Review of Preoperative Magnetic Resonance Imaging (MRI) in Breast Cancer
Should MRI Be Performed on All Women with Newly Diagnosed, Early Stage Breast Cancer?
Nehmat Houssami, MBBS, PhD and Daniel F. Hayes, MD

Abstract
Randomized controlled trials have shown equivalent survival for women with early stage breast cancer who are treated with breast-conservation therapy (local excision and radiotherapy) or mastectomy. Decades of experience have demonstrated that breast-conservation therapy provides excellent local control based on defined standards of care. Magnetic resonance imaging (MRI) has been introduced in preoperative staging of the affected breast in women with newly diagnosed breast cancer because it detects additional foci of cancer that are occult on conventional imaging. The median incremental (additional) detection for MRI has been estimated as 16% in meta-analysis. In the absence of consensus on the role of preoperative MRI, we review data on its detection capability and its impact on treatment. We outline that the assumptions behind the adoption of MRI, namely that it will improve surgical planning and will lead to a reduction in re-excision surgery and in local recurrences, have not been substantiated by trials. Evidence consistently shows that MRI changes surgical management, usually from breast conservation to more radical surgery; however, there is no evidence that it improves surgical care or prognosis. Emerging data indicate that MRI does not reduce re-excision rates and that it causes false positives in terms of detection and unnecessary surgery; overall there is little high-quality evidence at present to support the routine use of preoperative MRI. Randomized controlled trials are needed to establish the clinical, psychosocial, and long-term effects of MRI and to show a related change in treatment from standard care in women newly affected by breast cancer. CA Cancer J Clin 2009;59:290–302. ©2009 American Cancer Society, Inc.

Introduction
The remarkable evolution of breast cancer surgery from the radical mastectomy advocated by William Halsted to cosmetically appealing breast conservation has been championed by women and pioneering surgeons, and the safety and benefits of this approach have ultimately been confirmed through high-level scientific evidence. Randomized trials and subsequent experience with breast-conservation therapy (local excision and radiotherapy) have clearly established its efficacy, with a low, long-term risk of local (in-breast) recurrence, typically 0.5% to 1% per year. The increasing adoption of performing preoperative magnetic resonance imaging (MRI) scans in women

1Associate Professor and Principal Research Fellow, Screening and Test Evaluation Program (STEP), School of Public Health, Sydney Medical School, University of Sydney, Sydney, Australia, and Breast Physician at the Royal Hospital for Women, Sydney, Australia; 2Clinical Director of the Breast Oncology Program, University of Michigan Comprehensive Cancer Center, Ann Arbor, Michigan.

Corresponding author: Nehmat Houssami, MBBS, PhD, Screening and Test Evaluation Program (STEP), School of Public Health, Edward Ford Building (A27), University of Sydney, NSW 2006, Australia; nehmath@med.usyd.edu.au or hayesdf@med.umich.edu

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newly diagnosed with early stage (stage I and II) breast cancer, for the purpose of identifying additional (occult) foci of disease within the affected breast, has been based on assumptions that MRI’s detection capability in this setting will improve surgical treatment (and, hence, outcomes) in the absence of evidence of incremental clinical benefit. These assumptions, which are further discussed in relation to available evidence, are that: (1) preoperative MRI will improve surgical planning (or precision), thus leading to a reduction in re-excision surgery, and (2) MRI will reduce in-breast recurrences by guiding surgical intervention for MRI-detected additional disease.

Emerging data show that this approach to local staging of the breast leads to more women being treated with mastectomy without improvement in surgical outcomes or prognosis. Thus, it is timely and imperative to consider both current evidence and a way forward in determining the role of preoperative MRI. We review the data on breast MRI in women newly affected by breast cancer, highlighting the evidence on its potential benefit and associated harm, and discuss implications for management of women with early stage disease. We systematically discuss each of the key issues relevant to addressing the clinical question raised in the title of our article, based on summaries of published data, complemented by our perspectives on the evidence in the context of contemporary standards of care in breast cancer.

Background
Since the 1970s, studies have demonstrated that women with early stage breast cancer who are felt to have a single and resectable tumor as determined by clinical examination and conventional imaging have additional foci of cancer (foci other than the index cancer) on histology in about 20% to 60% of affected breasts. The multifocal (additional cancer in the same quadrant as the index cancer) and multicentric (additional cancer in a different quadrant to the index cancer) nature of breast cancer has long been identified by pathologists. However, the equivalence of mastectomy and breast-conserving therapy, which uses wide excision of the apparent tumor to achieve tumor-free margins, followed by breast radiation for long-term outcomes, such as metastasis-free and overall survival, has been established in several randomized controlled trials with decades of follow-up. These trials were based on conventional assessment (clinical, mammographic, and pathology correlation) with the assumption (and demonstration in randomized controlled trials) that unrecognized foci of disease would be eradicated by subsequent adjuvant radiotherapy. These randomized trials, and results from uncontrolled trials from several institutions, have demonstrated that the risk of local (in-breast) recurrence at 10 years after breast-conserving surgery and radiation is usually less than or equal to 10%. In centers with a decade or more of experience with breast-conserving therapy, this risk rarely exceeds 5%. The ability to achieve long-term, local control in women with early stage breast cancer who opted to have breast conservation and radiation therapy was demonstrated well before the introduction of breast MRI.

