Meta-analysis of the effect of preoperative breast MRI on the surgical management of ductal carcinoma \textit{in situ}

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\textbf{Background:} MRI has been used increasingly in the diagnosis and management of women with invasive breast cancer. However, its usefulness in the preoperative assessment of ductal carcinoma \textit{in situ} (DCIS) remains questionable. A meta-analysis was conducted to examine the effects of MRI on surgical treatment of DCIS by analysing studies comparing preoperative MRI with conventional preoperative assessment.

\textbf{Methods:} Using random-effects modelling, the proportion of women with various outcomes in the MRI versus no-MRI groups was estimated, and the odds ratio (OR) and adjusted OR (adjusted for study-level median age) for each model were calculated.

\textbf{Results:} Nine eligible studies were identified that included 1077 women with DCIS who had preoperative MRI and 2175 who did not. MRI significantly increased the odds of having initial mastectomy (OR 1.72, \(P = 0.012\); adjusted OR 1.76, \(P = 0.010\)). There were no significant differences in the proportion of women with positive margins following breast-conserving surgery (BCS) in the MRI and no-MRI groups (OR 0.80, \(P = 0.059\); adjusted OR 1.10, \(P = 0.716\)), nor in the necessity of reoperation for positive margins after BCS (OR 1.06, \(P = 0.759\); adjusted OR 1.04, \(P = 0.844\)). Overall mastectomy rates did not differ significantly according to whether or not MRI was performed (OR 1.23, \(P = 0.340\); adjusted OR 0.97, \(P = 0.881\)).

\textbf{Conclusion:} Preoperative MRI in women with DCIS is not associated with improvement in surgical outcomes.

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**Introduction**

Ductal carcinoma \textit{in situ} (DCIS) is the most common form of non-invasive cancer of the breast, and constitutes a spectrum of proliferating malignant cells that are confined within the basement membrane of the ductal epithelium\textsuperscript{1–3}. As a consequence of widespread mammographic screening, DCIS today accounts for 20–25 per cent of newly diagnosed breast cancers, with more than 63 000 cases diagnosed annually in the USA\textsuperscript{4–7}.

In women with DCIS, surgical planning traditionally follows ‘triple assessment’ with clinical examination, mammography and tissue diagnosis. However, in recent years, MRI has been used before surgery in women with DCIS, with the aim of better defining surgical treatment selection and reducing the need for additional surgery after breast-conserving surgery (BCS)\textsuperscript{8–10}.

The use of additional MRI after standard mammography may theoretically help to define the extent of DCIS better\textsuperscript{8,11,12}. Whether the use of preoperative MRI in women with DCIS translates into oncological advantages in terms of local control and survival is far from clear\textsuperscript{12–17}. In this regard, two recent studies\textsuperscript{12,18} reported no advantages for local control of DCIS in patients who underwent preoperative MRI and BCS. Furthermore, preoperative MRI has disadvantages, in that it increases the numbers of unnecessary surgical biopsies\textsuperscript{9,10,13,19}.

Thus, the effectiveness of preoperative MRI in patients with DCIS remains uncertain as recent studies\textsuperscript{9,16,20,21} have suggested that MRI does not lead to improved rates of complete excision and may increase rates of mastectomy. Most studies of MRI in patients with DCIS have
included relatively small numbers of patients, and individual studies to date may have limited statistical power. To examine the effect of preoperative MRI in the management of biopsy-proven DCIS, a systematic review and meta-analysis was conducted of studies comparing patients who had preoperative MRI (MRI group) with those who had triple assessment only (no-MRI group). The primary endpoint was to determine the effect of preoperative MRI on surgical outcomes, specifically the rates of reoperation for positive margins and the rate of mastectomy. A secondary endpoint was to estimate the proportion of patients who had an MRI-triggered change of treatment.

Methods

Study selection

A systematic literature search was performed using the PubMed and Cochrane databases, to identify studies reporting surgical outcomes of preoperative MRI in patients diagnosed with DCIS, using the following keywords: ductal carcinoma in situ, DCIS, intraductal, MRI, magnetic resonance imaging and breast. The ‘related articles’ function was used to broaden the search, and all abstracts, studies and citations scanned were reviewed, as were the references of relevant articles. The latest date for this search was 31 March 2014. No language restrictions were employed.

