# Precision biopsy of breast microcalcifications: An improvement in surgical excision

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Abstract. The aim of the present study was to improve the conventional wire-guided localization biopsy (WGLB) of breast microcalcifications to overcome disadvantages associated with the procedure, including inaccurate localization and large specimen volume. The novel approach described in the present study was termed double wire-guided localization and rotary cutting biopsy (DWGLB). Prior to surgery, the precise localization of the lesions was assessed using two wires under the assistance of mammography X-ray and ultrasound, followed by complete excision of the lesions using a novel rotary cutting tool. The cylindrical specimen was placed on a scaled specimen holder for pathological examination. DWGLB was performed in 108 patients with the classification of as Breast Imaging Reporting and Data System score 4A. Percutaneous localization of the lesions guided by a mammography X-ray and ultrasound were successful in all 108 lesions (100%) with one puncture attempt. The lesions were precisely excised in all of 108 patients, and included 13 malignant lesions (DCIS of breast in 7 cases, DCIS with focal invasive carcinoma in 3 cases and invasive ductal carcinoma in 3 cases). The average distance of the BARD Dualok to the lesion was 4.1 mm; the average weight of specimens was 8.5 g. Compared with WGLB, DWGLB offers several advantages, including more accurate localization of lesions, a more standardized biopsy method and a smaller specimen volume. DWGLB can also provide the precise position of lesions in the specimen for further pathological examination.

#### Introduction

Breast calcification lesions are notable imaging features of early breast cancer (1). In total, 20-30% of calcification lesions are pathologically confirmed to be of malignant breast cancer (2-4). Breast microcalcifications lesions are particularly significant for the early diagnosis of breast cancer (5). For example, the detection of 80-90% of ductal carcinoma in situ (DCIS) is attributed to the diagnostic analysis of the breast microcalcifications (6). It has been reported that the breast microcalcification lesions may be a unique positive feature of mammography X-ray imaging for patients with non-palpable disease (7,8). Mammography X-ray imaging is highly sensitive to breast microcalcifications lesions, and is therefore considered to be the gold standard of breast microcalcifications (9). However, breast microcalcifications exist in malignant and benign lesions (for example, hardening of breast disease, mammary dysplasia, hamartoma, scarring following radiotherapy, fibrocystic disease and fibroadenoma) (10). Thus, a breast biopsy is always required to identify the microcalcifications lesions.

However, breast microcalcifications lesions are non-palpable. Thus, the surgical operation of the breast microcalcifications lesions is different with that of the clinically palpable lesions. Identifying the accurate location of the microcalcification lesions is difficult, which can lead to inaccurate and/or incomplete excision, potentially resulting in misdiagnosis. Therefore, to localize the occult lesions clearly in the surgical process and excise the lesions completely, it is crucial to precisely localize the lesions prior to surgery. However, it is difficult to excise non-palpable breast lesions by established surgical biopsy. Thus, an easy, accurate, minimally invasive biopsy method is required for the breast microcalcifications lesions (11,12).

In 1965, Dodd *et al* (13) reported a method using wire to localize the breast lesions prior to surgery. In 1976, Frank *et al* (14) described the localizing of breast lesions using mammography X-ray imaging as a guide prior to the surgical excision of breast lesions for biopsy. Nowadays, the wire-guided location (WGL) biopsy method has been widely applied and is the gold standard for the biopsy of non-palpable breast lesions (15-17). In recent years, the application of vacuum-assisted breast biopsy (VABB) has reduced the

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percentage of patients that undergo conventional surgical biopsy (18,19). Barranger *et al* (20) claimed that VABB could replace WGL to become the gold standard method of biopsy of non-palpable breast lesions. However, VABB cannot excise the breast microcalcifications lesions completely. Thus, a second surgical procedure is required (21-23).

On the other hand, a major shortcoming of conventional WGL biopsy is that the wire may shift in the processes of lesion localization and removal (24), which usually leads to the incomplete excision of the lesion. It was reported that a second surgical procedure was required in ~50% patients who underwent the conventional WGL biopsy method (25,26). The other disadvantages involved in the conventional WGL biopsy include the large volume and irregular shape of the specimen, the breakage of breast structure, and the difficulty in localizing the lesion in the specimen for further pathological identification (27,28).

To overcome the aforementioned shortcomings, the present study reports on the development of a novel precision biopsy method of breast microcalcifications based on the double wire-guided localization and rotary cutting biopsy (DWGLB). Prior to surgery, the precise localization of the lesions was assessed by using two wires under the assistance of mammography X-ray and ultrasound, followed by the complete excision of the lesions using a novel rotary cutting tool (Fig. 1; Chinese patent no., ZL 2009 1 0099174.7).

