Clinical Usefulness and Future Prospects of MicroPure™

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Introduction

Mammography currently has a significant advantage over ultrasound in terms of its clinical usefulness for the detection of microcalcifications in breast examinations. The main reason is that in mammography, the probability of malignancy can be assessed using established categories that are based on the shape (small round, amorphous, pleomorphic, or fine linear) and distribution pattern (clustered, segmental, linear, regional, or diffuse) of microcalcifications.[1] In addition, there are established techniques for confirming the diagnosis, such as mammographic stereotactically guided biopsy and aspiration biopsy using the Mammotome Biopsy System.[2,3] Finally, a large number of studies have reported detailed comparisons of mammographic and pathologic findings.[4-7]

Ultrasound is effective for the detection of tumors and for the examination of patients with dense breasts, but this modality has trailed behind mammography because it displays only a part of the microcalcifications in a single plane, it cannot depict the exact size and shape of microcalcifications, and it lacks objective criteria such as those that have been established for mammography. Following the introduction of fully digital ultrasound systems, however, the detection of microcalcifications is no longer difficult thanks to the development of high-frequency imaging, the introduction of a wide-band nonlinear imaging technique known as Differential Tissue Harmonic Imaging (Diff-THI) and many other technological advances.[8,9]

MicroPure is an image processing function that is designed to improve the visualization of microcalcifications that can be detected but are difficult to visually identify in B-mode images due to the presence of speckle noise and surrounding tissues.

In the present study, MicroPure was evaluated in terms of its usefulness in visualizing microcalcifications that were found to have low mammographic density and low distribution density in mammographic images and were thought to be difficult to visually identify in ultrasound images. Whether or not high-echo spots, which are suggestive of microcalcifications, could be clearly visually identified in the ultrasound images was then investigated, and the results showed that a high visualization rate could be achieved.

Methods

The digital diagnostic ultrasound system SSA-790A (Toshiba Medical Systems Corporation, Otawara, Tochigi, Japan) and the PLT-850AT and PLT-1204AX transducers (Toshiba) operating at frequencies of 8 MHz and 12 MHz respectively, were used. Diff-THI, which visualizes the difference-tone components that arise due to nonlinear propagation, was employed to improve the spatial resolution. ApliPure™ Plus, which performs simultaneous transmission/reception compounding, was used to reduce speckle noise. The final images were generated by superimposing the original B-mode images displayed in blue (Blue Layer method) and the extracted microstructures displayed in white (referred to as “white spots”) to permit the locations of the white spots in the B-mode images to be visually identified.

Subjects

The objective of this study was to evaluate the usefulness of MicroPure in improving the visualization of microcalcifications. Therefore, microcalcifications that were judged to be difficult to visually identify in ultrasound images were selected as the targets for evaluation, and their clinical significance in terms of benign or malignant findings was not taken into consideration. Microcalcifications that were judged to be easily identifiable in standard B-mode images were excluded. Microcalcifications that can be visually identified without difficulty in B-mode images can of course be extracted with MicroPure.

The subjects were 40 patients who underwent mammographic and ultrasound examinations at our institution during the period from December 20, 2007, to February 12, 2008, (32 days of operation) and were confirmed to meet the above criteria. The age range of the subjects was 30 to 76 years, with an average age 48.8 years. All mammographic interpretations and ultrasound examinations were performed by specialists in the respective fields and by the author (as the supervising physician).

Based on the mammographic density and distribution density of the microcalcifications seen in the mammograms, the 40 subjects were classified into three groups: 1) small round or amorphous microcalcifications with low mammographic density and low distribution density, 2) microcalcifications with characteristics intermediate between those of group 1 and group 3, and 3) small round or amorphous microcalcifications with very low mammographic density and very low distribution density.

With regard to evaluation of the clinical usefulness of MicroPure, microcalcifications that were not visually identified as white spots were classified as grade 1 and those that were clearly visually identified as white spots were classified as grade 2 (Table 1).

Grouping of microcalcifications detected by mammography	
Group 1	Small round or amorphous, low mammographic density, low distribution density
Group 2	Intermediate between group 1 and group 2
Group 3	Small round or amorphous, very low mammographic density, very low distribution density

Evaluation of the clinical usefulness of MicroPure in improving the visualization of microcalcifications	
Grade 1	Cannot be visually identified
Grade 2	Can be clearly visually identified

Table 1. Grouping of calcifications and evaluation of the clinical usefulness of MicroPure in improving the visualization of microcalcifications

Results

1. Group classification based on the results of mammography

Of the 40 subjects, 10 were classified as group 1, 10 as group 2, and 20 as group 3.