Inclusion criteria

Studies reporting on patients with demonstration of DCIS on preoperative histology were considered for inclusion in the meta-analysis. The following inclusion criteria were used: comparison of surgical outcomes of patients who had preoperative MRI with those in patients who did not; a controlled study design (either a randomized clinical trial (RCT) or a comparative cohort design); and reporting of at least one of the defined surgical outcomes (described below).

Exclusion criteria

Studies were excluded according to the following criteria: comparison of MRI with no-MRI only in patients with invasive breast carcinomas; comparison of MRI with no-MRI in cohorts that included both invasive breast carcinoma and DCIS where it was not possible to extract data on DCIS separately; outcomes of interest, as specified below, were not reported or were not reported clearly, or where data could not be obtained or calculated separately for each of the MRI and no-MRI groups.

Data extraction and quality assessment

One author reviewed abstracts from the literature search and identified potentially relevant articles. Two authors extracted the following data: publication details, study population and time frame, number of subjects who had surgical treatment with and without preoperative MRI, total number of patients with DCIS, preoperative histology, tumour size, initial surgical intervention (BCS or mastectomy) and final surgical outcomes. To assess the quality of studies, the following information was also extracted: study design (whether randomization was used, and whether prospective or retrospective); whether consecutive subjects were included; and, if a non-randomized design was used, whether the comparison group was appropriate.

Data extraction was consistent between the two reviewers. Where data on surgical outcomes were reported but clarification was needed, the authors of the study were contacted to confirm the data or to obtain clarification. Contact with authors was required for two studies9,20. To avoid overlapping patient groups, where studies reported on the same patients in more than one publication, the most informative and/or most recent article was included.

Outcomes of interest

Surgical outcomes were defined as follows: initial operation (mastectomy or BCS); number of patients with positive margins after breast conservation as initial surgery; number of patients who had a reoperation after initial BCS (re-excision or conversion to mastectomy); overall number who underwent mastectomy (mastectomy as initial surgery plus mastectomy after initial BCS); and MRI-triggered change of treatment (patients for whom initial surgical planning was reported to have been modified because of MRI findings), including both change from breast conservation to mastectomy, and from unilateral to bilateral surgery.

Statistical analysis

Descriptive statistics (median and i.q.r.) were used to summarize across studies the study-level age, DCIS size and time frame. Random-effects logistic metaregression was used to model the proportion of subjects with the surgical outcomes in separate models defined above, with odds ratios (ORs) estimated for patients who had MRI versus those who did not (reference group). Random study effects were included in all models to allow for anticipated heterogeneity between studies beyond that which would arise from within-study sampling error alone. Allowing for such heterogeneity (both within and between studies) provides
Records identified through initial
literature search (PubMed and Cochrane databases)
\( n = 814 \)

Potentially relevant articles identified
after exclusion of duplicates
\( n = 780 \)

Articles excluded after screening
of title and abstract
\( n = 696 \)

Full-text articles assessed
for eligibility
\( n = 84 \)

Full-text articles excluded
\( n = 43 \)

Studies potentially eligible for
systematic review
\( n = 41 \)

Excluded \( n = 32 \)

- Reported data only for subjects who had MRI (no comparison group) \( n = 21 \)
- Reported only on invasive carcinoma \( n = 5 \)
- Did not report specified surgical outcomes \( n = 3 \)
- Impossible to extract data on patients with DCIS \( n = 2 \)
- Data also reported in a later article from same group (overlapping study) \( n = 1 \)

Studies eligible for meta-analysis
\( n = 9 \) (7 RCCs and 2 RCTs)

Fig. 1 Flow chart of systematic search and selection strategy. *The randomized clinical trials (RCTs) were the COMICE\textsuperscript{23} and MONET\textsuperscript{24} trials; reference 25 was also included, as it is a more detailed version of the COMICE trial\textsuperscript{23}, containing important data for the meta-analysis. DCIS, ductal carcinoma in situ; RCC, retrospective comparative cohort.

valid standard errors, confidence intervals and \( P \) values. Study-specific and pooled proportions (from the meta-regressions), and 95 per cent c.i., were estimated. Statistical significance was set at \( P < 0.050 \).

