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ORIGINAL ARTICLE – BREAST ONCOLOGY

Is there a Role for MRI in the Preoperative Assessment of Patients with DCIS?

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ABSTRACT

Background. Breast magnetic resonance imaging (MRI) is used to identify residual and additional disease in patients with invasive carcinoma. The use of MRI in assessing extent of disease for ductal carcinoma in situ (DCIS) is less well defined. This study assessed the value of MRI in the preoperative evaluation of DCIS.

Materials and Methods. We identified 98 patients with DCIS in 2007. Of these, 63 underwent stereotactic biopsy, followed by MRI. There were 35 who underwent stereotactic biopsy alone. Concordance between MRI and histopathology was defined as the presence or absence of residual disease.

Results. There was no significant difference in mastectomy rates between the MRI and non-MRI group (20.3% vs 25.7%, $P = .62$). In patients undergoing breast-conserving surgery (BCS), there were fewer positive margins in the MRI versus the non-MRI group (21.2% vs 30.8%, $P = .41$). Of the 64 cases that underwent preoperative MRI, 43 (67.2%) were concordant. Also, 15 of 43 cases (34.8%) had MRI results that accurately predicted pathologic size. In 28 of 43 patients (65.2%), MRI overestimated disease in 20, by a mean of 1.97 cm. In patients with MRI tumor size >2 cm, MRI overestimated disease by a mean of 3.17 cm. Of the 64 cases, 21 (32.8%) were discordant. Also, 10 of 21 (47.6%) had a positive MRI and no residual disease on histopathology, and 11 of 21 (52.3%) had negative MRI and residual disease on pathology.

Conclusions. MRI does not accurately predict extent of disease in patients with extensive DCIS. In patients with MRI tumor size ≤2 cm, MRI may assist in surgical planning. MRI results in patients with DCIS should be interpreted with caution; decision for mastectomy should not be made on MRI findings alone.

Prior to the routine use of screening mammography, ductal carcinoma in situ (DCIS) comprised approximately 1–2% of all breast cancers. Currently, with the widespread availability of screening mammography, patients with DCIS account for 20–25% of newly diagnosed breast cancer.[1] Mastectomy was once regarded as the gold standard for the treatment of DCIS. However, as data emerged regarding the oncologic efficacy of breast-conserving surgery (BCS) for DCIS, its use has increased over time and has essentially replaced mastectomy in patients with unifocal disease.[2]

The high percentage of positive margins for DCIS following BCS remains a major surgical challenge. Mammography may often underestimate the extent of disease because of its inability to detect noncalcified disease.[3] As a result, patients with positive margins often require additional surgery resulting in an inferior cosmetic result. Accurate preoperative assessment of extent of DCIS with more sensitive imaging studies may eliminate the need for additional surgery.

Magnetic resonance imaging (MRI) of the breast is a useful tool for the detection and characterization of breast disease, as well as assessment of local extent of disease. In patients with invasive breast cancer, MRI has been shown to be accurate in assessing extent of disease as well as additional foci of disease.[4] However, the ability of MRI to accurately assess disease extent in DCIS is less well defined.

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The present study was undertaken to address whether MRI should be used in the preoperative assessment of patients with DCIS and if its use would improve surgical outcomes.

METHODS

For calendar year 2007, 98 consecutive patients with a diagnosis of DCIS were identified in our 3-hospital, community-based health system as recorded by the system's tumor registry. A retrospective chart review was performed after permission was obtained from our institutional review board. Of the 98 patients, 63 were identified who underwent a preoperative MRI following stereotactic biopsy of a lesion yielding DCIS. One patient had synchronous bilateral lesions, giving rise to a total of 64 cases of DCIS. The 35 patients with DCIS who did not have a preoperative MRI prior to definitive surgery were evaluated for margin status and rates of re-excision. Positive margins were defined as cancer present at the inked margin.

Each patient had a mammogram that demonstrated an abnormality requiring biopsy. Subsequently, each patient underwent minimally invasive biopsy. A total of 23 patients had mammography performed at outside institutions that were not available for review. Of these 23 patients, 11 had their minimally invasive biopsy performed at an outside institution and presented to our health system with a diagnosis of DCIS prior to their MRI. All patients had an MRI at our institution.

