MRI-Guided Quadrantectomy in Patients with Ductal Carcinoma in Situ Detected Preoperatively by Mammographic Calcifications

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BACKGROUND: We designed MRI-guided quadrantectomy using 2-dimensional images reconstructed from MRI to enable virtual simulation of breast-conserving surgery. This study evaluated the efficacy of our approach, which involved projection of the 2-dimensional reconstruction images directly onto the breast to guide planned resection compared with the conventional approach with preoperative localization with hooked wires, for patients with ductal carcinoma in situ (DCIS) detected by mammographic calcifications.

STUDY DESIGN: Eighty-six patients with calcifications ≥2 cm in diameter on mammogram who were diagnosed with DCIS on preoperative percutaneous biopsy underwent breast-conserving surgery. In 32 patients, lesion localization was done using the conventional technique of hooked wires. In 54 patients, preoperative planning was performed using supine MRI and projection of reconstructed 2-dimensional images directly onto the breast surface. Surgical outcomes in the 2 groups were compared. In the latter group, we also compared accuracy of DCIS detection between supine MRI and specimen mammography.

RESULTS: Final pathologic assessment of the 86 patients was DCIS in 67 and DCIS with microinvasion (T1mic) in 19 patients. The rate of additional intraoperative margin resection and presence of DCIS at the surgical margin were significantly lower with our MRI-guided technique vs the hooked-wire approach. Supine MRI detected a considerably larger area of DCIS than did specimen mammography.

CONCLUSIONS: Compared with a conventional approach using hooked wires, our MRI-guided quadrantectomy might be useful for patients with DCIS and DCIS with T1mic detected by mammographic calcifications, due to the superior ability to detect DCIS on MRI compared with mammography. (J Am Coll Surg 2014;219:295–302. © 2014 by the American College of Surgeons)

With the development of breast screening by mammography1,2 and the establishment of biopsic methods for identifying abnormal calcifications on mammography,3,4 patients with ductal carcinoma in situ (DCIS) of the breast can now be diagnosed without surgical biopsy.5,6 Despite these situational changes, surgeons must perform an initial operation in patients with DCIS as with breast cancer patients with a mass lesion. As a corollary, patients with DCIS have desired breast-conserving surgery (BCS).7,8 Pioneers in the treatment of DCIS have succeeded in performing BCS using hooked wires for surgical biopsy in patients with abnormal calcifications.9,10

Surgeons would perform BCS actively in DCIS patients, as with breast cancer patients with mass lesions, if the cosmetic outcomes were preserved. Previous articles have reported that the resected volume is deeply engaged in the cosmetic outcomes of BCS in breast cancer patients.12-14 However, because of deformation of

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Drs Sakakibara and Yokomizo contributed equally to this work.

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breast shape at the time of mammography, preoperative estimation of the resected volume is difficult using conventional methods that target calcifications on mammography. New methods that can preoperatively predict the precise volume needed to be resected and allow direct resection of the DCIS lesion are needed. In other words, a new BCS guided by imaging without deformation of breast shape is necessary for patients with DCIS.

Many recent studies have shown the diagnostic superiority of MRI over mammography in patients with DCIS.15-18 In 2004, due to the diagnostic superiority of MRI for BCS, we were successful in developing a supine MRI procedure and surgical technique using a method of projecting reconstructed 2-dimensional (2D) MRI onto the breast surface.19 In DCIS patients with calcifications <2 cm in diameter on mammogram, lumpectomy using our approach substantially decreased the rate of positive margins compared with conventional lumpectomy using hooked wires.19 In addition, due to the difference in surgical technique, lumpectomy using our approach decreased the resected volume substantially compared with conventional lumpectomy.19

From these results, we considered the application of our approach to BCS in DCIS patients with calcifications ≥2 cm in diameter on mammogram. By combining our approach with quadrantectomy in these patients, we produced a new surgical technique that enables virtual simulation of BCS with reconstructed 2D images from MRI, preoperative prediction of the resected volume, and direct resection to the planned extent. In 2007, we started a feasibility study using this new surgical technique in these patients. Until 2006, we performed conventional quadrantectomy using hooked wires. From 2007, we used the new quadrantectomy guided by supine MRI. This study evaluated surgical outcomes of our MRI-guided quadrantectomy in these patients by historic comparison with conventional quadrantectomy using hooked wires. In addition, because our surgical technique produces precisely the same breast positions at the time of MRI and surgery, our surgical technique permitted direct comparison of reconstructed 2D MRI, calcifications on specimen mammography, and extent of DCIS in pathologic specimens. Using this comparison among the MRI-detected lesion, extent of calcifications, and pathologic extent, we discussed differences in surgical outcomes between our quadrantectomy targeting the MRI-detected lesion and conventional quadrantectomy targeting calcifications.

