Original Article

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Clinical Utility of MicroPure US Imaging for Breast Microcalcifications

유방 미세 석회에 대한 MicroPure 초음파

Heerin Lee, MD, Sung Hun Kim, MD*, Bong joo Kang, MD, Jeong Min Lee, MD

Department of Radiology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea

Purpose To evaluate the performance of MicroPure US imaging to detect and characterize microcalcifications.

Materials and Methods A total of 171 lesions with suspicious microcalcifications seen on mammography and B-mode US were included and simultaneously evaluated using MicroPure US imaging. The size of microcalcifications was divided into small (punctate, amorphous, fine pleomorphic, and fine linear) and large (coarse heterogeneous), and the extent was divided into narrow (grouped) and wide (others). MicroPure US imaging visibility was divided into four types based on the number of microcalcifications on the two images: B > M (more on B-mode), B = M (similar), B < M (more on MicroPure), and negative. Triple pairwise comparison was used to evaluate the imaging features according to the MicroPure US imaging visibility.

Results Among the 171 lesions examined, 157 lesions (91.8%) were detected by MicroPure US imaging. The proportion of Breast Imaging Reporting and Data System (BI-RADS) category 4A was significantly higher in the MicroPure positive group, and that of category 4B was significantly higher in the MicroPure negative group (p = 0.035). The other imaging features did not differ. Among the positive MicroPure subgroups, all features showed no significant difference.

Conclusion MicroPure US imaging demonstrated 91.8% positivity in detecting microcalcifications on B-mode US. MicroPure US imaging visibility correlated with the BI-RADS category of microcalcifications.

Index terms Breast; Calcinosis; Ultrasonography; Mammography

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***Corresponding author**
Sung Hun Kim, MD
Department of Radiology,
Seoul St. Mary's Hospital,
College of Medicine,
The Catholic University of Korea,
222 Banpo-daero, Seocho-gu,
Seoul 06591, Korea.

Tel 82-2-2258-1455
Fax 82-2-2258-1457
E-mail rad-ksh@catholic.ac.kr

ORCID iDs
Heerin Lee
https://orcid.org/0000-0003-2380-4434
Sung Hun Kim
https://orcid.org/0000-0003-4478-9720
Bong joo Kang
https://orcid.org/0000-0002-5991-6035
Jeong Min Lee
https://orcid.org/0000-0002-4266-7984

INTRODUCTION

Microcalcifications in both screening and diagnostic mammography are important diagnostic clues for breast cancer. Microcalcification is highly associated with ductal carcinoma in situ, and approximately 20% of invasive cancer is associated with micro-

calcifications (1, 2). Stereotactic biopsy is an accurate biopsy method for suspicious microcalcifications detected on mammography (3). Advances in US technology have enabled radiologists to identify and localize microcalcifications (4). US guidance is preferred in lesions that can be biopsied with both stereotactic or US guidance and is currently considered an effective and reliable alternative to stereotactic biopsy in such cases (4, 5). This is because US guidance has the advantages of simplicity and cost-effectiveness, radiation-proof procedure, and flexible needle insertion with real-time observation (6). However, microcalcifications without mass are difficult to detect on US because they are small and buried in the echogenic, fibroglandular breast tissue (7, 8). In addition, not all "hyperechoic foci" on US are microcalcifications, and collagen fibers and other changes might simulate microcalcifications (9).

MicroPure™ (Canon Medical Systems, Tustin, CA, USA) is a new US imaging processing technique to highlight microcalcifications by combining non-linear imaging and speckle suppression with a constant false alarm rate filter. This filter extracts only isolated high-brightness echoes against a heterogeneous background (10, 11). MicroPure US imaging marks suspected calcifications as white spots in a blue overlay image (12). A few studies have demonstrated superior detection of larger numbers of microcalcifications with MicroPure US imaging than with B-mode US (10, 11, 13, 14) .

To the best of our knowledge, no studies have analyzed detection and visibility capabilities of MicroPure US imaging based on imaging features. The purpose of this study was to evaluate the performance of MicroPure US imaging for detecting microcalcifications seen on mammography and B-mode US and to identify characteristics of microcalcifications detected with MicroPure US imaging.