2. Evaluation of the usefulness of MicroPure in improving the visualization of microcalcifications

Of the 40 subjects, 7 (17.5%) were classified as grade 1 and 34 (82.5%) were classified as grade 2, indicating a high visualization rate.

All of the 7 subjects classified as grade 1 were included in group 2 or group 3, and most of them were included in group 3 (microcalcifications with very low mammographic and distribution densities). With regard to the subjects classified as grade 2, no significant bias was observed between the groups. The number of subjects classified as grade 2 was highest (16 subjects) in group 3, indicating that MicroPure is effective in improving the visualization of microcalcifications with very low mammographic and distribution densities, which are considered to be difficult to visually identify in standard B-mode images (Table 2).

		Microcalcification group			
		1	2	3	Total
MicroPure grade	1	0	3	4	7 (17.5%)
	2	10	7	16	33 (82.5%)
	Total	10 (25.0%)	10 (25.0%)	20 (50%)	40 (100%)

Table 2. Relationship between MicroPure grades and calcification groups

B-mode images and the corresponding MicroPure images demonstrating a high degree of visualization are shown in Figs. 1-6.

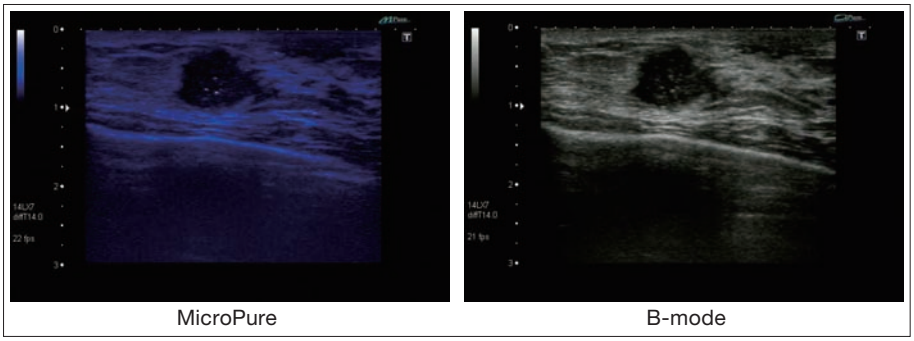

Figure 1. Case 1: Microcalcifications inside the mass of invasive ductal carcinoma (group 3, grade 2). Such microcalcifications are difficult to detect even by mammography. These are displayed amorphously in the B-more image, but after processing with MicroPure, the white spots can be clearly visually identified.

Discussion

1. Clinical usefulness of MicroPure

In order to improve the visualization of microcalcifications using MicroPure, it is necessary to extract and enhance true microcalcifications and, at the same time, to eliminate other high-echo spots that may lead to false-positive diagnostic findings.

The results of the present study confirmed that MicroPure can suppress the visualization of fat, the mammary

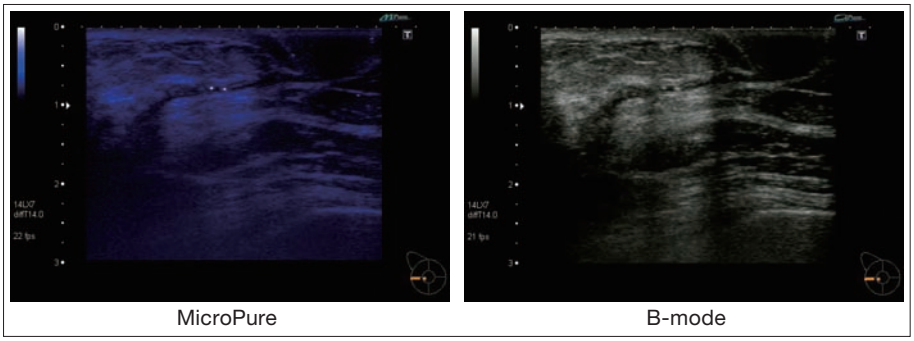

Figure 2. Case 2: Microcalcifications in invasive ductal carcinoma invading the lactiferous ducts (group 3, grade 2). White spots can be clearly visually identified in invasive ductal carcinoma invading the lactiferous ducts.

