

Sonographic Findings of High-Grade and Non-High-Grade Ductal Carcinoma In Situ of the Breast

Ji-Sung Park, MD, Young-Mi Park, MD, Eun-Kyung Kim, MD,
Suk-Jung Kim, MD, Sang-Suk Han, MD, Sun-Joo Lee, MD,
Hyun-Sin In, MD, Ji-Hwa Ryu, MD

Objective. The purpose of this study was to differentiate between high-grade and non-high-grade ductal carcinoma in situ (DCIS) of the breast on sonography. **Methods.** From October 2003 to August 2009, 76 DCIS lesions in 73 women who underwent sonography and mammography were included in this study. Lesions were confirmed by mastectomy, breast-conserving surgery, or surgical biopsy. Images were analyzed by 2 radiologists with consensus and were correlated with histologic grades. **Results.** Of the 76 lesions, 44 were classified as high-grade and 32 as non-high-grade DCIS. Fifty-seven lesions (75.0%) were identified on sonography, which revealed a mass in 30 cases, microcalcifications in 20, ductal changes in 4, and architectural distortion in 3. All cases with false-negative findings on sonography ($n = 19$) showed microcalcifications on mammography. On sonography, masses were more frequently found in non-high-grade (62.5%) than high-grade DCIS (22.7%; $P < .01$). No significant difference was seen in the sonographic features of masses between high-grade and non-high-grade DCIS. Microcalcifications were more common in high-grade (43.2%) than non-high-grade (3.1%) DCIS ($P = .02$). Most sonographically visible microcalcifications had associated findings such as ductal changes ($n = 11$), a mass ($n = 7$), or a hypoechoic area ($n = 5$). The detection rate of microcalcifications on sonography was higher in high-grade (62.9%) than non-high-grade DCIS (25.0%; $P = .023$). **Conclusions.** Microcalcifications with associated ductal changes (11 of 31 [35.5%]) were the most common sonographic findings in high-grade DCIS. An irregular hypoechoic mass with an indistinct and microlobulated margin (13 of 26 [50.0%]) was the most frequent finding in non-high-grade DCIS. **Key words:** breast neoplasm; ductal carcinoma in situ; pathologic assessment; sonography.

Abbreviations

BI-RADS, Breast Imaging Reporting and Data System; DCIS, ductal carcinoma in situ; ER, estrogen receptor; PR, progesterone receptor

Received April 14, 2010, from the Department of Radiology, Inje University College of Medicine, Busan Paik Hospital, Busan, Korea (J.-S.P., Y.-M.P., S.-S.H., S.-J.L., H.-S.I.); Department of Radiology, Yonsei University College of Medicine, Seoul, Korea (E.-K.K.); and Department of Radiology, Inje University College of Medicine, Haeundae Paik Hospital, Busan, Korea (S.-J.K., J.-H.R.). Revision requested June 8, 2010. Revised manuscript accepted for publication July 8, 2010.

This work was supported by a 2005 Inje University research grant and the Busan Paik Hospital Imaging Research Institute.

Address correspondence to Young-Mi Park, MD, Department of Radiology, Inje University College of Medicine, 633-165 Gaegeum-dong, Busanjin-gu, Busan 614-735, Korea.

E-mail: pymrad@yahoo.co.kr

Ductal carcinoma in situ (DCIS) is a spectrum of noninvasive breast cancers composed of malignant proliferation of ductal epithelial cells still surrounded by the normal basement membrane of the duct.¹ Nuclear grading of DCIS is based on the variability of the nuclear size (pleomorphism), the conspicuity and number of nucleoli, and the chromatic pattern. High-grade DCIS has large, variably sized nuclei with prominent nucleoli and clumped chromatin. Low-grade DCIS has small, uniform nuclei with inconspicuous nucleoli and a diffuse homogeneous chromatin pattern. Intermediate-grade DCIS is largely a miscellaneous category for tumors with intermediate nuclear features.² Current studies suggest that low- and high-grade DCIS follow different genetic routes.^{3,4} Low-grade DCIS is generally positive for estrogen receptor (ER) and progesterone receptor (PR) and negative for human epidermal

growth factor receptor 2, and displays chromosomal losses at 16q, gains in 1q, and near euploidy. High-grade DCIS tends to display a lack of ER and PR expression, human epidermal growth factor receptor 2 overexpression/amplification, a multitude of chromosomal changes, and aneuploidy.^{5,6} The distinct molecular genetic features found in different grades of invasive carcinoma are mirrored in preinvasive lesions of comparable morphologic grades. It has been thought that low-grade DCIS progresses to low-grade invasive ductal carcinoma, whereas high-grade DCIS progresses to high-grade invasive ductal carcinoma.⁵ Furthermore, White et al⁷ found that the predominant nuclear grade was the best predictor of local recurrence.

The mammographic features of DCIS have been well described in the literature.^{2,8-10} Calcifications of extensive necrosis usually associated with high-grade DCIS typically present mammographically as markedly pleomorphic, linear, branching, or casting microcalcifications in a clustered, ductal, or segmental distribution.² In contrast, mammography of low-grade DCIS has been reported to be less likely to show microcalcifications and more likely to show normal findings or noncalcified mammographic abnormalities.⁸

Although most cases of DCIS are diagnosed mammographically, 6% to 23% of DCIS lesions are not visible on mammography.^{9,11-12} Several recent studies have examined the sonographic findings of DCIS.¹³⁻¹⁶ Moon et al¹³ reported that the most common sonographic finding of DCIS included a microlobulated mass with mild hypoechogenicity, ductal extension, and normal acoustic transmission. To our knowledge, there have been only a few reports regarding the differences in the sonographic features of high-grade and non-high-grade DCIS.^{16,17} It would be helpful in treating patients with DCIS and planning management more confidently if the grade could be reliably predicted from sonography, especially in cases with negative mammographic findings or noncalcified mammographic abnormalities.¹⁸ The purpose of this study was to describe the differences between high-grade and non-high-grade DCIS of the breast on sonography and to evaluate the ability of sonography to predict the nuclear grade of DCIS.

