MRI and Breast Cancer: Role in Detection, Diagnosis, and Staging

By Richard J. Bleicher, MD and Monica Morrow, MD

Increasing experience with magnetic resonance imaging (MRI) has raised important questions about how it should be used in breast cancer screening, and for presurgical evaluation and posttherapy follow-up of women with this disease. Overall, the availability of MRI as an adjunct to mammography and ultrasound offers clear clinical benefit to women at increased risk of breast cancer development due to BRCA1 and BRCA2 mutations, and to women presenting with axillary adenopathy and an occult primary breast tumor. In contrast, its benefit for routine selection of breast conservation or further assessment of lobular carcinoma in women of average risk has not been demonstrated. This article reviews the use of MRI in these settings, with an emphasis on the clinical outcomes that have been observed to date.

Breast imaging has two distinct roles: to screen asymptomatic women in an effort to detect cancer that is likely to be cured by therapeutic interventions, and to assist in the selection of local therapy. For many years, mammography was the only modality available for these purposes. The local therapy of breast cancer has changed dramatically over the past 30 years, and breast-conserving therapy (BCT) and neoadjuvant therapy for operable cancers have become part of routine clinical practice. Our understanding of breast cancer risk has also evolved with the recognition of the BRCA1 and BRCA2 genetic mutations, allowing the identification of a subset of women at extremely high risk of breast cancer development.

In parallel with these changes, imaging techniques have also evolved. Ultrasound is now routinely used in the evaluation of the patient with known cancer, although its role in screening remains controversial. Magnetic resonance imaging (MRI) of the breast was added to the diagnostic armamentarium of the physician in 1984. Increasing experience with this technology has raised important questions about how it should be used in screening, and for presurgical evaluation and posttherapy follow-up of women with breast cancer. This article will review the use of MRI in these settings, with an emphasis on the clinical outcomes that have been observed to date.

Screening

Mammography remains the standard of care for screening and detection of breast cancer. It is the only breast screening tool that has been proven in randomized trials to reduce breast cancer mortality, and approximately 50% of the recently observed reduction in breast cancer mortality in the United States is attributed to the use of screening mammography.[1] Mammography, however, cannot distinguish between solid and cystic masses, misses approximately 10% to 15% of cancers, and has a lower sensitivity for the detection of lobular cancers, cancers in dense breasts, and cancers occurring in the presence of breast implants.[2]

Screening Known or Suspected BRCA1 and BRCA2 Carriers

The detection of cancer with MRI is dependent upon the increased vascularity of neoplasms, which results in enhancement after the injection of contrast material, and is not limited by the density of the breast tissue. Because benign lesions also enhance, the combination of the presence of enhancement, the kinetics of enhancement, and the morphology of the lesion are used to distinguish benign from malignant lesions.[3] Large-scale trials of screening with MRI in unselected populations have not yet been carried out. Screening studies to date have focused on high-risk populations, particularly women known or suspected to have mutations of BRCA1 or 2. There is a clear biologic rationale for seeking improved screening techniques for this group of women since studies have demonstrated a high rate of interval cancers in mutation carriers screened with annual mammography alone.[3]

Five prospective, nonrandomized screening trials comparing the use of mammography and MRI in high-risk women are summarized in Table 1.[3-7] Women were eligible for these trials if they had a lifetime risk of breast cancer development of at least 15%, and the proportion of proven BRCA1/2 mutation carriers ranged from 8% in the study by Kuhl et al[3] to 100% in the study by Warner et
al.[6] In spite of the heterogeneity in study designs, the results of these trials are remarkably similar. The sensitivity of MRI for the detection of cancer ranged from 77% to 100% and was substantially higher than that observed for mammography (25%–40%). In all of the studies, the specificity of MRI was lower than that of mammography, although in the majority of the reports the difference was less than 5% (Table 1).