## Materials and methods

*Patients*. A total of 108 mammographically detected non-palpable breast lesions in 108 patients, comprising 62 lesions on the left breast and 46 lesions on the right breast, were attempted between May 2012 and March 2014 at the department of Oncological Surgery, Hangzhou First People's Hospital (Hangzhou, China) using DWGLB. The age range of the patients was 24-69 years, with a mean age of 45.69 years. All the lesions were classified as being of Breast Imaging Reporting and Data System (BI-RADS) (29) category 4A (suspicious abnormality).

Surgical procedure. The surgical procedure included five steps. i) The 3D localization of the microcalcification was assessed by mammography using the Senographe DS Acquisition system (GE Healthcare, Chicago, IL, USA). Subsequently, a BARD Dualok (C. R. Bard, Inc., Murray Hill, NJ, USA) was inserted into the lesion and fixed. Mammographic imaging was performed mediolaterally or lateromedially to observe the position of the lesion and the BARD Dualok. Ideally, the lesion would be localized at the bifurcation of the BARD Dualok (Fig. 2). ii) Following transportation of the patients into an operating theatre, the relative position of the lesion and the BARD Dualok was further confirmed by an ultrasound scanner (MyLab Twice, Esaote SpA, Genoa, Italy). Subsequently, a mark line (3 cm) vertical to the BARD Dualok was made on the skin of the lesion, followed by insertion of a single hook needle vertically into the lesion. The junction point of two needles was the accurate position of the lesion (Fig. 3). iii) Local anesthesia (obtained with buffered 1% lidocaine injected into the skin and superficial tissues and with buffered 1% lidocaine



Figure 1. Rotary cutting tools (with a diameter of 2 cm) used in the report (Chinese patent no. ZL 2009 1 0099174.7).



Figure 2. Example of the optimal position of the BARD Dualok shown in mammographic image. The lesion is localized at the bifurcation of the BARD Dualok (as illustrated by arrow).



Figure 3. Image depicting a mark line (3 cm) vertical to the BARD Dualok made on the skin of the lesion with the assistance of an ultrasound scanner, and a single hook needle inserted vertically into the lesion. The junction point of two needles is the accurate position of the lesion.

containing epinephrine within the deeper breast tissues). iv) A 3-cm skin incision was made according to the mark line. Double wire-guided lesion sampling was performed using a rotary cutting device (Figs. 4 and 5). v) The lesion samples



Figure 4. Image depicting a 3-cm skin incision made according to the mark line, and exposure of the mammary gland and the single hook needle by scraping and separating the subcutaneous adipose tissue using a breast retractor.



Figure 5. Image depicting the excision of the lesion. A 2-cm rotary cut tool was used to make a round cut down to the breast tissue by the center of the single hook needle. The rotary cut tool was withdrawn when it contacted to the BARD Dualok in the deep breast tissue. The lesion was completely excised using an electric knife.

were reviewed by a pathologist (Figs. 6 and 7), followed by compression and dressing of the wound if they were benign calcifications, or proceeding to further surgical excision if they were malignant lesions.

Statistical analysis. All statistical analyses were done using SPSS 19.0 (IBM Corp., Armonk, NY, USA). The association between two categorical variables was evaluated using the  $\chi^2$  test. P<0.05 was considered to indicate a statistically significant difference.

# Results

*Results of puncture localization and specimen removal.* Percutaneous localization of the lesions guided by mammography and ultrasound were successful in all 108 lesions (100%) with one puncture attempt, which is consistent with the previous studies (98-100%) (30-32). No evident complication was observed. All 108 lesions were excised using DWGLB, with a mean distance between the needle and lesion of 4.1 mm (range, 0-20 mm) and mean specimen weight of 8.5 g (6-15 g). The mean surgical time was <1 h per biopsy. The complete excision rate of DWGLB was 100%. The comparison of DWGLB with the conventional WGLB is depicted in Table I (33-35).



Figure 6. Schematic illustration of the specimen marked at the top side of the cylinder using a suture on a scaled specimen holder. (A) Side view of the specimen. (B) Top view of the specimen.



Figure 7. X-ray image of the specimen. BARD Dualok was used to provide the precise position of lesions in the specimen for further pathological examination.

Association of breast cancer detection with the position and shape of lesions. A total of 108 mammographically detected non-palpable breast lesions in 108 patients, comprising 62 lesions on the left breast and 46 lesions on the right breast, included 62 lesions with cluster distribution, 38 lesions with regional distribution/segment distribution and 8 lesions with linear distribution. In total, 13 lesions (12.0%) were diagnosed as malignant (DCIS of breast in 7 lesions, DCIS with focal invasive carcinoma in 3 lesions and invasive ductal carcinoma in 3 lesions). There were 88 negative lesions, including 75 cases of adenosis of the breast, 10 of breast intracanalicular fibroma, 2 of intraductal papilloma and 1 of papillary hyperplasia (Table II). Of the 62 lesions with cluster distribution, breast cancer was diagnosed in 10 cases (16.1%) by biopsy. Of the 46 lesions with non-cluster distribution, DCIS was diagnosed by biopsy in 3 cases (6.5%) (Table III).

