INTRODUCTION

Breast cancer is a cancer of the epithelial cells lining the lobules and ducts of the breast. In Canadian women, it is the most commonly diagnosed cancer and ranks second in mortality behind lung cancer.1 Triple assessment is the standard approach for diagnosis, and consists of clinical assessment, imaging and pathology, to guide appropriate treatment. More recently, the use of preoperative MRI, which allows for superior tumour delineation, has become popular in efforts to reduce surgical re-excision rates and increase the efficacy of breast-conserving surgery. A variety of recently published studies, which have investigated the impact and efficacy of preoperative MRI on re-operation and recurrence rates, were reviewed. Notably, the COMICE trial concluded there was no statistical difference in re-operation rates (19%, 19%, p=0.77) between patients who received a preoperative MRI and those who received only standard triple assessment. A number of other studies showed variability in re-operation and recurrence rates for preoperative MRI. Based on this current evidence, preoperative breast MRI cannot be recommended solely to lower re-excision rates, however further research must be done in this area.

ABSTRACT

Breast cancer is the most frequently diagnosed cancer among Canadian women. Since early detection is associated with decreased morbidity and mortality, mammographic screening is standard protocol for women over the age of 50. Suspicious findings are evaluated using a triple assessment approach, consisting of a clinical assessment, imaging and pathology, to guide appropriate treatment. More recently, the use of preoperative MRI, which allows for superior tumour delineation, has become popular in efforts to reduce surgical re-excision rates and increase the efficacy of breast-conserving surgery. A variety of recently published studies, which have investigated the impact and efficacy of preoperative MRI on re-operation and recurrence rates, were reviewed. Notably, the COMICE trial concluded there was no statistical difference in re-operation rates (19%, 19%, p=0.77) between patients who received a preoperative MRI and those who received only standard triple assessment. A number of other studies showed variability in re-operation and recurrence rates for preoperative MRI. Based on this current evidence, preoperative breast MRI cannot be recommended solely to lower re-excision rates, however further research must be done in this area.

Efficacy of Preoperative MRI on Lumpectomy Re-Operation Rates in Breast Cancer

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Shawn Dason

INTRODUCTION

Breast cancer is a cancer of the epithelial cells lining the lobules and ducts of the breast. In Canadian women, it is the most commonly diagnosed cancer and ranks second in mortality behind lung cancer.1 Triple assessment is the standard approach for diagnosis, and consists of clinical assessment, diagnostic imaging and needle biopsy (Figure 1). The diagnosis and management of breast cancer requires the participation and cooperation of a multidisciplinary team, ranging from surgical oncology for excision to medical oncology for a chemotherapy regimen.2

Over the course of surgical treatment, the quantity of tissue to be excised becomes an important consideration. There is ample evidence to support breast conservation surgery in select cases over modified radical mastectomy, providing better cosmetic and psychosocial outcomes with no decrease in survival.3,4 However, inadequate tissue removal may leave positive margins and residual cancer, necessitating a second operation for re-excision. Current Canadian clinical practice guidelines suggest the use of preoperative mammography to determine whether to perform a lumpectomy or mastectomy; intraoperative margins are determined by inspection.7 Consequently, re-excision rates can be significant, ranging from 0% to 63%.6 While intraoperative frozen section or cytological techniques, such as imprint cytology, may be performed to guide margins and prevent re-excision, they are not always cost effective or available.2,8 The use of preoperative magnetic resonance imaging (MRI), a safe and widely available imaging modality, to reduce re-excision rates has been investigated in several recent trials.

The American College of Radiology and the European Society of Breast Imaging currently support the use of MRI for evaluation of the contralateral breast.12,13 Four percent of individuals may have a contralateral breast malignancy and early detection has been shown to increase relative survival from 27% to 47%.14,15 There is also evidence suggesting clinical outcomes may not be improved.16 Therefore, determining additional indications for preoperative MRI, such as reductions in re-operation rates, would be an important factor in encouraging its use.
Figure 1. Triple Assessment
1. Clinical History and Assessment
2. Imaging – Mammography is indicated for patients above the age 35, while ultrasound is indicated in high risk individuals to reduce the risk incurred with radiation
3. Biopsy – Core needle biopsy is indicated for suspicious masses, with the modality selection based on the presence of calcifications and quality of the mass

METHODS
Data Sources and Selection Criteria
A literature search with relevant keywords was performed using MEDLINE and the Cochrane Library to find articles published before December 2010 relating to the effect of preoperative breast MRI on re-excision rates following breast conserving surgery.