The exception to this trend was the study by Leach et al,[4] which included 22 centers in the United Kingdom, and reported a specificity of 81% for MRI and 93% for mammography. These results are probably more representative than those reported from single-institution studies, where high volumes of MRI were performed and interpreted by individuals with great levels of expertise. It is important to recognize that the lack of specificity of MRI potentially results in additional imaging in a significant number of women. In the study by Kreige et al,[7] the recall rate for additional imaging based on MRI findings was 10.7% compared to 3.9% for mammography, and the biopsy rates for these modalities were 3.1% and 1.3% respectively. While this may be an acceptable trade-off for increased cancer detection rates in populations at extremely high risk of breast cancer development (such as mutation carriers), it represents a significant drawback to the more widespread use of MRI screening in women at a lower level of risk.

Although a reduction in breast cancer mortality has not been demonstrated with MRI screening in high-risk women, the higher detection rate of cancer—particularly invasive cancer—with MRI, coupled with the earlier stage at detection led the American Cancer Society to conclude that sufficient evidence exists to recommend annual MRI screening for women proven to be mutation carriers, untested first-degree relatives of mutation carriers, and women with a lifetime risk of breast cancer development of 20% or greater as determined by models based on a family history of breast cancer.[8]

Screening Other High-Risk Women

Very little information is available to assess the benefits of MRI screening in women at risk for reasons other than family history. Port and coauthors[9] performed a retrospective study of 252 women with lobular carcinoma in situ (LCIS) and 126 with atypical hyperplasia followed with and without MRI. Patients selected for MRI screening were younger and had stronger family histories of breast cancer than their counterparts screened with mammography. Cancer was identified in 1% of the 478 MRIs performed, and 25% of the patients undergoing MRI received a biopsy recommendation during the study period, the majority of which were generated by findings seen on MRI alone. In comparison, abnormalities on physical exam or mammogram prompted biopsy in 11%
of patients. In addition, 48% of patients undergoing MRI had at least one study requiring short-interval follow-up. A total of 8 cancers were found in the MRI group, 6 by MRI alone. The sensitivity of MRI was 75%, the specificity 92%, and the positive predictive value was 13%. These data do not provide clear evidence of benefit for MRI screening in the population of women with LCIS and atypical hyperplasia, but they clearly illustrate the costs of screening in terms of follow-up examinations and biopsies. Further evaluation of the impact of recall, short-interval follow-up, and benign biopsies on compliance with screening is warranted before widespread adoption of MRI screening in populations at lower risk than women with known or suspected BRCA1/2 mutations is undertaken.

In a study of a subset of 611 women included in the United Kingdom MRI screening study,[4] 89% reported that they would definitely return for further screening, but 4% found MRI "extremely distressing" and 47% reported intrusive thoughts about the MRI exam 6 weeks later. The current American Cancer Society recommendations for breast MRI screening are summarized in Table 2.[8] It is important to note that breast MRI is an adjunct to mammography, not a replacement, and that clinical breast exam remains an important part of the surveillance of women at high risk. Cancers seen on mammography but not MRI continue to be observed, and although the problem of interval cancers is reduced by MRI screening, it is not eliminated.

<table>
<thead>
<tr>
<th>Table 2</th>
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</thead>
<tbody>
<tr>
<td><strong>American Cancer Society Guidelines for Screening With Magnetic Resonance Imaging</strong></td>
</tr>
<tr>
<td><strong>Recommended Annually Based on Evidence</strong></td>
</tr>
<tr>
<td>BRCA mutation carriers</td>
</tr>
<tr>
<td>Untested first-degree relative of BRCA carrier</td>
</tr>
<tr>
<td>Lifetime risk &gt; 20%–25% defined by BRCAPRO or other family history models</td>
</tr>
<tr>
<td><strong>Recommended Based on Expert Consensus Opinion</strong></td>
</tr>
<tr>
<td>Radiation to chest from age 10–30 yr</td>
</tr>
<tr>
<td>Li-Fraumeni syndrome and first-degree relatives</td>
</tr>
<tr>
<td>Cowden syndrome (and variants) and first-degree relatives</td>
</tr>
<tr>
<td><strong>Insufficient Evidence to Recommend For or Against</strong></td>
</tr>
<tr>
<td>Lifetime risk 15%–20%</td>
</tr>
<tr>
<td>Lobular carcinoma in situ</td>
</tr>
<tr>
<td>Atypical hyperplasia</td>
</tr>
<tr>
<td>Dense breasts on mammography</td>
</tr>
<tr>
<td>Personal history of intraductal or invasive breast cancer</td>
</tr>
<tr>
<td><strong>Recommend Against Based on Expert Consensus</strong></td>
</tr>
<tr>
<td>Lifetime risk &lt;15%</td>
</tr>
</tbody>
</table>