Materials and Methods

Patient Selection

This retrospective study of images and data was approved by the Institutional Review Board of our institution. From October 2003 to August 2009, 107 patients had a diagnosis of pure DCIS by breast-conserving surgery (n = 59), mastectomy (n = 43), or surgical biopsy (n = 5). Among this group, 76 cases of DCIS in 73 patients whose mammographic and sonographic records were available were included in the study cohort. Patients who had undergone mammography at outside hospitals within 1 year but whose outside mammographic records or interpretation reports were not available were excluded. Sonography was performed for mammographic abnormalities in 37 of 73 patients, for breast symptoms in 25, and for patient or physician requests regardless of negative mammographic findings in 11. Of the 73 patients, 8 had bilateral cancer. Five patients had invasive carcinoma in their contralateral breast. The remaining 3 patients had bilateral DCIS. We performed a retrospective review of these 76 cases to document the sonographic and mammographic features and correlated these findings with those from histopathologic evaluations.

Clinical Features

Before the sonographic examination, the radiologist asked the patient if she had symptoms, such as palpability, nipple discharge, or pain, and identified the clinician's concerns according to the referring clinician's records. The following clinical features were recorded: presence of a palpable mass, nipple discharge, Paget disease, and pain. Forty-eight women (65.8%) were asymptomatic, and 25 (34.2%) had symptoms. Of the 25 women with symptomatic DCIS lesions, 18 (72.0%) had a palpable mass; 3 (12.0%) had both a palpable mass and nipple discharge; 2 (8.0%) had Paget disease; 1 (4.0%) had pain; and 1 (4.0%) had nipple discharge. Asymptomatic DCIS lesions in 48 patients were found on either screening mammography (n = 37) or sonography (n = 11).

Sonography

One of 3 radiologists with 1 to 7 years of breast imaging and intervention experience performed

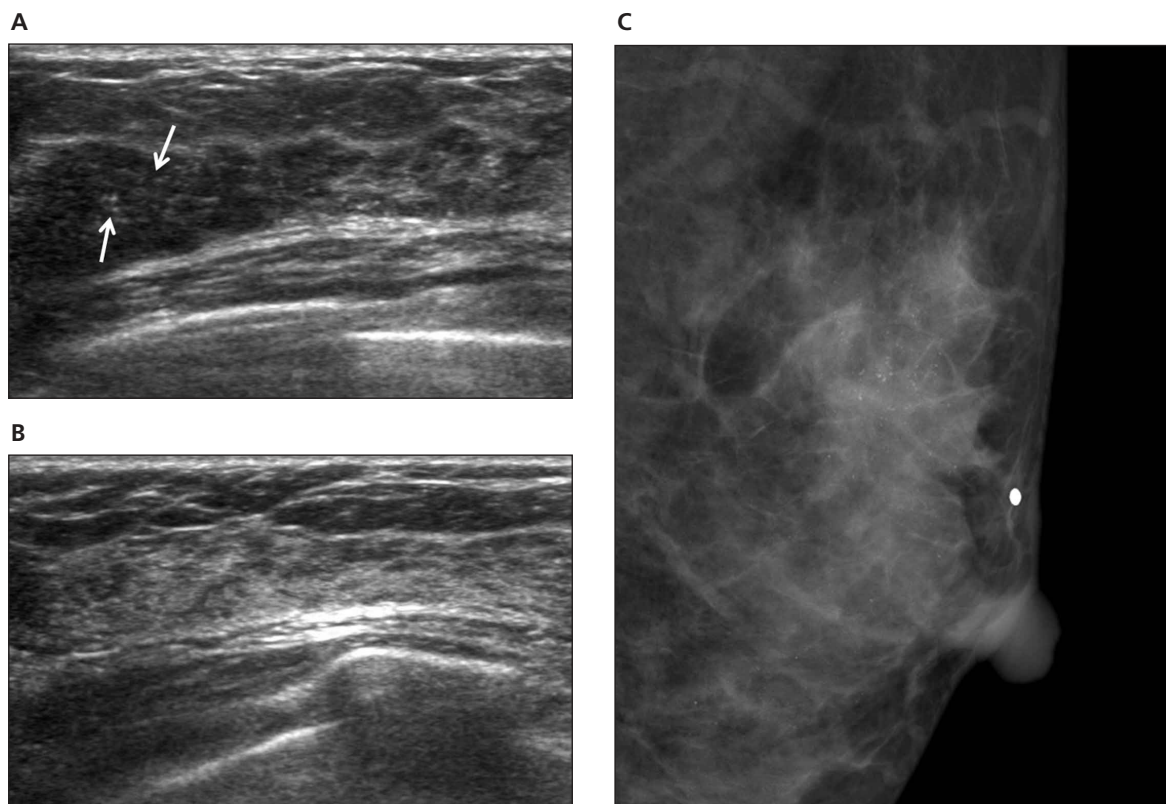
whole-breast sonography on all 73 patients using 10- to 14-MHz transducers on HDI 5000 and iU22 sonography units (Philips Healthcare, Bothell, WA). The radiologist was aware of the patients' mammographic results before the sonographic examinations. Sonograms were retrospectively reviewed with consensus. The sonographic findings were classified as negative, a mass, microcalcifications, ductal changes, or architectural distortion according to the Breast Imaging Reporting and Data System (BI-RADS) sonographic lexicon.¹⁹ If the lesion had more than 1 of these features, we recorded a dominant finding. When a mass was present, the sonographic findings were evaluated according to the BI-RADS sonographic lexicon, that is, the shape (oval, round, or irregular), orientation (parallel to the skin or not), margin (circumscribed or not circumscribed), lesion boundary (abrupt interface or echogenic halo), echo pattern (hypoechoic or complex), posterior acoustic feature