Because an earlier meta-analysis\textsuperscript{22} of preoperative MRI showed a correlation between receipt of MRI and median age, and based on the summary descriptive data for the median study-level age between the groups being compared, a simple adjustment for age was performed. This was done by fitting age as a binary variable, whereby the study-level median age (or mean age if median was not reported) was categorized as younger than the median value of the study-level median ages or older than that median value, to obtain an adjusted OR for each model\textsuperscript{22}. Because a limited number of studies reported age, an ‘unknown’ category was also included so that all studies could be retained in the analysis when adjusted for study-level age information. It should be noted that this represented a minimal study-level adjustment, and that more complex adjustments or adjustments for more variables were avoided owing to the modest number of studies providing data on co-variables. A sensitivity analysis that excluded one study using a historical comparison group was performed to assess whether excluding that study altered estimates of surgical outcomes.

All analyses were conducted in Stata\textsuperscript{®} version 13.1 (Stata Corp LP, College Station, Texas, USA).

Results

Study characteristics

The flow diagram summarizing the search and study identification for this systematic review is presented in Fig. 1. Nine studies\textsuperscript{9,12,20,23,24,26–29} were eligible for the meta-analysis; seven\textsuperscript{9,12,20,26–29} of these were studies that compared cohorts defined by whether or not MRI was performed, and two\textsuperscript{23,24} were RCTs of preoperative MRI. Four
BCS, breast-conserving surgery.

According to the number of studies reporting the specific surgical outcome and according to whether the analysis applied to all patients or only to those who did not (reference group).

§ Sensitivity analysis excluding one study29 that used a historical comparison group.

Table 2 Models comparing surgical outcomes in patients with ductal carcinoma in situ who had preoperative MRI and those who did not have MRI.

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of patients with DCIS Eligible subjects</th>
<th>Characteristics of the study and quality appraisal</th>
<th>Consecutive subjects with DCIS included or recruited</th>
<th>If not an RCT, was comparison group appropriate?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turnbull et al.23 (2010) (COMICE)</td>
<td>91 Patients with biopsy-proven primary breast cancer scheduled for wide local excision</td>
<td>RCT Yes Yes</td>
<td>Not applicable, as an RCT; patients randomized within same time frame (2002–2007)</td>
<td></td>
</tr>
<tr>
<td>Allen et al.26 (2010)</td>
<td>98 Patients with DCIS who underwent core biopsy</td>
<td>RCC No Yes</td>
<td>Yes, same time frame (2007)</td>
<td></td>
</tr>
<tr>
<td>Itakura et al.9 (2010)</td>
<td>149 Patients with DCIS who underwent core biopsy</td>
<td>RCC No Yes</td>
<td>Yes, same time frame (2000–2007)</td>
<td></td>
</tr>
<tr>
<td>Peters et al.24 (2011) (MONET)</td>
<td>80 Patients with non-palpable DCIS and IC who underwent core biopsy</td>
<td>RCT Yes Yes</td>
<td>Not applicable as an RCT; patients randomized within same time frame (2006–2010)</td>
<td></td>
</tr>
<tr>
<td>Kropcho et al.27 (2012)</td>
<td>158 Patients with DCIS undergoing BCS</td>
<td>RCC No Yes</td>
<td>Yes, same time frame (2002–2009)</td>
<td></td>
</tr>
<tr>
<td>Shin et al.20 (2012)</td>
<td>87 Patients with DCIS and IC scheduled for BCS</td>
<td>RCC No Yes</td>
<td>Yes, same time frame (2003–2009)</td>
<td></td>
</tr>
<tr>
<td>Davis et al.28 (2012)</td>
<td>218 Patients with DCIS who underwent core biopsy</td>
<td>RCC No Unclear</td>
<td>Yes, same time frame (2007–2011)</td>
<td></td>
</tr>
<tr>
<td>Pilewskie et al.12 (2014)</td>
<td>2321 Patients with DCIS who had BCS</td>
<td>RCC No Yes</td>
<td>Yes, same time frame (1997–2010)</td>
<td></td>
</tr>
</tbody>
</table>

DCIS, ductal carcinoma in situ; RCT, randomized clinical trial; RCC, retrospective comparative cohorts of patients with DCIS; IC, invasive carcinoma; BCS, breast-conserving surgery.

Table 2. Models comparing surgical outcomes in patients with ductal carcinoma in situ who had preoperative MRI and those who did not have MRI.

