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BREAST IMAGING
ORIGINAL ARTICLE

Causes of failure in removing calcium in microcalcification-only lesions using 11-gauge stereotactic vacuum-assisted breast biopsy

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PURPOSE
The aim of this study was to determine the causes and rate of failure in removing calcification in microcalcification-only lesions using 11-gauge stereotactic vacuum-assisted breast biopsy.

MATERIALS AND METHODS
In total, 1365 microcalcification-only lesions were included in this study. The breast biopsy database was reviewed retrospectively. The biopsies were divided into two groups based on whether the specimen X-ray showed calcium within the cores. Breast composition, lesion size, calcification distribution, density on mammography, and the number of specimens were compared between the two groups.

RESULTS
In 11 (0.8%) biopsies, no calcium in the specimen radiography could be identified. Re-biopsy was performed in five cases. The initial biopsy result was unchanged at the second biopsy in three cases containing calcium, while in the other two cases, a benign biopsy result was upgraded to atypical ductal hyperplasia and ductal carcinoma in situ, respectively. In six cases, the biopsy was not repeated despite the absence of calcium in the specimen X-ray. In three of these cases, calcifications were reported histopathologically and deemed to be too small to be identified on specimen X-ray. In two of six patients, sufficient information was found in the cores without microcalcification to indicate the need for surgery. One patient refused re-biopsy. A statistically significant higher failure rate was observed in low-density calcification compared with intermediate or high-density calcification on mammography.

CONCLUSION
The failure to retrieve microcalcification is uncommon when an 11-gauge vacuum-assisted breast biopsy is used. Low-density calcifications have a higher rate of failure. In cases in which no calcium is observed in specimen radiography, repeated biopsy is recommended.

Key words: • *vacuum-assisted breast biopsy* • *microcalcification* • *specimen X-ray*

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Breast calcifications are important mammographic features in the diagnosis of breast cancer (1). Clinical examination and ultrasound make limited contributions to discovering microcalcifications that are primarily detected using mammography. With the introduction of screening programs, identification of microcalcifications has increased. Although breast microcalcifications observed by mammography often represent difficult and complex diagnostic challenges, most are benign.

Current percutaneous biopsy techniques have reduced the number of women undergoing surgical biopsy for benign microcalcifications. Image-guided biopsies are often performed under stereotactic guidance using either spring-loaded 14-gauge needles or vacuum-assisted biopsy (VAB) devices with 14-, 11-, and more recently 8-gauge probes (2). Most microcalcifications can be accurately and effectively sampled using 14-gauge automated core biopsy; however, in 10%–20% of cases, a core biopsy may be insufficient for diagnosis (3–5). VAB was first introduced in 1995 to alleviate the limitations of spring-loaded biopsy techniques (4, 6). Because VAB allows more numerous and larger samples to be obtained (7), it provides a more accurate histological diagnosis, thereby reducing the need for re-biopsy. More specifically, for microcalcification only lesions, the use of VAB has been proven to be very effective (8, 9). Indeed, for microcalcification-only lesions, the cores containing calcium have been shown to be more accurate, while the cores without calcium may miss an important lesion (10, 11).

Radiography of core samples for microcalcification-only lesions has become a routine practice that is necessary to assess the adequacy of core specimens and improve the diagnostic yield. Liberman et al. (12) and Meyer et al. (13) were the first groups to introduce specimen radiography for detecting microcalcifications in stereotactic core biopsy specimens. When no calcification is identified within the specimen X-ray, re-biopsy may be required. The purpose of this study was to determine the causes and the failure rate in removing calcium in microcalcification-only lesions using 11-gauge VAB.

