ULTRASOUND DEMONSTRATION OF MAMMOGRAPHICALLY DETECTED MICROCALCIFICATIONS IN PATIENTS WITH DUCTAL CARCINOMA IN SITU OF THE BREAST


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**Background:** Breast microcalcifications are difficult to depict by ultrasound (US). However, recent advances in US equipment and the refinement of breast imaging techniques have improved the detection and characterization of small breast lesions. The present study attempts to determine whether US examination is able to demonstrate nonpalpable breast lesions associated with mammographically detected microcalcifications without mass density or distortion, and to evaluate the clinical reliability of US-guided procedures, especially in cases of ductal carcinoma in situ (DCIS) of the breast.

**Methods:** The subjects consisted of 73 patients with breast cancer diagnosed preoperatively as DCIS by stereotactic core needle biopsies, all of whom had microcalcifications without other abnormalities on mammography. The radiological appearance and size of the clustered microcalcifications were evaluated. US examinations were performed preoperatively, and the detection rates were assessed. Sonographically detected lesions underwent US-guided wire localization followed by surgical excision.

**Results:** The lesions associated with microcalcifications were identified sonographically in 54 of 73 cases (74%), and the pathological examination revealed breast cancer in all of the corresponding specimens. Lesions with linear-branching shape, segmental-linear distribution and category-5 calcifications on mammography had a high level of visibility on US. The US visible cases had a larger size of calcified area on mammography when compared with US invisible cases. Pathologically, the lesions were more frequently seen on US in cases with minimally invasive cancer or with comedo type DCIS.

**Conclusions:** US examination is an effective method for identifying and localizing breast microcalcifications, and can be used as an alternative to stereotactic localization in selected patients with early breast cancer.


Key words: Breast cancer, Calcification, Mammography, Ultrasound

The recent reduction of the mortality rate of breast cancer in Europe and the United States was influenced increased by the detection of early stage breast cancer due to mammographic screening for breast cancer*. Mammography is very sensitive in the detection of breast microcalcifications, which are associated with breast cancer.

Microcalcifications are probably the most reliable mammographic feature in early nonpalpable breast cancer*. Mammographically detected, suspicious clustered microcalcifications are usually diagnosed by either percutaneous core needle biopsy with stereotactic guidance or by surgical excision after mammographically guided wire localization. However, stereotactic biopsy equipment is expensive and the procedure is time consuming.

Ultrasound (US) has long been known as a reliable modality for the diagnosis of a cystic or solid breast lesion*. In general, a US-guided procedure is preferred by patients over a mammographically guided procedure because patients are more comfortable supine, the breast is not compressed, and
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the procedure is often quicker. Furthermore, no ionizing radiation is used, the needle insertion site is more flexible, and the needle can be observed in real time. The advances in US equipment and the refinement of breast imaging techniques enable better detection and characterization of small lesions, but the low capability of US to depict microcalcifications remains a major limitation. Microcalcifications are hardly visible with US, especially when they are located inside echogenic and fibroglandular breast tissue, because of the difficulty in differentiating them from the echogenic interfaces among tissues. Only a few studies exist on the US detection rate of microcalcifications within carcinoma in situ.

The present study attempts to determine whether US examination is able to demonstrate nonpalpable breast lesions associated with mammographically detected microcalcifications without mass density or distortion, and to evaluate the clinical reliability of a US-guided procedure, especially in cases of ductal carcinoma in situ (DCIS) of the breast.

Patients and Methods

The subjects consisted of 73 cases with breast cancer diagnosed preoperatively as DCIS by core needle biopsies, who had microcalcifications without other abnormalities on mammography. The patients were surgically treated at the Department of General Surgery, Chiba University Hospital, Chiba, Japan, from 2000 to 2003. All of the patients had undergone breast screening by mammography and suspicious microcalcifications had been noted on their mammograms. Stereotactic vacuum-assisted core needle biopsy (Mammotome; Johnson & Johnson Ethicon Endo-Surgery, Cincinnati, OH) was performed at Chiba Cancer Screening Center, Chiba, Japan, and pathological examinations revealed DCIS associated with microcalcifications. The cases with palpable breast lesions and/or with mammographically identified masses or architectural distortions were excluded from this series.

Mammography was performed using a conventional film-screen technique (Senographe DMR+; GE Medical Systems, Milwaukee, WI). Standard mediolateral oblique and craniocaudal images of the breasts, and additional spot compression magnification images of areas containing microcalcifications were also obtained in all patients. Categorization of microcalcifications was performed according to the Breast Imaging Reporting and Data System (BI-RADS) developed by American College of Radiology and the Japanese Mammography Guidelines. The calcifications were morphologically classified as small round, amorphous, pleomorphic or linear/branching. The distribution of calcifications was described as clustered or segmental/linear. The size of the clustered microcalcifications was measured and calculated by the greatest diameter and its perpendicular dimension of the calcified group on mediolateral oblique projections. The radiological appearances of the microcalcifications identified on mammograms were evaluated by two or more specialists who received the image-reading training course of the Central Committee in the Quality Control of Mammographic Screening and ranked as having ability for mammogram-reading.