<table>
<thead>
<tr>
<th>Design</th>
<th>No. having MRI†</th>
<th>No. having no MRI†</th>
<th>Estimated pooled proportion with outcome (%)</th>
<th>Model OR</th>
<th>OR adjusted for age‡</th>
<th>P for model‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI</td>
<td>No MRI</td>
<td>MRI</td>
<td>No MRI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial surgery: mastectomy (5 studies22,24,26,28,29)</td>
<td>319</td>
<td>279</td>
<td>27.6 (21.8–34.3)</td>
<td>18.2 (13.6–24.0)</td>
<td>1.72 (1.13–2.61)</td>
<td>0.012</td>
</tr>
<tr>
<td>Initial surgery: BCS (5 studies22,24,26,28,29)</td>
<td>319</td>
<td>279</td>
<td>71.5 (64.5–77.6)</td>
<td>82.0 (76.1–86.7)</td>
<td>0.55 (0.36–0.84)</td>
<td>0.006</td>
</tr>
<tr>
<td>Positive margins or incomplete excision after BCS as initial surgery (5 studies22,24,26,28,29)</td>
<td>764</td>
<td>1924</td>
<td>22.7 (16.7–30.1)</td>
<td>26.8 (20.1–34.6)</td>
<td>0.80 (0.64–1.01)</td>
<td>0.059</td>
</tr>
<tr>
<td>Reoperation: re-excision or conversion to mastectomy after BCS as initial surgery (6 studies22,24,26,28,29)</td>
<td>294</td>
<td>252</td>
<td>21.3 (15.6–28.5)</td>
<td>25.0 (18.6–33.0)</td>
<td>0.82 (0.65–1.03)</td>
<td>0.082</td>
</tr>
<tr>
<td>Sensitivity analysis*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall mastectomy rate: initial mastectomies plus mastectomies for positive margins after BCS (5 studies20,24,26,28)</td>
<td>383</td>
<td>263</td>
<td>37.9 (29.5–47.0)</td>
<td>34.5 (26.1–44.0)</td>
<td>1.16 (0.78–1.72)</td>
<td>0.475</td>
</tr>
</tbody>
</table>

Values in parentheses are 95 per cent c.i. *Sensitivity analysis excluding one study29 that used a historical comparison group. †Patient numbers vary according to the number of studies reporting the specific surgical outcome and according to whether the analysis applied to all patients or only to those who received initial breast-conserving surgery (BCS). ‡P value for model comparing estimates of each surgical outcome in those who had MRI relative to those who did not (reference group). §Adjusted for model outcomes using study-level median age (see Methods).
Initial mastectomy
Allen et al.\textsuperscript{26}
Itakura et al.\textsuperscript{9}
Peters et al.\textsuperscript{24} (MONET)
Davis et al.\textsuperscript{28}
Obdeijn et al.\textsuperscript{29}
Pooled: 27.6\% MRI versus 18.2\% no MRI

Initial breast conservation
Allen et al.\textsuperscript{26}
Itakura et al.\textsuperscript{9}
Peters et al.\textsuperscript{24} (MONET)
Davis et al.\textsuperscript{28}
Obdeijn et al.\textsuperscript{29}
Pooled: 71.5\% MRI versus 82.0\% no MRI

Positive margins (after BCS)
Turnbull et al.\textsuperscript{23} (COMICE)
Allen et al.\textsuperscript{26}
Kropcho et al.\textsuperscript{27}
Obdeijn et al.\textsuperscript{29}
Pilewskie et al.\textsuperscript{12}
Pooled: 22.7\% MRI versus 26.8\% no MRI

Reoperation or re-excision (after BCS)
Allen et al.\textsuperscript{26}
Itakura et al.\textsuperscript{9}
Peters et al.\textsuperscript{24} (MONET)
Shin et al.\textsuperscript{20}
Davis et al.\textsuperscript{28}
Obdeijn et al.\textsuperscript{29}
Pooled: 41.6\% MRI versus 40.1\% no MRI

Total mastectomy rate
Allen et al.\textsuperscript{26}
Peters et al.\textsuperscript{24} (MONET)
Kropcho et al.\textsuperscript{27}
Shin et al.\textsuperscript{20}
Davis et al.\textsuperscript{28}
Pooled: 13.9\% MRI versus 11.5\% no MRI

Fig. 2 Study-specific and estimated pooled proportions with each surgical outcome for MRI versus no-MRI groups. Study-specific proportions are shown as circles, and pooled proportions as squares; error bars represent 95 per cent c.i. with solid lines for MRI group and dashed lines for no-MRI group. BCS, breast-conserving surgery.
Fig. 3 Estimates of the effect of preoperative MRI on surgical outcomes in patients with ductal carcinoma in situ. Values in parentheses are the number of patients in each model. The adjusted odds ratio is based on study-level age adjustment (see Methods). BCS, breast-conserving surgery

studies20,23,24,29 included patients with both DCIS and invasive breast cancer, whereas five9,12,26–28 included patients with DCIS only. Four studies12,20,23,27 included patients undergoing BCS as primary surgery, whereas five9,24,26,28,29 evaluated preoperative MRI in patients scheduled for either mastectomy or breast conservation as initial surgery. The histological diagnosis of DCIS was obtained before surgery in most patients by means of core biopsy.