MATERIALS AND METHODS

SUBJECTS

The Institutional Review Board of our hospital approved this retrospective study, and the requirement for informed consent was waived (IRB No. KC19RESI0686).

This retrospective study performed from September 2017 to March 2019 included 171 cases. Mammographic reporting and US examination were performed by one of three radiologists with a breast subspeciality (5–19 years of experience). Breast Imaging Reporting and Data System (BI-RADS) category 4A or higher microcalcifications on mammography and that were also shown on B-mode US were included. Using mammography as a reference, the region of interest was scanned with B-mode US (4–18 MHz probe, Aplio i700, Canon Medical Systems). When echogenic foci on B mode US were matched with mammographic calcifications, a simultaneous MicroPure US image was obtained as a still image (MicroPure, Aplio i700, Canon Medical Systems). Pathologic diagnosis was performed with US-guided core-needle biopsy (n = 161), US-guided vacuum-assisted biopsy (n = 5), and stereotactic vacuum-assisted biopsy (n = 5). Specimen mammography after biopsy (n = 87) or pathologic report confirmed the presence of microcalcifications. With biopsy or surgery, final pathology was benign (n = 29) or malignant (n = 142) (Table 1).

Table 1. Pathologic Results (*n* = 171)

	Number of Lesions
Invasive breast cancer	107
Ductal carcinoma in situ	35
Atypical ductal hyperplasia	6
Lobular carcinoma in situ	1
Mucocele-like lesion	1
Fibrocystic change	14
Fibroadenoma	4
Sclerosing adenosis	3

IMAGE ANALYSIS

Medical records were reviewed, and images of mammography, B-mode US, and MicroPure US were reviewed with consensus by two radiologists (one with 14 years of experience in breast imaging and the other, a senior radiology resident) who were blinded to the pathologic results.

Morphology and distribution of the microcalcifications on mammography were evaluated using BI-RADS. Size and extent of microcalcifications were divided into two groups. Regarding size, the 'small' group was composed of punctate, amorphous, fine pleomorphic, and fine linear/linear branches smaller than 0.5 mm in size, and the 'large' group was composed of coarse heterogeneous calcifications. Regarding extent, the 'narrow' group was composed of grouped calcifications less than 2 cm in spread, and 'the wide' group was composed of regional, segmental, and linear distributions.

US images were evaluated whether the microcalcifications were associated with mass- or non-mass-like lesions and whether background echotexture was homogeneous or heterogeneous.

MicroPure US imaging was considered positive for microcalcification when a bright white spot was visible in an area of echogenic foci on B-mode. MicroPure US imaging visibility was divided into four types based on number of calcifications on two images: B > M (more calcifications on B-mode than on MicroPure), B = M (similar numbers), B < M (more on MicroPure than on B-mode), and negative (no microcalcifications on MicroPure) (Fig. 1).

STATISTICAL ANALYSIS

To assess pairwise differences between the two groups, Fisher's exact test was employed, because the negative MicroPure group comprised a small number of cells. The ANOVA test was used for triple pairwise comparison among MicroPure-positive groups. A p value < 0.05 was considered significant. Statistical analysis was performed using SAS Version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Mammographic and US findings of 171 lesions with microcalcifications are summarized in Table 2. There was 7.6% of large calcifications (coarse heterogeneous calcifications [*n* = 13, 7.6%]) and 92.4% of small calcifications (punctate [*n* = 6, 3.5%], amorphous [*n* = 59, 34.5%],

Fig. 1. Representative type of MicroPure visibility.
B-mode US (left) shows echogenic foci matched with microcalcifications detected on mammography (right). MicroPure US imaging (middle) shows bright dots.
A. In B > M type, MicroPure US imaging shows fewer bright dots than echogenic foci on B-mode.
B. In B = M type, MicroPure US imaging and B-mode US show similar patterns.
C. In B < M type, MicroPure US imaging shows more bright dots than echogenic foci on B-mode US.
D. B-mode US (left) shows echogenic foci matched with microcalcifications detected on mammography (right). MicroPure US imaging (middle) shows no bright dots.