MRI examinations were performed with a 1.5-T GE (Signa, General Electric Medical Systems, Milwaukee, WI), using an 8-channel breast-surface coil and VIBRANT software. All patients were scanned in the prone position. Imaging sequences included 1 sagittal series obtained before and 3 series obtained after the injection of 0.1 mmol/l of gadopentate dimeglumine (Magnevist®) per kilogram of body weight delivered through an intravenous catheter given via a power injector at a rate of 3 ml/s, followed by a 20-ml saline flush. A sagittal T2-weighted sequence with fat suppression followed by 3-dimensional, T1-weighted, gradient-echo sequences with fat suppression and delayed axial images was performed. Initial and delayed images were obtained within 4 and 8 min after the injection of contrast material. Spatial-resolution criteria included voxels smaller than 0.9 mm in the frequency-encoding direction, smaller than 1.8 mm in the phase-encoding direction, and 3 mm or smaller in the slice direction, providing full coverage of the breast.

MRI results were reviewed on the institutions' picture archiving and communication systems (PACS). Residual enhancement identified as "suspicious for malignancy" on MRI was considered a positive result and indicative of residual disease. Final pathology results were also reviewed on the institutions' patient chart archival system and compared with MRI results. The pathologic size of DCIS was calculated by using the maximum diameter of DCIS on 1 slide. Concordant patients were those who had MRI and histopathology results that demonstrated residual disease. Similarly, concordance was also defined as absence of residual disease on MRI and histopathology. Discordant patients were those who had MRI and pathology results that did not correlate (i.e., negative MRI and residual disease found on final pathology).

The size of DCIS on MRI used to determine overestimation or underestimation was the single largest diameter of enhancement on MRI. This was only calculated for the 43 concordant cases to determine accuracy. Accuracy in concordant cases was defined as a difference in MRI and pathologic measurements $\leq$1 mm. The size of residual enhancement measured on MRI by the radiologist was compared with the size of residual disease seen on final pathology. The extent of overestimation or underestimation was then calculated based on these measurements. If a patient was noted to have "enhancement at the periphery of the biopsy cavity" on MRI and "DCIS at the periphery of the biopsy cavity" on final pathology, the patients were classified as concordant with the same size on MRI and pathology.

Fisher's exact test was used to test whether mastectomy rates and re-excision rates were different among the MRI and non-MRI groups.

RESULTS

Clinical Characteristics

Table 1 shows the clinical characteristics of our 98 patients with DCIS according to the use of breast MRI. There were a total of 99 cases of DCIS: one patient had bilateral disease. Median age was 60.5 (range, 40–89). A total of 63 patients with 64 diagnoses of DCIS were identified who underwent preoperative MRI. Thirty-five patients underwent stereotactic biopsy alone, without preoperative MRI.

Breast-conserving surgery (BCS) was performed in 77 cases and mastectomy in 22. Table 2 demonstrates the reasons for mastectomy in the 22 patients who underwent this procedure, stratified by use of breast MRI. Patients in the MRI group had similar mastectomy rates as the patients in the non-MRI group (20.3% vs 25.7%, $P = .62$). In the MRI group, four patients elected mastectomy based on extent of disease on MRI. MRI overestimated the extent of disease in all four of these patients by an average of 2.95 cm. None of these patients had MRI biopsy confirmation of extensive disease prior to mastectomy. Of the four patients, three had disease that would have been

TABLE 1 Clinical characteristics of 98 patients with DCIS according to use of breast MRI

Characteristic	Total	Breast MRI performed		*P* value*
		Yes	No	
DCIS cases, *n* (%)	99	64 (64.6%)	35 (35.4%)	
Age at diagnosis				
Mean	61.9	60.5	64.4	
Median	60.5	59	67	
Range	40–89	40–83	41–89	
Surgery performed				
BCS	77	51[a] (79.7%)	26 (74.3%)	
Mastectomy	22	13 (20.3%)	9 (25.7%)	.62
Margin status[b]				
Positive	19	11 (21.2%)	8 (30.8%)	.41
Negative	59	41 (77.4%)	18 (69.2%)	
Re-excision rate	19/78	11/52 (21.2%)	8/26 (30.8%)	.41

BCS breast-conserving surgery

[a] 52 patients originally underwent BCS. One patient had mastectomy as definitive surgery due to positive margins

[b] Margin status was assessed only in those patients who had BCS

* *P* value was calculated using Fisher's exact test to compare the mastectomy and re-excision rates between the MRI and non-MRI groups

TABLE 2 Reasons for mastectomy in 22 patients according to the use of breast MRI

Reason for mastectomy	Breast MRI performed	
	Yes ($n = 13$)	No ($n = 9$)
Positive margins	1	1
Multifocal/multicentric disease	3	7
Local extent of DCIS on imaging	4	0
Family history breast cancer	1	0
Personal history breast cancer	2	0
Patient choice	2	1

amenable to breast conservation based on their pathologic size.