Magnetic Resonance Imaging
Remarkable advances in MRI technology have allowed sensitive detection and anatomic definition of cancer, and the introduction of MRI in several aspects of breast cancer diagnosis and management. These situations include screening women at high risk of breast cancer, selective “problem-solving”, or adjunct diagnosis where standard clinical and imaging evaluation do not provide a clear diagnosis, imaging of breast silicone implants, and monitoring response to neoadjuvant (primary), systemic therapy in locally advanced disease. In this overview, we focus on MRI in the specific setting of preoperative evaluation of women who are considering breast-conserving treatment after having received an established, new diagnosis of early stage breast cancer, and the application of MRI to identify additional foci of disease other than the proven index cancer (MRI-detected multifocal and/or multicentric cancer). This approach to staging the affected breast has been increasingly adopted in countries that have developed health care systems, and there are very divergent views on the merits and ramifications of preoperative MRI. Furthermore, this approach is now being extended to screen the contralateral, clinically unaffected breast. Although we applaud any intervention, be it preventive, diagnostic, or therapeutic, that improves care and/or prognosis in breast cancer, we
have concerns that the adoption of preoperative breast MRI has been based on assumptions (as outlined in the Introduction) rather than on evidence of improved patient outcomes. These concerns, and accumulating evidence on the potential for MRI to lead to worse clinical outcomes by virtue of unnecessary, more radical, breast surgery,25–26 are discussed to help clinicians judge the evidence on preoperative MRI and to clarify why we believe that randomized controlled trials are needed in this clinical context.

**Breast-Conserving Therapy Confers Equivalent Survival to Mastectomy**

For the first 80 years of the last century, mastectomy was considered the treatment of choice for women with newly diagnosed, early stage breast cancer. The long-term safety of breast-conserving surgery in the treatment of breast cancer has since been proven for more than 3 decades in randomized controlled trials and in meta-analysis of trials.5–9,27 These have all shown equivalent long-term survival in women treated with breast-conserving surgery or mastectomy.5–9,27 Primary tumor excision alone has, for most patient groups, been associated with high risks of local (in-breast) recurrence. Randomized controlled trials that compared breast-conserving surgery alone to breast-conserving surgery with radiation therapy have shown that the risk of local recurrence in those patients who receive radiotherapy is significantly reduced; an overview of all existing trials shows that radiation therapy provides a 70% proportional reduction in local recurrences with a 10-year risk of local recurrence of approximately 10%.28 Furthermore, these trials demonstrate a small, but significant, reduction in mortality for the patients who received radiation.28 Ten-year, local, recurrence rates of 5% to 10% are now reported in nonrandomized studies in many settings.10–15 In this regard, adjuvant radiotherapy plays a key role in achieving local control in women treated with breast-conserving surgery. Thus, the goal of breast-conserving therapy (breast-conserving surgery with adjuvant radiotherapy) is to achieve good local control, and to provide women who wish to conserve their breast a good cosmetic outcome.

Standards of care for breast cancer have been defined in clinical guidelines and at consensus meetings, have been advocated by experts,29–34 and provide women with early stage disease a choice between breast-conserving surgery and mastectomy. Selection for breast-conserving surgery is assisted by a large body of knowledge on clinical and histological factors that may increase risk of in-breast recurrence despite radiation and may help identify women who may not receive the best outcome from breast-conserving surgery. These include involvement of surgical margins, the presence of extensive cancer identified clinically and/or on mammography, or the presence of locally advanced cancer.12–15,29,33–37 When histology demonstrates cancer cells at the margins of the initial excision (surgical biopsy), then treatment may include re-excision surgery followed by radiotherapy. When clear margins cannot be achieved, mastectomy may be indicated. Whereas breast conservation confers the same survival outcomes as mastectomy, it is associated with a higher (but generally low) risk of local recurrence than mastectomy.5,6 Breast-conserving surgery has the advantage of improved psychosocial health in relation to body image and sexuality.38–40 Therefore, a strong recommendation for mastectomy over breast-conserving surgery, or the introduction of interventions leading to forgoing the opportunity for breast-conserving surgery, must be given very carefully and should be based on evidence that this will improve clinical outcomes.

