ORIGINAL ARTICLE

Incidence, Causes, and Implications of Unsuccessful Calcification Retrieval at Stereotactic Breast Biopsy — 5 Years' Experience

KMK Kwok,[1] CY Lui,[2] PYE Fung,[2] LK Chan,[2] HS Lam[2]

[1]Department of Radiology and Organ Imaging, United Christian Hospital, and [2]Department of Radiology, Kwong Wah Hospital, Hong Kong

ABSTRACT

Objective: *To determine the incidence, causes, and implications of calcification retrieval failure at stereotactic breast biopsy.*

Methods: *Retrospective review of the medical charts of 710 patients who underwent percutaneous stereotactic biopsy of calcifications at the Kwong Wah Hospital, Hong Kong, between January 2001 and December 2005 was performed. The outcomes for patients for whom calcification retrieval was unsuccessful were evaluated by repeat biopsy or mammographic follow-up for more than 1 year.*

Results: *Fifty five lesions (7.5%) were negative on the specimen radiographs. The causes of retrieval failure were significant bleeding (80.0%), perception factors (65.4%), targeting factors (40.0%), unfavourable calcification location (20.0%), patient movement (20.0%), use of short-throw needle for patients with thin breasts (8.4%), and technical factors (5.4%). The histology results for negative radiographs were as follows: malignancy (n = 4), high risk (n = 2), benign (n = 44), and inconclusive (n = 5). The 2 high-risk lesions on percutaneous biopsy were upgraded to malignant lesions on subsequent excision biopsy.*

Conclusions: *The failure rate of calcification retrieval for percutaneous stereotactic breast biopsy was 7.5%. The most common causes of unsuccessful biopsy were significant bleeding during biopsy and perception difficulties. Technical factors were the least common cause of failure, but could be avoided by meticulous technique and proper training. Mammographic follow-up and repeat biopsy are recommended for patients for whom calcification retrieval failed, particularly those with high-risk or inconclusive pathological results.*

Key Words: *Biopsy; Breast; Calcification; Mammography*

INTRODUCTION

Stereotactic breast biopsy was introduced in 1990 by Parker et al.[1] Stereotactic breast biopsy has become the main method for biopsy of non-palpable breast lesions, including calcifications because of its accuracy and non-invasiveness.[1] However, stereotactic biopsy can sometimes be technically demanding due to the nature of lesion and patient factors, which occasionally leads to failure in retrieving the targeted lesion. The failure rate of stereotactic biopsy of non-palpable breast lesions varies from 2% to 21%.[2-7]

Correspondence: Dr KMK Kwok, Department of Radiology and Organ Imaging, United Christian Hospital, 130 Hip Wo Street, Kwun Tong, Hong Kong.
Tel: (852) 3513 6575; Fax: (852) 3513 5637;
E-mail: kwokkimmy@gmail.com

Verkooijen et al identified factors leading to premature termination of stereotactic breast biopsy as extremely dense breast tissue, axillary location of the non-palpable lesion, body mass index below 20, <15 mm distance from the lesion to the chest wall, or the presence of more than 1 non-palpable lesion.[8] According to Jackman and Rodriguez-Soto, breast density, size of lesion, Breast Imaging Reporting and Data System category, type and size of the biopsy needle, amount of bleeding, number of specimens retrieved, and histology results are statistically significant factors causing calcification retrieval failure.[6]

The objective of this study was to retrospectively compare the standard of stereotactic biopsy at the Kwong Wah Hospital, Hong Kong, with other centres, to identify the causes of non-palpable calcification retrieval failure for patients who underwent stereotactic

breast biopsy, and to investigate ways to improve the success rate through modification of the procedure and technique.

METHODS
Patients
Retrospective review of the medical charts of 710 patients who underwent percutaneous stereotactic biopsy on the prone table for 734 non-palpable calcifications of the breast at Kwong Wah Hospital between January 2001 and December 2005 was performed. The median age of the women was 49 years (range, 34-87 years).