In the patients undergoing BCS, the rate of positive margins was lower in the MRI group of patients than in the non-MRI group (21.2% vs 30.8%, $P = .41$), although this did not reach statistical significance. Re-excision or mastectomy was performed in all cases of positive margins. In the MRI group, 10 of 11 patients with positive margins on initial segmental resection had re-excision with negative margins. Also, 1 of 11 patients went on to mastectomy without an attempt at re-excision. This patient had disease that was overestimated by MRI by 1.1 cm. In the non-MRI group, 8 of 8 patients underwent re-excision and had negative margins at the time of surgery.

Concordance Between MRI and Histopathology

Figure 1 demonstrates the breakdown of the 64 cases of DCIS by concordance and accuracy. Of 64 cases of DCIS, 43 (67.2%) demonstrated MRI and pathology results that were concordant. One patient had bilateral disease with both lesions in the concordant group. Of 43 cases, 15 (34.8%) had an accurate evaluation of residual disease; 10 were the same size on MRI and pathology, 2 were negative on both, and 3 had multifocal or multicentric disease on both. In the remaining 28 of 43 (65.2%) concordant cases, MRI inaccurately assessed the extent of residual disease. Table 3 is a comparison of the overestimation and underestimation of the 28 concordant cases of DCIS with preoperative MRI. In 20 of 28 cases, MRI overestimated the size of residual disease by a mean of 1.97 cm (range, 0.1–9.5 cm). In patients with MRI tumor size >2 cm ($n = 11$), mean overestimation was 3.17 cm (range, 1.1–9.5 cm). In cases of MRI tumor size ≤2 cm ($n = 9$), mean overestimation was 0.40 cm (range, 0.1–0.8 cm). In 8 of 28 cases, the pathologic size of DCIS was underestimated by MRI by a mean of 0.43 cm (range, 0.15–0.8 cm).

Of the 64 cases of DCIS, 21 (32.8%) demonstrated MRI and pathology results that were discordant. In this group, 10 of 21 (47.6%) had positive MRI results and no residual DCIS on final pathology, and 11 of 21 patients (52.3%) had negative MRI results and residual DCIS on final pathology. These false negatives represent 17.2% (11 of 64) of the total cohort of MRI patients, giving rise to a false negative rate of 21.2% (11 of 52). Of the 11 false negatives, one patient had multicentric disease that was not seen on MRI, three had residual DCIS at the periphery of the biopsy cavity, and seven had measurable disease (mean 0.76 cm, range, 0.1–1.9 cm). In the patient whose multicentric disease was not seen on MRI, mammography depicted her extent of disease preoperatively.

Table 4 demonstrates the concordance between MRI and histopathology in the 64 cases of DCIS. Sensitivity and specificity of MRI in determining residual DCIS following minimally invasive biopsy were calculated in our group of patients to be 78.8 and 16.7%, respectively. The positive predictive value of MRI in this setting was 80.4%, and the negative predictive value was 15.4%.

DISCUSSION

With the widespread availability of screening mammography, the incidence of DCIS is increasing over time. DCIS includes 20% of all breast cancers and 30–50% of all