Overall, of 3252 patients included in the analysis, 1077 had preoperative MRI and 2175 did not. Characteristics of each study including quality assessment are summarized in Table 1. Patients in the MRI and no-MRI groups were from the same time frame in all studies except one29, which used a historical comparison group. The study-level median age for the patients in the MRI and no-MRI groups was 54.2 (i.q.r. 51.7–57.7) and 60.7 (59.2–63.0) years respectively. The study-level median DCIS size was 2.6 (1.8–3.2) and 2.2 (1.6–2.5) cm respectively. The median study time frame (using mid-point of time frame) was 2005 (i.q.r. 2003–75–2007–5).

Four studies9,26,28,29 reported data for MRI-triggered changes of treatment. The proportion of patients who had changes to initial surgical treatment based on preoperative MRI findings was estimated as 15.7 (95 per cent c.i. 6.1 to 35.0) per cent.

Modelled estimates

The results of the models are summarized in Table 2. The numbers of subjects and studies contributing to each model are shown; subject numbers vary according to the number of studies reporting the specific surgical outcome and according to whether the analysis applied to all subjects or only those who received initial BCS. Table 2 also shows the estimated pooled proportions for each surgical outcome in the MRI versus no-MRI groups, as well as the OR estimated from each model.

In the present meta-analysis, there was evidence that preoperative MRI increased the odds of having mastectomy as initial surgery (OR 1.72, \( P = 0.012 \)); this finding did not change after adjustment for study-level age (adjusted OR 1.76, \( P = 0.010 \)). Conversely, the odds of having BCS were much higher for women who did not have MRI (OR 0.55, \( P = 0.006 \); adjusted OR 0.53, \( P = 0.004 \)). There were no statistical differences between the two groups in the odds of having positive margins or incomplete excision after BCS as initial surgery (OR 0.80, \( P = 0.059 \); OR from sensitivity analysis 0.82, \( P = 0.082 \); adjusted OR 1.10, \( P = 0.716 \)). There were no statistical differences in the odds of having reoperation for positive margins or incomplete excision after BCS (OR 1.06, \( P = 0.759 \); OR from sensitivity analysis 1.16, \( P = 0.475 \); adjusted OR 1.04, \( P = 0.844 \)). The overall mastectomy rate
(initial mastectomy plus mastectomy for positive margins after BCS), however, did not significantly differ according to whether or not MRI was performed (OR 1.23, \(P = 0.340\); adjusted OR 0.97, \(P = 0.881\)) (Table 2).

Figs 2 and 3 show the study-specific and estimated pooled proportions for each surgical outcome, the OR and the age-adjusted OR.

**Discussion**

The use of MRI in breast practice has progressively increased over the past decade. In particular, MRI has been used increasingly in the preoperative assessment of patients with both invasive and non-invasive breast cancer. However, its value remains controversial given that it has not been shown to be useful in improving surgical or long-term outcomes. A recent meta-analysis by Houssami and colleagues\(^1\) indicated an unfavourable harm–benefit ratio for surgical outcomes from the routine use of preoperative MRI, with evidence that it increased mastectomy rates. However, previous meta-analyses have focused mainly on invasive breast cancer\(^2\). The application and potential value of MRI in patients with pure DCIS has been less studied. Hence, the aim of the present systematic review and meta-analysis was to evaluate the role of preoperative MRI in patients with biopsy-proven DCIS with regard to surgical outcomes.

