The Breast 19 (2010) 7–9

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original Article

Counterview: Pre-operative breast MRI (magnetic resonance imaging) is not recommended for all patients with newly diagnosed breast cancer

Lawrence J. Solin*

Department of Radiation Oncology, Albert Einstein Medical Center, 5501 Old York Road, Philadelphia, PA 19141, United States

Keywords:
Magnetic resonance imaging
MRI
Early stage breast cancer
Breast conservation treatment
Radiation treatment
Local control

A B S T R A C T

For the woman with a newly diagnosed early stage breast cancer, the routine use of pre-operative breast MRI (magnetic resonance imaging) is not indicated beyond conventional breast imaging (i.e., mammography with correlation ultrasound as indicated). There is no consistent evidence that a pre-operative breast MRI confers a benefit to the patient by improving clinical outcomes or surgical procedures. In a meta-analysis of studies reporting on the use of pre-operative breast MRI for the patient with an established index cancer, multifocal or multicentric disease was found on breast MRI in 16% of the patients, a rate substantially higher than the rate of local recurrence after breast conserving surgery plus definitive radiation treatment. In the largest retrospective study of patients treated with breast conserving surgery plus radiation, no gain was found for adding a breast MRI to conventional breast imaging. No randomized clinical trial has been designed to evaluate long term clinical outcomes associated with adding a pre-operative breast MRI. Adding pre-operative breast MRI can alter clinical management in ways that are potentially harmful to patients, for example, increased ipsilateral mastectomies, increased contralateral prophylactic mastectomies, increased work-ups, and delay to definitive surgery. In summary, the routine use of pre-operative breast MRI is not warranted for the typical patient with a newly diagnosed early stage breast cancer.

It is axiomatic that a medical test or treatment should confer a benefit to patients to be used in routine clinical practice. For the typical patient with early stage breast cancer, no such benefit has been shown to date for the routine use of pre-operative breast MRI (magnetic resonance imaging), beyond the benefit already conferred by conventional breast imaging (i.e., mammography with correlation ultrasound as indicated). Thus, the routine use of pre-operative breast MRI for early stage breast cancer patients is not warranted.

Breast MRI gives detailed images of the breast. When breast MRI was developed in the 1990's, the initial promise was that detailed breast imaging on MRI would lead to an increased detection of occult foci of disease within the breast, which in turn would lead to more tailored surgery and improved long term clinical outcomes. In theory, local control might be improved in that patients with additional foci of disease identified on breast MRI could be managed with: (a) mastectomy, thus reducing the rate of local recurrence for the remaining cohort of patients by eliminating a high risk subset; (b) wider surgical excision of foci of disease in the breast, thus giving higher local control after definitive radiation treatment; or (c) higher doses of radiation treatment.

That breast MRI increases the detection of occult foci of disease in the breast has been shown in numerous studies. In a meta-analysis and review of the literature, Houssami et al. reported data from 2610 patients (with an established index breast cancer) in 19 studies.[1] In these 19 studies, the median prevalence of detecting additional multifocal or multicentric disease on MRI was 16% (range = 6%–34%).[1]

The addition of breast MRI leads to changes in surgery. However, this fact does not imply that surgery is necessarily improved with breast MRI, but merely changed, typically to more extensive surgery.[1,2] In the meta-analysis by Houssami et al., the rate of conversion from excision to mastectomy was 8.1%, and the rate of conversion from excision to more extensive surgery was 11.3%.[1] However, pathologic examination did not identify additional disease in 13.6% (1.1%/8.1%) of the former group and in 52.2% (5.9%/11.3%) of the latter group. Thus, at least 1.1% of the overall group had an unnecessary mastectomy, and the true number is likely higher because breast radiation treatment has been shown to achieve local

* Tel.: +1 215 456 6280; fax: +1 215 457 0270.
E-mail address: solin@einstein.edu

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doi:10.1016/j.breast.2009.11.004

control in most patients with microscopic disease in the breast. Further, at least 5.9% of the overall group had an unnecessarily wider local excision, which in turn, could lead to decreased cosmetic outcome.

Adding routine breast MRI can alter clinical management in ways that are potentially harmful to the patient. A number of studies have reported an increased rate of mastectomy associated with breast MRI, and in some cases, unnecessary mastectomy, as noted above.[1–6] Not only is the rate of ipsilateral mastectomy increased, but the rate of bilateral mastectomy is also increased.[4] Adding a breast MRI can result in increased work-up (for example, MRI guided biopsy), increased costs, and delay to definitive surgery.[1–3]

Perhaps the most important endpoint from a patient perspective is whether pre-operative breast MRI improves long term outcomes and decreases local recurrence after breast conservation treatment. Optimizing local recurrence is a key endpoint in the management of early breast cancer. In the Oxford overview and meta-analysis of randomized clinical trials, adding radiation after surgical excision (lumpectomy) dramatically reduced the rate of local recurrence by approximately 20% at 5 years and 10 years, and improved both breast cancer mortality and overall mortality by approximately 5–5½% at 15 years.[7] Further, local control was directly linked to overall mortality, and modeling of the Oxford overview and meta-analysis data demonstrated that four local recurrences directly led to one avoidable breast cancer death. Thus, local control is an important endpoint in breast cancer management, and is likely to be the most sensitive endpoint to measure the effectiveness, if any, of pre-operative breast MRI.