US examinations were performed with the patient in the supine position with the arms raised, using an Aloka model SSD 5500 (Aloka Co., Tokyo, Japan) ultrasound system with a 7.5-13 MHz broadband liner-array probe. The scans were performed with a knowledge of the mammographic findings for presence and areas of microcalcifications, focused on the suspicious area in the breast. Successful detection of the lesions on US was assessed based on whether a hypoechogenic area, local dilated ductlike structures and/or echogenic dots with or without acoustic shadowing were observed in the location of the mammographically visualized microcalcifications (Fig 1, 2). Sonographically detected lesions underwent US-guided wire localization using a 21-gauge hooked wire needle (Hakko Medical, Nagano, Japan), and lesions not seen on US underwent stereotactic procedure.

Sequential surgical excision was performed and specimen radiography was obtained in all cases to ensure the complete excision of the microcalcifications. The excised lesions were fixed in 10% formalin, paraffin embedded as tissue blocks, cut into multiple serial sections, stained by hematoxylin and eosin (H-E) and evaluated by our experienced pathologist. Pathological intraductal components were classified into comedo type and non-comedo type, depending on the existence of a comedo element.

Statistical differences were determined by the Mann-Whitney U test for continuous variables and
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Ultrasound Demonstration of Breast Calcifications

Table 1. Characteristics of Microcalcifications and Ultrasound Detection Rates for All Patients

<table>
<thead>
<tr>
<th>Shape</th>
<th>Count</th>
<th>Detection Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small round</td>
<td>12/17</td>
<td>(70.6%)</td>
</tr>
<tr>
<td>Amorphous</td>
<td>10/16</td>
<td>(62.5%)</td>
</tr>
<tr>
<td>Pleomorphic</td>
<td>23/30</td>
<td>(76.7%)</td>
</tr>
<tr>
<td>Linear/Branching</td>
<td>9/10</td>
<td>(90.0%)</td>
</tr>
<tr>
<td>Distribution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clustered</td>
<td>24/36</td>
<td>(66.7%)</td>
</tr>
<tr>
<td>Segmental/Linear</td>
<td>30/37</td>
<td>(81.1%)</td>
</tr>
<tr>
<td>Category</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>19/29</td>
<td>(65.5%)</td>
</tr>
<tr>
<td>4</td>
<td>11/14</td>
<td>(78.6%)</td>
</tr>
<tr>
<td>5</td>
<td>24/30</td>
<td>(80.0%)</td>
</tr>
</tbody>
</table>

Table 2. Characteristics of Microcalcifications and Ultrasound Detection Rates in Patients with Ductal Carcinoma in situ

<table>
<thead>
<tr>
<th>Shape</th>
<th>Count</th>
<th>Detection Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small round</td>
<td>10/15</td>
<td>(66.7%)</td>
</tr>
<tr>
<td>Amorphous</td>
<td>7/12</td>
<td>(58.3%)</td>
</tr>
<tr>
<td>Pleomorphic</td>
<td>8/14</td>
<td>(57.1%)</td>
</tr>
<tr>
<td>Linear/Branching</td>
<td>4/5</td>
<td>(80.0%)</td>
</tr>
<tr>
<td>Distribution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clustered</td>
<td>13/24</td>
<td>(54.2%)</td>
</tr>
<tr>
<td>Segmental/Linear</td>
<td>16/22</td>
<td>(72.7%)</td>
</tr>
<tr>
<td>Category</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>14/24</td>
<td>(58.3%)</td>
</tr>
<tr>
<td>4</td>
<td>7/8</td>
<td>(87.5%)</td>
</tr>
<tr>
<td>5</td>
<td>8/14</td>
<td>(57.1%)</td>
</tr>
</tbody>
</table>

chi-square test for categorical variables. P values of less than 0.05 were considered to indicate statistically significant differences.

Results

All the patients were female and the ages ranged from 29 to 74 years with a median of 54 years. The small round shaped microcalcifications were seen in 17 patients, amorphous in 16, pleomorphic in 30 and linear/branching in 10 cases. Microcalcifications of 36 cases showed a clustered distribution and 37 cases presented a segmental/linear distribution. The final assessment of mammographic findings was probably benign lesions (category 3) in 29 cases, suspicious lesions (category 4) in 14 cases, and highly suspicious lesions (category 5) in 30 cases. Mastectomies were performed in 31 cases (42.5%), and the other 42 cases (57.5%) received breast-conserving surgeries. The pathological examination revealed breast cancer in the resected specimens in all cases, including DCIS in 46 cases and minimally invasive ductal carcinomas in 27 cases. Among the DCIS cases, 15 (32.6%) had comedo components.