DCIS differs in many respects from invasive cancer through its biological behaviour, mammographic appearance, surgical perspectives, adjuvant treatments, and even MRI patterns\(^\text{3,11,13,11,32}\). Some studies\(^\text{11,33,34}\) have suggested that, in patients with biopsy-proven DCIS, MRI provides potentially a more accurate assessment than mammography of the presence of multicentricity and may provide better evaluation of disease extent. From a surgical perspective, the potential advantages of preoperative MRI in DCIS include fewer re-excisions for positive margins and detection of multifocal or multicentric disease if MRI does indeed provide a better assessment than mammography of disease extent. It is therefore plausible that MRI could assist in the surgical planning of patients with DCIS of the breast. However, data from the present meta-analysis provide no evidence that preoperative MRI does improve surgical outcomes. Just as has been shown for invasive cancer, preoperative MRI in women with DCIS in fact appears to lead to increased rates of mastectomy and surgical biopsy\(^\text{13,16,19,20,22}\). One reason for this is that MRI has limited specificity in patients with DCIS (ranging between 58 and 89 per cent) and variable positive predictive value (ranging from 25 to 84 per cent)\(^\text{25}\).

An important finding from the present meta-analysis was that preoperative MRI increased the odds of initial surgery being mastectomy (27.6 per cent in the MRI group versus 18.2 per cent in the no-MRI group). Conversely, the odds of having BCS were significantly higher for women who did not have preoperative MRI (82.0 per cent versus 71.5 per cent in the MRI group). These findings probably reflect the capacity of MRI to detect multifocal and multicentric disease, and thus results in more patients being considered unsuitable for BCS and better treated by mastectomy. In this regard, whether mastectomy is justified in lower-risk patients even if there is extensive DCIS is far from clear. Although MRI identifies more disease than conventional mammography and ultrasonography, there is no evidence in either invasive breast cancer or DCIS that treating this MRI-detected disease with more radical surgery improves outcome. In contrast, it can be argued that MRI does harm as mastectomy is usually advised when occult and multicentric foci are identified by preoperative MRI\(^\text{27,30,36}\).

In the present study the proportion of patients who had a change in their surgical treatment based on preoperative MRI findings was estimated to be 15.7 per cent. Interestingly, this proportion is similar to that in studies of preoperative MRI in invasive breast cancer. A meta-analysis from Houssami and co-workers\(^\text{14}\) estimated that a median of 16 per cent of patients with breast cancer had additional disease identified on preoperative MRI, leading to a change in surgical treatment. Fancellu and colleagues\(^\text{13}\) also found that 16.5 per cent of patients eligible for breast conservation had an MRI-triggered change of initial surgical treatment. Based on very limited information on conversion from initial BCS to mastectomy due to MRI findings with description of correlation with final pathology, it has been assumed that such conversion to mastectomy was appropriate, because in most patients (22 of 23 patients for the 3 studies\(^\text{9,26,28}\)) there was more extensive disease, either larger tumour, or multifocal or multicentric disease. Although this would seem a fair assumption, it remains unclear whether, for some of these patients, BCS would have led to the same prognostic outcomes had MRI not been performed, as suggested in a recent individual person data meta-analysis\(^\text{17}\), and this constitutes part of the ongoing controversy on MRI staging of the breast. Furthermore, although again based on limited data, there was an indication that MRI did not correlate well with exact tumour size measurement at pathology\(^\text{26,27}\), suggesting that the above-mentioned assumed ‘appropriate’ conversion to mastectomy may represent unnecessary radical surgery for at least some of the cases converted to mastectomy on the basis of MRI.

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Thus, it should be acknowledged that the issue of what is ‘necessary’ versus ‘unnecessary’ mastectomy in patients with DCIS is open to debate and interpretation. The presumed justified conversion from BCS to mastectomy, based on pathologically proven more extensive or multicentric disease, may not necessarily translate into patient benefit. Studies have reported that only 30–50 per cent of cases of DCIS evolve to invasive disease if left untreated. Given that much DCIS will not evolve to invasive carcinoma, it could be argued that most of the patients with DCIS treated with mastectomy receive overtreatment. Besides, patients with higher-risk DCIS undergo radiotherapy after BCS, and patients with oestrogen receptor-positive DCIS often receive adjuvant endocrine treatment. These treatments are effective because they treat occult disease in the breast and, therefore, if MRI detects disease that would otherwise have been treated effectively by radiotherapy or endocrine treatment, it is unlikely to improve outcomes. In this context, it is possible that the role of MRI in DCIS will become better defined when there is better understanding of DCIS biology.

