The Diagnostic Value of Micropure Imaging in Breast Suspicious Microcalcificaion

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Abbreviations

MI Micropure Imaging

B-US B-mode ultrasonography

DU Doppler ultrasonography

AUC area under the curve

DCIS ductal carcinoma in situ

CDFI color Doppler flow imaging

SD spectral Doppler

RI resistance index

NST invasive carcinomas of no special type

Rationale and Objectives: The purpose of this study was to evaluate the diagnostic value of Micropure Imaging (MI) in breast lesions differentiation by comparison with B-mode ultrasonography (B-US) and Doppler ultrasonography (DU).

Materials and Methods: A total of 135 consecutive patients (all females) with 135 suspicious lesions were examined and skin marked by MI before mammotome biopsies. All patients (age range, 20–86 years; mean age, 42.5 ± 15.6 years) were the first onset, not in the pregnancy or lactation and had no history of radiation or chemotherapy. The maximum diameter of lesions ranged from 0.2 to 9.6 cm (average 1.98 ± 1.3 cm). Their final diagnoses were obtained by histologic examination. The study protocol was approved by the hospital review board; each patient gave written informed consent.

Results: One hundred thirty-five breast lesions were classified into 90 nonmalignant and 45 malignant types. To 86 breast lesions with microcalcification, MI showed more microcalcification and coincided better with pathology results than B-US did ($P < .05$). The specificity of MI was higher than that of B-US and DU; the sensitivity of DU was significantly higher than that of B-US and MI ($P < .001$). By combining B-US, DU, and MI, the detection accuracy was 86.7%. Receiver-operator characteristic curves showed the area under the curve of B-US, DU, and MI was 0.865, 0.934, and 0.923($P = .000$), respectively. Moreover, the interobserver agreements of MI were the highest, 0.922 (observer 1 vs. observer 2), 0.866 (observer 1 vs. observer 3), and 0.916 (observer 2 vs. observer 3).

Conclusions: MI as an adjunct ultrasound modality holds some promise in locating and differentiating breast lesions.

Key Words: MI; microcalcification; B-US; DU.

INSTRUCTION

Breast cancer is one of the most malignant tumors in women. Early detection often spells excellent prognosis. Numerous pathologic subtypes of breast cancer with suspicious microcalcification are proved either ductal carcinoma in situ (DCIS) or invasive cancer, which could be an early stage of breast cancer (1). So microcalcification plays an important role in diagnosing breast diseases and leads to extensive research in digital mammography (2). However, not all microcalcifications in mammography are malignant, and digital mammography does not eliminate fundamental limitations of detecting breast cancers without calcification, especially in dense parenchyma (3). Owing to the potential carcinogenicity, whether and when we intensify screening mammography programs on breast cancer are controversial. To seek a more objective and accessible method to check, suspicious microcalcification has become a new research trend. Many research showed Asian women had small dense breast tissue and fit for screening by ultrasonography rather than mammography (4,5). Microcalcification is also a common finding and symbolized by bright spot on ultrasonography. Because the speckle pattern and some tissue structures look like microcalcification, traditional ultrasound imaging is not good enough in clinical evaluation of suspicious microcalcification to date. Micropure Imaging (MI; USA Patent No.8,696,575) is a patent that Toshiba company invented and added on traditional gray scale ultrasonography. The apparatus

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removes a speckle pattern using information on a direction (depth direction) that is substantially orthogonal to a plurality of ultrasonic images included in three-dimensional image data. Micropure technique highlights microcalcification (less than 0.5 μm) represented by white spot through suppressing surrounding tissue with blue overlay image (6–8). Thus far, although a few articles proved MI had a possibility to increase detectability of the microcalcification (9,10), no articles evaluated the capabilities of the application in differentiating breast lesions with pathologic tests as gold standard. The purpose of our study was to assess the capabilities of MI in revealing the nature of breast lesions and targeting at suspicious microcalcification in biopsy. The results were compared with those of B-mode ultrasonography (B-US) and Doppler ultrasonography (DU). DU included color Doppler flow imaging (CDFI) and spectral Doppler (SD).