(none, enhancement, shadowing, or combined), associated findings (none, microcalcifications, ductal changes, or architectural distortion), and size. When microcalcifications were present, the sonographic findings were classified as microcalcifications only, microcalcifications and ductal changes, microcalcifications and a mass, and microcalcifications and a hypoechoic area. In our study, we defined a hypoechoic area as a lesion that was different from the surrounding gland or the same area in the ipsilateral breast (Figure 1),²⁰ and we defined ductal changes as an abnormal caliber or arborization of ducts according to the sonographic BI-RADS lexicon.¹⁹

Mammography

Mammography in 2 standard imaging planes, mediolateral oblique and craniocaudal, was performed with a Senographe DMR scanner (GE Healthcare, Milwaukee, WI), with additional views being obtained as necessary. Mammograms were

Figure 1. High-grade DCIS in a 42-year-old woman who presented with a palpable mass. **A**, Sonogram showing hypoechoic areas, defined as focal heterogeneity distinguished from surrounding parenchyma, with microcalcifications (arrows) in the left breast. **B**, Sonogram of the mirror image region of the right breast as in **A** showing a normal parenchymal pattern. **C**, Left mediolateral oblique mammogram showing fine pleomorphic microcalcifications with regional distribution.



retrospectively reviewed with consensus by 2 breast radiologists for microcalcifications, masses, asymmetry/focal asymmetry, and architectural distortion according to the BI-RADS mammographic lexicon.²¹ If the lesion had more than 1 of these features, we recorded a dominant finding.

The mammographic parenchymal pattern was also recorded according to the BI-RADS mammographic lexicon (pattern 1, a fatty breast; pattern 2, a fatty breast with scattered fibroglandular densities; pattern 3, a heterogeneously dense breast; and pattern 4, extremely dense parenchyma).²¹

Histopathologic Assessment

Histopathologic findings from breast-conserving surgery (n = 44), mastectomy (n = 28), and surgical biopsy (n = 4) specimens served as the reference standards. One pathologist analyzed the following histologic parameters: nuclear grade, comedonecrosis, microinvasion, hormonal receptors, *c-erbB2* oncogene, and size. The nuclear grade was divided into high-grade and non-high-grade, including intermediate and low-grade. Lesions with pure DCIS and DCIS with microinvasion (invasive focus of ≤1 mm as defined by previously published criteria²²) were included in this study. Cases of DCIS associated with minimal invasion or infiltrative ductal carcinoma were excluded from the study.

Statistical Analysis

To determine whether there were differences in the sonographic, mammographic, and clinical findings between high-grade and non-high-grade DCIS, statistical analysis was performed using a statistical software system (SPSS for Windows version 12.0; SPSS Inc, Chicago, IL).

The Fisher exact test and χ^2 test were used for nonparametric independent variables, and the Mann-Whitney *U* test was used for variables such as age and size. Findings with *P* < .05 were considered statistically significant.

Results

Of 76 lesions in 73 women (age range, 28–81 years; mean, 53.4 years), 44 lesions in 43 women (age range, 38–81 years; mean, 54.4 years) constituted high-grade DCIS, and 32 lesions in 32 women (age range, 28–80 years; mean, 51.9 years) constituted non-high-grade DCIS, which included 2 intermediate- and 30 low-grade DCIS cases. Among the 44 high-grade DCIS cases, 14 were symptomatic, and among the 32 non-high-grade DCIS cases, 11 were symptomatic. Two of the 3 women with bilateral DCIS presented with unilateral breast symptoms. The remaining woman was asymptomatic. There was no statistical difference in age (*P* = .47) and patient symptoms (*P* = .81) between high-grade and non-high-grade DCIS.

The correlation between histologic grade and visibility on imaging is provided in Table 1. Seventeen of the 76 lesions (22.4%) were not visible on mammography. Of these cases, 6 had clinical symptoms, such as nipple discharge, a lump, or pain, and further sonographic examination revealed DCIS. The remaining 11 cases had no clinical symptoms and were diagnosed at screening sonography. In 30 cases of masses on sonography, 14 cases were not seen on mammography. In the other 16 cases, there were masses in 8, asymmetry or focal asymmetry in 4, calcifications in 3, and architectural distortion in 1 mammographically. All 8 cases of masses seen on mammography were detected sonographically.