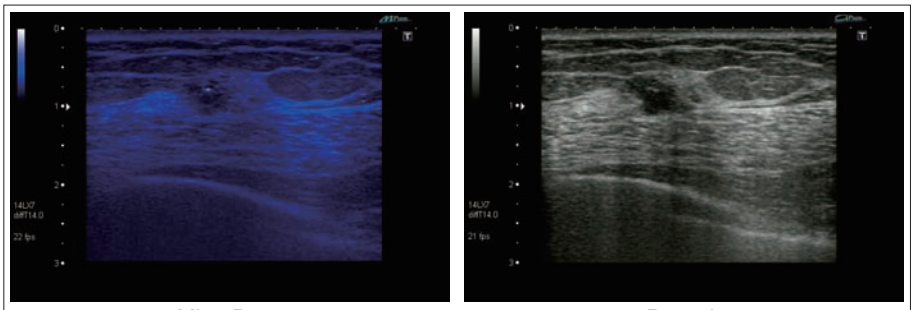

Figure 3. Case 3: Microcalcifications in invasive ductal carcinoma (group 2, grade 2).
White spots in invasive ductal carcinoma can be visually identified more clearly than in the B-mode image.

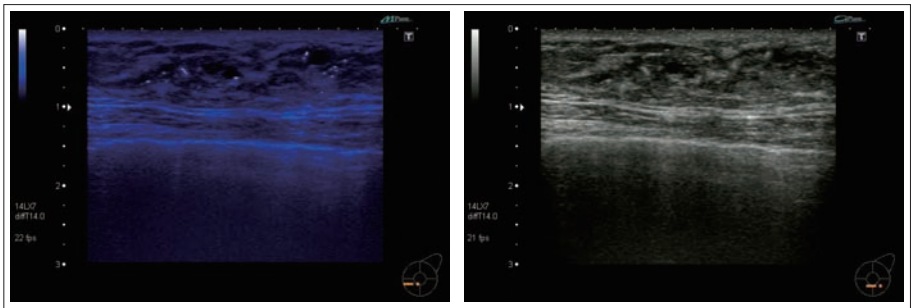

Figure 4. Case 4: Diffuse microcalcifications (group 1, grade 2).
Microcalcifications appear amorphously in the B-mode image, but many white spots can be visually identified in the MicroPure image. This lesion was confirmed to be benign by pathological examination.

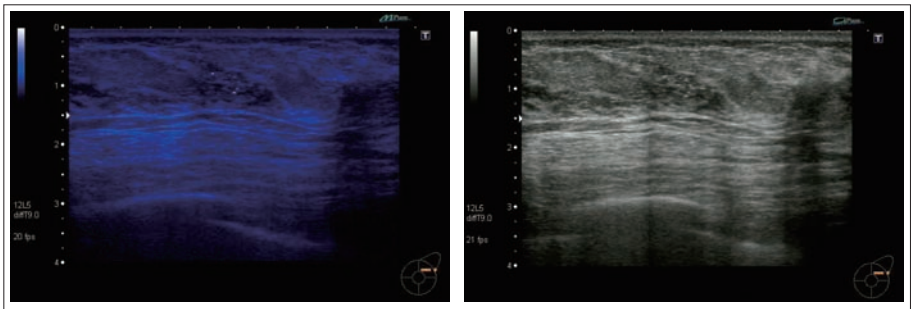

Figure 5. Case 5: Cluster of amorphous microcalcifications (group 3, grade 2).
The number of white spots is greater than the number of high-echo spots seen in the B-mode image, and the white spots can be visually identified with greater clarity. This lesion was confirmed to be benign by pathological examination.