A total of 95 benign lesions underwent segmental mastectomy (rotation biopsy). Hematoma was observed in 2 lesions following the procedure, which disappeared following conservative treatment. No cases of active bleeding were observed. All patients with malignant lesions underwent surgery later, although none of them exhibited residual tissue at the first follow-up with mammography, including modified radical

Study	Localization method	Surgical method	Distance between needle and lesion, mm	Specimen weight, g	Patients, n	Lesion localization	(Refs.)
Mariscal Martinez et al	WGL	Surgical biopsy	<20	67.3	68	Not assessed	(33)
Rampaul et al	WGL	Surgical biopsy	<20	31	47	Not assessed	(34)
Rahusen et al	WGL	Surgical biopsy	Not assessed	53	23	Not assessed	(35)
Present study	DWGLB	Rotary cutting biopsy	4.1	8.5	108	Submillimeter accuracy	-

Table I. Comparison of DWGLB with the conventional WGLB.

WGL, wire-guided localization; DWGLB, double wire-guided localization and rotary cutting biopsy.

Table II. Clinicopathological features of patients.

Variable	Patients, n		
Pathological diagnosis (n=108)			
DCIS	7		
DCIS with invasive	3		
Invasive ductal carcinoma	3		
ADH	7		
Adenosis	75		
Fibroadenoma	10		
Intraductal papilloma	2		
Papillary hyperplasia	1		
Selection of operation (n=13)			
Modified radical mastectomy	7		
BCS+SLNB	2		
Mastectomy+SLNB	4		
Invasive carcinoma TNM staging (n=6)			
IA	4		
IIA	2		
Molecular subtyping (n=6)			
Luminal A	3		
Luminal B	1		
Triple negative	1		
HER2 overexpression	1		
Postoperative adjuvant therapy (n=18)			
Endocrinotherapy	10		
Chemotherapy	3		
Radiotherapy	3		
Targeted therapy	2		

DCIS, ductal carcinoma *in situ*; ADH, atypical ductal hyperplasia; BCS, breast conservative surgery; SLNB, sentinel lymph node biopsy; HER2, human epidermal growth factor receptor 2.

mastectomy for breast cancer in 7 cases, the breast conservation surgery plus sentinel lymph node biopsy in 2, and the unilateral mastectomy plus sentinel lymph node biopsy in 4. In total, 10 of 13 malignant lesions following surgical operation were given the endocrinotherapy. In total, 3 patients were first

given chemotherapy, followed by radiotherapy in 1 patient with the lymphatic metastasis and the targeted therapy using trastuzumab in 2 with human epidermal growth factor receptor 2 (HER2) expression. The other 2 patients with BCS underwent radiotherapy. In the follow-up period of 16-38 months, no metastasis and recurrence were identified in the 13 malignant lesions and no new tumor formation in 95 benign lesions was observed, neither.

# Discussion

Breast carcinoma is the most common malignant tumor in female patients, with the second highest mortality rate (36). The early diagnosis of breast cancer significantly decreases the recurrence, metastasis and mortality rate of the disease (37-39). Breast microcalcification is a manifestation of early breast cancer; it is therefore vital to localize the lesions precisely and excise them completely for the following pathological examination and the treatment.

The distance between the needle and lesion was mostly 20 mm measured by the mammography (40), which further increased subsequent to releasing the pressure plate of the molybdenum target. As a result, there were usually certain residual lesions and the second surgery was needed (15,25,41). To avoid shifting the needle, the needle core was pushed out of the needle sheath by ~1 cm after the puncture needle reached to the lesion, which made the BARD Dualok insert into breast tissue from two sides. Meanwhile, the needle core was kept under pressure to cause it to continuously puncture into breast tissue whilst withdrawing the needle sheath and releasing the plate, until the breast restored itself to a natural state. It was observed that the needle could puncture the breast several cm deep, varying with the volume of the breast and the position of the lesion. In the series of patients in the present study, the mean distance between the needle and lesion was 4.1 mm, and the majority of lesions were located at the bifurcation of the BARD Dualok. Thus, the precision of localization under the mammography was significantly improved compared with the previous reports, where the mean distance between the needle and lesion was <20 mm (33,34).