Reoperation for tumour-involved margins or incomplete excision after BCS remains a primary concern for breast surgeons and patients. In fact, although DCIS is a non-obligate precursor of invasive carcinoma, it can recur locally as in situ or invasive disease, and positive margins are one of the most important risk factors for local recurrence. In the literature, the rate of reoperation ranges between 10 and 68 per cent, and depends on multiple variables, including differences in selection criteria for breast conservation, surgeon expertise, definition of positive margins, surgical techniques and tumour histotype. The rates of reoperation after BCS are, in general, higher for patients undergoing surgery for DCIS than for those with invasive carcinoma. In a retrospective study, it was reported that 29.5 per cent of women with DCIS in England had at least one reoperation within 3 months after primary BCS. In the present analysis, the rates of positive margins or incomplete excision after BCS, as well as reoperation rates, did not differ statistically between MRI and no-MRI groups, despite the fact that MRI should theoretically have provided a more accurate assessment of tumour extent compared with conventional imaging. These data may be explained by the possibility of discrepancy between the MRI estimate of DCIS size and pathology size, as observed in MRI-specific studies, and perhaps by difficulty in translating MRI images into surgical procedures.

The present meta-analysis showed that the overall mastectomy rate did not differ significantly between patients who had MRI and those who did not, even though the odds of having initial mastectomy were higher in the MRI group. Reoperation rates (including conversion to mastectomy) were also not statistically different between the two groups. This partly reflects that different studies contributed to the different models in the statistical analysis. There was the suggestion of slightly higher reoperation rates in the MRI group, but the lack of significant differences probably also reflects the limited power in some of the models that were based on only a few studies. The model for ‘positive margins or incomplete excision’ included the largest data set in this meta-analysis, and indicated the lack of an effect from preoperative MRI for this important surgical endpoint. It is also possible that at reoperation more of the MRI group had wider excisions, whereas more of the no-MRI group had mastectomy, which would have the effect of rendering similar final overall mastectomy rates for both groups despite the initially higher mastectomy rate for the MRI group.

Histological studies have shown that most DCIS is unicentric. Much of the multifocal disease identified by MRI may be in continuity rather than truly a second focus. Multifocality is not in itself a contraindication to BCS in either DCIS or invasive breast cancer, and satisfactory rates of local control are possible with BCS assuming that the appropriateness of BCS is determined by the ability to excise all of the disease with a good cosmetic result. Some authors have discussed a possible role for MRI in patients with particular subsets of DCIS. Unfortunately, only three studies were randomized trials and most studies eligible for the present meta-analysis reported data on preoperative MRI according to tumour characteristics; hence, there were limited outcome data suitable for subgroup analyses. Recent literature suggests that DCIS is a heterogeneous disease also from a molecular perspective, including different subtypes with different biological behaviour. Identification of subsets of patients with DCIS who might benefit from MRI, if any, awaits further definition of the biology associated with progression to invasive disease or recurrence.

The costs of MRI are of concern in the current era of spending accountability, and the increased time usually taken for obtaining MRI images and results is an important aspect when considering routine use of preoperative MRI. Many have raised concerns also about possible delay in surgical treatment as a result of the time implications of preoperative MRI. These issues are particularly relevant when dealing with a disease typically with an excellent lifetime prognosis, such as DCIS of the breast.

A limitation of this work is the small number of studies that were available for inclusion in the analysis, and that not all outcome data were available for all studies. Furthermore, as identified in the quality assessment, only two studies were randomized trials and most studies...
used a comparison group rather than randomization; therefore selection bias may have affected the results of the primary studies and also of the meta-analysis. The use of a historical comparison group in one study was of concern from a methodological perspective, so its effect on estimated ORs was explored by including or excluding that study through a sensitivity analysis. Despite these acknowledged limitations, the present work represents a large comparative analysis of preoperative MRI in women with DCIS, and the analyses were adjusted for observed imbalances in study-level age between MRI and no-MRI groups, as identified in previous preoperative MRI studies. When interpreting the age-adjusted estimates, it is important to recognize that a study-level adjustment does not entirely account for the potential effect of age, and further adjustment (either more complex statistically, or including more variables) is not appropriate given that so few studies were available.

The present meta-analysis shows that preoperative MRI in women with DCIS is not associated with an improvement in surgical outcomes. MRI increases the initial rate of mastectomy, although the overall mastectomy rate is not significantly increased as a result of MRI. Importantly, this meta-analysis shows that preoperative MRI does not reduce the odds of having negative margins after BCS, nor does it reduce the odds of patients requiring reoperation for positive margins. On the basis of the collective evidence summarized in this meta-analysis, preoperative MRI does not improve the surgical treatment of women with DCIS of the breast.

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