Perspective

Practical Considerations for the Use of Breast MRI for Breast Cancer Evaluation in the Preoperative Setting

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Preoperative contrast-enhanced (CE) breast magnetic resonance imaging (MRI) remains controversial in the newly diagnosed breast cancer patient. Additional lesions are frequently discovered in these patients with CE breast MRI. As staging and treatment planning evolve to include more information on tumor biology and aggression, so should our consideration of extent of disease. Directing CE breast MRI to those patients most likely to have additional disease may be beneficial. We sought to develop practical guidance for the use of preoperative CE breast MRI in the newly diagnosed breast cancer patient based on recent scientific data. Our review suggests several populations for whom preoperative breast MRI is most likely to find additional disease beyond that seen on conventional imaging. These can be viewed in three categories: (1) tumor biology—patients with invasive lobular carcinoma or aggressive tumors such as triple negative breast cancer (estrogen receptor negative, progesterone receptor negative, and human epidermal growth factor receptor 2 (HER2) negative) and HER2 positive tumors; (2) patient characteristics—dense breast tissue or younger age, especially those age <60; and (3) clinical scenarios—patients with more sonographic disease than expected or those who are node positive at initial diagnosis. Focusing breast MRI on patients with any of the aforementioned characteristics may help utilize preoperative breast MRI where it is likely to have the most impact.

Key Words: Breast MRI; breast cancer; preoperative breast MRI; breast cancer staging; breast imaging.

INTRODUCTION

Contrast-enhanced (CE) breast magnetic resonance imaging (MRI) has many uses in breast imaging, including screening for women at high risk for developing breast cancer, evaluation of extent of disease in the newly diagnosed breast cancer patient, evaluation in the neoadjuvant chemotherapy setting, and for diagnostic dilemmas not resolved with standard breast imaging techniques (1–3). Of these, the most controversial is the use of breast MRI in the preoperative setting in those newly diagnosed with breast cancer. While it is known that CE breast MRI is the most sensitive detection method for invasive breast cancer, there is discussion regarding the usefulness of finding additional disease in newly diagnosed breast cancer patients. Is the extent of disease important and in which patients is CE breast MRI most likely to be helpful? While these questions seem to defy simple answers, a review of recent literature gives guidance to a practical approach.

CE Breast MRI and Extent of Disease

Newly diagnosed breast cancer patients often have more disease than is suspected from standard, or conventional, imaging with mammography and ultrasound (4). The oldest meta-analysis summarizing data from 19 studies and 2610 patients showed additional disease in 16% (5); a larger analysis of 50 studies and 10,811 patients confirmed additional lesions in 20% of newly diagnosed breast cancer patients (6). Not all of these lesions seen at MRI were malignant, but the positive predictive value given in both analyses suggests additional malignant lesions occurred in 11%–14% of patients. Newer studies suggest the additional malignancy rate is at least 14% or higher. Recent studies from the United States, Germany, and Canada, together including 5432 patients, showed additional malignancy rates at MRI of 14%, 23%, and 34%, respectively, for newly diagnosed breast cancer patients, with additional lesions seen in up to 45% of patients (7–9). Concern has been raised about whether or not this disease is important, because its discovery is unlikely to affect prognosis (or stage) and because early literature suggested that surgical management is not positively affected.

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Additional MRI-only Lesions and Breast Cancer Stage