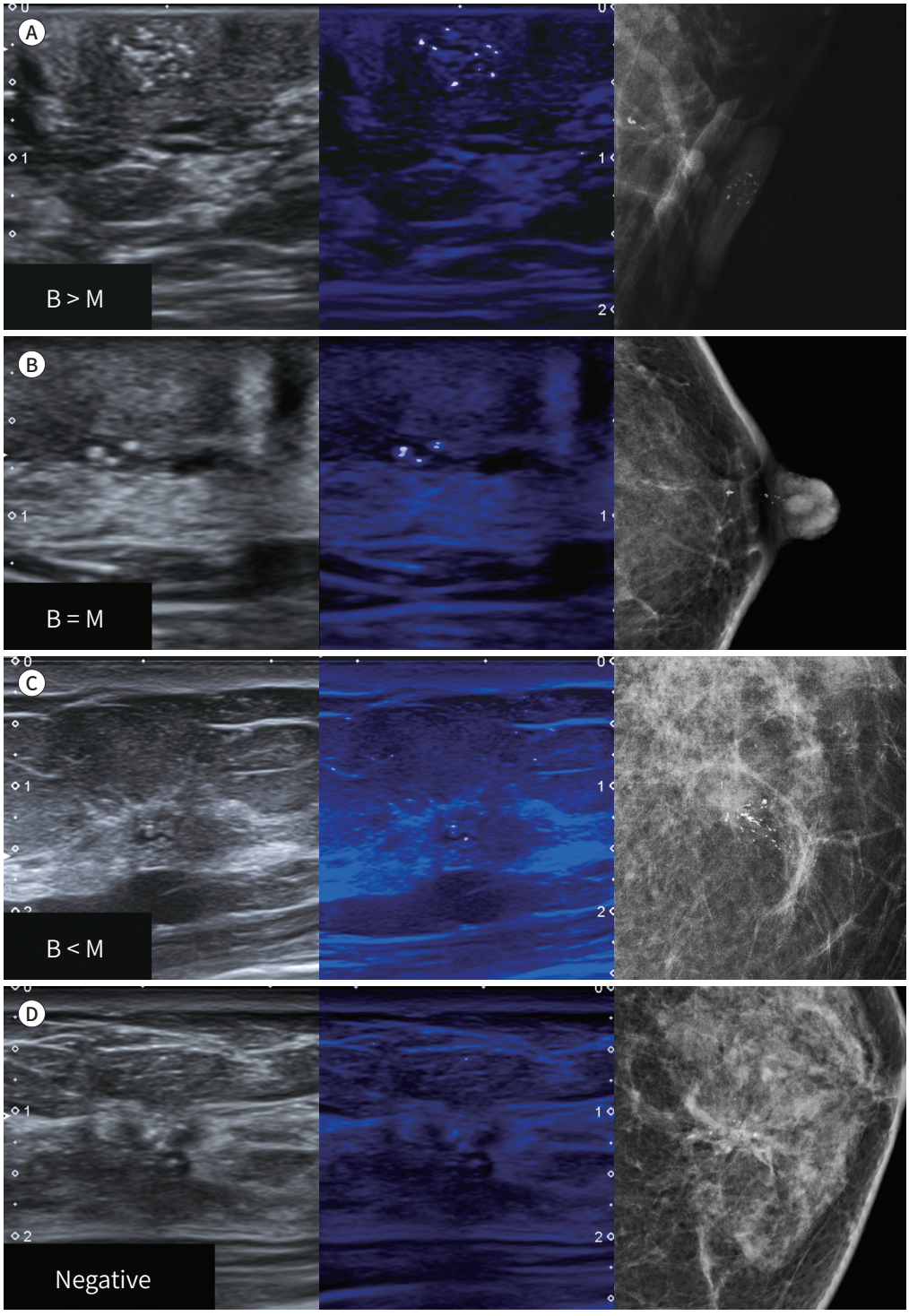


Table 2. Mammographic and Ultrasonographic Findings of Microcalcifications (*n* = 171)