Only two published studies have addressed the issue of long term clinical outcomes after breast conservation treatment.[8,9] Long term outcomes in this context refers to clinical endpoints (for example, local control), and should be distinguished from surgical endpoints, such as the rate of re-excision or the rate of obtaining clear margins at the time of lumpectomy. No current randomized clinical study has reported a clinical outcome as the primary study endpoint. Houssami and Hayes have estimated that a randomized clinical study with local recurrence as the primary study endpoint would require between 2900 and 14,000 patients for adequate statistical power.[2]

In a retrospective study of 224 patients, Fischer et al. reported a decrease in local recurrence after breast conservation treatment from 6.5% (9/138) for patients without a breast MRI to 1.2% (1/86) for patients with a breast MRI ($p < .001$).[8] However, the 6.5% rate of local recurrence for patients without breast MRI is higher than would be expected in contemporary practice, given the mean follow-up of 3.4 years in this study.

In a study of 756 patients after breast conservation treatment, Solin et al. reported no benefit for adding a breast MRI for the 8-year rates of local failure (3% versus 4%, respectively; $p = .51$), contralateral breast cancer (6% versus 6%, respectively; $p = .39$), overall survival (86% versus 87%, respectively; $p = .51$), cause specific survival (94% versus 95%, respectively; $p = .63$), or freedom from distant metastases (89% versus 92%, respectively; $p = .16$).[9] The absence of benefit was confirmed on multivariate analysis (all $p \geq .19$). No benefit for local control was found from adding breast MRI for the subset of 620 patients with invasive breast carcinoma (3% versus 3%, respectively; $p = .62$) or for the subset of 136 patients with ductal carcinoma in situ (6% versus 6%, respectively; $p = .58$). Unpublished data from Duke University also showed no benefit for local control by adding a breast MRI.[10]

The absence of a clinical benefit from adding a breast MRI for patients undergoing breast conservation treatment plus radiation may be due to a number of factors. In contemporary studies, the baseline risk of local recurrence after breast conservation treatment using conventional breast imaging (i.e., mammography with correlation ultrasound as indicated), without a breast MRI, is low. For example, in the study by Solin et al., the rate of local recurrence without a breast MRI was 4% at 8 years.[9] Thus, the ability to detect an improvement in local failure with breast MRI would be difficult, if not impossible, in a retrospective cohort study, and would require thousands of patients in a prospective, randomized study, as noted above.[2] Radiation treatment substantially reduces the rate of local recurrence by controlling subclinical disease, as demonstrated by randomized clinical trials.[7,11–13] In other words, regardless of whether a pre-operative breast MRI detects occult foci of disease in the breast for the patient undergoing breast conservation treatment, adding breast MRI confers no additional benefit because radiation treatment is known to be effective in controlling such microscopic foci of disease.

The first results of the COMICE (Comparative Effectiveness of Magnetic Resonance Imaging in Breast Cancer) study were presented at the San Antonio Breast Cancer Symposium in 2008.[6] After conventional breast imaging, 1625 patients were randomized to undergo a pre-operative breast MRI versus not. The primary study endpoint was the re-operation rate, a surgical endpoint, and there was no difference in the re-operation rate between the two arms of the study (18.8% versus 19.3%, respectively; $p = .77$). Further, no difference was seen in the disease-free survival rate (94% versus 96%, respectively), with a median follow-up of 3.1 years.

The above comments should not be construed to indicate that breast MRI is never warranted. On the contrary, there are a number of accepted indications for using breast MRI, for example, high risk women for screening, patients with an axillary lymph node presentation (i.e. with no primary breast carcinoma on physical examination, mammography, and ultrasound), patients with an augmentation breast implant, assessing response to neoadjuvant chemotherapy, and clinical problem solving. On balance, these indications constitute a relatively small fraction of patients in routine practice (excluding certain specialized clinics, for example, high risk screening clinics). Thus, for most physicians, adding a breast MRI is indicated for only a small fraction of the overall patient population.

In summary, the current evidence does not support adding a pre-operative breast MRI for all patients with early stage breast cancer. There is no consistent evidence that adding a pre-operative breast MRI confers a benefit by improving clinical outcomes or surgical procedures for patients with early stage breast cancer. No randomized clinical trial has been designed to evaluate long term outcomes, and the largest retrospective study found no gain for adding a breast MRI to conventional breast imaging.[9] Although breast MRI is indicated in a limited number of clinical settings, these patients are the minority of cases in most clinical practices. In the setting of early stage breast cancer, the routine use of pre-operative breast MRI is not warranted.

Conflict of Interest Statement

None declared.

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