Materials and methods

From February 2000 to December 2010, 1480 stereotactic VABs were performed for microcalcifications, architectural distortions, asymmetrical density, and mass lesions detected by mammography. Screen-detected and symptomatic patients were included and all these patients had a breast ultrasonography at their first assessment that showed no abnormality; hence, stereotactic biopsy was performed. In total, 1365 microcalcification-only lesions were included in the present study. Informed consent was obtained from each patient prior

to biopsy. The information was prospectively entered into a stereotactic breast biopsy database and reviewed retrospectively. If no microcalcification was found in specimen radiography, it was recorded as a failure. Ethics committee approval was not required as this was a retrospective survey and no patients were individually identified.

Biopsy procedure

All stereotactic VABs were performed on a digital prone table (Fischer Imaging, Denver, Colorado, USA) using 11-gauge vacuum probes (Mammotome, Ethicon Endo-Surgery, Norderstedt, Germany). The target lesion was identified following the scout and two 15° stereotactic images, and after infiltration with 10 cc of 2% lidocaine local anaesthetic, the needle was inserted into the center of the lesion. A second set of stereotactic images was taken to confirm the correct position of the needle. Needle-tip location was modified, if necessary, to ensure its vicinity in the target. When more than one lesion was targeted, a new probe was used. On completion of the biopsy, a radiopaque biopsy marking clip was inserted into the biopsy cavity. Post-biopsy mammograms were obtained to confirm accurate clip placement.

Radiographs of specimens

The core specimens were visualized using a digital imaging machine (Faxitron X-ray Corporation, Lincolnshire, Illinois, USA) with four levels of magnification. The exposure factors of 16 kV and 10 mA were used to confirm the presence of microcalcification in the specimen. The procedure was considered complete when radiographically visible microcalcifications were identified in the core samples. The specimen radiograph was assessed while the patient was still in position. If no calcium was retrieved following three attempts, it was accepted as a failure. The tissue specimens were then placed in formalin and processed at the Department of Cellular Pathology.

All cases were reviewed by the same radiologist retrospectively. The density of microcalcification was classified in three categories subjectively: 1, low density; 2, intermediate density; and 3, high density (Figs. 1–3).

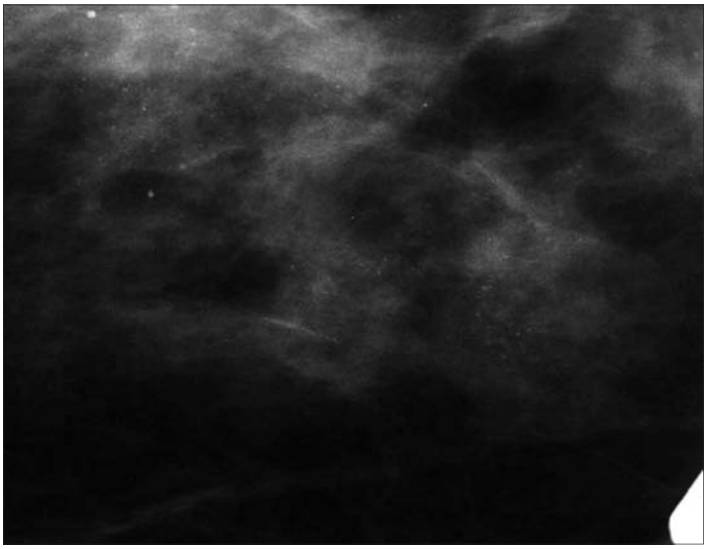

Figure 1. Mammogram shows low-density microcalcification.