**Selection of Local Therapy in the Patient With Carcinoma**

As breast-conserving surgery with radiation has matured from an experimental treatment to an accepted standard of care, important lessons have been learned about patient selection for the procedure and the detection and management of local recurrence. Absolute contraindications to BCT include a history of prior therapeutic irradiation to the breast region, the inability to obtain negative margins after a reasonable number of surgical attempts, first and second trimester pregnancy, and clinically or mammographically detected multicentric cancer.[10] These contraindications appear to be reliably identified with a history and physical examination and diagnostic mammography. Morrow et al reported that of 216 consecutive patients...
thought to be candidates for BCT after clinical evaluation and diagnostic mammography, BCT was successfully carried out in 210 (97.2%).[11]

Even when the subset of patients with tumors that are palpable but not seen on imaging studies is considered, it is difficult to find evidence that the performance of BCT is problematic. Morrow et al[12] compared 52 patients with clinically evident but mammographically occult breast cancer to 217 women with both clinically and mammographically evident tumors treated during the same time period. Eligibility for BCT did not differ between groups, and BCT was successfully carried out in an equal proportion of patients who elected to have the procedure in both groups.

A study of 77 patients with infiltrating lobular carcinoma suggested that the selection of surgical therapy was more problematic than for those with ductal carcinoma, with a 2.5 times greater likelihood of conversion from lumpectomy to mastectomy in patients with lobular carcinoma.[13] In contrast, Morrow et al [14] compared outcomes of 318 patients with lobular carcinoma (pure or mixed) to those of 636 patients with ductal carcinoma who were matched for year of diagnosis, menopausal status, and pathologic stage. Using clinical and mammographic evaluation, 25% of patients with lobular cancer were not considered candidates for BCT compared to 20% of those with ductal carcinoma (P = .04). Among the remaining women felt to be candidates for BCT, the procedure was equally successful in those with ductal and lobular carcinoma after adjustment for tumor size and patient age, and no significant difference in the number of surgical excisions required to obtain negative margins was seen.

In patients selected for BCT using clinical and mammographic evaluation, local recurrence in the breast has decreased significantly as experience with BCT has been gained. In a variety of National Surgical Adjuvant Breast and Bowel Project adjuvant therapy trials[15] including both estrogen-receptor–positive and estrogen-receptor–negative patients receiving adjuvant systemic therapy, local recurrence rates at 10 years were 7% or less.

Impact of MRI on Surgical Therapy

The background information discussed above is useful when considering the role of MRI in treatment selection for the woman with known carcinoma. At present, local recurrence due to improper patient selection or inadequate local therapy is infrequent. Yet a substantial number of studies have demonstrated that the performance of MRI in women with localized cancers identifies additional tumor foci in 11% to 31% of cases (Table 3).[16-25] The demonstration of these additional tumor foci has been used to argue that MRI should be a routine part of the preoperative evaluation of women with breast carcinoma.
Table 3