METHODS

Patients

Participants included 220 patients who showed calcifications ≥2 cm in diameter and underwent surgery at our hospital between January 2004 and December 2009. All patients were diagnosed with DCIS preoperatively based on vacuum-assisted core-needle biopsy. In the first period between January 2004 and December 2006, a total of 104 patients underwent surgery. In the second period between January 2007 and December 2009, a total of 116 patients underwent surgery. To estimate the extent of DCIS, both mammography and prone MRI were performed in the first period, and mammography and supine MRI were performed in the second period. Among DCIS patients with nonfocal distribution who showed calcifications ≥2 cm in diameter, DCIS patients with calcifications >10 cm in diameter and multifocal or regional distributions were excluded. In addition, among the DCIS patients with segmental distribution who remained, patients who were predicted to require resection of >20% of the breast were excluded. Those who remained included 32 patients who underwent conventional quadrantectomy using hooked wires in the first period and 54 patients who underwent MRI-guided quadrantectomy in the second period. All patients who underwent surgery received follow-up with mammography and clinical examination every year. The latest recurrence data were collected on December 1, 2012 (first period group: mean follow-up 82 months; range 61 to 107 months; second period group: mean follow-up time 49 months; range 36 to 59 months). The study protocol was approved by the ethics committee of our institute and written informed consent was obtained from all patients before participation.

Supine breast MRI in surgical position acquisition and MRI-guided quadrantectomy

Acquisition of supine MRI in the surgical position was performed as described previously.19 The MRI examinations were performed using 1.5-T scanner units (NT Intera; Philips Medical Systems) with a flex-M coil. Patients lifted the arm on the affected side and were then fixed in the supine oblique position with use of an oblique board placed at an angle of 10 degrees (Fig. 1A). The lesion site was reconfigured in the maximal intensity projection (MIP) image.
and extent of the lesion was precisely evaluated by the radiologist and surgeons on the MIP image (Fig. 1B). We performed a virtual simulation of the resection line on the 2D MIP image with a 15-mm margin. By measuring the angle of expected resection for the specimen from quadrantectomy, we predicted the expected resection volume and judged whether BCS was indicated (Fig. 1C). A transparent seat scaled down for the projection was created from this MIP image, including the detected lesion and expected resection line (Fig. 1D). Preoperatively, the detected lesion and expected resection line on the transparent seat was projected onto the breast surface using the linac instruments. (F) The extent of DCIS and expected resection line on the transparent seat were projected onto the breast surface.

Figure 1. A 55-year-old woman was preoperatively diagnosed with ductal carcinoma in situ (DCIS) based on vacuum-assisted core-needle biopsy. The major axis of calcifications on mammography was 4 cm long. The patient requested breast-conserving surgery. (A) We performed supine MRI in the surgical position (the patient was placed on an oblique board, with the arm on the affected side lifted; the patient was then fixed in position) to judge the indications for MRI-guided quadrantectomy. (B) Maximal intensity projection (MIP) image showing enhancing segmental lesion in the upper inner quadrant of the right breast. Yellow marker shows position of the nipple. (C) We performed a virtual simulation of the resection line on the MIP image with a 15-mm margin (yellow dashed line). The angle of expected resection for quadrantectomy was about 45 degrees. We therefore predicted a resection volume of about 12.5%, and considered the patient as a candidate for MRI-guided quadrantectomy. (D) Profile of the extent of DCIS and expected resection line on the transparent seat for projection. (E) The patient was placed on an oblique board and the arm on the affected side was lifted. The patient was fixed in the surgical position using the linac instruments. (F) The extent of DCIS and expected resection line on the transparent seat were projected onto the breast surface.

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By measuring the angle of expected resection for the specimen from quadrantectomy, we predicted the expected resection volume and judged whether BCS was indicated (Fig. 1C). A transparent seat scaled down for the projection was created from this MIP image, including the detected lesion and expected resection line (Fig. 1D). Preoperatively, the detected lesion and expected resection line on the transparent seat was projected onto the breast surface using the linac instruments (Figs. 1E, 1F). Methylene blue dye was injected and quadrantectomy was performed (Figs. 2A–2C). Intraoperatively, calcifications present in the specimen were detected using specimen mammography; if there was a possibility of residual calcifications, re-excision was performed immediately.