	Total
Mammographic abnormalities	
Calcification	98 (57.3)
Calcification with mass	73 (42.7)
Morphology of calcifications	
Punctate	6 (3.5)
Amorphous	59 (34.5)
Coarse heterogeneous	13 (7.6)
Fine pleomorphic	67 (39.2)
Fine linear/linear branching	26 (15.2)
Size of calcifications	
Large	13 (7.6)
Small	158 (92.4)
Distribution of calcifications	
Grouped	70 (41.0)
Regional	45 (26.3)
Segmental	53 (31.0)
Linear	3 (1.7)
Extent of calcifications	
Wide	101 (59.0)
Narrow	70 (41.0)
Mammographic category (BI-RADS)	
C4A	12 (7.0)
C4B	66 (38.9)
C4C	48 (28.0)
C5	45 (26.3)
Ultrasonographic abnormalities	
Echogenic foci	43 (25.1)
Echogenic foci with mass	102 (59.7)
Echogenic foci with nonmass	26 (15.2)
Background echotexture	
Heterogeneous	95 (55.6)
Homogeneous	76 (44.4)
Pathology	
Benign	29 (17.0)
Malignant	142 (83.0)

Numbers in parentheses are percentage.
BI-RADS = Breast Imaging Reporting and Data System

fine pleomorphic [*n* = 67, 39.2%] and fine linear [*n* = 26, 15.2%]). Extent according to distribution was wide in 59% of the calcifications (regional, segmental, linear distribution) and narrow in 41% (grouped distribution).

Among 171 lesions, 91.8% (157/171) were detected on MicroPure US imaging (Table 3). MicroPure US imaging did not detect calcifications in 14 cases (8.1%). Most of the negative

Table 3. Mammographic and Ultrasonographic Findings according to MicroPure US Imaging Visibility

	Positive (*n* = 157)	Negative (*n* = 14)	*p*-Value
Mammographic abnormalities			0.084
Calcification	89 (56.7)	9 (64.3)	
Calcification with mass	68 (43.3)	5 (35.7)	
Morphology of calcifications			0.064
Punctate	6 (3.8)	0 (0.0)	
Amorphous	54 (34.4)	5 (35.7)	
Coarse heterogeneous	12 (7.6)	1 (7.1)	
Fine pleomorphic	62 (39.5)	5 (35.7)	
Fine linear/linear Branching	23 (14.6)	3 (21.4)	
Size of calcifications			0.108
Large	66 (42)	6 (42.9)	
Small	91 (58)	8 (57.1)	
Distribution of calcifications			0.062
Grouped	60 (38.2)	10 (71.4)	
Regional	44 (28)	1 (7.1)	
Segmental	50 (31.8)	3 (21.4)	
Linear	3 (1.9)	0 (0.0)	
Extent of calcifications			0.153
Wide	97 (61.8)	4 (28.6)	
Narrow	60 (38.2)	10 (71.4)	
Mammographic category (BI-RADS)			0.035
C4A	12 (7.6)	0 (0.0)	
C4B	59 (37.6)	7 (50.0)	
C4C	45 (28.7)	3 (21.4)	
C5	41 (26.1)	4 (28.6)	
Ultrasonographic abnormalities			0.345
Echogenic foci	38 (24.2)	5 (35.7)	
Echogenic foci with mass or nonmass	119 (75.8)	9 (64.3)	
Background echotexture			0.084
Heterogeneous	88 (56.1)	7 (50.0)	
Homogeneous	69 (43.9)	7 (50.0)	
Pathology			0.389
Benign	28 (17.8)	1 (7.1)	
Malignant	129 (82.2)	13 (92.9)	

Numbers in parentheses are percentage.
BI-RADS = Breast Imaging Reporting and Data System

group were calcifications without mass on mammography (9/14, 64.3%), grouped distribution (10/14, 71.4%), small size (13/14, 92.9%), narrow extent (10/14, 71.4%), and malignancy (13/14, 92.9%). Grouped distribution was more frequently shown in MicroPure negative group than in MicroPure positive group (71.4% vs. 38.2%, respectively), but there was no significant difference ($p = 0.062$). The proportion of C4A was significantly higher in the MicroPure positive group and that of C4B was significantly higher in the MicroPure negative group ($p = 0.035$)

(Figs. 2, 3). Mammographic abnormalities, morphology, size, distribution and extent of calcifications, US abnormalities, background echotexture and pathology were not different between MicroPure positive and negative group.