Design
The lesions were biopsied on a dedicated stereotactic biopsy prone table using a digital imaging system (Lorad, Danbury, USA). Vacuum-assisted biopsies were performed with an 11-G needle on the Mammotome breast biopsy system (Ethicon Endo-Surgery, Cincinnati, USA); core biopsies were performed with a 14-G long-throw (22-mm excursion or 25-mm excursion) automatic biopsy needle and gun (ProMag 2.2 or 2.5; Manan Medical Systems, Northbrook, USA) or 14-G short-throw (14-mm excursion) automatic biopsy needle and gun (ProMag 1.4).

Radiographs of biopsied tissues were immediately taken for the presence of the targeted calcifications and the specimens were sent for histological examination. A negative specimen radiograph was defined as one with no calcification present, and the procedure was regarded as failed. The diagnostic mammograms, including magnification views, digital images taken during the biopsy procedure, and specimen radiographs, were reviewed by

2 radiologists. The cause of calcification retrieval failure for each lesion was identified and categorised. During the joint mammogram meeting, the technical aspects of specimen retrieval, quality of specimens, and presence of calcifications were presented by the radiologists. The pathological findings were correlated with the mammographic and clinical features to determine whether the results were concordant.

A joint decision on the management plan was made. For patients with negative specimen radiographs, follow-up in the form of repeat mammogram and re-biopsy by percutaneous or excisional biopsy was done. The follow up period ranged from 1 to 6 years.

RESULTS
Among the 734 non-palpable calcifications biopsied, specimen radiographs were negative for 55 (7.5%). Seven causes leading to calcification retrieval failure were found. The most common cause was significant bleeding encountered during biopsy (n = 44; 80.0%), followed by the calcification being too faint to perceive (n = 36; 65.4%), the calcification being too scattered (n = 22; 40.0%), unfavourable location of the calcification (close to the chest wall, nipple, or fat-gland interface) [n = 11; 20.0%], patient movement (n = 11; 20.0%), short-throw needle with 14-mm stroke margin (due to limited compressed breast thickness) [n = 6; 10.9%], and technical error (n = 3; 5.4%) [Figure 1].

Of the 55 lesions, 44 had benign pathological results (Figure 2). Thirty five of the 44 patients underwent repeat mammography, 32 of which showed no disease progression, compatible with benignity. Of the remaining
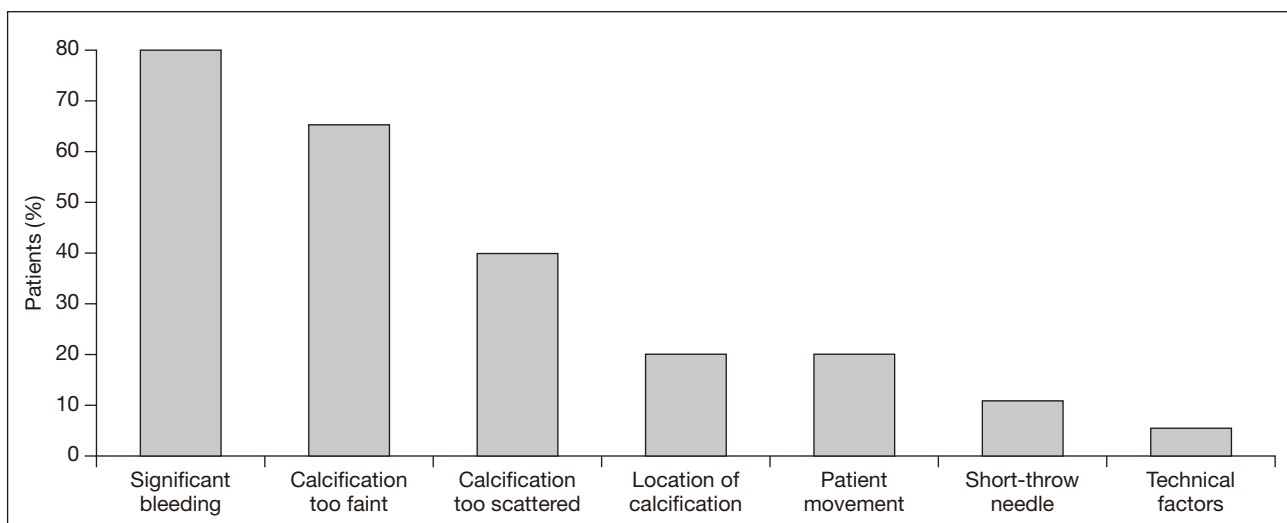