Prone MRI acquisition and conventional quadrantectomy using hooked wires

Conventional prone-position MRI acquisition was performed as described previously. MRI was performed using 1.5-T MR units (Signa Horizon; GE Medical Systems). Information on lesion extent as detected by MRI was used as a reference. Preoperatively, placement of hooked wires (mean 2.2 wires; range 1 to 4 wires) was performed using mammographic equipment. In all patients, positional relationships of hookwires and calcifications were carefully evaluated on mammography. Locations of calcifications were detected by hooked wires...
and resection lines were determined with a 15-mm safety margin around these lesions on the breast surface. Dye-guided quadrantectomy was performed. Intraoperatively, calcifications present in the specimens were detected using specimen mammography; if there was a possibility of residual calcifications, re-excision was performed immediately.

Pathologic assessments and postsurgical treatments
All specimens were sliced into contiguous 5-mm sections and reviewed by pathologists. For the purposes of this study, conservative criteria for negative margins were used. A negative margin was defined as a negative surgical margin ≥2 mm from the cut end. Patients with tumor exposure close to the surgical margin were considered to have positive margins. When the final pathology indicated positive margins, patients routinely underwent additional excision to obtain negative margins. All patients received radiotherapy after surgery. No patients with DCIS received systemic therapies. In patients with invasive lesion, all patients showing estrogen receptor–positive results received tamoxifen (tamoxifen citrate) or an aromatase inhibitor and no patients received chemotherapy.

Direct comparison of area on images and specimens and statistical analysis
The area of detected lesion on the MIP image from supine MRI (Fig. 2D), 2D extent of calcifications on specimen mammography (Fig. 2E), 2D extent of DCIS in the pathologic specimen (Fig. 2F), and area of resected specimen, including intraoperative additional resection, were all calculated using NIH Image software. In the evaluation of patient characteristics, tumor characteristics, and surgical outcomes, t-tests and chi-square analyses were used. In comparison of the 3 areas (ie, detected lesion on MIP image from supine MRI, extent of calcifications on specimen mammography, and extent of DCIS on pathologic specimen), paired t-tests were used. Values of p < 0.05 were considered statistically significant.

RESULTS
Patient characteristics
In the first period, 32 (30.8%) of 104 patients who showed calcifications ≥2 cm in diameter and were
preoperatively diagnosed with DCIS underwent conventional quadrantectomy using hooked wires (group 1). In the second period, 54 patients (46.6%) of 116 patients who showed calcifications 2 cm in diameter and were preoperatively diagnosed with DCIS underwent MRI-guided quadrantectomy (group 2). Final pathologic assessment of the 86 patients was DCIS in 67 patients and DCIS with microinvasion (T1mic) in 19 patients. Patients and tumor characteristics of the 2 groups, including the 32 patients in group 1 and 54 patients in group 2, are shown in Table 1. Mean lesion size was significantly smaller for patients in group 1 (3.58 cm) than for patients in group 2 (4.08 cm; \( p = 0.017 \)). Age, mean nuclear grade of DCIS, presence of comedo necrosis, and presence of invasive lesions did not differ markedly between groups.

**Surgical outcomes**

Surgical outcomes in patients who received MRI-guided quadrantectomy in group 2 and conventional quadrantectomy in group 1 are shown in Table 2. No difference in mean area of the resected specimen was seen between groups. Mean area of the resected specimen was 45.8 m² in group 1 and 37.6 m² in group 2 (53.1%; \( p = 0.00001 \)). No difference in rate of positive margins was seen between group 1 (37.5%) and group 2 (37.5%). In contrast, rate of additional intraoperative resection after detection of specimen mammography was significantly lower in group 2 (9.3%) than in group 1 (53.1%; \( p = 0.00001 \)). In contrast, rate of exposure of DCIS in a surgical margin was significantly lower in group 2 (3.7%) than in group 1 (18.8%; \( p = 0.02 \)). The preoperative projection of MRI onto breast surface took a mean of 12.5 minutes (range 7 to 20 minutes). Preoperative placement of hooked wires took a mean of 33.6 minutes (range 25 to 45 minutes). Mean time required for projection of MRI in our approach was significantly shorter than that for placement of hooked wires in conventional approach (p < 0.00001). Local recurrence was observed in 2 patients from group 1 (6.3%) and 2 patients from group 2 (3.7%). All local recurrences represented DCIS and were not invasive. No difference in rate of local recurrence was seen between the 2 groups.