MRI of the Ipsilateral Breast in Women With Known Carcinoma

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of Cancers</th>
<th>Additional Tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orel et al[16]</td>
<td>64</td>
<td>20%</td>
</tr>
<tr>
<td>Boetes et al[17]</td>
<td>61</td>
<td>15%</td>
</tr>
<tr>
<td>Muntaz et al[18]</td>
<td>92</td>
<td>11%</td>
</tr>
<tr>
<td>Fischer et al[19]</td>
<td>336</td>
<td>16%</td>
</tr>
<tr>
<td>Drew et al[20]</td>
<td>178</td>
<td>23%</td>
</tr>
<tr>
<td>Bedrosian et al[21]</td>
<td>267</td>
<td>15%</td>
</tr>
<tr>
<td>Liberman et al[22]</td>
<td>70</td>
<td>27%</td>
</tr>
<tr>
<td>Blumke et al[23]</td>
<td>428</td>
<td>13%</td>
</tr>
<tr>
<td>Berg et al[24]</td>
<td>96</td>
<td>31%</td>
</tr>
<tr>
<td>Deurloo et al[25]</td>
<td>116</td>
<td>23%</td>
</tr>
</tbody>
</table>

MRI = magnetic resonance imaging.

A smaller number of studies have examined the actual impact of MRI findings on surgical therapy, and these are summarized in Table 4.[21,24-26] In three of the four studies,[21,24,25] performance of a mastectomy that would not otherwise have been done was the most common outcome. Berg et al[24] observed that MRI resulted in wider excision than initially planned in 30% of women undergoing breast-conserving surgery, although disease extent was overestimated in 20 of the 29 patients. Overall, MRI resulted in management changes in 20% to 55% of women in these studies.

Table 4

MRI-Related Changes in Surgical Therapy in the Ipsilateral Breast of Patients With Carcinoma

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of Cases</th>
<th>Conversion to Mastectomy</th>
<th>Wider Excision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bedrosian et al[21]</td>
<td>267</td>
<td>16.5%</td>
<td>9.4%</td>
</tr>
<tr>
<td>Berg et al[24]</td>
<td>121</td>
<td>25.0%</td>
<td>3.0%</td>
</tr>
<tr>
<td>Deurloo et al[25]</td>
<td>116</td>
<td>15.5%</td>
<td>6.0%</td>
</tr>
<tr>
<td>Bilimoria et al[26]</td>
<td>155</td>
<td>6.5%</td>
<td>13.5%</td>
</tr>
</tbody>
</table>

MRI = magnetic resonance imaging.
In contrast to studies examining the role of MRI in breast cancer patients in general, where approximately one-quarter of patients have additional tumor identified, studies in patients with lobular carcinoma suggest that approximately 50% will have their management altered.[27-29] This has led both the American College of Radiology and the American Society of Breast Surgeons to include a diagnosis of lobular carcinoma as an appropriate indication for MRI, and would suggest that the treatment of lobular cancer with less than mastectomy would be unsuccessful in a significant number of cases.

This assumption is not borne out by the available clinical data. The lack of difference in conversion rates from BCT to mastectomy on the basis of tumor histology has been discussed previously.[14] In addition, local failure rates for patients with lobular carcinoma do not differ significantly from those seen in patients with infiltrating ductal cancer who are treated with BCT,[30-32] even with long-term follow-up.

The study by Peiro et al[30] included 1,624 patients with a median follow-up of 133 months for survivors. Pathology slides were reviewed in 82% of cases; 93 patients were found to have pure lobular carcinoma and an additional 59 had mixed ductal and lobular cancer. Local recurrence rates did not differ on the basis of histology, and in multivariate analysis histologic type was not a significant predictor of survival or recurrence. Winchester et al[32] used data from the National Cancer Data Base on 1,953 patients treated with BCT between 1985 and 1988, and noted no differences in 5-year local disease free survival between women with ductal and lobular carcinoma, supporting observations from single-institution reports with longer follow-up periods.[30,31]

Proof of Benefit?