Table 1. Correlation Between Histologic Grade and Visibility on Images in 76 Cases of DCIS

Visibility	High-Grade (n = 44)	Non-High-Grade (n = 32)	Total (n = 76)
Sonography, n (%)			
Visible	31 (70.5)	26 (81.3)	57 (75.0)
Nonvisible	13 (29.5) ^a	6 (18.7) ^a	19 (25.0)
Mammography, n (%)			
Visible	37 (84.1)	22 (68.7)	59 (77.6)
Nonvisible	7 (15.9) ^b	10 (31.3) ^b	17 (22.4)

^aAll of the cases showed microcalcifications on mammography.

^bFourteen cases were masses, and 3 showed ductal changes on sonography.

Sonographic Features

Sonography revealed a mass in 30 cases (39.5%), microcalcifications in 20 cases (26.3%), ductal changes in 4 cases (5.3%), and architectural distortion in 3 cases (3.9%). There were 19 false-negative cases (25.0%) on sonography, which included 13 high-grade (13 of 44 [29.5%]) and 6 non-high-grade (6 of 32 [18.8%]) cases of DCIS. All false-negative cases showed microcalcifications on mammography. Masses were more common in non-high-grade ($n = 20$ [62.5%]) than high-grade ($n = 10$ [22.7%]) DCIS ($P < .01$), whereas microcalcifications were more common in high-grade ($n = 19$ [43.2%]) than non-high-grade ($n = 1$ [3.1%]) DCIS ($P = .02$). Cases with ductal changes did not show a significant difference between high-grade ($n = 2$ [4.5%]) and non-high-grade ($n = 2$ [6.3%]) DCIS. All 3 cases showing architectural distortion were confirmed as non-high-grade DCIS (Table 2).

A total of 30 masses were detected on sonography (Table 3). Masses visible on sonography typically revealed hypoechogenicity and an irregular shape with indistinct and microlobulated margins (Figures 2 and 3). Usually, no posterior acoustic feature or abrupt interface was present. No significant difference was seen in the sonographic features of masses between high-grade and non-high-grade DCIS, including shape, margin, echogenicity, orientation, lesion boundary, and posterior acoustic feature. In cases with a mass, associated microcalcifications were more often seen in high-grade (3 of 10 [30.0%]) than non-high-grade (2 of 20 [10.0%]) DCIS. Associated ductal changes and architectural distortion were seen in non-high-grade but not high-grade DCIS. The mean sizes of a mass on sonography were 1.47 cm in high-grade and 1.54 cm in non-high-grade DCIS. No significant difference was seen in the sizes of high-grade and non-high-grade DCIS ($P = .69$).

Twenty-five of 47 cases with mammographically detected microcalcifications were identified sonographically (Table 4). Of the 25 cases, microcalcifications were a dominant finding in 20, and dominant masses with associated microcalcifications were detected in the remaining 5. Ductal changes were the most common associated finding (11 of 25 cases; Figure 4), followed by a mass in 7 cases, a hypoechoic area in 5 cases, and normal parenchymal tissue in only 2 cases. In addition, microcalcifications associated with high-grade DCIS (22 of 35 [62.9%]) were more likely to be seen on sonography than those associated with non-high-grade DCIS (3 of 12 [25.0%]). There was a statistical difference in the detection rates of microcalcifications between the two groups ($P = .023$).

In non-high-grade DCIS detected by sonography, an irregular hypoechoic mass with an indistinct and microlobulated margin was the most frequent finding (13 of 26 [50.0%]), and in high-grade DCIS, microcalcifications with associated ductal changes was the most common sonographic finding (11 of 31 [35.5%]).

Mammographic Features

The mammographic parenchymal patterns of the 73 patients were pattern 4 in 4 patients (5.5%), pattern 3 in 59 (80.8%), pattern 2 in 8 (11.0%), and pattern 1 in 2 (2.7%). Among 17 patients who had mammographically occult lesions, mammography showed dense parenchyma in 15 (BI-RADS pattern 3 or 4 [88.2%]).

Microcalcifications were the most common finding and were noted in 44 of the 76 cases (57.9%), followed by the presence of a mass in 8 cases (10.5%) and asymmetry or focal asymmetry in 5 (6.6%). Architectural distortion was noted in only 2 cases (2.6%; Table 5). There were 17 false-negative cases on mammography, which included 7 high-grade (7 of 44 [15.9%]) and 10

Table 2. Dominant Sonographic Findings in 76 Cases of DCIS

Sonographic Finding	High-Grade (n = 44)	Non-High-Grade (n = 32)	Total (n = 76)
Microcalcifications, n (%) ^a	19 (43.2)	1 (3.1)	20 (26.3)
Mass, n (%) ^a	10 (22.7)	20 (62.5)	30 (39.5)
Ductal changes, n (%)	2 (4.5)	2 (6.3)	4 (5.3)
Architectural distortion, n (%)	0	3 (9.4)	3 (3.9)
Negative finding, n (%)	13 (29.5)	6 (18.8)	19 (25.0)

^aStatistically significant ($P < .05$).

non-high-grade (10 of 32 [31.3%]) DCIS. Of 17 false-negative cases, 14 showed masses and 3 showed ductal change on sonography (Table 1).

Microcalcifications were more frequently found in high-grade than non-high-grade DCIS ($P < .05$). Noncalcified abnormalities, including a mass, asymmetry/focal asymmetry, and architectural distortion, were more frequently found in non-high-grade than high-grade DCIS ($P = .01$).