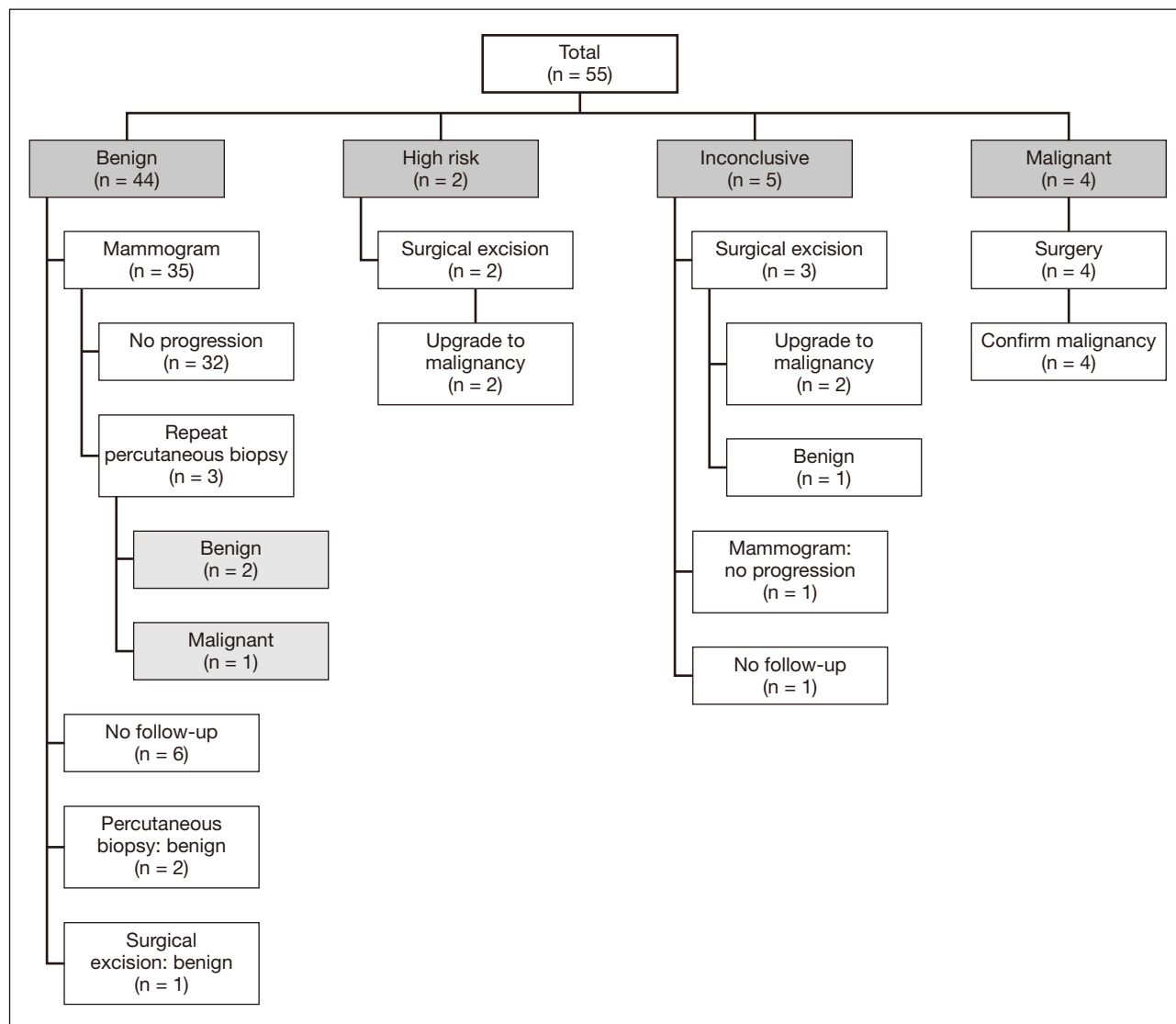**Figure 1.** Factors leading to unsuccessful calcification retrieval.