All lesions according to MicroPure US imaging visibility were divided into B > M (n = 92, 53.8%), B = M (n = 51, 29.8%), B < M (n = 14, 8.1%), and negative (n = 14, 8.1%) (Tables 3, 4). All imaging features including distribution of calcifications and pathology showed no difference among the three MicroPure US imaging visible groups.

DISCUSSION

We evaluated the effectiveness of a new ultrasound image processing technique, MicroPure US imaging, in detecting microcalcifications in female with suspicious microcalcifications on mammography and B-mode US.

MicroPure US imaging demonstrated positivity in 91.8% of the microcalcifications detect-

Fig. 2. A 41-year-old female with suspicious microcalcifications and positive MicroPure findings.
A. Magnification view shows regional, amorphous microcalcifications, with Breast Imaging Reporting and Data System category 4A.
B. B-mode US (left) shows a few echogenic foci of microcalcifications (arrowheads) and MicroPure US imaging (right) shows one bright dot of microcalcification (arrowhead).
C. Specimen mammography after US-guided core needle biopsy confirms the presence of microcalcifications and fibrocystic change.

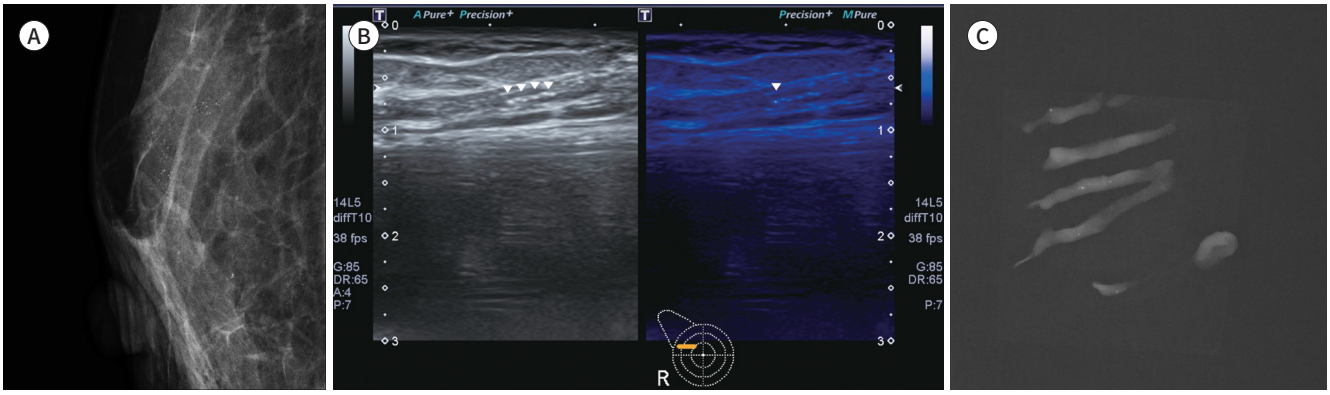


Fig. 3. A 56-year-old female with suspicious microcalcifications and negative MicroPure findings.
A. Magnification view shows grouped, fine pleomorphic microcalcifications, with Breast Imaging Reporting and Data System category 4B.
B. B-mode US (left) shows few echogenic foci of microcalcifications (arrowheads). MicroPure US imaging shows no bright dots.
C. Specimen mammography after US-guided core needle biopsy confirms the presence of microcalcifications and invasive breast carcinoma.