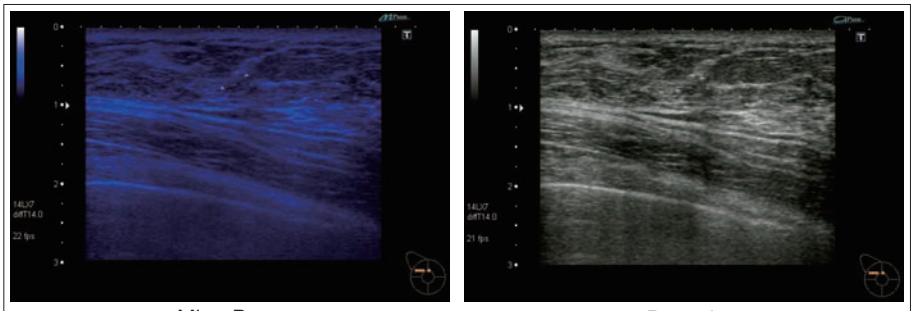

Figure 6. Case 6: Amorphous microcalcifications (group 2, grade 2).
White spots can be clearly visually identified. This lesion was confirmed to be benign by pathological examination.

gland borders, and the pectoralis major muscle, which are likely to appear as high-echo spots in B-mode images, and thus reduce or almost completely eliminate high-echo spots other than microcalcifications. The results also confirmed that the superimposition of a blue background (original B-mode image) and the white spots (indicating calcifications) makes it easier to clearly visually identify the presence and locations of white spots, as compared with standard B-mode images. We feel that the finding that visual identification was possible in 82.5% of the subjects provides strong evidence for the clinical usefulness of MicroPure. In addition, we must emphasize that the greatest advantage of this technique is its ability to provide a high degree of visualization without sacrificing real-time characteristics.

In terms of subjective visual assessment, the number of white spots in MicroPure images was slightly less than the number of high-echo spots in the corresponding B-mode images. In some cases, the white spots appeared smaller than the high-echo spots in the corresponding B-mode images. However, it has been reported that the size of a high-echo spot seen in a B-mode image does not accurately reflect the size of the micro calcification, and the finding that white spots appear smaller is therefore not considered to be a disadvantage.

In some cases, white spots were displayed but visualization was not improved. Such microcalcifications were difficult to detect as high-echo spots even in B-mode images.

There were also cases in which a microcalcification was not detected by mammography but a white spot was displayed in MicroPure images. In order to accurately diagnose microcalcifications using MicroPure, it is necessary to first assess their locations and shapes in mammographic images, then to confirm their expected locations and distribution by ultrasound examination, and then to determine whether or not the displayed white spots are exactly those intended to be depicted. The Guidelines for Breast Ultrasound caution us that high-echo spots do not always represent calcifica-

tions because a high-echo spot may appear due to the posterior echo of a very small cystic lesion or a Cooper's ligament crossing the echo tomographic plane at right angles.[10] In addition, ensuring an accurate focus setting is of crucial importance. It was confirmed that the false-positive rate can be reduced by setting the focus accurately on the mammary gland.

2. Suggestions for dealing with microcalcifications using MicroPure

Because of the increasing popularity of mammographic screening, an increasing number of patients visit hospitals for the detailed evaluation of microcalcifications.[11,12] In order for ultrasound to provide a level of performance equivalent or superior to mammography in dealing with microcalcifications, it is necessary to expand its capabilities so that it can serve as a modality for guidance during interventional procedures to confirm the diagnosis (Table 3). The steps for dealing with microcalcifications are: 1) improving the microcalcification detection rate, 2) improving the visualization of microcalcifications, 3) clarifying the low-echo areas around microcalcifications, and 4) providing quantitative guidance for biopsy of low-echo areas around microcalcifications. Specifically, it is necessary to develop an ultrasound system that can display the microcalcifications identified by mammography with a high degree of visualization by employing MicroPure to determine the clinical value of the displayed microcalcifications, and eventually to support guidance in interventional procedures. Most of the microcalcifications identified by mammography and considered to require detailed evaluation (especially those classified as category 3) are found to be benign lesions or noninfiltrating cancers, but mammographic stereotactically guided intervention is an invasive procedure. Considering the above situation, the establishment of a less invasive and simpler echo-guided biopsy procedure is eagerly awaited.[13,14]

Conclusion

In the present study, white spots could be extracted in MicroPure images in 82.5% of the subjects. This finding indicates that MicroPure can improve the visualization of microcalcifications and also suggests that it is a clinically useful imaging technique. In mammographically guided interventional procedures, the needle is simply advanced until it reaches the displayed calcification, and the presence of cellular components cannot be displayed directly in the image. In ultrasound examinations with MicroPure, on the other hand, white spots that indicate calcified lesions and low-echo cellular components can be displayed simultaneously. This is an important advantage of ultrasound over mammography. Low-echo areas around calcified lesions (cellular components) are exactly the target we should deal with, and providing effective support for precise needle biopsy is the next challenge for MicroPure.