Figure 2. Flow chart summarising the outcomes for 55 patients for whom calcification retrieval was unsuccessful.

3 mammograms, the calcifications had either increased in number or irregularity, so repeat stereotactic biopsies were performed. Malignancy was found in 1 patient and benign pathologies were found in the remaining 2. Further biopsies were performed for 3 of the 44 patients; 1 underwent excisional biopsy, which yielded benign pathology, and 2 underwent repeat percutaneous stereotactic biopsies, both of which had benign results. Six of the 44 patients were not followed up at Kwong Wah Hospital.

Five of the 55 lesions had inconclusive pathology results. Three patients underwent excisional biopsy, 2 of which yielded malignancy while 1 was benign, 1 had follow-up mammogram, which showed no disease progression, and 1 was not followed up at Kwong Wah Hospital.

Four patients had biopsy-proven carcinoma. All 4 patients underwent surgery and malignancy was confirmed in the surgical specimens.

The remaining 2 patients with high-risk histology results had atypical ductal hyperplasia. Excision biopsy showed malignancy for both patients.

DISCUSSION

Calcifications on mammograms are either found incidentally during screening of asymptomatic patients or are associated with other abnormalities in patients with symptoms. Microcalcifications are analysed according to their morphology, distribution, and size. While the majority of calcifications are benign, some are typically malignant due to their pleomorphism, ductal distribution, and/or associated mass or architectural distortion.[9]

The remaining calcifications are too small for characterisation. This group of calcifications has an overall malignancy rate of 22% to 37%,[10-13] therefore, further histological evaluation is needed.

Percutaneous stereotactic biopsy has become a widely accepted biopsy method for obtaining samples of breast calcifications because of its accuracy and relative non-invasiveness.[14-28] The presence of calcifications in the sampled tissue suggests that the sample is representative of the area of interest and improves the diagnostic accuracy. Therefore, routine specimen radiographs are taken immediately after the biopsy procedure. The presence of calcifications on specimen radiographs significantly increases the chance that a histopathological diagnosis will be made.[20-33]

Failure of calcification retrieval is defined as absence of a calcification on the specimen radiograph, which accounted for 7.5% of specimens in this study. This is similar to results from studies conducted in regional hospitals in other countries.[5,7,33]

Significant bleeding during the biopsy procedure can affect the quality of tissue samples, such that blood clots may be harvested instead of glandular tissue. Two methods can be adopted to reduce the amount of bleeding. First, by careful selection of the puncture site on the pre-procedural stereotactic images, puncture of major blood vessels can be avoided. Second, diluted adrenaline can be added to the local anaesthetic and injected before biopsy. Minimising the size of the skin incision and number of cores and checking for a history of bleeding tendency or use of anticoagulants, are general principles for biopsy procedures that also apply to stereotactic breast biopsy.

Faint calcifications are difficult to see. For such patients, higher mAs and higher resolution, for example, 1024 x 1024 pixels instead of 512 x 512 pixels, and careful adjustment of the window settings and sharpening tools can improve the perception of calcifications and improve the chance of successful biopsy.

Scattered microcalcification locations within the breast will be difficult to target, as it is technically challenging to identify the same calcification focus on the stereotactic images. If the same calcification focus on the stereotactic paired images is not targeted, there would be an error in the calculation of x, y, and z coordinates, leading to retrieval of tissue from an incorrect site. This problem can be solved by specifying the group of calcifications to be biopsied to the radiologist responsible for the biopsy procedure. The decision as to which group of calcifications should be biopsied should be made at a joint meeting of clinicians and radiologists. Different groups of calcifications on a single mammogram may represent different pathologies in a heterogeneous lesion; therefore, it is important to biopsy the area that is radiologically most suspicious. Secondly, the z coordinate of a specific calcification focus on a stereotactic mammogram can be estimated based on its location on the initial mammogram. The information can be used to crosscheck with the values on the stereotactic images to ensure that the same calcification focus is being targeted on the paired images.

