Preoperative Breast Magnetic Resonance Imaging for the Assessment of the Size of Ductal Carcinoma In Situ

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Purpose: The purpose of this study was to determine whether magnetic resonance imaging (MRI) could assess the size of ductal carcinoma in situ (DCIS) more accurately compared to mammography and ultrasonography using the histopathological dimension of the surgical specimen as the reference measurement. Methods: This was a retrospective review study using data from our institution database of breast cancer. Preoperative contrast-enhanced MRI, mammography and ultrasonography were performed to detect and assess the size of DCIS in 131 patients. The greatest dimensions of DCIS determined by the imaging modalities were compared with the histopathological dimensions of the surgical specimens. Intraclass coefficients were calculated to examine the agreement among the MRI, mammography and ultrasonography measurements. The Wilcoxon signed-rank test was used to evaluate the statistical significance of the differences in size among MRI, mammography or ultrasonography and histopathology findings. Results: Of the 131 DCIS lesions, 126 (96.2%) were detected by MRI, 103 (78.6%) were detected by mammography, and 121 (92.4%) were detected by ultrasonography. The mean lesion size was 38.8 mm on histopathology, 36.0 mm on MRI, 28.8 mm on mammography, and 23.3 mm on ultrasonography, and there were no significant differences between sizes determined by histopathology and MRI, while there were significant differences between histopathology and the other modalities. The correlation coefficient between histopathological measurement and MRI was 0.837, versus 0.461 between histopathology and mammography and 0.284 between histopathology and ultrasonography. The lesion size was correctly estimated (± 5 mm), under-estimated (< 5 mm), or over-estimated (> 5 mm), respectively, by MRI in 52.7%, 30.5%, and 16.8% of cases; by mammography in 32.0%, 51.2%, and 16.8% of cases, respectively; and by ultrasonography in 24.4%, 62.6%, and 13.0% of cases, respectively. Conclusion: In our study, MRI was more accurate for detection and assessment the size of DCIS compared to mammography and ultrasonography.

Key Words: Breast neoplasms, Ductal carcinoma in situ, Magnetic resonance imaging

INTRODUCTION

Ductal carcinoma in situ (DCIS) is a noninvasive form of ductal carcinoma, limited to the confines of the basement membrane of the duct. DCIS is a multiform disease with different growth patterns and a heterogeneous set of clinical signs and symptoms [1]. Before the era of screening mammography, DCIS was a relatively uncommon presentation of breast cancer. However, since the introduction of mammography screening programs for breast cancer, the incidence of DCIS has risen consistently. DCIS currently accounts for 15% to 25% of all breast cancers and 30% to 50% of all clinically occult cancers [2,3]. Approximately 40% of cases of DCIS evolve into invasive cancer [4].

Accurate information regarding the extent and distribution of DCIS is important in determining the extent of surgery required. Mammography is the primary tool of radiologists for the detection and assessment of size of microcalcifications. However, mammography is relatively limited in its ability to detect DCIS and assess tumor size because it only detects the calcified portion of DCIS, and it can underestimate or overestimate the histopathological tumor size. Consequently, surgical resection is too often insufficient, resulting in a 30% rate of re-excision because of persistent margin involvement [5], as well as a higher risk of local recurrence [6,7].

Studies have shown that magnetic resonance imaging (MRI) is more accurate than mammography for detecting and assessing tumor size in patients with invasive cancer [8]. The sensitivity of MRI has been reported to vary between 90% and 94% in larger studies and meta-analyses [9,10]. However, few studies have investigated the value of MRI for assessing the extent of DCIS; the initial results are encourag-
ing and demonstrate a fairly good correlation between size determined with MRI and histopathological size [11-13]. However, MRI of the breast in patients with DCIS is not routinely performed and remains experimental. Few studies have examined the effects of breast MRI on surgical management specifically for DCIS [14-16].

The aim of this study was to evaluate the value of MRI for the staging of DCIS, and particularly for the accurate assessment of tumor size in comparison with mammography and ultrasonography, using the histopathological measurements as a reference.