**Evidence on MRI in Preoperative Staging of the Breast**

**Detection of Additional Disease in the Ipsilateral (Affected) Breast**

Numerous nonrandomized (mostly case-cohort) studies during the past 10 years have demonstrated that MRI increases detection of tumor foci, in addition to the index cancer, not identified with conventional imaging25,41–59 (Figs. 1–3). Meta-analysis of all observational studies of preoperative MRI has shown that the median prevalence of detection of additional foci of cancer within the affected breast is 16% (interquartile range, 11% to 24%) based on 2,610 women with recently diagnosed cancer.25 In Table 1, we present evidence for MRI’s incremental (additional) detection on the basis of studies that have quantified both detection of additional cancer foci (ordered from the highest to the lowest proportion of incremental detection).
and their distribution in the affected breast (multifocal or multicentric). Experts have pointed out that the detection of additional malignant disease by MRI parallels the distribution that has been recognized in landmark histological studies, namely that the vast majority of additional cancer foci are within the same quadrant as the index cancer. If this were the case, then it would be an indicator that MRI is unlikely to contribute to improvement of clinical outcomes, because the additional MRI-detected disease would reflect that which has been treated successfully with radiation therapy for almost 4 decades.

Our summary of the evidence (Table 1) shows diverse estimates of percentages of patients in whom additional, multifocal, or multicentric cancer was detected by preoperative breast MRI. Incremental MRI-only detection varies between approximately 1% and 28% for multifocal cancer and between 2% and 15% for multicentric cancer. It may be argued that the variability in reported data for MRI’s detection of additional cancer foci is a reflection of changes in MRI technology. In a recent systematic review, Warren et al examined MRI technical parameters (such as slice thickness, or number of sequences after administration of contrast medium) and found that neither technical variables nor study time-frame were significantly associated with MRI’s incremental detection in this clinical context.

It is these findings on MRI’s detection capability that have led to widespread adoption of preoperative MRI in early stage breast cancer, because, in theory,
detection and removal of these previously unrecognized cancer deposits would lead to improved outcomes, either with regard to surgical planning or with regard to fewer locoregional recurrences, or even fewer distant metastases and deaths. However, in addition to detecting previously occult cancer foci, MRI is also associated with false-positive findings—the pooled estimate of true-positive to false-positive MRI-detection was 1.9:1 in a recent overview. Thus, regardless of the clinical significance of the cancer deposits detected by MRI, patients should be informed of the increased costs and the additional diagnostic procedures (which may include further imaging, needle and/or surgical biopsy, or second-opinion consultations) that this approach will entail. Women should also be informed of surgical implications including potential impact on cosmetic outcome, as will be further outlined.

The Impact of Preoperative MRI on Surgical Treatment and Planning

Because of the enhanced detection of previously occult tumor deposits compared with routine imaging evaluation, MRI has been applied in preoperative breast staging, particularly in North America and in some European countries. MRI has been adopted in this setting on the basis of assumptions outlined earlier in this article, despite the absence of evidence demonstrating clinical benefit. Specifically, the assumption that MRI will improve surgical care by helping to plan the extent of local resection of the tumor, thus avoiding the need for re-excision surgery, is not supported by data. In Table 2, we summarize the evidence from studies reporting surgical outcomes attributable to preoperative MRI in women with newly diagnosed breast cancer. Data on the effect of MRI on re-excision surgery is limited to evidence from 1 randomized controlled trial and 2 observational (retrospective) studies. None of these studies demonstrated that preoperative MRI improves surgical planning or precision as shown in the data (Table 2).

The only evidence from a randomized trial on the impact of MRI on surgical planning comes from 1 randomized controlled trial that was designed to measure the effect of MRI on re-excision rates as its primary endpoint, and which has been reported only in abstract form. In this trial (COMICE, Comparative Effec-
tiveness of MRI in Breast Cancer), 1,625 women scheduled for breast-conserving surgery were randomly assigned to preoperative evaluation with MRI or not. Re-excision rates were almost the same in women randomized to receive conventional assessment (19.3%) or to receive MRI in addition to conventional assessment (18.8%); $P = .8$. Two additional, nonrandomized studies have also recently reported that MRI was not associated with a significant reduction in positive margins after local excision (Table 2). In 1 of these