As calcifications are small, even slight movement by a patient can result in a sampling error. There are several methods to reduce patient movement during the procedure. First, patients should be educated about the importance of keeping still throughout the procedure. Second, patient discomfort during positioning should be minimised, for example, providing cushions at pressure points. Third, patients should be alerted before each core is taken to prevent sudden jerky movements as a result of unexpected noise and manipulations. Lastly, local anaesthetics can be used liberally for pain control.

The least common cause of calcification retrieval failure is the operator's technical deficiency, which was noted for 3 of the 55 unsuccessful procedures. Two biopsies were performed with a mammotone and 1 with a core biopsy needle. On review of the stereotactic images of the biopsy procedures, the group of calcifications were not correctly positioned at the sampling notch of the needle for the 2 patients for whom a mammotome was used, and the needle tip was not positioned to the target for the patient for whom a core biopsy needle was used. With proper training and accumulation of experience, such failure can be avoided.

Two of the causes of calcification retrieval failure were intrinsic and could be not corrected by adjustment of the technique. The causes were specific unfavourable location of the calcifications and thin breasts requiring the use of a short-throw needle.

Calcifications at particular locations in the breasts can be difficult to target. Lesions close to chest wall would be lifted upwards on slight patient movement, while those near the nipple are relatively mobile as the areolar
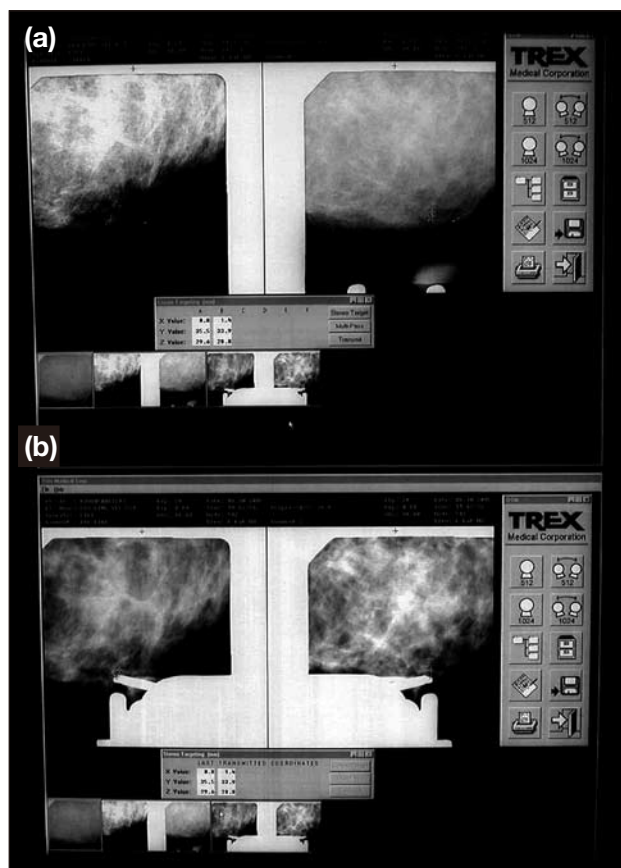
Figure 3. Imaging showing that (a) the areolar region is not well confined by the compression paddle, and remains relatively mobile; and (b) calcifications close to the nipple are difficult to biopsy since they tend to move during penetrance of the needle.

region is not well confined by the compression paddle (Figure 3). Tissues respond differently to compression, such that fat is more compressible than glandular tissue. If the lesion is located at the fat-gland tissue interface, the lesion moves towards the more compressible fatty tissue on penetrance of the needle; the extent of the movement cannot be predicted from the preprocedural film.