Keywords included combinations of: “breast cancer”, “MRI”, “re-operation” and “re-excision”. Studies classified as “case report”, “letter” or “editorial” were excluded. Language of publication was not a direct exclusion criterion.

The retrieved articles were reviewed if they were primary studies that addressed the question as to how preoperative MRI might affect re-excision rates.

RESULTS
Out of the 39 articles initially retrieved, four met the inclusion criteria.

Comparative Effectiveness of MRI in Breast Cancer (COMICE), Turnbull et al.
COMICE was a randomized controlled trial (open, parallel group) conducted in 45 UK centers. A total of 1,623 women scheduled for lumpectomy of a biopsy-proven breast cancer were randomly assigned to receive a preoperative MRI (n=816) or no further imaging (n=807). The primary endpoint of the study was the proportion of patients undergoing a repeat operation within six months of random assignment or a pathologically avoidable mastectomy at initial operation. This study concluded that there was no significant difference in re-operation rates between the two groups (19% in both groups, p=0.77).

Mann et al.
These investigators performed a retrospective cohort study on a consecutive series of patients with invasive lobular carcinoma presenting at one of two tertiary care centers between 1993 and 2005. A total of 267 patients met the inclusion criteria, with 99 having undergone a preoperative MRI and 168 having not. Patients who had received a MRI before operation had a re-excision rate of 9%, while those who did not had a re-excision rate of 27% (p=0.010). There was also a trend toward a lower final mastectomy rate when a preoperative MRI had been done (48%) than when it had not (59%, p=0.098). These investigators concluded that preoperative MRI reduces re-excision rates without increasing the rate of mastectomies.

McGhan et al.
These investigators conducted a retrospective study of patients diagnosed with invasive lobular carcinoma at a single institution from 2001 to 2008. Re-operation rates were compared between patients who underwent MRI and those who received conventional management. MRI was not found to significantly lower re-operation rates for close or positive margins (p>0.05). These investigators also noted that MRI had a better correlation (r=0.75) with tumor size at pathology than mammography (r=0.65), clinical breast exam (r=0.63) and ultrasound (r=0.45, all p<0.01). MRI-based tumor size was concordant with pathologic size in 56% of tumors and overestimated tumor size by >0.5 centimetres in 31% of tumors.

Hwang et al.
This prospective cohort study was conducted at Princess Margaret Hospital, Toronto, from 1999 to 2005. The study investigated ipsilateral breast tumor recurrence (IBTR) as well as re-operation rates in patients who received preoperative MRI versus those who did not. The study selected 463 patients diagnosed with invasive carcinoma, whose lumpectomies were performed by a single surgeon, to limit the inherent variability of lumpectomy techniques. The investigators found no significant improvements in IBTR for MRI compared to non-MRI groups (1.8% vs. 2.5%, p=0.4) and no significant differences in re-operation rates.


Table 1. Re-operation Rates for MRI vs. Standard Triple Assessment Only

<table>
<thead>
<tr>
<th>Study</th>
<th>Re-operation Rate, No MRI</th>
<th>Re-operation Rate with MRI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMICE</td>
<td>19%</td>
<td>19%</td>
<td>0.77</td>
</tr>
<tr>
<td>Mann et al.</td>
<td>27%</td>
<td>9%</td>
<td>0.01</td>
</tr>
<tr>
<td>McGhan et al.</td>
<td>17%</td>
<td>7%</td>
<td>0.20</td>
</tr>
<tr>
<td>Hwang et al.</td>
<td>13.3%</td>
<td>11.8%</td>
<td>0.50</td>
</tr>
</tbody>
</table>

