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Review Article

The role of breast MRI in newly diagnosed breast cancer: An evidence-based review

Jessica L. Thompson [a, b, *], G. Paul Wright [a, b, c]

[a] Spectrum Health General Surgery Residency Program, 100 Michigan Street NE, Suite A501, Grand Rapids, MI, 49503, United States
[b] Michigan State University College of Human Medicine, Department of Surgery, 15 Michigan Street NE, Grand Rapids, MI, 49503, United States
[c] Spectrum Health Medical Group, Division of Surgical Oncology, 145 Michigan Street NE, Suite 5500, Grand Rapids, MI, 49503, United States

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ABSTRACT

The utility of pre-operative MRI in patients with newly diagnosed invasive breast cancer remains a topic of debate. Those who advocate for pre-treatment imaging contend that MRI may detect additional disease not otherwise appreciated on conventional imaging and may provide more accurate staging information to guide treatment. Additionally, it has been proposed that MRI can be utilized to assess extent of residual disease in patients undergoing neoadjuvant chemotherapy. Conversely, those in opposition maintain that routine pre-operative MRI subjects patients to unnecessary ipsilateral mastectomies and prophylactic contralateral mastectomies with no difference in oncologic outcome. When stratified based on tumor biology and patient characteristics, the data suggests that pre-treatment MRI may be advantageous in certain subsets when compared to the general cohort of breast cancer patients. This review recapitulates the current literature on the impact of breast MRI on the surgical management and outcomes of newly diagnosed breast cancer.

Introduction

The utility of breast magnetic resonance imaging (MRI) in the staging and surgical planning of breast cancer remains controversial despite a myriad of studies published on the topic. Due to a lack of evidence-based recommendations, the decision to order pre-operative breast MRI is based on clinical judgement and provider preference. The use of breast MRI was first described in 1986 as an adjunctive imaging modality to mammography and sonography.[1] Over time, breast MRI was incorporated into clinical practice to supplement the conventional imaging modalities.[2] A survey sent to members of the American Society of Breast Surgeons (ASBrS) in 2010 revealed that 41% of practicing surgeons reported routine MRI utilization, defined as greater than 75% of the time, in patients with newly diagnosed breast cancer.[3] Using the Surveillance, Epidemiology, and End Results (SEER) Medicare-linked database, Killelea et al. found that between 2008 and 2009, 25% of their patient cohort underwent preoperative MRI compared to only 0.8% between 2000 and 2001.[4] In a Canadian population-based study, Arnaout, et al. reported an eight-fold increase, from 3% to 24%, in MRI use from 2003 through 2012.[5]

With respect to breast cancer detection, several studies have demonstrated the sensitivity of contrast-enhanced MRI is superior to that of mammography and ultrasound, with published rates ranging from 89% to 100%.[6,7] Identification of suspicious foci inevitably prompts biopsy, however, discrimination between benign lesions and malignancies on breast MRI is challenging due to similarities in kinetic patterns, contrast enhancement, and morphologic features. As a result, breast MRI has low to moderate specificity with rates ranging from 65% to 86% leading to diagnostic ambiguity.[8,9] A meta-analysis conducted by Houssami et al. concluded that pre-operative MRI detects tumor foci in the ipsilateral breast in 16% of females with newly diagnosed breast cancer.[10] Brennan et al. conducted a systematic review of studies on contralateral breast MRI screening in cases of recently diagnosed cancer and calculated a positive predictive value of 47.9%. Based on pooled data, MRI identified mammographically and clinically occult abnormalities in the contralateral breast in 9% of patients, but the estimated incremental cancer detection rate was only 4% resulting in a true-positive to false-positive ratio of 0.9–1.[11] Considering its capability to define the extent of disease and detect previously

* Corresponding author. 100 Michigan NE Suite A501 Mail Code 188, Grand Rapids, MI, 49503.
E-mail addresses: jessica.thompson@spectrumhealth.org (J.L. Thompson), paul.wright@spectrumhealth.org (G.P. Wright).

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unrecognized cancer, pre-treatment breast MRI can be perceived as a tool to enhance surgical planning and improve local control. However, based on the findings of numerous studies and meta-analyses, MRI has not translated into improved short-term or long-term outcomes in females with early-stage breast cancer.