**Direct comparison of extent of detected lesion on MRI, extent of calcifications on specimen mammography, and extent of DCIS in pathologic specimen**

In this study, rate of exposure of DCIS in a surgical margin was significantly lower in group 2 using supine MRI projection than in group 1 using hooked wires. However, we intraoperatively detected the presence of calcifications from specimen mammography in both group 1 and group 2. Therefore, theoretically, the extent of resection in group 2 was decided by supine MRI and specimen mammography finally, and that of group 1 was decided by usual MRI and specimen mammography finally. Calcifications on specimen mammography were generically clearer than on standard mammography. These findings might suggest a difference between extent of calcifications on specimen mammography and extent of the detected lesion on supine MRI. Our approach with the same position in supine MRI acquisition and operation allows for direct comparison of the extent of detected lesions on supine MRI (Fig. 2D), extent of calcifications on specimen mammography (Fig. 2E), and extent of DCIS and DCIS with T1mic in the pathologic specimen (Fig. 2F). As a result, we evaluated the difference in area (ie, 2D extent) in patients from group 2 using these 3 values. Mean extent of the MRI-detected lesion, extent of calcifications, and extent of pathologic DCIS and DCIS with T1mic were 8.04 cm², 5.65 cm², and 10.37 cm², respectively. Mean difference between

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<th><strong>Table 1.</strong> Patient and Tumor Characteristics</th>
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*Major axis of calcifications on mammography before biopsy. \( *p < 0.05 \).
extent of MRI-detected lesion and extent of pathologic DCIS and DCIS with T1mic was 2.33 cm², and extent of the MRI-detected lesion was significantly smaller than extent of pathologic DCIS and DCIS with T1mic (p < 0.001; Fig. 3). Mean difference between extent of pathologic DCIS and DCIS with T1mic and extent of calcifications was 4.72 cm², and extent of calcifications was significantly smaller than extent of pathologic DCIS and DCIS with T1mic (p < 0.001; Fig. 3). Mean difference between extent of the MRI-detected lesion and extent of calcifications was 2.39 cm², and extent of calcifications was significantly smaller than extent of the MRI-detected lesion (p < 0.001; Fig. 3). These data indicated that MRI-guided quadrantectomy was theoretically superior as a surgical method for breast cancer patients with DCIS and DCIS with T1mic detected by mammographic calcifications compared with hooked wire-guided quadrantectomy.

DISCUSSION

We succeeded in developing MRI-guided quadrantectomy, which enables virtual simulation of BCS on 2D images reconstructed from MRI, to predict resected volume preoperatively and to directly resect to the planned extent in DCIS and DCIS with T1mic patients with calcifications ≥2 cm in diameter on mammogram. Our surgical procedure decreased rates of intraoperative additional resection and exposure of DCIS in the surgical margins compared with conventional methods using hooked wires according to histologic examination. To the best of our knowledge, this is the first investigation to directly compare the extent of the detected lesion on MRI and the extent of calcification on specimen mammography, and the surgical superiority of MRI-guided surgery over hooked wire-guided surgery was clearly demonstrated.

Because combination therapy including BCS and radiation therapy offers comparable curability and superior cosmetic outcomes compared with mastectomy,20-26 BCS has been selected by many breast cancer patients. However, previous articles have reported that cosmetic outcomes after BCS decayed if the resected volume exceeded 10% to 20%.12-14 In addition, with the development of immediate breast reconstruction using autologous tissue or implants, BCS is no longer the only method for patients seeking to avoid mastectomy.27-29 Due to such changes in background conditions, patients with palpable breast cancer who desire highly cosmetic outcomes after breast surgery are generally recommended to undergo BCS if the predicted resection volume is relatively small, and mastectomy with immediate breast reconstruction if the predicted resection volume is relatively large. In diversifying breast surgery, predicted resection volume has become critical for selecting surgical procedures in breast cancer patients.