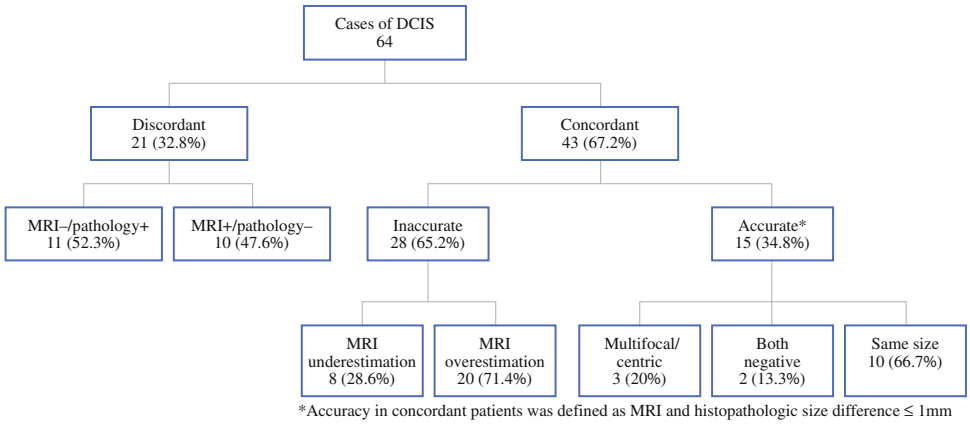

FIG. 1 Breakdown of DCIS patients undergoing MRI by concordance and accuracy

TABLE 3 Comparison of overestimation and underestimation in 28 cases of DCIS with preoperative MRI

DCIS cases	Overestimated	Underestimated
Total	20 (71.4%)	8 (28.6%)
Size (mean)	1.97 cm	0.43 cm
MRI group		
>2 cm	3.17 cm	N/A
≤2 cm	0.40 cm	0.43 cm

TABLE 4 Concordance between MRI and histopathology in 64 cases of DCIS

	Histopathology	
	Positive	Negative
MRI		
Positive	41 (TP)	10 (FP)
Negative	11 (FN)	2 (TN)

TP true positive, *FP* false positive, *FN* false negative, *TN* true negative

mammographically detected cancers.[5] BCS has emerged as the standard of care for the treatment of DCIS. However, surgical management continues to be plagued by our inability to accurately evaluate the extent of disease with standard imaging. Although mammography can detect close to 83% of DCIS lesions, it has limitations and can underestimate the extent of disease.[6] Poor preoperative assessment of extent of disease may lead to high re-excision rates secondary to positive margins. Breast MRI has emerged as an exquisitely sensitive imaging modality to evaluate patients with invasive carcinoma. Its utility in patients with DCIS remains controversial.

MRI detects malignant lesions by demonstrating enhancement after injection of gadolinium-based contrast agents.[7] Enhancement is related to tumor-induced angiogenesis that produces increased blood flow and therefore contrast enhancement.[8] The sensitivity of MRI with regards to DCIS is variable in the literature ranging from 50 to 100%, and this may be related to a slower growth rate of DCIS and lower angiogenesis as seen by Bazzocchi et al.[9–11] Even among DCIS lesions, there is some evidence that MRI is more sensitive in detecting high-grade lesions than low-grade lesions because tumor angiogenesis is more prominent.[12]

In the literature, MRI has been criticized for its increased mastectomy rate in invasive carcinoma.[4] In our study, we found no clinically significant increase in mastectomy rates in patients who underwent preoperative MRI versus those who did not. Interestingly, we did notice that four of the patients in the MRI group underwent mastectomy based on size of MRI enhancement. None of these patients had preoperative MRI-guided biopsy to confirm extensive disease. Three of these patients would have been candidates for breast conservation based on the pathologic size of their cancer. Therefore, although MRI did not show a significant increase in mastectomy rates, three mastectomies may have been avoided had MRI not been performed. As our study is small and retrospective, this may have limited our ability to demonstrate a difference in mastectomy rates. In a study performed at the Mayo Clinic in Rochester, they found that MRI led to a significant increase in mastectomy rate (54% vs 36%) in patients with invasive carcinoma as compared with those who did not undergo MRI.[13] Bleicher et al. found a 1.8-fold increase in the odds ratio of patients undergoing mastectomy and concluded that the increase in mastectomy rate was multifactorial resulting from overestimation of extent of disease in MRI and patient choice.[14] Caution should be used when interpreting size of residual enhancement in patients with DCIS; mastectomy should not be offered based on MRI results alone without biopsy confirmation of extensive or multicentric disease.

In the patients who underwent BCS, we found a lower re-excision rate in those who had preoperative MRI. This did not reach statistical significance, although our study may have been underpowered to detect a small difference,

even if one existed. Other studies have likewise demonstrated that MRI may help limit the need for re-excision in patients undergoing BCS.[6] Schouten van der Velden et al. demonstrated that patients who underwent MRI had fewer positive margins than those who did not (50% vs 81%). Moreover, he found that the MRI group underwent fewer reoperations compared with patients who underwent mammography alone (mean number of operations, 1.5 vs 1.9).[12] In patients undergoing BCS, MRI may assist in surgical planning. In these patients, their smaller volume of disease leads to less overestimation by MRI, allowing for more accurate interpretation of extent of disease. Accurate knowledge of extent of disease may assist in improved preoperative planning, leading to fewer positive margins at initial surgery and fewer re-excisions.