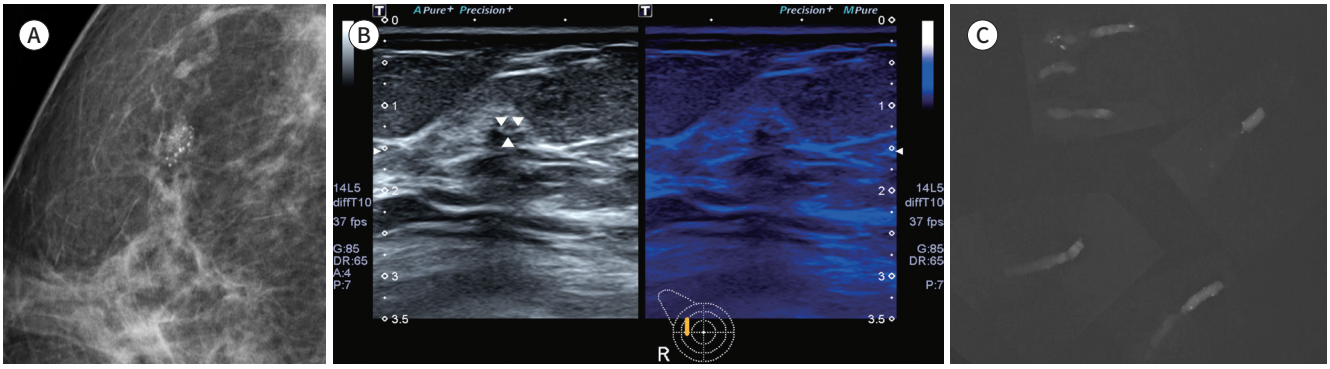


Table 4. Comparison of Imaging Features and Pathology among the Groups Stratified by MicroPure US Imaging Visibility

	B > M (*n* = 92)	B = M (*n* = 51)	B < M (*n* = 14)	*p*-Value
Mammographic abnormalities				0.205
Calcification	49 (53.3)	29 (56.9)	11 (78.6)	
Calcification with mass	43 (46.7)	22 (43.1)	3 (21.4)	
Size of calcifications				0.972
Large	8 (8.6)	3 (5.8)	1 (7.1)	
Small	84 (91.4)	47 (94.2)	13 (92.9)	
Extent of calcifications				0.087
Wide	63 (68.5)	28 (54.9)	6 (42.9)	
Narrow	29 (31.5)	23 (45.1)	8 (57.1)	
Mammographic category (BI-RADS)				0.172
C4A	6 (6.5)	4 (7.8)	2 (14.3)	
C4B	28 (30.4)	23 (45.1)	8 (57.1)	
C4C	28 (30.4)	14 (27.5)	3 (21.4)	
C5	30 (32.6)	10 (19.6)	1 (7.1)	
Ultrasonographic abnormalities				0.376
Echogenic foci	22 (23.9)	13 (25.5)	3 (21.4)	
Echogenic foci with mass	52 (56.5)	31 (60.8)	11 (78.6)	
Echogenic foci with nonmass	18 (19.6)	7 (13.7)	0 (0.0)	
Background echotexture				0.461
Heterogeneous	55 (59.8)	25 (49.0)	8 (57.1)	
Homogeneous	37 (40.2)	26 (51.0)	6 (42.9)	
Pathology				0.083
Benign	12 (13.0)	11 (21.6)	5 (35.7)	
Malignant	80 (87.0)	40 (78.4)	9 (64.3)	

Numbers in parentheses are percentage. B > M: MicroPure shows fewer microcalcifications as bright dots than does B-mode. B = M: MicroPure and B-mode show microcalcifications in similar numbers. B < M: MicroPure shows more microcalcifications as bright spots than does B-mode.
BI-RADS = Breast Imaging Reporting and Data System