Histopathologic Findings

Forty-four lesions were classified as being in a high-nuclear-grade group, whereas 32 were classified as being in a non-high-nuclear-grade group, which included 2 intermediate- and 30 low-nuclear-grade groups. Comedonecrosis was more frequently found in high-grade (36 of 44 [81.8%]) than non-high-grade (5 of 32 [15.6%]) DCIS ($P < .01$). No statistically significant difference was seen in microinvasion between high-grade (4 of 44 [9.09%]) and non-high-grade (2 of 32 [6.25%]) DCIS. Data regarding biological

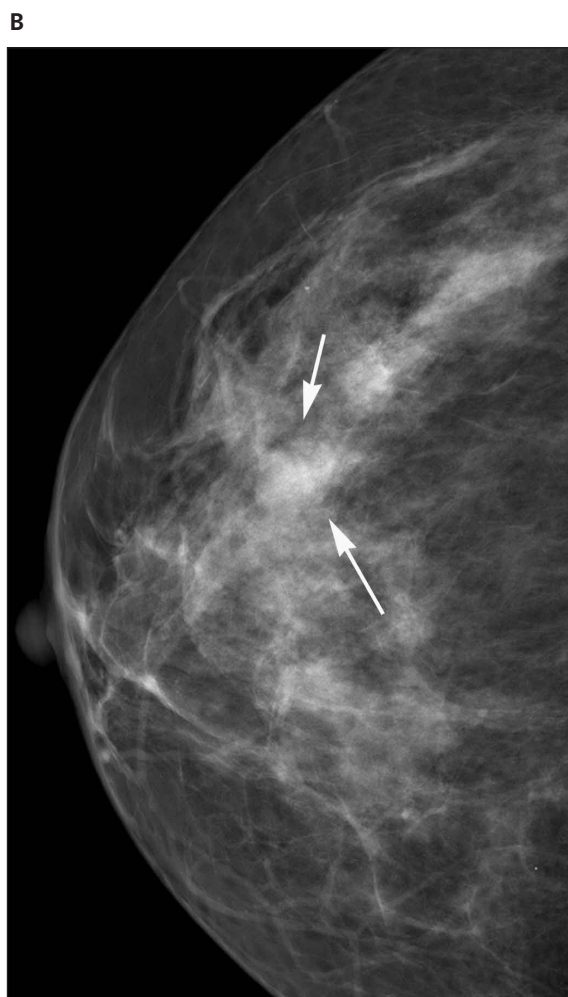
Figure 2. Low-grade DCIS in an asymptomatic 41-year-old woman. **A**, Sonogram showing an irregularly shaped hypoechoic mass with an indistinct margin in the left breast. **B**, Left mediolateral oblique mammogram showing no abnormality.



Table 3. Comparison of Sonographic Findings in 30 Cases of DCIS With Masses

Sonographic Finding	High-Grade (n = 10)	Non-High-Grade (n = 20)
Shape, n		
Oval to round	2	7
Irregular	8	13
Margin, n		
Circumscribed	0	5
Not circumscribed		
Microlobulated	4	5
Indistinct	5	10
Angular	1	0
Echogenicity, n		
Hypoechoic	8	18
Complex	2	2
Orientation, n		
Parallel	9	17
Not parallel	1	3
Lesion boundary, n		
Abrupt interface	9	15
Echogenic halo	1	5
Posterior feature, n		
None	4	12
Enhancement	3	5
Shadowing	1	2
Combination	2	1
Associated finding, n (%)		
Microcalcifications	3 (30)	2 (10)
Ductal changes	0	7 (35)
Architectural distortion	0	1 (5)
Size, cm, mean ± SD	1.47 ± 0.63	1.54 ± 1.13

Figure 3. High-grade DCIS in an asymptomatic 49-year-old woman. **A**, Sonogram showing an oval hypoechoic mass with an indistinct margin in the right breast. **B**, Right craniocaudal mammogram showing an isodense mass (arrows) with an obscure margin and oval shape in the right breast.



markers, including hormone receptors and the *c-erbB2* oncogene, were available in 40 cases with high-grade and 28 cases with non-high-grade DCIS. Expression of the *c-erbB2* oncogene was significantly higher in high-grade than non-high-grade DCIS ($P < .01$). Expression of ER and PR was significantly higher in non-high-grade than high-grade DCIS ($P < .05$; Table 6). The sizes of the DCIS lesions on pathologic specimens were available in 35 cases with high-grade and 26 cases with non-high-grade DCIS. The mean sizes of the DCIS lesions on pathologic specimens were 2.30 cm (range, 0.2–6.0 cm) in high-grade and 1.58 cm (range, 0.5–8.0 cm) in non-high-grade DCIS. There was no statistical difference in sizes on pathologic specimens between the two groups ($P = .86$).

Discussion

As the incidence of breast cancer is increasing and screening mammography is more widely used, the detection rate of DCIS is increasing.²³ Sonography has traditionally had a relatively small role in the diagnosis and evaluation of DCIS. Although the use of sonography in symptomatic patients is widely accepted, there is some debate as to the utility of this modality in screening or in those with a diagnosis of DCIS. Nonetheless, the emergence of newer high-resolution transducers and the increasing experience of physicians with sonography have resulted in improved sensitivity and specificity of sonography as well as confidence in the technique.^{13,14,18,24–26} Although DCIS is typically depicted on mammography as calcifications, it may also appear masslike in its noncalcified form.^{5,11–12} Sonography is an important diagnostic tool as an adjunct to mammography, especially in breasts with a dense parenchymal pattern or in cases of noncalcified lesions. It is still useful to detect another incidental carcinoma in the ipsilateral or contralateral breast in patients with a diagnosis of DCIS, although sonography depends on the ability of the examiner and the equipment. At the same time, it can show small satellite nodules around DCIS, which may not be found on mammography. These may affect planning treatment for the patients.^{13,27} Furthermore, it would be helpful in treating patients with DCIS

and planning management more confidently if the grade could be reliably predicted with sonography, especially in cases with negative mammographic findings or noncalcified mammographic abnormalities.¹⁸ In this study, 17 of 76 cases (22.4%) could not be detected on mammography. Six of these 17 cases had clinical symptoms, and further sonographic examination revealed DCIS. However, the remaining 11 cases had no clinical symptoms, and screening sonography was the only modality able to show the lesions.