Concordance between MRI and histopathology in patients with DCIS has been reviewed in the past. Our study revealed that 67.2% of the cases demonstrated concordant results between MRI and histopathology. Accurate evaluation of residual disease, however, was seen in only 34.8% of cases. Similarly, Sardanelli et al. found that only 46% of the DCIS lesions in his study were concordant with MRI.[15]

Overestimation of tumor size on MRI compared with histopathology may be caused by ischemic reduction during fixation; however, overestimation appears more pronounced in patients with pathologic tumor size greater than 2 cm.[16] Our study revealed that 31.3% of our patients had overestimation of final pathologic size by MRI similar to the 38% of patients with DCIS reported by Schouten van der Velden.[12] We found a mean overestimation of 3.17 cm in our group of patients with MRI tumor size greater than 2 cm. Onesti et al. had similar results, demonstrating a mean overestimation of 2.40 cm for MRI DCIS lesions greater than 2 cm.[16] Because of the overestimation, more radical surgery is often elected by either the surgeon or the patient to treat their disease. While overestimation may also lead to additional unnecessary biopsies prior to surgery, as demonstrated by Berg et al., this option is preferred to mastectomy in confirming extensive or multicentric disease.[17]

Reported sensitivity and specificity of MRI in the literature has been variable over time. Reported sensitivity of MRI for DCIS ranges from 50 to 100%.[9,10] Differences in tumor size, subtype, and vascularity, as well as differences in MR imaging technique and interpretation may explain the variation in reported sensitivities.[18] Higher specificities are obtained when integrating both morphologic and dynamic criteria. However, the relatively low specificity makes the availability of MRI-guided biopsy mandatory.[9] In our study, the sensitivity and specificity of MRI was 78.8 and 16.7%, respectively. The low sensitivity and specificity of MRI in DCIS compared with invasive tumors may be a result of enhancement in only a fraction of DCIS.[19] False-negative rates have been reported to range from 5 to 80%.[20] Our false-negative rate was calculated to be 21.2%. Peribiopsy cavity inflammation may make it difficult to decipher residual disease from postbiopsy changes on MRI. In addition, an elevated false-negative rate may also indicate that MRI cannot accurately predict the removal of the entire tumor.[19]

Our study has several limitations. It is a nonrandomized, retrospective analysis of a small cohort of patients. Selection bias may have also contributed, limiting our results further, since the use of MRI was left to the clinical discretion of the breast surgeon. Furthermore, the MRI and non-MRI groups were not matched with respect to personal or family history of breast cancer. This history also influenced patients' decision for mastectomy. Finally, in our study, we had a strict definition of accuracy that influenced our calculation of underestimation or overestimation. Perhaps with a less strict definition, MRI could be considered more accurate in DCIS.

In summary, an analysis of 99 cases of DCIS demonstrated equivocal results with regard to the use of MRI in preoperative planning. The use of MRI did not lead to a higher mastectomy rate in this series. However, three patients in the MRI group who would have been amenable to BCS based on pathologic size, underwent mastectomy as a result of overestimation of disease by MRI. In patients undergoing BCS, MRI led to a fewer number of re-excisions compared with the non-MRI group, although this did not reach statistical significance.

MRI and histopathology demonstrated concordant results in 67.2% of patients with DCIS. In this subset of patients, MRI accurately assessed the extent of disease 34.8% of the time. MRI had a tendency to overestimate the extent of residual DCIS, particularly in patients with MRI tumor size >2 cm. Decision for mastectomy based on extent of disease on MRI should be discouraged. Biopsy confirmation of local extent of disease or multicentricity is mandatory prior to recommending aggressive surgery. In patients with MRI tumor size $\leq$2 cm, MRI tumor size more closely correlated with pathologic size. The use of MRI in preoperative planning for patients undergoing BCS led to fewer re-excisions; however, the number of patients in each group is small, and it is difficult to assess whether a true difference exists. A prospective study is needed to determine whether preoperative MRI in patients with DCIS would improve surgical outcomes. In addition, care should be taken when interpreting MRI results in patients with extensive DCIS, as overestimation of tumor size may lead to unnecessary mastectomy.

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