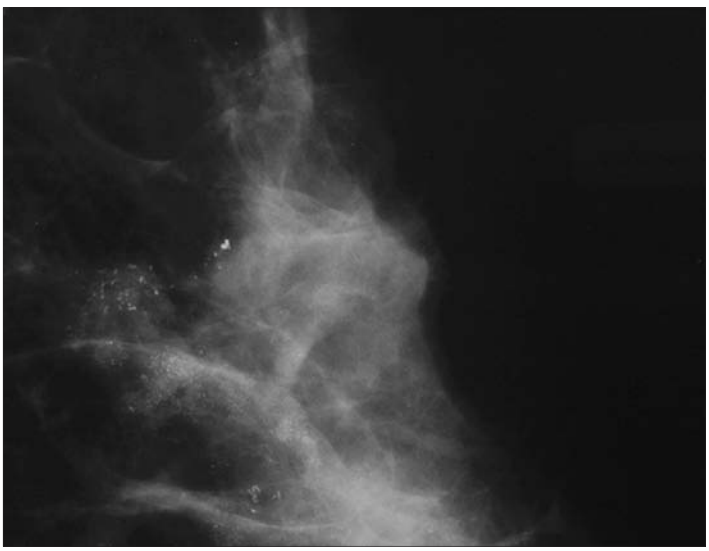

Figure 2. Mammogram shows intermediate density microcalcification.

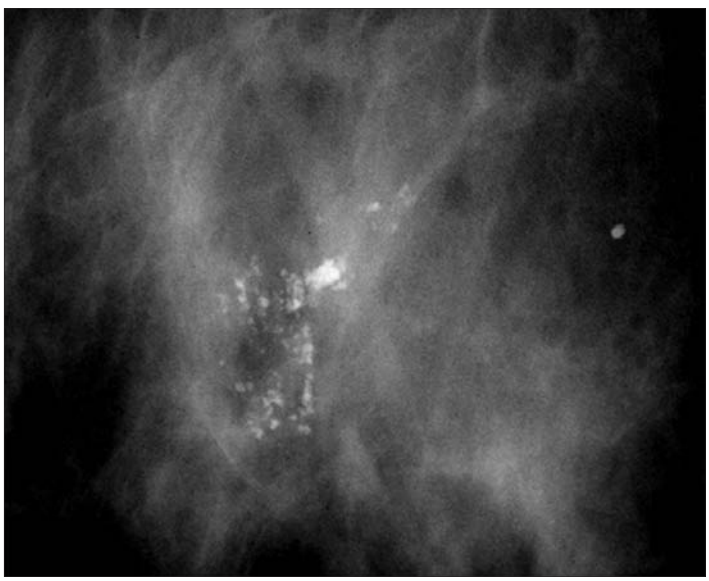

Figure 3. Mammogram shows high-density microcalcification.

Data collection and analysis

Pathology results and mammography variables were recorded. Biopsies depending on the specimen X-ray results were divided in two groups: Group 1 comprised the biopsies in which the specimen X-ray showed calcium within the cores. Breast composition, lesion size, calcification distribution, calcification density on mammography, and the number of specimens were compared between the two groups.

Statistical analysis

Statistical analyses were performed using Statistical Package for the Social Sciences (SSPS) software (SPSS for Windows, version 13.0, SPSS Inc., Chicago, Illinois, USA). Data are presented as the mean±standard deviation or n (%). A one-sample Kolmogorov-Smirnov test was used to evaluate the distribution of data. The differences between the subgroups were analyzed by chi-square or Fisher's exact, Student's *t*, and Mann-Whitney *U* tests. A P value < 0.05 was considered to be statistically significant.

Results

From February 2000 to December 2010, 1480 stereotactic VABs were performed, of which 1365 (92.2%) were conducted for microcalcification-only lesions. The median patient age was 55 years (range, 20–88 years). A specimen X-ray was performed in all cases. In 1354 cases (99.2%), classified as Group 1, calcium was visualized within the cores by an X-ray of the biopsy specimen.

In Group 2, 11 (0.8%) lesions were found in which no microcalcification was detected by specimen radiography. Re-biopsy was performed in five cases, and an X-ray on a subsequent specimen confirmed the presence of microcalcification. No difference was found in the second-round biopsy results of low-density and higher-density calcifications. These five patients are summarized in Table 1. In the remaining six cases, biopsy was not repeated although no calcium was detected in the specimen X-ray. In three of these cases, calcification was reported histopathologically and found to be too small to be identified on X-ray. In two of six patients, sufficient histological information was obtained in the cores without microcalcification to recommend surgery. One patient refused re-biopsy and opted for follow-up. She was placed on six-month follow-up, early-recall schemes for three years, which revealed no change, and she was subsequently discharged back to the national screening program. These six patients are summarized in Table 2.