**METHODS**

**Patient selection**

This was a single-center retrospective review from a Samsung Medical Center database of breast cancer. All patients diagnosed with pure DCIS, proven by core needle biopsy or vacuum-assisted biopsy, between January 2013 and December 2014, were included. Patients were excluded if they did not undergo MRI. Patients with multifocal or multicentric lesions were also excluded because of the difficulty in estimating the exact tumor size; thus, 131 patients were eligible for the study. Data obtained for each patient included age; sex; and results of the clinical breast examination, mammography, ultrasonography, MRI, and histopathological examination of the biopsy and surgical specimens. Clinical examination included the patient’s history, hormone receptor status, and physical breast examination.

**Imaging techniques**

Mammography was performed using the Senographe 2000D system (General Electric Medical Systems, Buc, France). Spot compression and magnification views were also obtained in patients with microcalcifications visible on mammography. Assessment of mammograms considered breast density, and abnormalities were scored using the Breast Imaging-Reporting and Data System (BI-RADS) mammography classification [17].

Ultrasonography was performed systematically using the HDI 5000 (Advanced Technology Laboratories, Bothell, USA), iU22 (Philips Medical Systems, Bothell, USA) or LOGIQ700 (GE Medical Systems, Milwaukee, USA), ultrasonography scanner, respectively equipped with commercially available 12- to 7-MHz, and 10- to 7-MHz, linear-array transducers. The examinations were interpreted using the BI-RADS ultrasonography classification system [18].

MRI was performed using a 1.5-T (Sigma; GE Healthcare, Milwaukee, USA) or 3.0-T (Philips Achieva; Philips Healthcare, Best, The Netherlands) MRI system. Three-dimensional, fat-suppressed, gradient-echo, contrast material-enhanced, and dynamic images before and seven times after a bolus injection of 0.1 mmol/kg of gadopentetate dimeglumine (Magnevist; Berlex Laboratories, Wayne, USA) were acquired in the sagittal or axial plane. The image acquisition time per one dynamic scan was 60 to 90 seconds. Standard subtraction images were obtained by subtracting the precontrast images from the early peak (or serial) postcontrast images on a pixel-by-pixel basis. Reverse subtraction images were obtained by subtracting the last postcontrast images from the early peak postcontrast images. Abnormalities were scored according to the BI-RADS MRI classification system [19].

The findings obtained on all the imaging studies were analyzed, and the size of the DCIS was measured as the single greatest measurement by an experienced radiologist.

**Biopsy, surgery, and histopathology**

The diagnosis of DCIS was obtained via core needle biopsies or vacuum-assisted biopsies, prior to the preoperative MRI and mammography. All patients underwent surgery at our institution. Following lumpectomy or mastectomy, gross specimens were reviewed by a pathologist with expertise in breast pathology. The DCIS grade (high, intermediate or low), presence or absence of microinvasive clusters or an associated invasive tumor component, and nodal status were recorded. The histopathological size was recorded as the single greatest measurement in one long axis dimension, regardless of the spatial plane used.

**Statistical analysis**

Quantitative data are presented in a histogram, and as medians with range and means and standard deviation (SD). The criterion used for the accuracy of size assessment was a size within ± 5 mm compared with the histological size. Two types of statistical analyses were performed for correlations. Intraclass coefficients were calculated to examine the agreement between the MRI, mammography and ultrasonography measurements and the histopathological size, with a 95% confidence interval. The Wilcoxon signed-rank test was used to
evaluate the statistical significance of the differences in size between MRI, mammography or ultrasonography and histopathology. A p-value less than 0.05 was considered to indicate statistical significance. All statistical analysis were performed using SAS version 9.4 (SAS Institute, Cary, USA). The requirement for informed consent was waived because of the low risk posed by this investigation. This study adhered to the ethical tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Samsung Medical Center in Seoul, Korea (IRB number: 2016-04-006).

**RESULTS**

The mean age ± SD was 48.6 ± 9.8 years overall (range, 35–78 years) (Table 1); estrogen receptor expression was observed in 97 patients (74.1%), while progesterone receptor expression was observed in 90 patients (68.7%). Of the 131 DCIS lesions, 126 (96.2%) were detected by MRI, 103 (78.6%) were detected by mammography, and 121 (92.4%) were detected by ultrasonography (Table 2).