| STUDY AUTHOR AND DESIGN* | STUDY POPULATION. NO. OF SUBJECTS (% WITH DCIS-ONLY INDEX CANCER WHERE INCLUDED); MEAN OR MEDIAN AGE, Y [RANGE] | NO. (%) WITH ADDITIONAL MRI-ONLY DETECTION† | ESTIMATED PPV OF MRI-ONLY DETECTION | NO. (%) WITH MRI DETECTION IN SAME QUADRANT; MULTIFOCAL CANCER | NO. (%) WITH MRI DETECTION IN DIFFERENT QUADRANT; MULTICENTRIC CANCER‡ |
|--------------------------|-------------------------------------------------------------------------------------------------|-----------------------------------------------|--------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------------|
| Godinez60 R | Candidates for BCS and eligible for PBI. N=79 (15%); 48 [29-75] | 30/79 (40.0) | 57.0% | 22 (27.8) | 8 (10.1) |
| Zhang46 P | Fine-needle cytology diagnosis of breast cancer, confined to 1 quadrant, candidates for BCS. N=54 (22%); 55 [33-75] | 14/491 (28.6) | 73.4% | 7 (14.3) | 7 (14.3) |
| Liberman45 R | Core needle biopsy-proven breast cancer, confined to 1 quadrant, and candidates for BCS. N=70; 51 [32-78] | 19/70 (27.1) | 52.8% | 14 (20.0) | 5 (7.1) |
| Drew58 P | Women with breast cancer who had MRI. N=178; 56 [47-66] | 41/178 (23.0) | 69.5% | 15 (8.4) | 26 (14.6) |
| Orel54 R | Women with breast cancer who had MRI. N=64; 56 [35-88] | 13/64 (20.3) | 72.2% | 7–9§ (10.9–14.1) | 4 (6.3) |
| Sardanelli55 P | Candidates for mastectomy (whole-breast sectioning as reference standard to define MRI accuracy). N=90; 58.6 [± 16] | 13/801 (16.3) | 41.9% | 4 (5.0) | 9 (11.3) |
| Fischer53 NR | Women with breast cancer who had MRI. N=336 with MRI data from 463; 54 [21-89] | 54/336 (16.1) | 98.2% | 30 (8.9) | 24 (7.1) |
| Boetes56 NR | Candidates for mastectomy (whole-breast sectioning as reference standard). N=60; 53 [32-72] | 8/60 (13.3) | 72.7% | 7 (11.7) | 1 (1.7) |
| Mumtaz59 P | Women with breast cancer confined to 1 quadrant and candidates for BCS. N=90 (7.6%); 49 [29-80] | 10/851 (11.8) | 71.4% | 1 (1.2) | 9 (10.6) |
| Deurloo42 P | Women with breast cancer confined to 1 quadrant and candidates for BCS. N=116; 54 [26-86] | 13/116 (11.2) | 50.0% | 8 (6.9) | 5 (4.3) |
| Bilimoria41 R | Women with breast cancer who were eligible for BCS and had MRI. N=155 (21%); 53 [34-75] | 13/155 (8.4) | 19.1% | 5 (3.2) | 8 (5.2) |
| Al-Hallaq61 R | Candidates for BCS who would have been eligible for PBI based on NSABP trial B-39 criteria. N=110; 57 [34-87] | 9/110 (8.2) | 56.5% to 72.2%¶ | 4 (3.6) | 5 (4.5) |

BCS indicates breast conserving surgery; DCIS, ductal carcinoma in-situ; PBI, partial breast irradiation; PPV, positive predictive value; NSABP, National Surgical Adjuvant Breast and Bowel Project.

*All studies were nonrandomized: P, prospective; R, retrospective; NR, not reported and unclear.

†Subject total in denominator may differ from number of initial subjects in each study because of eligibility for inclusion in analysis of MRI-only incremental detection, as defined by Houssami et al.‡

‡Cases with additional detection in both the same and a different quadrant are included as multicentric.

§Two cases not clearly specified in the same quadrant but are probably multifocal.

¶Estimate may include 2 subjects with lesions in the contralateral breast; however, these have not been included in numbers for multifocal or multicentric detection.

TABLE 2. Incremental MRI Detection in Women with Newly Diagnosed Breast Cancer Based on Studies Reporting MRI-Only Detection and Specifying Quadrant of Additional Disease Foci Relative to the Index Cancer in the Affected Breast

| STUDY AUTHOR AND DESIGN* | STUDY POPULATION. NO. OF SUBJECTS (% WITH DCIS-ONLY INDEX CANCER WHERE INCLUDED); MEAN OR MEDIAN AGE, Y [RANGE] | NO. (%) WITH ADDITIONAL MRI-ONLY DETECTION† | ESTIMATED PPV OF MRI-ONLY DETECTION | NO. (%) WITH MRI DETECTION IN SAME QUADRANT; MULTIFOCAL CANCER | NO. (%) WITH MRI DETECTION IN DIFFERENT QUADRANT; MULTICENTRIC CANCER‡ |
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TABLE 2. Impact of MRI on Surgical Treatment and Planning in Women with Newly Diagnosed Breast Cancer