In contrast, among patients with nonpalpable breast cancer as typified by DCIS, because precise prediction of the resection volume is difficult, mastectomy with immediate breast reconstruction is often selected.10 In fact, in this study, we used the same indications for BCS of predicted resection volume <20% in both group 1 and group 2. However, among patients treated in group 1 who were evaluated by prone MRI, extent of DCIS and DCIS with T1mic were significantly smaller than in patients treated in group 2 who were evaluated by supine MRI. A previous study has reported that prone MRI is more likely to overestimate the size of DCIS.30

Our MRI-guided quadrantectomy makes it possible to precisely predict the resection volume for patients with...
nonpalpable breast cancer. Because quadrantectomy is basically a 2D resection, it offers a good match for our method for deciding on resection volume using a 2D MIP image from supine MRI. Because we decide the resection line on the basis of diagnosis of the extent of DCIS on the 2D MIP image, the resection volume was easy to predict. In addition, because this diagnosis on the 2D MIP image with surgical margins was projected onto the breast surface and we performed resection on the basis of this projected resection line, diagnosis on the 2D MIP image linked directly to the 2D extent of calcifications on specimen mammography and 2D extent of DCIS and DCIS with T1mic in the pathologic specimen. This direct link between diagnostic imaging and surgery is another advantage of our procedure. Because these links enable comparison of the extent of detected lesion on supine MRI, extent of calcifications on specimen mammography and extent of DCIS and DCIS with T1mic in the pathologic specimen, diagnostic imaging on MRI always provides feedback about surgical results and contributes to continued progress. In this study, we made direct comparisons of the extent of detected lesion on supine MRI, specimen mammography, and pathologic specimen obtained in the same position. The extent of the lesion detected by calcifications on specimen mammography was significantly smaller than that on supine MRI. Many previous studies have shown the diagnostic superiority of MRI compared with mammography in patients with DCIS. This study confirmed those results in a straightforward manner. This superior detection ability of supine MRI compared with specimen mammography was considered one of the central causes of the decreased exposure rate among patients in group 2. In contrast, the rate of positive margins in patients from group 2 was not decreased. However, considering the difference in the mean size of the lesion in the 2 groups, surgical outcomes in group 2 were relatively satisfactory. Because all patients with positive margins received additional resection postoperatively, rates of local recurrence did not differ significantly between groups. In this regard, because the follow-up period for group 2 was shorter than that for group 1, continued and careful observation is required.

Another merit of our approach with supine MRI was a simple surgical procedure after accurate projection compared with the conventional approach with hooked wires. This was considered one of the central causes of the decreased rate of additional intraoperative resection. In contrast, resected volume did not decrease in group 2. This was thought to be causally related to the difference in mean size of lesion in the 2 groups. Because the rate of additional intraoperative resection was lower compared with the conventional approach, and the predicted and actual resected volumes were congruent, our approach with projection of an image from MRI was superior for preserving cosmetic appearance compared with the conventional approach with hooked wires.

A study limitation was that the current study was a nonrandomized, retrospective analysis from a single institution. In this study, we used the same indications for BCS in both group 1 and group 2. However, among patients treated in group 1, extent of DCIS and DCIS with T1mic was significantly smaller than that in patients treated in group 2. This must be confirmed by a prospective study. Another limitation of the current study was the short follow-up period in group 2 (mean follow-up time 49 months; range 36 to 59 months). In this regard, because the follow-up period for group 2 was shorter than that for group 1, continued and careful observation is required.

**CONCLUSIONS**

MRI-guided quadrantectomy enables virtual simulation of BCS using a 2D image reconstructed from MRI to preoperatively predict resected volume and to directly resect to the planned extent in DCIS and DCIS with T1mic patients with calcifications ≥2 cm in diameter on mammogram. In addition, due to the superior detection of DCIS and DCIS with T1mic and the simple surgical procedure after projection, MRI-guided quadrantectomy might decrease rates of additional intraoperative resection and exposure of DCIS and DCIS with T1mic in a surgical margin. Although judging the surgical indications for BCS or immediate breast reconstruction is difficult in those patients with calcifications ≥2 cm in diameter on mammogram, this approach might have promise as a method of judgment. In addition, our diagnosis and procedure for MRI-guided quadrantectomy can receive feedback from the results of pathologic estimation. In the future, advances in this procedure will hopefully lead to substantial improvements in surgical outcomes for those patients with calcifications ≥2 cm in diameter on mammogram.

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Critical revision: Sakakibara, Yokomizo, Miyazaki
REFERENCES