The final histopathological study found 34 low-grade (26.0%), 59 intermediate-grade (45.0%), and 38 high-grade DCIS lesions (29.0%). The mean histopathological size of the DCIS lesions was 38.8 mm (± SD, 26.2 mm). The mean size of lesions determined by mammography was 28.8 mm (± SD, 25.7 mm) (Table 1). The difference in the mean size determined by mammography and histopathology was -10.0 mm (± SD, 25.6 mm), a difference that was statistically significant (p < 0.001) (Table 3). The graph showed wide variation between sizes determined by mammography and histopathology (Figure 1).

The correlation coefficient between the histopathological size and mammographic size was 0.461. Mammography correctly assessed the lesion size (± 5 mm) in 33 cases (32.0%), underestimated the size in 53 cases (51.2%), and overestimated the size in 17 cases (16.8%) (Table 2). Among our patient population, 25 patients (19.0%) had dense breasts in which the lesions could not be visualized, while three patients (2.3%) did not show lesions.

The mean ultrasonographic size of DCIS was 23.3 mm (± SD, 18.0 mm). The difference in mean size between ultrasonography and histopathology was -15.6 mm (± SD, 23.9 mm), a difference that was statistically significant (p < 0.001) (Table 3). The graph depicted a variation between the ultrasonographic and histopathological sizes (Figure 1).

The correlation coefficient between the histopathological and ultrasonographic sizes was 0.284. Ultrasonography correctly assessed the lesion size (± 5 mm) in 29 cases (24.4%), underestimated the size in 76 cases (62.6%), and overestimated the size in 16 cases (13.0%) (Table 2).

The mean MRI size of the DCIS lesions was 36 mm (± SD, 24.3 mm). The difference in the mean size between MRI and histopathology was -2.9 mm (± SD, 14.2 mm), a difference that was statistically significant (p = 0.011) (Table 3). A close fit was graphically depicted between the MRI and histopathological sizes (Figure 1). The size discrepancy and span were smaller for the MRI measurements than for the mammographic and ultrasonographic differences. The correlation coefficient between the histopathological and MRI sizes was

### Table 1. Mean age and mean size of DCIS as determined by ultrasonography, mammography, MRI, and histopathology

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>131</td>
<td>48.6</td>
<td>9.8</td>
</tr>
<tr>
<td>Pathology size (mm)</td>
<td>131</td>
<td>38.8</td>
<td>26.2</td>
</tr>
<tr>
<td>Ultrasonography size (mm)</td>
<td>121</td>
<td>23.3</td>
<td>18.0</td>
</tr>
<tr>
<td>Mammography size (mm)</td>
<td>103</td>
<td>28.8</td>
<td>25.7</td>
</tr>
<tr>
<td>MRI size (mm)</td>
<td>126</td>
<td>36.0</td>
<td>24.3</td>
</tr>
<tr>
<td>DCIS = ductal carcinoma in situ; MRI = magnetic resonance imaging.</td>
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</table>

### Table 2. Size assessment correlation coefficients between ultrasonographic, MRI imaging sizes and histological size

<table>
<thead>
<tr>
<th>No. of detection</th>
<th>Ultrasonography</th>
<th>Mammography</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>121</td>
<td>92.4</td>
<td>78.6</td>
<td>96.2</td>
</tr>
<tr>
<td>29 (24.4)</td>
<td>33 (32.0)</td>
<td>67 (52.7)</td>
<td></td>
</tr>
<tr>
<td>76 (62.6)</td>
<td>53 (51.2)</td>
<td>38 (30.5)</td>
<td></td>
</tr>
<tr>
<td>16 (13.0)</td>
<td>17 (16.8)</td>
<td>21 (16.8)</td>
<td></td>
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<tr>
<td>Correlation coefficient, all Nuclear grade</td>
<td>0.284</td>
<td>0.461</td>
<td>0.837</td>
</tr>
<tr>
<td>Low</td>
<td>0.367</td>
<td>0.434</td>
<td>0.872</td>
</tr>
<tr>
<td>Intermediate</td>
<td>0.236</td>
<td>0.391</td>
<td>0.815</td>
</tr>
<tr>
<td>High</td>
<td>0.234</td>
<td>0.527</td>
<td>0.829</td>
</tr>
<tr>
<td>MRI = magnetic resonance imaging.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 3. Differences between ultrasonography, mammography or MRI assessments and histopathological assessment