All of the studies of the impact of MRI on choice of surgical procedure make the assumption that the identification of additional tumor corresponding to the MRI abnormality is proof that the MRI was beneficial to the patient. This is an assumption that is open to question and lies at the crux of the debate regarding what evidence of clinical benefit is needed prior to the adoption of MRI into routine clinical practice. Although clinically multicentric carcinoma is recognized in fewer that 10% of patients[33] the multifocal/multicentric nature of breast cancer has long been recognized by pathologists. Studies employing serial subgross sectioning to evaluate clinically and mammographically normal tissue from the breasts of women thought to have localized tumors have demonstrated additional tumor foci in 21% to 63% of cases. (Table 5).[34-41]

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of Cases</th>
<th>Population</th>
<th>Multifocal/ Multicentric</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qualheim and Gall[34]</td>
<td>157</td>
<td>Not stated</td>
<td>54%</td>
</tr>
<tr>
<td>Rosen et al[35]</td>
<td>203</td>
<td>Invasive carcinoma</td>
<td>33%</td>
</tr>
<tr>
<td>Lagios[36]</td>
<td>85</td>
<td>Not stated</td>
<td>21%</td>
</tr>
<tr>
<td>Egan[37]</td>
<td>118</td>
<td>Not stated</td>
<td>60%</td>
</tr>
<tr>
<td>Schwartz et al[38]</td>
<td>43</td>
<td>Nonpalpable cancer</td>
<td>44%</td>
</tr>
<tr>
<td>Vaidya et al[39]</td>
<td>30</td>
<td>Invasive carcinoma</td>
<td>63%</td>
</tr>
<tr>
<td>Anastassiades et al[40]</td>
<td>366</td>
<td>Invasive ≤7 cm, noninvasive</td>
<td>49%</td>
</tr>
<tr>
<td>Holland et al[41]</td>
<td>282</td>
<td>Clinically unicentric</td>
<td>63%</td>
</tr>
</tbody>
</table>

The work by Holland et al[41] demonstrated that all carcinoma was confined to the site of primary tumor in only 37% of cases and was within 2 cm in an additional 20%. However, the majority of foci of residual disease were found within 4 cm of the primary site, and the likelihood of identifying residual tumor was not related to the size of the primary tumor. Pathology studies such as these were used to strongly argue that the treatment of breast cancer with less than total mastectomy was inappropriate. However, extensive clinical experience has demonstrated that the majority of these
subclinical foci are controlled with radiotherapy, as demonstrated by the 10-year local recurrence rates of 7% or less in women treated with radiotherapy and systemic therapy discussed previously.[15]

It is reasonable to ask whether the additional tumor foci identified by MRI are the same tumor foci identified by the pathologist. The available evidence would suggest that they are. Sardanelli et al.[42] performed MRI on 90 patients who were scheduled to undergo mastectomy. Serial subgross sectioning was performed on the mastectomy specimens and tumor location was mapped and correlated with the findings of the MRI examination. The overall sensitivity of MRI was 81%—89% for invasive foci and 40% for in situ disease. The mean diameter of malignant lesions not seen by MRI was 5 mm (range: 0.5–15.0 mm). In the 90 breasts studied, MRI failed to identify microscopic multifocal or multicentric disease in 19 and incorrectly suggested additional foci of malignancy in 30 cases. These findings strongly suggest that MRI is capable of detecting some but not all of the tumor foci found with detailed pathologic sectioning.

The findings of Berg et al.[24] and Liberman et al.[22] also support the idea that the same tumor is identified with both techniques. Berg et al.[24] observed that in 40 of 46 breasts (87%) with additional tumor foci on MRI, the foci were within 4 cm of the index lesion. Liberman et al.[22] also noted that the majority of additional tumor foci were in the same quadrant as the index lesion. These patterns correspond well to the pathologic distribution of tumor described by Holland et al.,[41] where 96% of tumor foci were within 4 cm of the index tumor.

If the cancer identified by MRI is the same cancer that has been successfully treated with radiotherapy for the past 30 years, how does its identification improve clinical management? One study has attempted to address the influence of preoperative MRI on local recurrence rates in patients treated with BCT. Fischer et al.[43] retrospectively compared the local failure rate of 86 patients who underwent conventional imaging studies plus an MRI prior to BCT to that of 138 patients who had only conventional imaging. After a mean follow-up of 40 months, local recurrences were observed in 1.2% and 6.8% of patients, respectively (P < .001).