ed on both mammography and B-mode US. In previous studies, both B-mode and MicroPure US imaging showed 100% detection positivity in diffuse microcalcifications (*n* = 20 patients) (13), grouped microcalcifications (*n* = 10 patients) (10), and microcalcifications (*n* = 20 surgical specimens) (11). Another study with 70 cases of pathologically proven microcalcifications revealed a higher detection rate for MicroPure US imaging than for B-mode (100% vs. 71.4%). In the present study, MicroPure US imaging did not detect microcalcifications in 8.2% of cases (14/171). We analyzed the characteristics of imaging features in MicroPure negative case, and only the BI-RADS category was meaningful. The proportion of of category 4B was significantly higher in the MicroPure negative group and that of category 4A was significantly higher in the MicroPure positive group in this study. On B-mode US, it was more difficult to identify isolated microcalcification than to find microcalcifications within a hypoechoic mass because of the lack of contrast between the parenchyma and the microcalcifications (13). However, associated US abnormalities did not differ between the MicroPure US imaging visi-

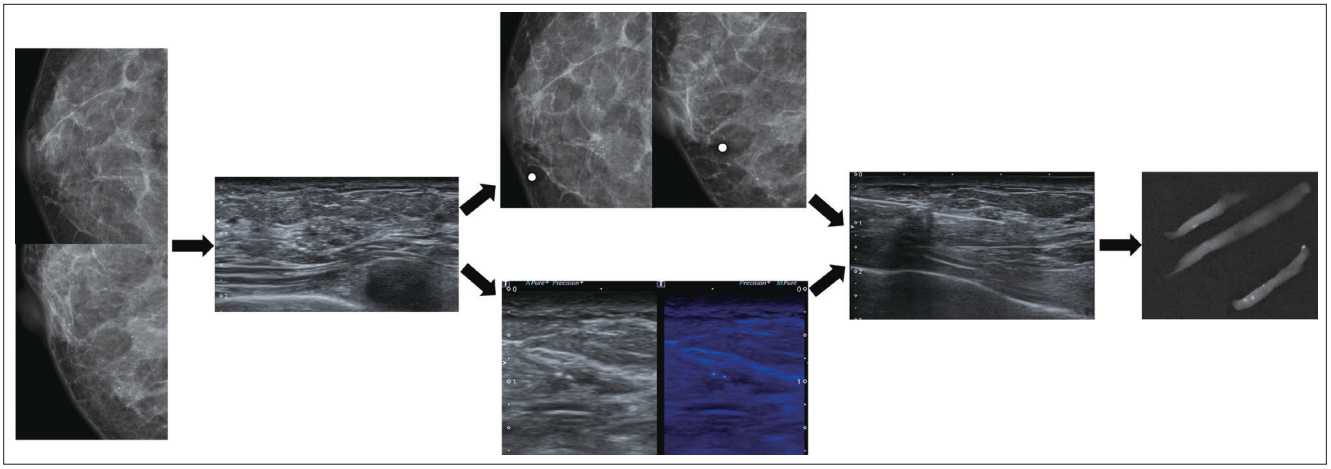
ble group and the negative group in this study.

Study results showed that 91.8% of microcalcifications were visible with MicroPure US imaging and B > M type was the most frequent (53.8%), followed by B = M (29.8%) and B < M types (8.1%). In previous studies, clinicians saw more calcifications with MicroPure US imaging than with B-mode in all cases (11, 13). One study showed B < M (60%) and B = M (40%) in 10 cases (10). The present study showed the B < M group to be smallest in proportion, which was inconsistent with previous studies (10, 11, 13). The B < M group was possibly related to MicroPure US imaging artifacts due to Cooper's ligaments (13) and fibrosis and hyaline change (14). The presence of artifacts had no effect on the accuracy of identification of microcalcifications (15).

Biopsy with US guidance is preferred to stereotactic biopsy for suspicious microcalcifications on mammography and US due to several advantages (4-6). Accurate US-guided biopsy for suspicious microcalcifications needs two steps confirming precise correlation of mammographic and US findings. First, additional mammography is obtained after placing the adhesive marker on the skin at the area of suspicious microcalcifications on B-mode. Second, specimen mammography is performed after biopsy. MicroPure US imaging improved visualization of microcalcifications and allowed physicians to perform biopsy of microcalcifications (10, 16). When microcalcifications are found on B-mode and are also shown as bright dots on MicroPure US imaging, the confidence of detection on US is increased. Considering the high detection positivity of MicroPure, it can replace additional mammography after skin marking in US-guided biopsy for microcalcifications detected both on B-mode and MicroPure US imaging (Fig. 4).