The type of needle throw to be used is determined by the compressed breast thickness and the z values of the calcifications. Commonly used needle throws have 22-mm and-25 mm excursion, which produces tissue samples up to 15 mm and 18 mm long, respectively. A short-throw needle of 14-mm excursion has to be used for thin breasts, which limits the sample length to 7 mm. The amount of tissue retrieved is therefore reduced.

The pathological results are classified as benign, inconclusive, high risk, and malignant. The result is regarded as benign if a histology diagnosis of benign breast disease is made or if there is an absence of malignant or precancerous changes in the samples. For this group of lesions,

the radiology and pathology diagnoses will be discussed to ascertain whether they are concordant. Follow-up mammograms will be done for lesions with a low radiology grading, while repeat biopsy will be needed for those with radiological-pathological discordance.

The malignant category includes carcinoma in situ as well as invasive carcinoma. Patients will require surgical excision of the tumour and axillary lymph node sampling.

Inconclusive samples are those for which there is absent or inadequate representative breast tissue in the specimens. Whether this group of patients requires excisional biopsy or follow-up mammogram will depend on the level of confidence during the biopsy procedure and the level of suspicion of the lesion radiologically. As the missed cancer rate for this group of lesions was as high as 40%, careful planning for future management is needed. Mammograms should be reviewed during the joint mammogram meeting and the need for repeat biopsy, either percutaneously or by excision, will be decided if the calcifications are radiologically suspicious.

The 2 high-risk lesions were both atypical ductal hyperplasia, which is known to have a 4- to 5-fold increased risk of coexisting malignancy.[34] Atypical ductal hyperplasia diagnosed at percutaneous stereotactic biopsy is known to be associated with malignancy, which is underdiagnosed at a rate of 19% to 44%.[35,36] According to Liberman et al, atypical ductal hyperplasia and associated malignancy may not be distinguishable mammographically.[37] Therefore, it may not be possible to specifically target the malignant areas within a heterogeneous lesion composite, with a spectrum ranging from atypia to invasive carcinoma, during stereotactic biopsy. Nowadays, surgical excision of the biopsied area for a larger volume of tissue is standard practice when the percutaneous biopsy result yields atypical ductal hyperplasia.[27,35,36] This study confirms the need for further surgical excision, as both patients with atypical ductal hyperplasia turned out to have malignancy.

Twenty seven patients (49%) with no calcification seen on specimen radiographs had calcifications identified microscopically. None of these lesions were upgraded histologically on re-biopsy. Histological diagnosis was made for all but 1 of the patients in this group. Among the rest of the patients in whom no calcification was seen in the sampled tissues microscopically, histological upgrade to malignancy and inconclusive pathology reports were observed in 5 and 4 patients, respectively.

Calcification only seen microscopically is likely to be too faint or small to be perceived by the human eye. The presence of microscopic calcifications on tissue samples suggests that the retrieval of tissue from the area of interest has been successful. This study supports Liberman et al's opinion that calcification observed histologically improves the chance that a specific pathological diagnosis will be made.[29] The failure rate for calcification retrieval for percutaneous stereotactic breast biopsy was 7.5% in this study, which is close to the results of studies conducted in regional hospitals in other countries.[5,7,33]

Percutaneous stereotactic biopsy has become a well-recognised biopsy method for breast calcifications. Several factors leading to failure of calcification retrieval have been identified in this study, the most important being the significant bleeding encountered during biopsy, the ability to visualise only faint calcifications, and their scattered locations preventing precise targeting.

For patients with unsuccessful calcification retrieval, further management is based on a consensus reached by clinicians, radiologists, and pathologists. The 2 patients with high-risk results proved the importance of further excisional biopsy as both were upgraded to malignancy subsequently. The missed cancer rate in the group with inconclusive pathological results was 40%, implying that repeat biopsy is required. For patients with calcifications identifiable microscopically but not on specimen radiographs, the chance for a histological diagnosis to be made is higher than for patients without microscopic calcification. This further illustrates the importance of precise targeting of the calcification in the area of interest on the success of percutaneous biopsy of breast calcifications.

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