Unfortunately, the retrospective nature of the study resulted in some imbalances among the groups, which render the results extremely difficult to interpret. For example, only 5% of patients in the MRI group did not receive adjuvant therapy compared to 18% in the conventional imaging group. It is well documented in randomized trials that the use of adjuvant systemic therapy decreases the risk of local failure by approximately 50%,[44,45] so this imbalance could be responsible for the observed difference in the rates of local failure. Due to these problems, this study cannot be considered evidence of a clinical benefit for MRI.

At present, there is no convincing evidence that the use of MRI for patient selection improves local control in women undergoing BCT. It has been suggested that the use of preoperative MRI, by allowing better definition of the extent of disease, would decrease the need for reexcision due to positive margins.[46] In practice, however, it may be difficult to translate imaging findings to the three-dimensional surgical setting. An initial report of a 43% positive margin rate in 21 patients undergoing MRI-guided localization and excision does not provide convincing evidence of the utility of MRI to achieve negative margins.[47]

Occult Breast Cancer

One of the most clinically relevant uses for MRI has been for the detection of occult breast cancers. Detection of an occult ipsilateral primary is important in two settings—in women presenting solely with axillary nodal disease, and in those with Paget's disease of the breast. Although BCT has been established as a treatment equivalent to mastectomy, with low rates of local recurrence for the majority of women with stage II breast cancer, mastectomy has remained the traditional treatment of occult primary carcinoma.

One goal of resecting the primary tumor is to minimize the residual tumor burden that must be controlled by radiotherapy, thereby decreasing the risk of local recurrence. Although studies examining the utility of MRI for identifying occult primary breast cancers are small, most series demonstrate that detection of a primary lesion occurs in at least 60% of women (Table 6).[48-55] False-positive findings occur in 0% to 29% of cases,[48,49,51] but false-negative results are uncommon. Identification of the primary tumor allows both resection and the use of a boost dose of radiotherapy to maximize local control. Good local control can be achieved with breast conservation for lesions seen solely on breast MRI, indicating that an axillary presentation is not indicative of a biologic tumor type that should be preferentially treated by mastectomy.[49]
Not every primary breast cancer is visible on MRI, as noted in Table 6. Mastectomy provides a higher likelihood of finding such a lesion, but between 33% and 100% of patients who present with axillary metastases and negative mammograms, physical examinations, and MRIs will have no tumor found in the breast on pathologic evaluation.[50-52] Both observation of the breast without radiotherapy and whole-breast radiotherapy without surgery have been investigated in this circumstance. The limited available data suggest that observation alone is associated with a high rate of local failure,[56] but radiotherapy to the intact breast provides local control in 75% to 100% of women with mammographically and MRI-occult tumors.[56,57]

Paget's Disease

Patients with Paget's disease of the nipple are a separate clinical entity, but half of them also present without a palpable mass, and a minority of these women have a normal mammogram. Characteristics of an occult primary tumor associated with Paget's disease vary, but tumors can present at a considerable distance from the nipple or as multicentric disease in one-third of patients.[58] Primary tumors at a distance from the nipple and multicentricity are considered contraindications to BCT.

Although not confirmed by large trials, it stands to reason that identification of a locally resectable primary in Paget's disease may improve patient selection for BCT, minimizing local recurrence. One case series of three women with Paget's disease noted suspicious enhancement on MRI in each patient.[59] Two of the patients' MRI enhancements were found to be DCIS, whereas the third patient's lesions were found to be fibroadenomas. In particular, women with Paget's disease who have dense breasts or a difficult breast examination may benefit by the addition of MRI when their mammogram and physical examination are unremarkable.