Impact on surgical management

A retrospective review of newly diagnosed breast cancer cases from 2004 through 2009 reported a change in surgical management based on the results of pre-treatment MRI in 18% of subjects. Adjustments in local therapy included 16 conversions to larger lumpectomy, 38 unilateral surgeries changed to bilateral, and 187 lumpectomies converted to mastectomies.[8] In addition to reporting that 49% of their patient population underwent pre-operative breast MRI between the years 2011 and 2013, Romanoff et al. found that one-third of the MRI cohort had a resultant change in management.[2] Data from thirteen studies targeting women with multifocal and/or multicentric breast cancer was analyzed to determine the impact of MRI staging on surgical treatment. Pooled estimates showed the rate of conversion from wide local excision to more extensive surgery (mastectomy or wider/additional resection) was 11% in women with biopsy-proven additional cancer deposits identified by MRI. An additional 5.5% of women underwent more extensive surgery for false-positive MRI findings.[12] Nineteen studies and 85,975 patients were included in a systematic review that examined pre-treatment MRI and surgical outcomes in invasive breast cancer. The age-adjusted analyses demonstrated an increased likelihood of ipsilateral mastectomy (odds ratio 1.39; $P < .001$) and contralateral prophylactic mastectomy (odds ratio 1.9; $P = .003$) in women who underwent MRI.[13]

The MONET trial was a multicenter randomized control trial designed to study the effectiveness of pre-treatment breast MRI on the proportion of additional surgical procedures. The investigators found the addition of MRI was associated with a paradoxical increase in re-excision rates, with 34% of subjects in the MRI group undergoing re-excision due to positive resection margins compared to only 12% in the control arm.[14] Data from two randomized controlled trials and seven comparative cohort studies were included in a meta-analysis that found despite statistically significant increased rates of upfront and overall mastectomy, pre-operative MRI did not reduce rates of re-excision or re-operation. The authors concluded that routine use of pre-treatment MRI in newly diagnosed breast cancer patients produces an unfavorable harm-benefit ratio.[15]

Oncologic outcomes

Debate regarding the long-term effect of staging MRI was addressed by an individual patient-level meta-analysis that examined the potential correlation between MRI and breast cancer recurrence. Despite statistical adjustments and sensitivity analysis, pre-operative MRI was not associated with reduced risk of local recurrence nor distant recurrence.[16] With the advances in adjuvant systemic treatment and effective multimodality therapies currently available, subclinical disease detected by MRI may not necessitate resection. These findings correlate with other studies such as NSABP B-04 and ACOSOG Z0011 that demonstrate complete surgical removal of all microscopic disease is not necessarily associated with improved outcomes.[17,18]

Breast density

Romanoff et al. reported that the variables associated with pre-operative MRI included increased breast density, lobular pathology, mammographically occult disease, commercial insurance, and genetic testing.[2] In their retrospective review Elder et al. hypothesized that when stratified by mammographic density, pre-operative MRI would confer additional benefit in females with dense breasts. While 42% of patients with dense breasts had additional concerning foci identified on MRI in the ipsilateral breast and 25% had suspicious lesions in the contralateral breast, the proportions of biopsy-proven malignancies did not differ among density cohorts. Furthermore, re-excision rates and local recurrence rates were similar between low-density and high-density patients.[19]

Infiltrating lobular carcinoma

Infiltrating lobular carcinoma (ILC) can be challenging to detect on conventional imaging due to its diffuse infiltrative growth pattern and similar density to the surrounding breast parenchyma. With respect to ILC, the reported sensitivity of MRI ranges from 83% to 100%, surpassing that of mammography and ultrasonography.[7] Brennan et al. reported that conventional imaging underestimated pathologic measurements in 57% of ILC cases and had a concordance rate, defined as within 20-mm of histological size, of 41%. By comparison, MRI underestimated size in 28% of ILC cases and had a concordance rate of 67%.[20] A survey by Morrow et al. revealed that 72% of surgeons endorsed pre-treatment MRI in patients with ILC.[21] Despite better concordance rates and size estimates, a recent systematic review performed a subgroup analysis for ILC based on data from six studies did not find an association between pre-operative MRI and the odds of re-excision or the odds of undergoing mastectomy.[13]

Implicit ramifications

A consequence of breast MRI's limited specificity is the need for additional workup for false-positive findings. Bleicher et al. reported that pre-operative MRI was associated with a mean 22-day delay in surgical treatment.[22] A more recent study found patients who underwent pre-treatment MRI waited an average of 39 days compared to 27 days for those who did not receive MRI. While delays related to MRI use may not be of consequence with respect to clinical outcomes, they have the potential to be anxiety-provoking for patients.[23] Using SEER Medicare-linked data, Onega, et al. compared the costs of imaging and biopsy in females with a breast cancer diagnosis between 2005 and 2009. The unadjusted median costs were $2251 in the diagnostic MRI group in contrast to $1151 for those who did not undergo pre-operative MRI.[24] In addition to longer wait times and increased costs, MRI subjects recipients to the risk of contrast reaction and the unknown long-term impact of gadolinium-based contrast agent administration.[25]