In this study, the most frequent sonographic feature of DCIS was a mass, followed by microcalcifications, ductal changes, and architectural distortion. A mass was more common in non-high-grade than high-grade DCIS (62.5% versus 22.7%; $P < .01$). Yang and Tse¹⁵ analyzed the sonographic findings of 60 symptomatic patients with DCIS and reported that an irregularly shaped mass with indistinct or angular margins and no posterior acoustic phenomena was more likely to be associated with Van Nuys group 3 and a cystic ovoid mass with circumscribed margins and posterior enhancement was more likely to be associated with Van Nuys group 1. However, in our study, no significant difference was seen in the sonographic features of masses between high-grade and non-high-grade DCIS.

Several studies reported that microcalcifications associated with malignant breast lesions were more likely to be seen on sonography than those associated with benign lesions because most malignant calcifications occur in a mass.^{13,14,18} Identifying isolated microcalcifications within normal breast tissue is thought to be more difficult with sonography because of the lack of contrast between normal parenchyma with a hyperechoic heterogeneous fibrous structure and microcalcifications.²⁸ Thus, malignant microcalcifications are more easily visualized on sonography and are usually associated with a

mass or ductal changes. Yang and Tse¹⁵ also reported that the microcalcifications visible on sonography and mammography were associated with a high Van Nuys classification. The findings in our study concur with those of Yang and Tse.¹⁵

Figure 4. High-grade DCIS of the left breast in an asymptomatic 48-year-old woman. **A**, Left and right sonograms showing microcalcifications (arrows) within irregularly distended ducts in a series. **B**, Left mediolateral oblique mammogram showing fine pleomorphic microcalcifications with a segmental distribution in the left breast.

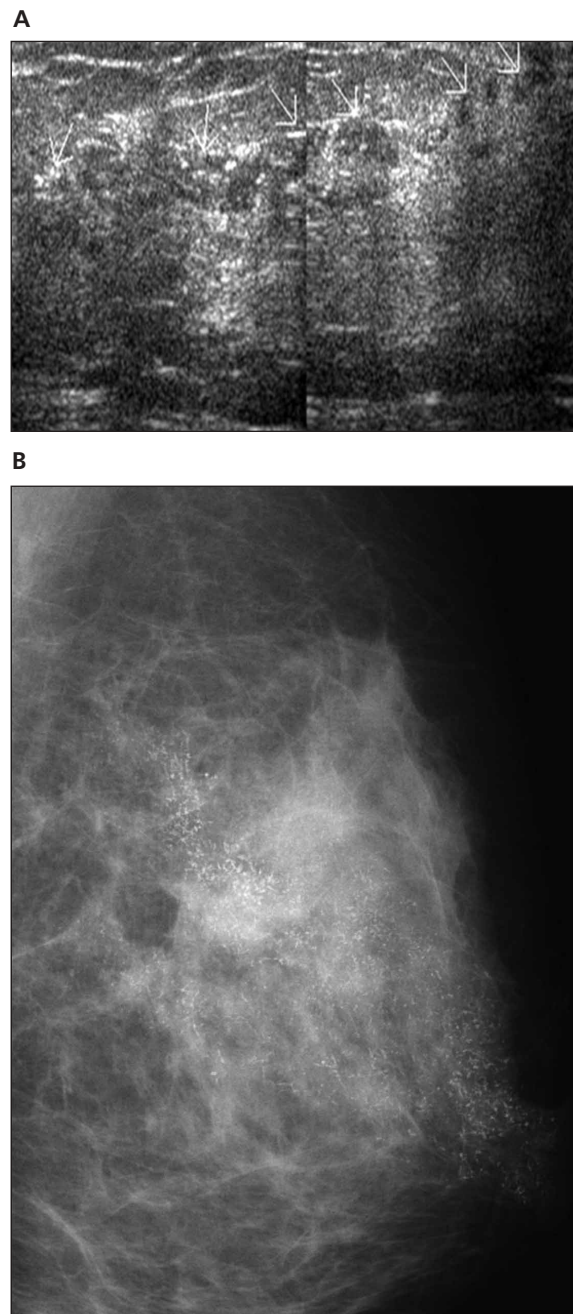


Table 4. Comparison of Sonographic Findings in 25 Cases of DCIS With Microcalcifications

Sonographic Finding	High-Grade (n = 22)	Non-High-Grade (n = 3)
Microcalcifications only, n (%)	2 (9.1)	0
Microcalcifications and ductal changes, n (%)	11 (50.0)	0
Microcalcifications and mass, n (%)	5 (22.7)	2 (66.7)
Microcalcifications and hypoechoic area, n (%)	4 (18.2)	1 (33.3)

Table 5. Dominant Mammographic Findings in 76 Cases of DCIS

Mammographic Finding	High-Grade (n = 44)	Non-High-Grade (n = 32)	Total (n = 76)
Microcalcifications, n (%) ^a	33 (75.0)	11 (34.4)	44 (57.9)
Mass, n (%)	3 (6.8)	5 (15.6)	8 (10.5)
Asymmetry and focal asymmetry, n (%)	1 (2.3)	4 (12.5)	5 (6.6)
Architectural distortion, n (%)	0	2 (6.3)	2 (2.6)
Negative finding, n (%)	7 (15.9)	10 (31.3)	17 (22.4)

^aStatistically significant ($P < .05$).