<table>
<thead>
<tr>
<th>Pathology difference</th>
<th>No.</th>
<th>Mean (mm)</th>
<th>SD (mm)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasonography</td>
<td>121</td>
<td>-15.6</td>
<td>23.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Mammography</td>
<td>103</td>
<td>-10.0</td>
<td>25.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>MRI</td>
<td>126</td>
<td>-2.9</td>
<td>14.2</td>
<td>0.011</td>
</tr>
</tbody>
</table>

MRI = magnetic resonance imaging.
MRI correctly assessed the lesion size (± 5 mm) in 67 cases (52.7%), underestimated the size in 38 cases (30.5%), and overestimated the size in 21 cases (16.8%) (Table 2). In patients with dense breast tissue, MRI showed the lesion in 24 out of 25 patients.

According to histological grade, in low-grade DCIS, the mean size determined by mammography was 21.4 mm (Table 4); the difference between the mean mammographic size and the mean histopathological size was -6.1 mm (± SD, 24.4 mm), which was not statistically significant (p = 0.067) (Table 5). On ultrasonography, the mean size was 19.5 mm; the difference in the mean MRI and histopathological sizes was -0.2 mm (± SD, 10.3 mm), which was not statistically significant (p = 0.758) (Table 5).

For intermediate grade DCIS, the mean size determined by mammography was 28.1 mm (Table 4). The difference between the mean mammographic size and the mean histopathological size was -13.5 mm. The correlation between the histopathological ductal carcinoma in situ (DCIS) size and corresponding DCIS size as measured by MRI, mammography and ultrasonography is shown in Figure 1.

Table 4. Mean size of DCIS by ultrasonography, mammography, and MRI and histopathological size according to histological grade

<table>
<thead>
<tr>
<th>Grade</th>
<th>No.</th>
<th>MRI size* (mm)</th>
<th>Mammography size† (mm)</th>
<th>Ultrasonography size‡ (mm)</th>
<th>Pathology size (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Low</td>
<td>34</td>
<td>27.3</td>
<td>20.7</td>
<td>21.4</td>
<td>26.3</td>
</tr>
<tr>
<td>Intermediate</td>
<td>59</td>
<td>36.4</td>
<td>25.0</td>
<td>28.1</td>
<td>25.3</td>
</tr>
<tr>
<td>High</td>
<td>38</td>
<td>43.0</td>
<td>24.5</td>
<td>36.4</td>
<td>24.5</td>
</tr>
</tbody>
</table>

DCIS = ductal carcinoma in situ; MRI = magnetic resonance imaging.

*5 Patients were excluded because they were not detected by MRI; †28 Patients were excluded because they were not detected by mammography; ‡10 Patients were excluded because they were not detected by ultrasonography.
mm (± SD, 27.7 mm), which was statistically significant (p < 0.001) (Table 5). On ultrasonography, the mean size was 20.9 mm (Table 4). The difference between the mean ultrasonographic and histopathological sizes was -20.8 mm (± SD, 24.5 mm), which was statistically significant (p = 0.000) (Table 5). On MRI, the mean size was 36.4 mm (Table 4). The difference between the mean MRI size and the mean histopathological size was -5.24 mm (± SD, 15.6 mm), which was statistically significant (p = 0.007) (Table 5).

In high-grade DCIS, the mean size determined by mammography was 36.4 mm (Table 4). The difference between the mean mammographic and histopathological sizes was -8.2 (± SD, 23.3 mm), which was statistically significant (p = 0.039) (Table 5). On ultrasono-
raphy, the mean size was 30.4 mm (Table 4). The difference between the mean ultrasonographic and histopathological sizes was 14.3 mm (± SD, 26.0 mm), which was statistically significant (p = 0.001) (Table 5). On MRI, the mean size was 43 mm (Table 4). The difference between MRI and histopathological sizes was 1.6 (± SD, 14.6 mm), which was not statistically significant (p = 0.392). The correlation coefficient between the histopathological and MRI sizes was greater than 0.8 for all grades, but this was not the case for the sizes determined by mammography or ultrasonography (Table 2).