We think that MicroPure US imaging will be useful for radiologists who do not have much experience in breast US for the detection of microcalcifications. Also MicroPure US imaging will help the guidance of needle and be useful in reducing the biopsy procedure time through improved visualization of microcalcifications.

Fig. 4. Schematic diagram of conventional US-guided biopsy and the newly proposed method using MicroPure imaging.
Conventional US-guided biopsy for suspicious microcalcifications consists of four processes to confirm the precise correlation between mammography and US and the presence of microcalcifications: detection with B mode, additional mammography after skin marking, biopsy, and specimen mammography. Considering its high detection positivity, MicroPure US imaging might become an alternative to additional mammography after skin marking.



This study had some limitations in that it was a retrospective study from a single institution with a limited number of cases. There might have been selection bias, and the results might not be applicable to the general population. Including only cases where mammographic calcifications were visible on B-mode US, this study did not evaluate and compare the detection rates of B-mode and MicroPure US imaging for mammographic suspicious microcalcifications.

Finally, still images of B-mode and MicroPure US were reviewed instead of video images. Therefore, limited area was included for evaluation and artifacts and microcalcifictions were not properly distinguished.

In conclusion, MicroPure US imaging showed comparable positivity to B-mode US in detecting microcalcifications. BI-RADS category of microcalcifications significantly differed according MicroPure US imaging visibility.

Author Contributions

Conceptualization, all authors; investigation, all authors; methodology, all authors; visualization, L.H., K.S.H.; writing—original draft, all authors; and writing—review & editing, all authors.

Conflicts of Interest

Sung Hun Kim has been a Deputy Editor of the Journal of the Korean Society of Radiology since 2017; however, she was not involved in the peer reviewer selection, evaluation, or decision process of this article. Otherwise, no other potential conflicts of interest relevant to this article were reported.

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유방 미세 석회에 대한 MicroPure 초음파

이희린 · 김성헌* · 강봉주 · 이정민

목적 MicroPure 초음파 영상의 미세 석회 발견 성능을 평가하고, MicroPure 초음파 영상 소견을 이용하여 미세 석회의 특징을 파악하고자 하였다.

대상과 방법 유방촬영술과 B-mode 초음파에서 모두 보이며, 악성으로 의심되는 총 171개의 미세 석회를 대상으로 MicroPure 초음파 영상을 평가하였다. 미세 석회의 크기는 작거나(점상, 무정형, 미세 다형성, 미세 선형), 큰(거친 불균질) 군으로 구분하였고, 미세 석회의 범위는 좁거나(군집), 넓은(기타) 군으로 나누었다. MicroPure 초음파 영상 가시성은 B-mode와 MicroPure 초음파 영상의 미세석회 개수를 비교하여 4가지로 나누었다: B > M (B-mode에서 더 많은 병변이 보임), B = M (비슷한 개수가 보임), B < M (MicroPure에서 더 많은 병변이 보임), 음성(보이지 않음). MicroPure 초음파 영상의 가시성과 관련된 영상 소견들에 대해 다중비교를 시행하였다.

결과 171개 중 157개의 병변이 MicroPure 초음파 영상에서 확인되었다(91.8%). Breast Imaging Reporting and Data System (이하 BI-RADS) 범주 4A의 비율은 MicroPure 양성군에서 범주 4B의 비율은 MicroPure 음성군에서 유의하게 더 높았다(p = 0.035). 다른 영상 소견에는 차이가 없었다. MicroPure 양성 세부군에서 모든 특징은 유의한 차이를 보이지 않았다.

결론 MicroPure 초음파 영상은 B-mode 초음파에서 보이는 미세 석회의 91.8%를 발견하였다. MicroPure 초음파 영상 가시성은 미세 석회의 범주와 관련이 있었다.

가톨릭대학교 의과대학 서울성모병원 영상의학과