Evaluation of Response to Neoadjuvant Treatment

Neoadjuvant chemotherapy may render locally advanced breast cancer operable or convert a tumor requiring mastectomy to one that may be treated with BCT. Approximately 80% of breast cancers will respond measurably to neoadjuvant chemotherapy, and between 6% and 19% will demonstrate a complete pathologic response.[60] Assessment of response has traditionally been performed using physical examination, mammography, and more recently ultrasound. Because an accurate assessment of the degree of response is critical to determine the extent of surgical excision required, there has been interest in using MRI to improve the preoperative assessment of response for patients with both locally advanced and operable disease.[61,62] The results of trials assessing the utility of MRI in determining the presence of residual disease after neoadjuvant chemotherapy are varied, demonstrating its ability to underestimate, overestimate, and accurately size residual tumor in the same series.[63] Overall, MRI has been found to allow a more

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of Patients</th>
<th>True Positives*</th>
<th>False Negatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buchanan et al[48]</td>
<td>55</td>
<td>26/55 (47%)</td>
<td>2/13 (15%)</td>
</tr>
<tr>
<td>McMahon et al[53]</td>
<td>18</td>
<td>12/18 (67%)</td>
<td>0</td>
</tr>
<tr>
<td>Olson et al[49]</td>
<td>40</td>
<td>NA</td>
<td>1/5 (20%)</td>
</tr>
<tr>
<td>Stomper et al[54]</td>
<td>8</td>
<td>2/8 (25%)</td>
<td>NA</td>
</tr>
<tr>
<td>Orel et al[50]</td>
<td>22</td>
<td>17/20 (85%)</td>
<td>2/3 (66%)</td>
</tr>
<tr>
<td>Henry-Tillman et al[51]</td>
<td>10</td>
<td>8/8 (100%)</td>
<td>0/2 (0%)</td>
</tr>
<tr>
<td>Tilanus-Linthorst et al[55]</td>
<td>4</td>
<td>4/4 (100%)</td>
<td>0</td>
</tr>
<tr>
<td>Morris et al[52]</td>
<td>12</td>
<td>9/12 (75%)</td>
<td>0/2 (0%)</td>
</tr>
</tbody>
</table>

*True-positive percentage defined as MRIs demonstrating a pathologically confirmed malignancy over all MRIs performed.

MRI = magnetic resonance imaging, NA = not available.
precise estimation of the presence of residual disease when compared with mammography, accurately determining the extent of postneoadjuvant disease nearly twice as often,[46,64] possibly due to the inability of mammography to differentiate tumor from peritumoral fibrosis and scarring.[65] A recent comparison of MRI to ultrasound for assessment of postneoadjuvant therapy tumor size in 68 patients demonstrated that MRI was significantly more accurate than both ultrasound and physical examination.[61] A size discrepancy of 1 cm or less with final pathologic tumor size occurred in 76% of MRIs, 66% of ultrasounds, and 54% of physical examinations. Detection of a complete pathologic response by MRI varies widely by series, ranging from 13% to 100%.[61,65-67]

Despite its sensitivity, breast MRI is not a substitute for excision. Limitations in the detection threshold of MRI mean that small residual foci of in situ and invasive cancer may remain undetected. This is particularly important in the neoadjuvant chemotherapy setting, because tumors shrink unpredictably and not concentrically. In one study evaluating MR imaging of 40 patients undergoing neoadjuvant chemotherapy, MRI underestimated final lesion size by ≥ 15 mm in 6 cases where multiple foci of residual invasive cancer remained.[68] Although some microscopic disease may not be detectable by breast MRI, it appears to be the most accurate staging modality after neoadjuvant chemotherapy, and can effectively be used to evaluate a patient's candidacy for BCT.