| STUDY AUTHOR | STUDIES REPORTING CHANGE IN SURGICAL MANAGEMENT ATTRIBUTED TO MRI BASED ON MRI-ONLY DETECTION OF LESIONS OTHER THAN THE INDEX CANCER |
|--------------|-----------------------------------------------------------------------------------------------------------------------------------|
|              | CHANGE IN MANAGEMENT DUE TO MRI-DETECTED MALIGNANT FOCI | CHANGE IN MANAGEMENT DUE TO MRI-DETECTED LESIONS NEGATIVE ON HISTOLOGY (FALSE POSITIVE MRI) |
| STUDIES OF WOMEN WHO WERE BREAST-CONSERVATION SURGERY CANDIDATES AND HAD AN MRI |                                                                                   |
| Bilimoria41  | Mastectomy 8/155 (5.2%)                                                                                                        | Mastectomy 2/155 (1.3%) |
|              | Wider excision 5/155 (3.2%)                                                                                                      | Wider excision 16/155 (10.3%) |
| Deurloo42    | Mastectomy 7/116 (6.0%)                                                                                                         | Mastectomy (none reported) |
|              | Wider excision 6/116 (5.2%)                                                                                                      | Wider excision 1/116 (0.9%) |
| Berg43       | Mastectomy 6/96* (6.3%)                                                                                                         | Mastectomy 5/96 (5.2%) |
| Bagley44     | Mastectomy 6/27 (22.2%)                                                                                                         | Mastectomy 3/27 (11.1%) |
| Zhang46      | Mastectomy 5/54† (9.3%)                                                                                                         | Mastectomy (none reported) |
| Tan 48       | Mastectomy 2/83 (2.4%)                                                                                                          | Mastectomy 1/83 (1.2%) |
|              | Wider excision 3/83 (3.6%)                                                                                                       | Wider excision or additional separate biopsy 7/83 (8.4%) |
| Godinez60    | Mastectomy 8/79 (10.1%)                                                                                                         | Mastectomy 2/79 (2.5%) |
|              | Wider excision 11/79 (13.9%)                                                                                                     | Wider excision 9/79 (11.4%) |
| REPORTED DATA FOR BREAST-CONSERVATION SURGERY CANDIDATES FROM STUDIES OF WOMEN WITH BREAST CANCER WHO HAD MRI |                                                                                   |
| Hollingsworth49 | Mastectomy 24/312 (7.7%)                                                                                                       | Mastectomy 6/312 (1.9%) |
|              | —                                                                                                                                  | Additional separate biopsy 8/312 (2.6%) |
|              | Wider excision (NA)‡                                                                                                            | Wider excision (NA)‡ |
| Schelfout50  | Mastectomy 18/170 (10.6%)                                                                                                       | Mastectomy (none reported) |
|              | Wider excision 24/170 (14.1%)                                                                                                    | Wider excision 9/170 (5.3%) |
|              | Additional separate biopsy 6/170 (3.5%)                                                                                           | — |
| Bedrosian51  | Mastectomy 44/267 (16.5%)                                                                                                       | Mastectomy 2/267 (0.8%) |
|              | Wider excision or additional separate biopsy 5/267 (1.9%)                                                                      | Wider excision 10/267 (3.7%) |
|              | —                                                                                                                                  | Additional separate biopsy 8/267 (3.0%) |
| Hlawatsch52  | Mastectomy or wider excision 5/101 (5.0%)                                                                                         | Mastectomy (none reported) |
|              | —                                                                                                                                  | Wider excision 3/101 (3.0%) |
| Fischer53    | Mastectomy 32/463 (6.9%)                                                                                                        | Mastectomy (NR) |
|              | Wider excision 19/463 (4.1%)                                                                                                     | Wider excision (NR) |
| Orel54       | Mastectomy 5/64 (7.8%)                                                                                                          | Mastectomy (none reported) |
| REPORTED IMPACT ON SURGICAL PLANNING IN WOMEN WHO HAD ROUTINE ASSESSMENT VERSUS THOSE WHO ALSO HAD MRI FROM STUDIES OF WOMEN PLANNED FOR BREAST-CONSERVATION SURGERY |                                                                                   |
| Surgical Outcome | Did not Have MRI | Had MRI | P |
| Did not Have MRI | No. (%) with Outcome | No. (%) with Outcome |
| Turnbull62¶ (COMICE) | Reoperation/Re-excision | 156/807 (19.3) | 153/816 (18.8) | .77 |
| Pengel63     | Positive margins | 35/180 (19.4) | 22/159 (13.8) | .17 |
| Bleicher56   | Positive margins (adjusted for T classification) | 33/239 (13.8) | 11/51 (21.6) | .2 |

Data in Table 2 are partly adapted from Houssami et al25 and updated to include studies published up until January 2009. Study by Turnbull62 was a randomized controlled trial (RCT); all other studies were nonrandomized. COMICE is the Comparative Effectiveness of MRI in Breast Cancer trial; NA indicates not applicable; NR, not reported.