Previous research demonstrates that detection rate of breast microcalcifications using ultrasound alone is low, and it is only 30-50% of detection rate of mammography X-ray (42,43). It

Table III. Association between breast cancer incidence and the position and snape of the lesion	Table	III. /	Association	between	breast	cancer	inc	idence	and	the	position	and	shape of	the	lesion.
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Position and shape of lesions	Breast cancer	Benign lesions	$\chi^2$ -value	P-value
Left side	7	55	0.08	>0.05
Right side	6	40		
Cluster distribution	10	52	2.30	>0.05
Non-cluster distribution	3	43		

was reported that the combination of ultrasound and X ray mammography was useful to detect the non-palpable lesions and identify the breast lesions (benign or malignant) (44,45). To overcome the disadvantages of conventional WGL, including inaccurate localization, difficulty for localization of the lesions (46), DWGLB utilized dual localization using mammography and ultrasound. Following the localization of microcalcifications by mammography, the patient lay in the supine position in order to achieve the flattest state of the breast. The ultrasound probe was used to detect the position of the BARD Dualok. Subsequently, a mark 3 cm vertical to the BARD Dualok was made on the skin of the lesion, followed by the insertion of a single hook needle vertically into the lesion. The junction point of the two needles was the accurate position of the lesion (Fig. 3). Finally, a 3-cm skin incision was made according to the mark and the lesions could be found along with the single hook needle. Compared with the conventional WGL, DWGLB could provide a more accurate localization of the lesions and substantially decrease the surgical area.

In conventional WGL, the excision of breast tissues is highly dependent on the experience of the surgeon. On the contrary, the surgical approach and the size and shape of the specimen are standardized following the dual localization using the mammography and the ultrasound: A 3 cm incision was first made on the skin according to the mark line, followed by scraping and separating the subcutaneous adipose tissue to expose the mammary gland and the single hook needle. In this way, the whole surgical operation could be performed only in the breast tissue. Subsequently, a 2-cm rotary cut tool was used to make a round cut down to the breast tissue by the center of the single hook needle. The rotary cut tool was withdrawn when it contacted the BARD Dualok in the deep breast tissue. The lesion was then completely excised using an electric knife by comparing of the position of lesion shown in Fig. 2 and the relative distance between the BARD Dualok and lesion shown in Fig. 5.

The specimen excised using conventional WGL is usually irregular. Thus, it is difficult for the pathologists to determine the position of the lesion in the specimen, resulting in a potential missed diagnosis (24). On the contrary, the specimen excised by using DWGLB was cylindrical breast tissue, with the top side of the cylinder marked by using a suture. The specimen was placed on a scaled specimen holder (Fig. 6), enabling the pathologists to find the lesion by pathological examination more easily. It was observed that 12% (13/108) of the breast microcalcifications of BI-RADS score 4A were diagnosed as early-stage breast cancer in the present study.

There is no confirmed standard yet concerning the weight of the surgically excised biopsy specimen. The guidelines of British Association of Surgical Oncology state that the weight of the specimen of at least 80.0% benign lesions excised by using wire-localization techniques should be less than 20 g (47). However, this goal has become difficult to achieve since the mammography screening was widely applied. The mean weight of biopsy specimen of benign lesions was 28 g between 1997 and 1998, with 47.0% of benign lesion biopsy specimens weighing <20 g (48). In the present study, the mean weight of specimen was <8.5 g, which was significantly decreased compared with that of the minimum group in the previous studies (31 g) (34). Thus, the shape of the breasts was retained.

In conclusion, compared with conventional WGL, DWGLB has several advantages, including the precise localization of calcifications, the small specimen volume, the complete excision of the lesions and the increased accuracy of pathological examination. Therefore, DWGLB should be recommended for the early diagnosis and treatment of patients with breast cancer.

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#### Availability of data and materials

All data or analyzed during this study are included in this published article.

# **Author's contributions**

ZYL contributed to trial design and protocol development. YP performed statistical analysis, drafted the report and approved the final version of the article. WHC, JiZ, JHF and PZ contributed to mammography, ultrasound, pathological diagnosis and data monitoring. JN was involved in the surgical biopsy and postoperative data management and was involved in revising the manuscript critically for important intellectual content. HDC and BL collected and verified all data. AZX, JuZ and JWD analyzed and interpreted the results.

## Ethics approval and consent to publish

This clinical trial was approved by Hangzhou First People's Hospital Ethics Committee (approval number: 2010-004-01). The trial was registered with the Chinese Clinical Trial Registry (registration number: ChiCTR-DDT-14004231).

#### **Consent for publication**

All participants gave informed consent for publication of any associated data and accompanying images were obtained from all subjects.

## **Competing interests**

The authors declare that they have no competing interests.

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