The microcalcifications on sonography were more common in high-grade than non-high-grade DCIS (43.2% versus 3.1%; $P = .02$). The most common associated findings with microcalcifications on sonography were ductal changes, especially in high-grade DCIS (11 of 22 [50.0%]). Ductal carcinoma in situ with microcalcifications was visible on sonography in 25 of 47 cases (53.2%). Moreover, the microcalcifications associated with high-grade DCIS (22 of 35 [62.9%]) were more frequently detected on sonography than those associated with non-high-grade DCIS (3 of 12 [25.0%]; $P = .023$).

Cho et al²⁹ analyzed the sonographic findings of 22 noncalcified DCIS cases and reported that all 3 patients with ductal changes had Van Nuys group 1 DCIS, and ductal changes were more frequently associated with group 1 DCIS ($P = .017$). Although the number of cases with ductal changes alone on sonography was too small to compare in our study, ductal changes alone did not show a significant difference between high-grade (n = 2 [4.5%]) and non-high-grade (n = 2 [6.3%]) DCIS. Isolated ductal changes on sonography are rare in DCIS but easily found in patients with benign diseases. However, ductal changes in DCIS may represent distended ducts with proliferated cancer cells at histologic analysis.¹³ Therefore, isolated ductal changes may be an important finding in diagnosing DCIS.

In our study, architectural distortion was seen in 3 of 76 DCIS cases (3.9%), which were confirmed as non-high-grade DCIS. Low-grade tumors grow more slowly, incite a more aggressive host immune response, and often provoke a desmoplastic reaction in the surrounding breast parenchyma.^{30,31} This explains the correlation between a small stellate tumor presenting as architectural distortion and a histologic low-grade tumor. This hypothesis can also be applied to low-grade DCIS.

On mammography, 62% to 98% of DCIS cases are detected because of the presence of microcalcifications, with 2% to 23% manifesting as a mass or asymmetric density only.^{9,11-12} Mammographic abnormalities were noted in 77.6% of the cases in this study. These comprised microcalcifications (57.9%), masses (10.5%), asymmetry/focal asymmetry (6.6%), and architectural distortion (2.6%). High-grade DCIS includes most cases of comedonecrosis, and it is the necrotic debris produced by this high-grade tumor that undergoes calcification.⁴ Mammography of low-grade DCIS without comedonecrosis has been reported to be less likely to show microcalcifications and more likely to either be mammographically normal or show noncalcified abnormalities.⁸ Our results were similar to those of previous studies. Microcalcifications were more frequently found in high-grade than non-high-grade DCIS ($P < .05$). Noncalcified abnormalities, including masses, asymmetry/focal asymmetry, and architectural distortion, were more frequently found in non-high-grade than high-grade DCIS ($P = .01$).

The major limitations of this study were the relatively small number of patients and its retrospective nature. Larger prospective studies are needed to differentiate the sonographic features between high-grade and non-high-grade DCIS.

Table 6. Comparison of Histopathologic Findings in High- and Non-High-Grade DCIS

Histopathologic Finding	High-Grade (n = 40)	Non-High-Grade (n = 28)
Positive ER, n	22	25
Positive PR, n	17	27
Positive <i>c-erbB2</i> oncogene, n	17	0

All statistically significant ($P < .05$).

In conclusion, our results show differences in the sonographic features of high-grade and non-high-grade DCIS. On sonography, microcalcifications were more common in high-grade than non-high-grade DCIS, whereas masses were more frequently found in non-high-grade than high-grade DCIS ($P < .05$). Microcalcifications with associated ductal changes (11 of 31 [35.5%]) were the most common sonographic finding in high-grade DCIS, and an irregular, hypoechoic mass with an indistinct and microlobulated margin (13 of 26 [50.0%]) was the most frequent finding in non-high-grade DCIS. High-grade DCIS had a higher detection rate of microcalcifications on sonography than non-high-grade DCIS ($P < .05$). Thus, sonography might be helpful in predicting the histologic grade of DCIS as a supplement to mammography.