No other controlled studies were found that primarily investigated the effect of preoperative MRI on re-operation rates, although several made relevant observations. Grobmyer et al. found that the incidence of margin-positive partial mastectomy requiring re-excision was low (10%) in their uncontrolled retrospective series of 79 patients who received a preoperative MRI.20 In an uncontrolled prospective study, Bhattacharya et al. similarly discuss low re-operation rates (9.5%) and superiority of correlation to histopathological size (r=0.71) in patients receiving a preoperative MRI rather than ultrasound or mammography.21 Conversely, Bleicher et al. and Pengel et al. both found that preoperative MRI did not significantly decrease the incidence of positive margins at lumpectomy.22,23 Finally, at the 2010 meeting of the Radiological Society of North America, Jie et al. reported no significant differences in ipsilateral recurrence rates (3.6% vs. 4.9%, p=0.4) or contralateral recurrence rates (2.0% vs. 3.2%, p=0.6) for patients who received pre-operative MRI vs. patients who did not.24

**DISCUSSION**

**Efficacy**

Compared to other imaging modalities, MRI is best able to define the histopathological extent of the tumor. In theory, the use of preoperative MRI to guide surgical margins should reduce re-excision rates, however, the evidence for its use has been varied. Notably, the COMICE trial makes clear conclusions that there appears to be no link between preoperative MRI and re-excision rates on a large scale.17

In a review of the COMICE trial, Morris raises some important points, which could impact its generalizability. She suggests that the trial may have been conducted in a setting where tissue margins of the initial surgical excision were quite wide.24 With a more radical approach to excision, the usefulness of MRI relative to standard triple assessment is difficult to elicit, as the surgeon would be more likely to successfully excise all malignant foci regardless of any extra information MRI may provide.

It is also noted that the trial spanned six years, over which advancements in MRI-guided biopsy and localization may provide a larger mean resource cost per patient (GBP £5,508.40 vs. £5,213.50), but this was not statistically significant after controlling for other covariates. While the COMICE trial concluded that preoperative MRI did not detection of contralateral breast cancer (1.6%), either reflecting a real difference or the quality of imaging and interpretation. Finally, a large number of subjects (14%) who were enrolled in the trial were recruited by physicians who recruited only one to two patients per year, introducing a potential selection bias. Curiously, the trial also assessed re-operation rates as the primary endpoint rather than recurrence or mortality, which may be more clinically significant.

**Invasive Lobular Carcinoma**

It may be that preoperative MRI reduces re-excision rates under specific conditions. When only invasive lobular carcinoma (ILC) was included in the study by Mann et al., re-excision rates were 27% and 9% in the no-MRI and MRI groups, respectively.18 The McGhan et al. study makes a similar conclusion when distal recurrence is considered with re-operation.19 Perhaps some intrinsic property of ILC, such as its increased propensity to be incompletely excised, causes a preoperative MRI to decrease re-excision rates.18 It was noted in the COMICE trial that ILC tended to have higher absolute re-excision rates.17 Further study of this phenomenon may identify a set of criteria for which preoperative MRI should be used in consideration for surgery.

**Surgical Use**

Although groups in the studies examined were divided based on whether they received an MRI or not, the actual extent to which the images were used in surgical planning was not evaluated. It would be important to determine the mechanisms by which MRI may guide margins and therefore affect re-excision rates. For example, margin width has been found to have an impact on ipsilateral recurrence rates and would be an important variable to consider in multicenter studies.26 Further, adoption of preoperative MRI on a large scale would require creation of guidelines outlining specific indications for its use, the nature of consultation with the interpreting radiologist, and effective surgical planning techniques.

**Cost**

The COMICE trial investigators conducted a concurrent economic analysis.27 They found that the group receiving a preoperative MRI had a larger mean resource cost per patient (GBP £5,508.40 vs. £5,213.50), but this was not statistically significant after controlling for other covariates. While the COMICE trial concluded that preoperative MRI did not
lower re-operation rates overall nor improve quality of life, it is important to note that there is evidence for its use in detecting contralateral breast cancer and in reducing re-operation rates in specific types of breast cancer.14,18,27 These additional benefits suggest that a preoperative MRI can be recommended without a significant cost increase. Since the COMICE trial was conducted in the United Kingdom, further study in a Canadian context is necessary to determine its applicability to the Canadian healthcare system.

CONCLUSION

With conflicting evidence, preoperative breast MRI cannot currently be recommended solely to lower re-excision rates. However, breast MRI does have other important uses, including contralateral breast cancer detection. Further research into preoperative breast MRI is needed to determine under what conditions it is indicated. Decreasing costs, improved technology and interpretation, and wider availability of MRI should be important factors in strengthening this recommendation in the future.

REFERENCES