**DISCUSSION**

The current study investigated the impact of MRI in preoperative assessment of the size of DCIS compared with that of mammography and ultrasonography. The findings showed that MRI assessed the extent of DCIS much more accurately than mammography and ultrasonography. Mammography is widely accepted as the most important imaging method for the detection of DCIS, which is usually visualized as clusters of microcalcifications [20]. However, its sensitivity was 78% in the current study. In a prospective study of 167 cases of DCIS, Kuhl et al. [21] reported a diagnostic sensitivity of only 56% with mammography. In addition, the modality has some limitations in dense breasts, which were found in 19% of participant in our study.

Ultrasoundography is an adjunct modality used routinely in patients diagnosed with DCIS. Previous studies [22,23] have reported the ultrasonographic features of DCIS as an architectural distortion, an intracystic lesion or a bulky, hypoechoic vascular mass with ductal extension and prominent microlobules. In our study, DCIS was observed as a nonmass abnormality, a round or oval-shaped, microlobulated, mildly hypoechoic mass or a microcalcification (Figure 2), a result similar to those obtained in previous studies [22,23]. In addition, microcalcification was also observed. The ability to visualize microcalcifications on ultrasonography has been described previously [24,25]. In our study, ultrasonography detected DCIS lesions in 121 patients with a sensitivity of 92.4%. Lee et al. [25] reported the sensitivity of ultrasonography in DCIS as 86.5%.

MRI is not currently used as a systematic diagnostic modality in DCIS, and controversy remains regarding its use for preoperative planning. Previous studies have found that suspicious MRI findings for DCIS include nonmass enhancement, especially in a ductal or segmental/linear pattern, and variable perfusion patterns, including delayed washout, plateau, and persistent kinetics [26]. Although in our study MRI showed enhancement in 126 patients, it showed nonmass enhancement with an excellent sensitivity of 96% for DCIS detection. Previous studies have reported sensitivities ranging from 60% to 100% [12,13,27-28]. MRI is a useful adjunct modality for dense breast tissue; in our study, it revealed the lesions in 96% of patients with dense breasts and negative findings on mammography.

Regarding the preoperative size assessment of DCIS, mammographic and ultrasonographic assessments of the lesion size were mediocre in our study because the correlation coefficients between these measurements and the size determined by histology were only 0.461 and 0.284, respectively. In our study, mammography tended to underestimate the size of DCIS. This finding did not differ significantly from those reported in the literature [29]. Furthermore, in our study, ultrasonography tended to underestimate the size of lesions by 10% compared to mammography.

Can MRI palliate the limitations of mammography and ultrasonography to serve as an effective tool for the staging of DCIS? The correlation coefficient between size determined by MRI and size determined by histology in our study was very satisfactory (0.837), with excellent reliability. MRI accurately estimated the DCIS size in 52.7% of cases. Other studies [11-13,30], which included 30, 22, 72, and 33 patients, respectively, all reported accurate MRI estimation of size in 57% to 72% of cases. Only a few studies [11,30] considered an accurate size assessment as one that was within ± 5 mm. In the study of Schouten van der Velden et al. [30], size assessment with MRI was accurate in 38% of cases versus 27% with mammography, with no statistical significance; however, in the study of Marcotte-Bloch et al. [11], size assessment had an accurate rate of 60% with MRI versus 38% with mammography (this difference was statistically significant).

The results obtained in our study showed statistical significance in favor of better size assessment for all histological grades of DCIS by MRI compared with size determinations by mammography and ultrasonography. However, our study had limitations. First, it employed a retrospective design, with data from a single institution. Second, multicentric or multifocal cancer was excluded, possibly limiting the reliability of the results. Third, breast images were performed after core needle or vacuum-assisted biopsies, generating a bias in imaging and pathological measurements. Fourth, all lesions analyzed were
pure DCIS in the final histopathology; lesions with associated micro-invasive or invasive clusters were also included. Despite these limitations, our findings are significant and warrant further investigations.

In conclusion, our study confirmed that preoperative MRI staging of DCIS assessed the extent of these tumors much more accurately than mammography and ultrasonography. Precise preoperative assessment of tumor size should improve surgical planning and reduce the risk of secondary recurrence.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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