*MRI-based findings recommended mastectomy in 19/96; however, this included some recommendations based on ultrasound and/or the woman’s preference; we have provided data clearly attributable to MRI-only detection.

†MRI recommended mastectomy in 7/54 (however, 2 declined).

‡Study of detection of multicentric cancer.

§Proportion may include cases changed partly because of MRI-defined tumor size.

¶Data obtained from published abstract.
studies, preoperative MRI was associated with an average delay in pretreatment evaluation of 22.4 days; \( P = .01 \). Furthermore, for women who had a preoperative MRI, mastectomy was the initial surgery in 27.7% compared with only 19.5% for women who did not have MRI (odds ratio, 1.8; \( P = .024 \)).

The above findings are underscored by data from a recent meta-analysis of published, nonrandomized studies of MRI in preoperative breast evaluation. This meta-analysis emphasized that MRI evaluation of the affected breast in women newly diagnosed with breast cancer may increase potentially unnecessary surgery (Table 2). Pooled estimates of the impact of MRI on surgical treatment, based on change in surgery attributed to MRI-detection in 12 primary studies (providing data for 1,908 women) showed that 11.3% (95% CI, 6.8–18.3) had more extensive surgery than initially planned, either mastectomy or wider resection of the preserved breast. Although perhaps less drastic than unnecessary mastectomy, the latter may compromise cosmetic outcome, because this is significantly affected by the volume of tissue removed. Pooled estimates showed that 8.1% (95% CI, 5.9–11.3) of all women eligible for breast-conserving surgery were treated with mastectomy because of MRI-only detection of additional disease. A further 5.5% (95% CI, 3.1–9.5) of women had more extensive surgery (wider excision or mastectomy) because of false-positive findings on MRI including 1.1% (95% CI, 0.3–3.6) who were converted to mastectomy. Table 2 illustrates the impact of MRI in individual studies and is partly based on this overview. At the least, these pooled results suggest that if MRI is performed, the false-positive rate dictates that abnormal findings should be investigated with image-guided needle biopsy to establish a diagnosis before surgical treatment.

Of note, the pooled estimates for incremental MRI detection and related change in surgical treatment are derived from random effects logistic-regression models. This method takes into account both the within-study variability and the between-study variability; hence, smaller studies will have less weight in the overall estimate than larger studies. Point estimates for MRI-attributable conversion of surgery may, therefore, seem conservative relative to the study-specific data shown in Table 2. Study-specific data on conversion to mastectomy (counting both true-positive and false-positive MRI detection) range from 3.6% to 33.3% (Table 2), so the impact of MRI on surgical treatment will vary between breast services.

In summary, with regard to surgical care, there is consistent evidence that MRI changes surgical management (generally from breast conservation to more radical surgery); however, there is no evidence that it improves surgical treatment or outcomes. The expectation that MRI would help decrease the need for re-excision surgery is, thus, not supported by existing evidence (based on a limited number of studies), whereas data in Table 2 demonstrate evidence of conversion to mastectomy attributed to preoperative MRI (based on a larger body of evidence). Overall, there is growing evidence that MRI does not improve surgical care, and it could be argued that it has a potentially harmful effect.

**Does Preoperative MRI Improve Long-Term Outcomes?**

The second assumption about preoperative MRI is that by identifying foci of cancer, which would have remained occult on the basis of standard assessment, and ensuring surgical removal of MRI-detected, additional disease, MRI will potentially reduce in-breast recurrence. This assumption has not been addressed in randomized trials, and data from 2 observational studies have reported conflicting findings. In a retrospective study, Fischer and colleagues (University of Gottingen) reported that women evaluated by MRI had a significantly lower local recurrence rate (1.2%) at 40 months than women who had standard preoperative assessment (6.8%; \( P < .01 \)). This study is limited by imbalances in surgical treatment and adjuvant systemic therapy between the groups being compared, which would be expected to bias estimate-of-effect in favor of MRI. In a second, nonrandomized study, Solin and colleagues (University of Pennsylvania) compared longer term outcomes in women who had or had not received preoperative MRI in a well-defined clinical cohort of women with early stage breast cancer. They observed that MRI staging was not associated with any differences in the 8-year rates for the following (had MRI vs did not have MRI): any local recurrence (3% vs 4%; \( P = .51 \)), local-only first site of recurrence (3% vs 4%; \( P = .32 \)), overall survival (86% vs 87%; \( P = .51 \)), cause-specific survival (94% vs 95%; \( P = .63 \)), or freedom from distant metastases (89% vs 92%; \( P = .16 \)).
Perspectives on the Evidence