References

1. Schnitt SJ, Silen W, Sadowsky NL, Connolly JL, Harris JR. Ductal carcinoma in situ (intraductal carcinoma) of the breast. *N Engl J Med* 1988; 318:898-903.
2. Poplack SP, Wells WA. Ductal carcinoma in situ of the breast: mammographic-pathologic correlation. *AJR Am J Roentgenol* 1998; 170:1543-1549.
3. Vos CB, ter Haar NT, Rosenberg C, et al. Genetic alterations on chromosome 16 and 17 are important features of ductal carcinoma in situ of the breast and are associated with histologic type. *Br J Cancer* 1999; 81:1410-1418.
4. Sewell CW. Pathology of high-risk breast lesions and ductal carcinoma in situ. *Radiol Clin North Am* 2004; 42:821-830.
5. Simpson PT, Reis-Filho JS, Gale T, Lakhani SR. Molecular evolution of breast cancer. *J Pathol* 2005; 205:248-254.
6. O'Malley F, Pinder SE (eds). Molecular genetics of ADH/DCIS and ALH/LCIS. In: *Breast Pathology*. New York, NY: Churchill Livingstone; 2006:185-189.
7. White J, Levine A, Gustafson G, et al. Outcome and prognostic factors for local recurrence in mammographically detected ductal carcinoma in situ of the breast treated with conservative surgery and radiation therapy. *Int J Radiat Oncol Biol Phys* 1995; 31:791-797.
8. Wright B, Shumak R. Part II: medical imaging of ductal carcinoma in situ. *Curr Probl Cancer* 2000; 24:112-124.
9. Stomper PC, Connolly JL, Meyer JE, Harris JR. Clinically occult ductal carcinoma in situ detected with mammography: analysis of 100 cases with radiologic-pathologic correlation. *Radiology* 1989; 172:235-241.
10. Evans AJ, Pinder S, Ellis IO, et al. Screening-detected and symptomatic ductal carcinoma in situ: mammographic fea-

tures with pathologic correlation. *Radiology* 1994; 191:237-240.

11. Dershaw DD, Abramson A, Kinne DW. Ductal carcinoma in situ: mammographic findings and clinical implications. *Radiology* 1989; 170:411-415.
12. Ikeda DM, Andersson I. Ductal carcinoma in situ: atypical mammographic appearances. *Radiology* 1989; 172:661-666.
13. Moon WK, Myung JS, Lee YJ, Park IA, Noh DY, Im JG. US of ductal carcinoma in situ. *Radiographics* 2002; 22:269-281.
14. Hashimoto BE, Kramer DJ, Picozzi VJ. High detection rate of breast ductal carcinoma in situ calcifications on mammographically directed high-resolution sonography. *J Ultrasound Med* 2001; 20:501-508.
15. Yang WT, Tse GM. Sonographic, mammographic, and histopathologic correlation of symptomatic ductal carcinoma in situ. *AJR Am J Roentgenol* 2004; 182:101-110.
16. Shin HJ, Kim HH, Kim SM, Kwon GY, Gong G, Cho OK. Screening-detected and symptomatic ductal carcinoma in situ: differences in the sonographic and pathologic features. *AJR Am J Roentgenol* 2008; 190:516-525.
17. Kim JH, Ko ES, Kim do Y, Han H, Sohn JH, Choe du H. Noncalcified ductal carcinoma in situ: imaging and histologic findings in 36 tumors. *J Ultrasound Med* 2009; 28: 903-910.
18. Moon WK, Im JG, Koh YH, Noh DY, Park IA. US of mammographically detected clustered microcalcifications. *Radiology* 2000; 217:849-854.
19. Mendelson EB, Baum JK, Berg WA, Merritt CR, Rubin E. Ultrasonography. In: *Breast Imaging Reporting and Data System*. 4th ed. Reston, VA: American College of Radiology; 2003:3-68.
20. Endo T, Kubota M, Konishi Y, et al. Draft Diagnostic Guidelines for Non-Mass Image-Forming Lesions by the Japan Association of Breast and Thyroid Sonography and the Japan Society of Ultrasonics in Medicine. Tokyo, Japan: Japan Association of Breast and Thyroid sonography; 2004:35-37.
21. D'Orsi CJ, Bassett LW, Berg WA, et al. Mammography. In: *Breast Imaging Reporting and Data System*. 4th ed. Reston, VA: American collage of Radiology; 2003:7-228.
22. Lagios MD. Microinvasion in ductual carcinoma in situ. In: Silverstein MJ (ed). *Ductal Carcinoma In Situ of the Breast*. Baltimore, MD: Williams &Wilkins; 1997:241-246.
23. Frykberg ER. An overview of the history and epidemiology of ductal carcinoma in situ of the breast. *Breast J* 1997; 3:227-231.
24. Zonderland HM, Coerkamp EG, Hermans J, van de Vijver MJ, van Voorthuisen AE. Diagnosis of breast cancer: contribution of US as an adjunct to mammography. *Radiology* 1999; 213:413-422.
25. Rahbar G, Sie AC, Hansen GC, et al. Benign versus malignant solid breast masses: US differentiation. *Radiology* 1999; 213:889-894.

26. Stavros AT, Thickman D, Rapp CL, Dennis MA, Parker SH, Sisney GA. Solid breast nodules: use of sonography to distinguish between benign and malignant lesions. *Radiology* 1995; 196:123–134.
27. Moon WK, Noh DY, Im JG. Multifocal, multicentric, and contralateral breast cancers: bilateral whole-breast US in the preoperative evaluation of patients. *Radiology* 2002; 224:569–576.
28. Gufler H, Buitrago-Téllez CH, Madjar H, Allmann KH, Uhl M, Rohr-Reyes A. Ultrasound demonstration of mammographically detected microcalcifications. *Acta Radiol* 2000; 41:217–221.
29. Cho KR, Seo BK, Kim CH, et al. Non-calcified ductal carcinoma in situ: ultrasound and mammographic findings correlated with histological findings. *Yonsei Med J* 2008; 49:103–110.
30. Alexander MC, Yankaskas BC, Biesemier KW. Association of stellate mammographic pattern with survival in small invasive breast tumors. *AJR Am J Roentgenol* 2006; 187: 29–37.
31. De Nunzio MC, Evans AJ, Pinder SE, et al. Correlations between the mammographic features of screen detected invasive breast cancer and pathological prognostic factors. *Breast* 1997; 6:146–149.