MATERIALS AND METHODS

Patients, Procedure, and Examination Technique

The study was conducted in a general hospital from November 2013 to March 2015, 135 consecutive patients (all females) with 135 nonpalpable suspicious breast lesions were examined by B-US and MI before mammotome biopsy and after surgery dissection. All patients (age range, 20–86 years; mean age, 42.5 ± 15.6 years) were the first onset, not in the pregnancy or lactation and had no history of radiation or chemotherapy. The maximum diameter of lesions ranged from 0.2 to 9.6 cm (average, 1.98 ± 1.3 cm). Their final diagnoses were obtained by means of histologic examination. The study protocol was approved by the hospital review board; each patient gave written informed consent.

During the whole ultrasound examination, patients maintained a supine position with arms abduction to fully exposed lesions. The scanning process was carried out by the same sonographer using an Aplio400 14L5 ultrasound scanner (Toshiba Corporation, Tokyo, Japan) equipped with a 5–14 MHz linear-array transducer. No compounding or other image processing techniques were applied. Time-gain compensation and 2-D gain setting were optimized for each subject individually. It should be noticed that a single imaging mode was used for B-US and CDFI but split-screen mode for MI to obtain identical images. SD was measured three times in excision regions, and resistance index (RI) was recorded by average. The lesions' maximum diameter as well as border, margin, internal echo, posterior acoustic, and presence of calcifications were documented. We skin marked lesion under the guidance of MI and acquired regional biopsy by the mammotome biopsy system (Johnson & Johnson Corp., New Brunswick, NJ). Eight-gauge needles (inside diameter, 3.9 mm; outer diameter, 4.3 mm; length, 9.27 cm) were used, and the biopsy operated by a surgeon with 20 years of experience. After biopsy, each specimen was placed in standard biocassettes for tissue sample embedding, formalin fixed, and sent to the pathologist for histologic examination. All images were stored in hard disks and analyzed by three reviewers who had at least 5 years of experience in sonography diagnosis and gave their impressions individually without any clinical data.

B-US, DU, and MI Evaluation

We referred BI-RADS(2003) (11) and defined irregular, speculated, or angulated border, indistinct margin, heterogeneous echogenicity with or without calcification, boundary echo, and posterior acoustic shadowing as malignant characteristics. With previously mentioned three or more than three characteristics in images, reviewers could judge the lesions as malignant. CDFI consulted Adler classification (12) as follows: pattern 0 showed bare vascularization in lesion; pattern I showed a small amount of color flow signals and displayed as a point or a thin rod whose diameter was less than 1 mm. Pattern II showed a main blood vessel with or without 2 and 3 small blood vessels at the same time. The length of the main vessel usually exceeded the radius of lesion. Pattern III showed prominent vascularization with vessel signals distributed chaotically within the lesion. We referred Choi HY et al (13) and defined that RI more than or equal to 0.7 suggested that lesions were malignant. With pattern II or pattern III or RI $\geq$0.7, we defined lesion malignant and the rest with pattern 0 or pattern I or RI <7 nonmalignant. MI criteria were classified into four maps as follows: map 1 indicated no bright spot appeared in visual field; map 2 indicated some bright spot outside lesion and less than or equal to 3 bright spots in lesion. Map 3 indicated more than 3 bright spots in central lesion. Map 4 indicated more than 3 bright spots in peripheral lesion. MI with map 1 or map 2 suggested malignant and those with map 3 or map 4 nonmalignant. Besides, we recorded the number of white spot (less than 0.5 μm) in B-US and MI separately. B-US, CDFI, and MI scoring criteria were sketched in Figure 1.

Pathologic Examination

All patients underwent mammotome biopsy after skin marking in lesions. After biopsy, we re-examined the region to prove whether the same lesion had been excised out.

The specimens were selected and fixed in 10% formalin and embedded in paraffin. Then 4-mm sections were obtained at 20-mm to 30-mm intervals for standard hematoxylin and eosin staining. All pathologic diagnoses were made by a pathologist with 20 years of working experience. All pathologic types of breast tumors referred to World Health Organization classification of tumors of the breast (14).

Statistical Analysis

SPSS for Windows version 19.0(SPSS Inc., IBM) was used for statistical analysis. Measurement data were described as mean ± standard deviation. Differences in continuous measurements