Our view is that the evidence on preoperative MRI indicates that it is of little benefit for the average woman with newly diagnosed, early stage breast cancer. It does not appear to improve surgical planning (as had been previously assumed), and there is very limited and inconsistent evidence on its long-term impact on clinical outcomes. Taken as a whole, there are 2 persistent concerns based on current evidence. First, the technical false positives cause unnecessary diagnostic biopsies that may compromise cosmesis and may further raise anxiety in patients who are already, by virtue of their recent diagnosis, under stress. Second, and perhaps more important, is the concern that although MRI detects previously unrecognized, but pathologically confirmed, cancer deposits, these deposits may be biologically and clinically irrelevant in a patient who will undergo standard excision and breast irradiation. Because the overall, long-term, local-recurrence rates for breast-conserving surgery using standard breast imaging and pathology criteria are routinely less than 10%, the 15% to 20% detection rate of additional cancer foci reported in MRI series clearly underestimates or ignores the beneficial effects of postoperative breast irradiation, and overestimates the risk of subsequent in-breast recurrence if the test was not performed. The assumption that detection and surgical treatment of previously occult tumor deposits is beneficial also ignores the effect of systemic therapy, which has been shown to reduce the risk of local recurrence in women treated with breast-conserving surgery.29

Pertinent to this discussion is that the small risk of in-breast relapse is present long term, with trials reporting cumulative incidence rates between 8.8% and 14.3% at 20-year follow-up.5,6 Most of the in-breast recurrences occurring after the first 10 years post-breast-conserving therapy are believed to be new primary breast cancers66 and not cancers recurring as a result of therapeutic failure. Because these late recurrences are not biologically present on initial diagnosis, an informed choice for women, some of whom may prefer to have mastectomy for their treatment to reduce the very small but relentless risk of in-breast recurrence, is unrelated to preoperative MRI evaluation.

There may be a potential role for preoperative MRI in assisting patient selection for partial breast irradiation. However, at present, the results of randomized controlled trials evaluating the efficacy and long-term safety of partial breast irradiation as a therapeutic option in early stage breast cancer are unavailable.67

What Are the Data for the Contralateral (Unaffected) Breast?

We have focused on MRI in evaluation of the affected breast. In addition, the adoption of pretreatment MRI for screening the contralateral (unaffected) breast in newly diagnosed women warrants discussion. Studies have shown that MRI detects synchronous, contralateral breast cancer that is not detected clinically or with conventional imaging in approximately 1% to 18% of newly affected women.24,41–44,49,50,52,53,68–70 It is also associated with false-positive findings,24,41–44,49,50,52,53,68–70 which may necessitate further imaging, needle biopsy, and/or surgical biopsy. In a systematic review of the evidence (22 observational studies) on MRI screening of the contralateral breast in 3,253 women with an established, invasive cancer of the affected breast, Brennan et al71 recently identified the following outcomes:

- MRI-only–detected abnormalities (true-positives and false-positives) were identified in 9.3% (95% CI, 5.8–14.7) of women.
- Less than half of these MRI-detected lesions were cancers, so the estimated, incremental cancer detection rate for contralateral breast cancer, based on pooled data, was 4.1% (95% CI, 2.7–6.0).
- A summary estimate for MRI’s incremental, positive predictive value was 47.9% (95% CI, 31.8–64.6) or a true-positive to false-positive ratio of 0.9 to 1.
- Tumor histology, based on data for 114 MRI-only–detected, contralateral breast cancers, was ductal carcinoma in situ in 35.1% and invasive cancer in 64.9%.
- Individual tumor size (reported for only 43 of the MRI-detected contralateral breast cancers) was consistent with early stage cancer; mean size was 6.9 mm (range, 1 mm to 25 mm) for ductal carcinoma in situ and 9.3 mm (range, 3 mm to 17 mm) for invasive cancer.
- Lymph-node status (reported for only 21 invasive
cancers) showed that most of the MRI-detected, contralateral breast cancers were node-negative (pN0 = 17; pNmi = 1; pNx = 3).

- Mastectomy was performed in 10 women with a positive contralateral MRI who did not have a definitive diagnosis: 3 of these 10 women had malignancy in the mastectomy specimen; the remaining 7 had only benign breast changes.71