Neoadjuvant chemotherapy

Several studies have shown breast MRI to be the most accurate imaging modality for assessing response to neoadjuvant chemotherapy (NAC).[26,27] The I-SPY trial demonstrated that in the post-NAC setting MRI findings were a stronger predictor of pathologic response compared to clinical assessment.[28] The goal of breast MRI after NAC is to assess the extent of residual disease to facilitate operative planning and acquisition of adequate surgical margins at the time of index operation.[29] Jochelson et al. conducted a retrospective study to evaluate if MRI alone and with mammography could predict breast-conserving therapy (BCT) candidates after NAC. The investigators found MRI alone accurately identified 53 of 60 patients suitable for BCT, and MRI combined with mammography was correct in 55 of 60 patients. Current evidence suggests

that tumor subtype has a role in MRI's ability to assess pathologic complete response and warrants further investigation.[30–32]

Societal recommendations

The current version of the National Comprehensive Cancer Network (NCCN) guidelines (v.6.2020) has a section addressing clinical indications and applications of dedicated breast MRI testing. According to NCCN, MRI of the breast can be helpful for assessment prior to and after NAC to determine the extent of cancer, treatment response, and possibility for BCT. A category 2B recommendation includes the use of breast MRI for staging by defining the extent of disease, evaluating for the presence of ipsilateral multifocal or multicentric cancer, or screening for contralateral breast cancer at the time of initial diagnosis. The guidelines acknowledge that no high-quality evidence has shown MRI use to improve local recurrence or survival rates. Furthermore, the guidelines state that the role of MRI in ductal carcinoma in situ (DCIS) management is unclear and the NCCN panel advocates for pre-treatment breast MRI only in "select circumstances where additional information is warranted". In cases of axillary nodal adenocarcinoma and occult breast cancer, the guidelines do support the use of breast MRI to facilitate the identification of the primary malignancy.[33]

The ASBrS addressed the use of MRI in the Consensus Guideline on Diagnostic and Screening Magnetic Resonance Imaging of the Breast released June 2017. The Society recommended against routine diagnostic breast MRI in cases of newly diagnosed cancer. The ASBrS did describe exceptions to the recommendation including research study participants, patients undergoing neoadjuvant systemic therapy, cases of occult breast cancer with an unidentified primary lesion on conventional imaging, and lastly patients with both a biopsy proven malignancy in addition to associated indeterminate clinical or radiographic findings concerning for malignancy. In 2016, the ASBrS contributed a list of appropriate care measures to the Choosing Wisely® campaign in an effort to avoid overutilization of unnecessary services. One of the five guidelines included the omission of routine breast MRI in new breast cancer patients.[34]

The American College of Radiology (ACR) has published a document outlining the technical standards for performing breast MRI. The current indications, as defined by the ACR document, include delineating the extent of disease. The practice parameter describes breast MRI as a useful tool to identify multifocality and multicentricity in both the preoperative setting and postoperatively in cases of margin positivity. Additionally, ACR mentions staging MRI can be used to evaluate for subfascial invasion. The guidelines acknowledge that despite its superior accuracy, breast MRI has not corresponded with reduction in the rates of re-excision or recurrence.[35]

Surgeons' practice beliefs

In a survey of ASBrS members regarding MRI use, 63% of respondents selected personal experience as the resource that most strongly influenced their practice patterns. The results revealed surgeons in private practice were more likely to recommend preoperative MRI compared to those in an academic setting. Rates of MRI utilization were 49% in highly specialized practices compared to 26% in practices with less breast specialization. Consensus for MRI usage varied based on specific clinical settings. The majority of respondents recommended breast MRI in the setting of increased mammographic density, strong family history, and invasive lobular carcinoma. Conversely, responses to MRI use in DCIS, invasive ductal carcinoma, and pursuit of breast conservation were dissonant.[3] The objective of the Individualized Cancer Care study was to determine surgeon characteristics and perspectives associated with MRI use based on a scenario-centered survey. The survey results revealed significant provider variation (10%–72%) but overall frequent use of MRI, with higher volume surgeons exhibiting a stronger tendency to obtain MRI. The misconceptions about the benefits of testing were more prevalent among surgeons identified as high MRI users.[21]

Conclusion

The value of pre-treatment testing should be contingent on a study's capability to modify outcomes. Staging MRI has been integrated into practice under the assumption that its detection capabilities would improve treatment and outcomes. At present, there is no clear consensus on the indications for obtaining pre-operative MRI in patients with newly diagnosed breast cancer. Based on incongruent practice patterns, it can be inferred that a high degree of uncertainty continues to besiege the breast cancer community. Despite differing opinions on the clinical benefit of pre-treatment MRI in newly diagnosed breast cancer patients, most authors acknowledge a need for further prospective trials to validate the long-term effects and to optimize patient outcomes. While individual studies have conflicting conclusions, the published meta-analyses to date suggest that pre-operative MRI may be overutilized with little to no additional benefit. While availability of breast MRI is ubiquitous and often recommended by our radiology colleagues, it is prudent for surgeons to consider the literal and figurative costs prior to ordering this exam outside the setting of a properly designed clinical trial.

Declaration of competing interest

The authors have no conflict of interest or sources of funding to disclose.

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