First, we should consider how these lesions affect stage, typically used historically to determine prognosis but more recently to encompass therapy. In the American Joint Committee on Cancer staging handbook 7th edition, currently in use, tumor size is determined only by the largest lesion in the tumor/node/metastasis (TNM) system of staging (10). Assuming that the largest lesion will be discovered by conventional imaging, additional cancers found only by CE breast MRI will not change the patient's stage unless they are found to involve skin or chest wall. However, MRI-only lesions have been found to be larger than the index lesion 23% of the time and biologically more important in 5% of patients (8). In addition, the TNM system, which was started in 1959 in the absence of screening mammography or effective chemotherapy, has been slow to change with increasing knowledge of tumor biology. The current TNM system in use fails to account for tumor grade, receptor status, or multifocal/multicentric disease. Because lumpectomy and mastectomy have historically been shown to have equivalent survival, it is assumed that additional tumors that existed in the breast but were undiscovered in the pre-MRI era are unimportant. However, survival is not the only important outcome measure. The increased tumor burden of multifocal/multicentric disease has been shown to increase the likelihood of axillary metastasis, suggesting that the importance of total tumor burden has been underappreciated (11). Recent work by Weissenbacher and colleagues showed that patients with multifocal/multicentric disease had statistically significantly more local recurrence (17.4% vs 7.3%), shorter relapse-free survival (170 months vs 206 months), and shorter overall survival (203 months vs 222 months) than matched patients with unifocal disease (their patients were also matched for grade and receptor status) (12). Multifocal/multicentric disease was an independent predictor of decreased breast cancer-specific survival and decreased relapsed-free survival. Multifocal/multicentric disease has also been linked to more aggressive tumor biology (13–15). In 2018, the American Joint Committee on Cancer 8th edition cancer staging manual recommendations are scheduled to take effect, and tumor biology in the form of tumor grade and receptor status will be incorporated into the staging scheme (16), largely because they are currently in wide use for treatment planning and have been for years. The view on multifocal/multicentric disease is also evolving over time and may need to be given renewed consideration in the future.

Additional MRI-only Lesions and Surgical Planning

Older analyses showed CE breast MRI in the preoperative setting to be ineffective in reducing re-excision rates after attempts at breast conserving surgery, with an increase in overall mastectomy rates (5,17). However, more recent data have emerged, which not only reflects current MRI techniques, including MRI-guided biopsy, but also controls better for variations in surgeons and surgical approach (18–21). Obdeijn and colleagues showed a statistically significant reduction in both positive margins at initial surgery (15.8% vs 29.3%) and reoperation rate (18.9% vs 37.4%) when preoperative MRI was utilized compared to no preoperative MRI (19). Similarly, Sung and colleagues, in a study that controlled for the treating surgeon, showed that re-excision rate with the use of preoperative MRI was 29% vs 45% in patients who did not have MRI (20). The surgeon is an important variable and yet few studies control for this factor. A recent randomized controlled study in Sweden showed that both overall reoperation rate (5% vs 15%) and reoperation in patients who were scheduled for breast conserving therapy (5% vs 22%) significantly improved with the use of preoperative breast MRI in younger patients compared to those treated without preoperative MRI (21). This study also showed that the overall mastectomy rate was the same with or without breast MRI and that the time to treatment was similar. Concern about mastectomy rate is also addressed in the Multicenter International Prospective Meta-Analysis of Individual Woman Data trial in Europe, which began in 2012 and involves 34 centers in 14 countries. Preliminary results reported at the European Congress of Radiology 2017 showed that per-patient reoperation rate for close/positive margins was significantly less in the MRI group (8% vs 13.4%) and that the actual mastectomy rate after preoperative MRI was increased by only 1% (22). In summarizing the MIPA results, the authors state that already planned mastectomies prompted MRI in many cases, not vice versa. Overall, there is emerging evidence that current CE breast MRI techniques can bring significant benefits in reducing reoperation and directing appropriate management.

Maximizing Impact of Preoperative Breast MRI

Although CE breast MRI is certainly an asset in many cases, it is clear that some patient populations will be more likely to benefit than others. A review of recent literature shows which patients tend to have more additional disease at preoperative MRI, suggesting patient populations that might be targeted for its routine use. These populations can be grouped in terms of tumor biology, patient characteristics, and clinical scenario.

Tumor Biology

It has been clear for some time that invasive lobular carcinoma (ILC) is often underappreciated on conventional imaging. Patients with ILC have significantly more additional disease at MRI than patients with other types of tumor biology (7,23–26). This has clinical implications; preoperative breast MRI has been shown to significantly decrease reoperation rate by as much as 40% without increasing mastectomy rate in patients with ILC (27,28). Patients with tumors that are positive for human epidermal growth factor receptor 2 (HER2) have worse prognosis (29); this tumor subtype is twice as likely to have to have four or more metastatic lymph nodes and 1.6 times more likely to have multifocal disease than patients with