Summary data reported by Brennan et al71 confirm MRI’s increased detection capability for the contralateral breast, although these authors cautioned that most primary studies in their systematic review did not include consecutive women, so their data were prone to selection bias.71 Selection bias would be expected to overestimate MRI’s detection yield.71 The question of whether this “upfront” detection for the contralateral breast provides a clinical benefit cannot be answered from current evidence—there are several complex issues that factor into the interpretation of data on MRI in the context of contralateral breast cancer. The cumulative incidence rates for metachronous, contralateral breast cancer (in women with a past history of breast cancer) after 10 years of routine follow-up are less than or equal to 5% in contemporary series.10,72 In one of the largest population studies of contralateral breast cancer with long-term follow-up, Gao et al73 reported actuarial rates for contralateral breast cancer of 3% at 5 years, 6.1% at 10 years, 9.1% at 15 years, and 12% at 20 years.74 This risk produces an annualized incidence rate for contralateral breast cancer in the range 0.4% to 0.6% in women with a history of breast cancer. The epidemiology of contralateral breast cancer is increasingly modified by the use of highly effective systemic therapies, including endocrine therapy (particularly in postmenopausal women) and chemotherapy, which may either prevent contralateral breast cancer or inhibit its progress.72,74 The majority of MRI-detected contralateral breast cancer appears to be early stage disease as indicated in a recent overview of contralateral MRI in newly affected women,71 and a considerable proportion is pure ductal carcinoma in situ.71 Whether early detection of contralateral breast cancer in this specific scenario confers benefit in women whose prognosis may be largely determined by an established, invasive cancer is unknown.

The only relevant evaluation, based on the observational study of Solin and colleagues,53 found no significant difference in the 8-year rates of contralateral breast cancer between women who had or did not have preoperative breast MRI staging. If, as we discuss next, randomized trials of preoperative MRI are conducted, the incidence of contralateral breast cancer should be examined as a clinical endpoint allowing sufficient years of follow-up. Randomized controlled trials would also allow valid estimation of the effect of MRI of the contralateral breast on prognosis by removing the biases inherent in cancer screening,75 specifically lead-time and length bias.

Randomized Studies Are Needed Before We Modify Standards of Care in Breast Cancer

The appearance of novel medical technologies, whether directed toward therapy or diagnosis, at times creates enthusiasm over potential clinical utility and adoption of the technology with the assumption, albeit without evidence, that clinical outcomes are improved. Demonstrating a test’s detection yield or capability does not equate with evidence on clinical utility and does not constitute evidence that it improves clinical decisions or patient outcomes.75–78 The current article does not challenge the role of MRI in screening unaffected women with genetically high-risk profiles16,17 or for specific clinical indications where it provides valuable information,18,79 for example, in evaluation of women who present with axillary-node metastases without obvious, primary breast cancers on clinical or mammographic evaluation.19 However, routine use of preoperative MRI in women with established, early stage breast cancer should be discouraged until (and if) high levels of evidence demonstrate that preoperative MRI either improves surgical care, reduces the number of required surgeries, or (more importantly) that it reduces at least local recurrence, if not distant metastases and death due to breast cancer.

Appropriate evaluation of the impact of MRI in local staging of the breast should be determined through well-designed, randomized controlled trials to quantify potential benefit and harm, including careful evaluation of its impact on quality of life. One may argue that the incidence of in-breast recurrence is so low already that the size of such a trial would be prohibitive and impractical to conduct. We do not disagree with this perception, which could be stated as the primary reason that incorporation of MRI into
routine management of patients contemplating breast-conserving therapy may be unwarranted. Surprisingly, preoperative MRI has already been incorporated into clinical practice in the absence of high-level evidence of its clinical utility. We argue that, as for any new medical intervention in the evidence-based era, efforts should be directed to evaluations that generate high-level evidence to clearly define the role of MRI (if any) in this setting and to guide future practice. We, therefore, estimate that approximately 6,600 women would need to be accrued to a randomized controlled trial to determine whether use of preoperative MRI reduces 10-year local recurrence rates in early stage breast cancer by 20% (or 2,900 women for a 30% reduction), assuming a baseline 10% prevalence of local recurrence. If local recurrence rates are only 5%, the sample size would need to be 14,000 women (or 6,000 for a 30% reduction). If one wishes to use an even more important clinical endpoint, such as distant recurrence and/or breast-cancer mortality, the estimated numbers of required patients would be substantially higher. Alternately, it would be reasonable (and more feasible in terms of patient recruitment) to assume that randomized controlled trials demonstrating a relative reduction in local-recurrence rates of the magnitude hypothesized in the above estimates would provide a surrogate indicator of a reduction in breast-cancer deaths. We acknowledge that logistics and costs of conducting such large-scale, multicenter trials are enormous. If the technology is truly as beneficial as its proponents claim, then these costs are worth it. If it is not, then they are outweighed by the costs of adopting expensive technology and associated intervention without evidence of clinical benefit.

The history of breast cancer treatment over the last century is riddled with examples in which expert-supported, presumably “better” treatment has been proven to be nonbeneficial or even harmful in appropriately designed trials. These include radical mastectomy versus modified radical mastectomy, mastectomy versus breast-conservation treatment, and high-dose chemotherapy with bone marrow transplantation versus standard-dose chemotherapy, to name a few past dogmas in breast-cancer care. In each clinical scenario, the randomized controlled trial has provided answers that have guided the way toward evidence-based, effective patient care.

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