The only statistical significance detected between the groups was the calcification density on mammography. The failure rate was higher in low-density calcification than in

Table 1. Data of five failed patients who had re-biopsy

	Breast density	Histopathologic results in first biopsy	Histopathologic results in second biopsy	Core number in first biopsy	Core number in second biopsy	Final results
1	HD	Normal	FCC	12	12	Discharged
2	SD	CCC	ADH	18	20	Followed up
3	EF	Normal	DCIS	18	7	Operated
4	SD	Normal	DH	3	14	Discharged
5	SD	DH	SC	17	12	Discharged

HD, heterogeneous density; SD, scattered density; EF, entirely fat; CCC, columnar cell change; DH, ductal hyperplasia; FCC, fibrocystic change; ADH, atypical ductal hyperplasia; DCIS, ductal carcinoma in situ; SC, stromal calcification.

Table 2. Data of six failed patients who had no re-biopsy

	Breast density	Core number	Histopathologic results	Calcification on pathology specimen	Final results
1	EF	13	ADH	No	Upgraded to DCIS on final pathology
2	SD	14	Normal	No	Followed up for three years (patient's choice)
3	SD	18	IDC	No	Same histopathologic result after surgery
4	HD	18	ALH	Yes	Followed up for two years
5	SD	12	FCC	Yes	Discharged
6	SD	14	ALH	Yes	Same histopathology result after surgery

EF, entirely fat; SD, scattered density; HD, heterogenous density; ADH, atypical ductal hyperplasia; IDC, invasive ductal carcinoma; ALH, atypical lobular hyperplasia; FCC, fibrocystic change; DCIS, ductal carcinoma in situ.

intermediate- or high-density calcification on mammography ($P = 0.039$). No significant difference was observed between the two groups for breast composition, lesion size, microcalcification distribution, or number of specimens (Table 3).

Discussion

Microcalcifications viewed on mammography are important findings because breast carcinoma may be associated with microcalcification. The superiority of cores containing microcalcifications has been reported (11, 14, 15). Biopsy of a sufficient amount microcalcifications is essential to allow an accurate diagnosis (15). The use of surgical biopsy in microcalcification-only lesions has been abandoned because the image-guided biopsy technique was proven to be successful in adequate sampling and diagnosis. Despite the occasional role of ultrasonography in the biopsy of microcalcifications, the biopsy technique most commonly performed for these lesions is conducted under stereotactic guidance (16). The adequacy of core specimens, along with the improvement of the diagnostic yield, can be assessed by specimen radiography (12, 17).

VAB with stereotactic guidance has become a viable method of choice in the biopsy of microcalcification-only lesions. It has been shown to be more accurate than conventional spring-loaded biopsy (18, 19). A single probe insertion with directional sampling, rapid collection of larger samples (16), and a lower potential sampling failure have been demonstrated (20). The rate of failure to retrieve breast microcalcifications after an 11-gauge VAB prone to stereotactic biopsy is reported to be between 0% and 5% (5, 18, 19, 21–26). This rate was lower than the rate of failure to retrieve breast microcalcifications with 14-gauge core biopsy, which was 0%–16% (5, 19, 21, 23, 27) (Table 4).