MRI for Follow-up of the Breast Cancer Patient

Identification of Local Recurrence

The current recommendations for the detection of local recurrence after BCT are patient self-examination monthly, physician exam every 3 to 6 months for 5 years, then annually, and a mammogram 6 to 12 months after the completion of radiotherapy and then yearly.[11] With this approach, one-half to one-third of local recurrences are detected by mammography alone and 85% to 90% of patients have operable disease when a local recurrence is detected.[69] Mastectomy is the standard treatment of an isolated local recurrence following BCT, and in the majority of studies examining prognostic factors after local recurrence, the size of the recurrent tumor is not a prognostic factor.[69,70]

Thus, it is not clear that the idea of "earlier" identification of local recurrence with MRI will improve outcome or change treatment. In addition, most studies indicate that a short interval to the development of local recurrence is an indicator of aggressive tumor biology rather than being due to early detection as a result of aggressive surveillance. Veronesi et al reported that the risk of distant metastases after a local recurrence occurring within 1 year of initial treatment was 6.6-fold higher than the risk seen in patients developing local recurrence more than 3 years after surgery (P = .004).[71] Based on this information, it seems unlikely that patients undergoing MRI to detect local recurrence will derive a significant benefit.

Detection of Contralateral Cancer

Another proposed role for MRI is surveillance of the contralateral breast of the woman who has been treated for carcinoma. Lehman and coauthors[72] reported the results of a multi-institutional study that included 987 women diagnosed with unilateral breast cancer within 60 days. All women had a normal contralateral breast examination and mammogram. During a 12-month follow-up period, MRI identified carcinoma in 30 women (3.1%), including 12 intraductal cancers and 18 invasive cancers. The positive-predictive value of MRI was 31% for postmenopausal women compared to 11% in pre- or perimenopausal women (P = .002).

Although women with unilateral breast carcinoma are recognized to be at increased risk of developing a second contralateral breast carcinoma, their absolute level of risk is often relatively low. In a population-based study of 134,501 breast cancer patients from the Surveillance Epidemiology, and End Results (SEER) registry, the 5-year incidence of contralateral breast carcinoma was 3.0%.[73] In addition, adjuvant therapy with tamoxifen is well documented to reduce the incidence of contralateral breast cancer by 50%.[74] While treatment with the aromatase inhibitors results in a somewhat larger degree of risk reduction, the use of adjuvant chemotherapy also results in a 20% reduction in contralateral breast cancers.[74]

These observations, coupled with the SEER report[73] that the 5-year incidence of breast cancer in an unselected population is equal to the 1-year incidence reported by Lehman et al,[72] raise the definite possibility that some cancers detected by MRI would never have become clinically apparent. Additional follow-up of participants in the study of Lehman et al[72] will provide valuable information on the incidence of contralateral cancer at 5 years. Because of these uncertainties, The American Cancer Society has listed unilateral breast carcinoma (invasive or intraductal) as a clinical circumstance in which there are insufficient data to recommend for or against routine screening with MRI (Table 2). It should be noted that for many women treated with adjuvant endocrine therapy, the...
lifetime risk of contralateral cancer development is less than 15%, a level of risk for which the American Cancer Society recommends against the performance of MRI.[8]

Summary and Conclusions
The availability of MRI as an adjunct to mammography and ultrasound offers clear clinical benefit to women at increased risk of breast cancer development due to BRCA1 and BRCA2 mutations, and to women presenting with axillary adenopathy and an occult primary breast tumor. In addition, MRI provides a more accurate assessment of the response to neoadjuvant therapy than conventional breast imaging; whether this translates into improved identification of women who are able to undergo BCT remains to be demonstrated.

The greatest controversy regarding the use of MRI involves the woman with known breast carcinoma. While there is no doubt that MRI demonstrates additional tumor in the breast, the majority of this tumor is controlled with radiotherapy, and its detection may lead to unnecessary additional surgery. The selection of local therapy and local recurrence after BCT are a problem for a small minority of women with breast cancer. The appropriate role for MRI in the cancer patient would be best addressed by identifying unresolved clinical problems to which this technologic advance could be applied in properly conducted trials.

Disclosures:
The authors have no significant financial interest or other relationship with the manufacturers of any products or providers of any service mentioned in this article.

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