



Long-term impact of staging breast magnetic resonance imaging – a risk for overtreatment?

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Since the introduction of contrast enhanced breast magnetic resonance imaging (MRI) as an additional modality in breast imaging in 1989, there has been much debate regarding its role in clinical practice (1). Although it has an impressive sensitivity (reportedly 94–100%) for detecting breast lesions, this advantage has to be balanced with its markedly decreased specificity, ranging between 34–70% (2). The relatively high incidence of false positive findings and patient call backs coupled with the increased cost and the need for radiologists trained in breast MRI interpretation, have limited the application of this technology to date.

Given these barriers, MRI for breast cancer screening has been recommended only for certain high risk populations. The current American College of Radiology (ACR) recommendations state that MRI screening is indicated in women with a lifetime breast cancer risk of greater than 20–25%, individuals with known *BRCA* germline mutations or the untested first-degree relative of a *BRCA* carrier, and women that received chest wall radiation prior to age 30 years old (3). The role for MRI in follow-up of high risk lesions such as atypical ductal hyperplasia and lobular carcinoma in situ or women that have a personal history of breast cancer is still being debated. Meanwhile, it is categorically discouraged in patients at an average lifetime risk of breast cancer.

Similarly, the role for preoperative breast MRI in the patient with a known cancer diagnosis continues to evolve. MRI has been advocated in this setting for several reasons. First, the increased sensitivity of MRI may better delineate tumor size and associated margins when compared to mammography and ultrasound, so MRI has been used

to ascertain the extent of disease (4). The other potential advantages of obtaining a preoperative MRI are to diagnose mammographically occult multicentric disease in the ipsilateral affected breast or to identify a contralateral breast cancer.

Current NCCN guidelines note that preoperative breast MRI may be used as part of staging evaluation. However, given the lack of data supporting an improvement in local recurrence or survival when MRI is used in surgical decision making, MRI should be incorporated at the discretion of the clinical provider (5).

The current literature definitively demonstrates the effect of preoperative breast MRI on surgical decision making. An Australian analysis of 181 patients receiving preoperative breast MRI found that 38.1% altered their surgical plan based on the results, including a change to a wider excision, mastectomy or bilateral surgery (6). Similarly, Brooke Army Medical Center reviewed their experience prospectively after implementing preoperative breast MRI for all new breast cancer diagnoses (7). In this series, mastectomy rates increased from 29% to 52% when breast MRI was used for staging in all cancers. Not only is preoperative MRI increasing ipsilateral mastectomy, it also has an effect on the rate of contralateral prophylactic mastectomy (CPM). A prospective analysis of women electing mastectomy at the University of Iowa found that 53 of 134 patients (39.6%) also elected CPM (8). Approximately half of these patients had undergone preoperative MRI (66/134). Univariate analysis showed that patients who had received preoperative MRI were more likely to choose CPM [odds ratio (OR), 2.74], particularly if they were given a follow up

recommendation from MRI (OR, 7.6).

One hypothesized benefit to preoperative MRI is that better knowledge of disease extent would increase rate of negative pathologic margins. Authors at UCSF examined the impact of preoperative MRI specifically in patients treated for ductal carcinoma in situ (DCIS) (9). Their retrospective review of 149 patients identified 38 patients had preoperative MRI; these tended to be younger patients with larger area of involvement. The MRI group had a mastectomy rate of 45% compared with 14% in the non-MRI group. As expected with increased mastectomy performance, they also saw a significant increase in the use of sentinel node biopsy in the MRI group. Unfortunately, despite the more aggressive surgical approach, no difference was seen in margin status or rate of re-excision.

The above studies all corroborate the findings of a recent review of the National Cancer Database that showed a national trend of increasing mastectomy rates in all patients with breast cancer (regardless of MRI usage) from 34% in 1998 to 37% in 2011 (10). Another study of 20,000 patients with stage 0–II breast cancer receiving primary surgical treatment noted a 45% rate of mastectomy (11). Both analyses cite the rising use of breast MRI as one of multiple factors contributing to this trend. Other factors include the rise of prophylactic mastectomy and the increasing availability of breast reconstruction. However, it remains to be seen as to whether an increase in identification of multicentric/multifocal and contralateral disease and subsequent changes in surgical planning will yield any impact on patient outcomes in terms of local control and survival.

In the recent issue of *Cancer*, Vapiwala *et al.* present their single-institution experience with breast MRI in the early stage breast cancer patient planning breast conservation therapy and evaluated the effect on long term outcomes (12). This longitudinal series with a median follow up time of 13.8 years (mean 12.7 years; range, 0.1–23.6 years) noted that 28% of patients received breast MRI in as part of their preoperative assessment. These patients undergoing MRI tended to be younger and were treated more recently. At follow up there was no difference observed in either local recurrence or overall survival between groups receiving preoperative MRI versus those without. Thus, although breast MRI can detect otherwise occult foci of disease, this may not be clinically relevant in the setting of standard breast conservation therapy, consisting of lumpectomy followed by whole breast radiation. If anything, these findings serve to highlight the ability of post lumpectomy

radiation to clear microscopic disease. Similar to the group at UCSF, no difference was seen in the final pathologic margin status. Limitations of this study include its single-institution, retrospective nature and the relatively low incidence of local failure and mortality, which would require a large patient group to have detected a small benefit.

A similar retrospective review was performed in Korea to analyze the impact of preoperative MRI on survival in early breast cancer (13). In this study, 743 of 954 (77.8%) patients were assessed with preoperative MRI and these patients were followed for a median of 5 years to evaluate local regional recurrence free survival, recurrence free survival and overall survival. All of these metrics were similar between the two groups, in keeping with the findings of Vapiwala *et al.*

It is likely that the continued use of perioperative MRI will increase the mastectomy rate, but Vapiwala *et al.*, as well as the work of other groups, continue to demonstrate that the use of preoperative MRI has not been shown to impact breast-cancer related survival and likely has little impact on surgical outcomes such as re-excision. This raises legitimate concern for possible overtreatment, spurred by the acquisition of preoperative MRI. However, there is likely a small subset of patients that would benefit from this additional imaging prior to surgery. This group likely includes those with lobular histology, which is known to be poorly visualized on mammogram and sonogram, and therefore more likely to be underrepresented on standard imaging (14). A review of 46 patients with invasive lobular cancer who underwent preoperative MRI had a 37% chance of newly identified multifocal disease and 10.9% chance of a contralateral lesion (13). Another cohort that may benefit is those patients who have discordant radiology and pathology where there is high concern for carcinoma despite a negative biopsy result.

In light of these findings, more investigation is needed to clarify the role of preoperative staging with breast MRI. The present study has the longest reported follow-up, exceeding 10 years, and still fails to demonstrate a survival benefit. Given the relatively infrequent events, a larger cohort is likely needed to detect a benefit. Similarly a larger study and preferably multicenter study population is needed to show a difference in the rate of margin re-excision.

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Footnote

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