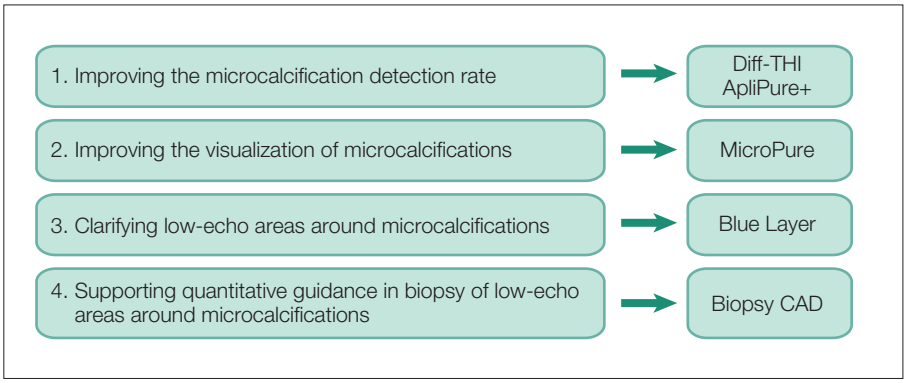

Table 3. Steps for dealing with microcalcifications using ultrasound

References

1) Guidelines for Mammography, Second Edition. Japan Radiological Society, MMG Guidelines Committee, 2004.
2) Matsuzaki S, Shiba E, Kobayashi Y, et al. Usefulness of stereotactically guided Mammotome biopsy for calcified lesions detected by mammography. Japanese Journal of Breast Cancer 2003;18(4):327-331.
3) Sato N, Hino M, Sano M, et al. Diagnostic approach to impalpable lesions using stereotactically guided aspiration needle biopsy. Japanese Journal of Breast Cancer 2004;19(6):557-560.
4) Watanabe R, Namba K, Furusawa H, et al. Diagnosis and treatment of breast cancers based on microcalcification images. Journal of Japan Association of Breast Cancer Screening 2004;13(2):159-166.
5) Koyama T, Shimooka H, Iijima K, et al. Pathological studies on mammary gland microcalcifications in comparison with mammography. Journal of Japan Association of Breast Cancer Screening 2004;13(2):154-158.
6) Tsunoda H, Kikuchi M, Oikado K, et al. Relationship between calcification and cancer lesion in specimens sampled by stereotactically guided aspiration needle biopsy. Japanese Journal of Breast Cancer 2005;20(3):245-249.
7) Onuki K, Ouchi A. Advances in image-based diagnosis and diagnostic imaging systems, 3. Mammography. Advanced Medicine for Breast Cancer. Advanced Medicine Technology Research Institute, Tokyo. 87-92, 2003
8) Kurita T. Usefulness of Differential Tissue Harmonic Imaging in breast examinations. Eizo Joho Medical 2006;38:558-569.
9) Kurita T. Latest ultrasound diagnostic imaging for the mammary gland: Establishment of new image concept with 4D images and MicroPure. New Medicine 2008;35(5):66-69.
10) Japan Association of Breast and Thyroid Sonology: Guidelines for Breast Ultrasound Diagnosis, 2nd Edition. Nankodo, Tokyo, 2008.
11) Usami S, Onuki K, Ishida T, et al. Study on diagnostic methods for microcalcifications found in screening. Journal of Japan Association of Breast Cancer Screening 2004;13(2):176-183.
12) Onuki K, Ouchi N, Yoshida K, et al. Approaches to calcifications found in mammographic screening: Aiming at higher precision. Journal of Japan Association of Breast Cancer Screening 1997;6:43-49.
13) Mizutani M, Toyama T, Kamei K, et al. Medical care system for impalpable breast cancers that appear only as microcalcification in mammography at Aichi Prefectural Cancer Center, Breast Surgery Department. Journal of Japan Association of Breast Cancer Screening 2004;13(2):167-175.
14) Sakurai O. Echo-guided Mammotome biopsy (two-person method: advantages and tips). Japanese Journal of Breast Cancer 2007;22(4):121-126.

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