Among 73 cases examined, the lesions of microcalcifications were identified sonographically in 54 cases (74%). The linear/branching shape (detection rate 90.0%) and segmental/linear distribution (81.1%) on mammography had a higher level of visibility on US examination, compared with other types (Table 1). Category 5 lesions were also more likely to be seen on US (80.0%), followed by category 4 and 3. In patients with DCIS, a similar tendency was demonstrated between the US visibility and characteristics of
microcalcifications (Table 2). However, there was no statistically significant difference among the groups of microcalcifications concerning US detection rates. The US visible cases had a larger size of calcification containing area on mammography than the invisible cases ($P = 0.019$, Table 3).

Table 4 shows the correlation between pathological subtypes and US detection rates. The breast lesions were more frequently observed on US in cases with minimally invasive cancers (92.6%) than DCIS (63.0%, $P = 0.006$). The lesions were more frequently indicated on US in the comedo type (73.3%) than in the non-comedo type (58.1%) of DCIS.

### Discussion

Mammography is the gold standard for the detection and characterization of microcalcifications. In contrast, US examination has been reported to be less sensitive for the demonstration of microcalcifications than mammography.\(^{15-17}\). This low capability to visualize microcalcifications remains a major limitation for using US as a screening tool for early breast cancer. However, the marked improvement of current transducer technology has improved spatial resolution and contrast, allowing better and more frequent visualization of breast microcalcifications.\(^{1,18,20}\). The main benefit of identifying the lesions corresponding to mammographically detected microcalcifications is to allow the use US procedures, such as needle biopsy and needle localization. US allows echogenic breast lesions to be directly targeted in real time, and the biopsy needle can be seen penetrating the target, thus ensuring accurate sampling. In addition, US-guided procedures are less expensive and faster than stereotactically guided procedures. At the institutions that do not have stereotactic equipment, the use of US in selected patients would extend the role of biopsy of early breast cancer.\(^{18,21}\).

Calcifications that occur within masses are easily seen on US.\(^{6,22,23}\). This is partly because most malignant solid tumors provide a very hyperechoic background, which enhances the US demonstration of the bright punctate calcification echoes. Previous studies have shown that sonography can reveal lesions containing microcalcifications. In 1982, Kasumi et al. succeeded in detecting microcalcifications within breast carcinomas by US.\(^{24}\). Hastrich et al.\(^{25}\) sonographically evaluated isolated microcalcifications in 76 patients and identified 45% of microcalcifications with a 7.5 MHz probe. In reported series, high-resolution US is capable of visualizing microcalcifications within breast cancers with a sensitivity of 95%\(^{22,26,27}\). Of course, US detectability of breast lesions is strongly dependent on the examiners' experience and technique, the size of the lesions, and the histopathologic characteristic of the lesions. With no knowledge of mammographic findings, some microcalcifications or small lesions may be missed by US examination.

Identifying isolated microcalcifications within normal breast tissue, which is comprised of much hyperechoic and heterogeneous fibrous tissue, is thought to be more difficult with US. This is mainly due to the lack of contrast between normal parenchyma with hyperechoic heterogeneous fibrous structures and the microcalcifications.\(^{28}\) Thus, the microcalcifications associated with DCIS are not easily visualized sonographically unless a mass effect develops.\(^{29}\). Consequently, little is known about the detailed US features of DCIS. In our study, 74% of microcalcific lesions without other mammographic findings were identified on US, and US guidance could be used successfully to help wire localization techniques. The breast lesions with a linear/branching shape or segmental/linear distributed microcalcifications were more frequently demonstrated on US. The detection rate was higher when the size of the microcalcification containing area became larger. Pathologically, minimally invasive cancers were more frequently detected on US than DCIS, and the comedo type of DCIS had a higher detection rate compared with the non-comedo type. These results coincided with the pathological reports that the
comedo type showed invasive nests significantly more often and the rate of invasion increased with the extent of the calcifications.

Our results do not lead to a definitive consensus concerning the management of DCIS with microlcalifications by US techniques, because of the small number of cases. Further investigations of a large number of cases are needed to delineate the proper selection of clinically suitable cases with microlcalifications to undergo US guided procedures. However, US examination is an effective non-invasive method of identifying and localizing breast microlcalifications, and can be used as an alternative to stereotactic localization in the majority of cases with early breast cancer.

References


