address the former, we have shown a very low re-excision rate of 8.8%, theorizing that this outcome is accomplished through the preoperative identification of satellite nodules and irregular tumor extensions.

Although concerns persist that patients who undergo preoperative mapping with MRI might be overstaged and steered toward mastectomy when breast conservation would suffice, downstaging is a likely counterbalance, reassuring patients through the strong negative predictive power of MRI that breast conservation is safe. Our breast conservation rate of

60% overall, and 65% when preventive bilateral mastectomy patients are excluded, supports this notion.

Specificity is comparable with that of mammography, but all suspected multicentric and contralateral enhancements on MRI should undergo biopsy for histologic confirmation of malignancy if treatment plans are to be adjusted accordingly.

The findings reported here with regard to occult contralateral cancers discovered through MRI are arguably enough to warrant the recommendation of preoperative MRI. However, the ipsilateral findings, especially with regard to multicentric foci in this era of accelerated partial breast irradiation, add considerable weight to incorporating preoperative MRI routinely in newly diagnosed breast cancer patients.

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