Microcalcification was observed in the pathological examination of three of 11 patients, although it was not viewed in specimen radiography. In one of three patients, histopathology showed fibrocystic change and this patient was discharged. Two of three patients had atypical lobular hyperplasia (ALH). One of two patients with ALH underwent surgical excision, and histology of the excised specimen confirmed ALH-only. The other patient with ALH was followed up for two years in line with local guidelines. No malignancy diagnosed after two years follow-up. According to our unit policy, patients with ALH are usually followed up instead of surgical treatment. With these three cases excluded, the success rate in retrieving microcalcification was 99.4%. In two patients, despite failure to retrieve breast microcalcifications, biopsies revealed invasive ductal carcinoma and atypical ductal

Table 3. Statistical comparison between study groups

Variables	Negative radiographs (n)	Positive radiographs (n)	*P*
Breast composition			0.687
Fatty density	2	137	
Extremely dense	0	60	
Heterogeneously dense	2	353	
Scattered dense	7	804	
Lesion size			0.274
1–10 mm	7	638	
>10 mm	4	716	
Calcification distribution			0.690
Cluster	8	935	
Diffuse	0	74	
Linear	1	202	
Segmental	2	143	
Calcification density			0.039
High-intermediate	5	1008	
Low	6	346	
Number of specimen			0.159
1–12	3	658	
>12	8	696	

Table 4. Rates of negative radiography of specimen at 14-gauge core biopsy and 11-gauge VAB

	14-gauge core biopsy (n/n [%])	11-gauge VAB (n/n [%])
Jackman and Rodriguez-Soto 2006 (5)	30/182 (16)	19/1423 (1)
Burbank 1997 (18)	0	0/47 (0)
Philpotts et al. 1999 (19)	17/190 (9)	4/189 (2)
Reynolds et al. 1998 (21)	6/42 (14)	0/64 (0)
Berg et al. 2001 (22)	0/9 (0)	0/102 (0)
Apesteguia et al. 2002 (23)	0	5/106 (5)
Liberman et al. 2002, 2001 (24, 27)	15/146 (10)	11/565 (2)
Kettritz et al. 2004 (25)	0	8/2013 (0.4)
Penco et al. 2010 (26)	0	39/4086 (1)
The present study	0	11/1365 (0.8)

VAB, vacuum-assisted biopsy.

hyperplasia. Based on the biopsy result, surgical treatment was planned without the need for re-biopsy. In one case, the patient declined to have a re-biopsy. No malignancy diagnosed after three years follow-up.

Jackman and Rodriguez-Soto (5) reported that the number of cores, lesion size, and breast density were influential on the failure of stereotactic VAB biopsy for microcalcified breast lesion, and that the effect was statistically significant. However, no significance was found between these parameters in our study. To the best of our knowledge, no previous study has reported the failure rate of VAB in low-density microcalcifications. In our study, we found that the failure rate was significantly higher in low-density calcified lesions than in intermediate- or high-density lesions. Our classification of density, however, was subjective and not quantitatively made. We also discovered that the calcification distribution was not associated with the failure rate in VAB.

In five cases, re-biopsy was performed because the initial procedure showed no calcium on either specimen X-ray or histopathology. The second attempt for the five cases was successful, revealing calcium on the specimen X-ray. In one case, the initial biopsy confirmed normal breast tissue while the subsequent biopsy revealed ductal carcinoma in situ. Columnar cell change was upgraded to atypical ductal hyperplasia in another case. These two cases, in which upgrading occurred, verified the importance of calcium retrieval in biopsy specimens. The remaining three cases showed benign changes with no evidence of malignancy.

A few limitations of this study deserve comment. The study was designed as a retrospective study, and the calcification density was defined subjectively, which depends on the radiologist's experience. The number of cases without calcification on specimen mammograms was very low compared with the other groups. Thus, the statistical significance of the results was of limited strength, and the numbers in the subgroups were even lower.

In conclusion, VAB remains an important biopsy technique for accurate diagnosis of non-palpable microcalcified breast lesions that can only be viewed by mammography. Failure in microcalcification retrieval is possible but the rate of failure is very low (0.8%) when using the prone table technique. Calcification density affects the failure rate. In two of five subsequent re-biopsies in failed patients, a significant pathological diagnosis was established. Thus, for microcalcification-only lesions, unless calcification can be observed in specimen radiographs, a second biopsy should be conducted. Obtaining large numbers of specimens may not prove to be useful for an accurate diagnosis, but an adequate number of correctly targeted specimens is essential.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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