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Application of Localization and Needle Placement Guided by Mammographic, Ultrasound and Fiberoptic Ductoscopy for Resection of Non-palpable Breast Lesions

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Abstract. *Aim: To evaluate the usefulness of localization needles under mammographic, ultrasound or fiberoptic ductoscopy guidance for non-palpable breast lesions. Patients and Methods: Eighty-three patients undergoing needle localization and biopsy of non-palpable breast lesions under mammographic, ultrasound or fiberoptic ductoscopy guidance from June 2013 to December 2014 in Beijing Friendship Hospital were included in the study. The preoperative imaging assessment, application of localization needles, surgical operation and pathological examination were recorded and analyzed retrospectively. Results: A total of 83 localization and biopsies were carried out, of which 27 were performed under mammographic guidance, 32 under ultrasound guidance and 24 under fiberoptic ductoscopy guidance. Twenty-seven cases of breast microcalcifications were localized under mammographic guidance and surgically removed, of which eight cases were pathologically diagnosed as malignant. Thirty-two cases of non-palpable breast lesions were localized under ultrasound guidance and 30 pathologically diagnosed, of these, four cases were pathologically diagnosed as malignant. Twenty-four cases of intraductal space-occupying lesions were localized under ductoscopy guidance and surgically removed, of which five cases were pathologically diagnosed as malignant. Conclusion: Utilization of localization needles under mammographic, ultrasound or fiberoptic ductoscopy guidance for non-palpable breast lesions is a safe and effective procedure, and is helpful in the diagnosis of breast cancer. With the help of this procedure, more malignant lesions can be localized and surgically removed.*

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With the development of imaging technology, more and more non-palpable breast lesions (NPBL) are being detected in the clinic (1). Accurate positioning is a prerequisite for the accurate incisional biopsy of NPBL, and imaging-guided puncture localization is helpful in the qualitative diagnosis of NPBL, which is conducive to the early detection and diagnosis of breast cancer (2, 3). At present, amongst the biopsy techniques for NPBL, the most widely used methods are localization and incisional biopsy guided by mammography, ultrasound and fiber-optic ductoscopy (4, 5).

From June 2013 to December 2014, 83 patients with NPBL underwent surgery at the Beijing Friendship Hospital. According to the different imaging methods and the characteristics of the detected lesions, the localization needle was placed and guided by mammography, ultrasound, or fiberoptic ductoscopy before surgery for resection of lesions. The clinical effects were satisfactory. The patient's imaging examination results, puncture positioning method, operative situations, histopathology and comprehensive treatment were retrospectively analyzed in this study in order to investigate the applied range and value of localization and needle placement guided by mammography, ultrasound and fiberoptic ductoscopy in the diagnosis and treatment of NPBL.

Patients and Methods

Clinical data. A total of 83 female patients with NPBL, who were admitted to Beijing Friendship Hospital, were selected for this study. The age of these patients ranged between 23 and 70 years, with a median age of 45 years. These patients underwent routine physical examination, or suffered from breast pain or nipple discharge and were subsequently diagnosed with NPBL. Sandy or cluster-like calcified breast lesions were diagnosed in 27 patients by mammography, and all had a diameter of <1 cm. According to the diagnostic criteria of the Breast Imaging Reporting and Data System (BI-RADS) developed by the American College of Radiology (6), three patients were diagnosed with BI-RADS grade 3 by mammography, 19 with BI-RADS grade 4, and five with BI-RADS grade 5. Ultrasound revealed NPBL in 32 patients, and the lesion diameter was ≥0.4 cm and <1 cm. According to ultrasound results,

seven patients were diagnosed with BI-RADS grade 3, 22 with BI-RADS grade 4, and three with BI-RADS grade 5. Fiber-optic ductoscopy revealed intra-ductal space-occupying lesions in 24 patients. Among these patients, six patients were diagnosed with intra-ductal papillary epithelioma, 15 with intra-ductal papillomatosis, and three with intra-ductal carcinoma.

Inclusion criteria. Patients were required to have the following: (i) Negative breast palpation results. (ii) One of the following examination results: diagnosed with BI-RADS grade 3-5 calcified breast lesions by molybdenum; diagnosis with BI-RADS grade 3-5 breast lesions; diagnosed with intraductal space-occupying lesions by fiber-optic ductoscopy, such as intra-ductal papillary epithelioma, intra-ductal papillomatosis and intra-ductal carcinoma. (iii) No severe heart or lung disease. (iv) No history of breast surgery within 3 months. (v) No history of neoadjuvant or chest radiation therapy.

Instruments and equipment. The GE breast mammography X-ray three-dimensional positioning system was used, which was equipped with a breast-specific computed X-ray imaging (CR) system (GE,Connecticut. USA). A SSD-a5 color Doppler flow imaging instrument was used (ALOKA, Tokyo, Japan). The fiber-optic ductoscopy and ancillary equipment were purchased from Polydiag (POLYDIANOST, Bavaria, Germany). Breast localization needles with a hook-like barb (Accura™ BLN2110. 21ga) were purchased from Angiotech (Angiotech, Vancouver, Canada).

Localization method. Puncture localization guided by mammography: Patients were placed in the sitting position, the chest was compressed by a localization-compression plate, and the X and Y axes were adjusted by the knob under the monitor to determine the puncture point. The skin underwent local disinfection, and local infiltration anesthesia was induced by 0.5% lidocaine. The Z-axis and the depth of needle insertion were determined according to the calculated data of the three-dimensional positioning system. The needle was inserted towards the calcified lesions from the puncture point vertical to the skin (90˚). The X and Y axes were then adjusted again, and photographs were taken for correction to ensure the puncture needle reached the target calcified lesions. The needle sheath was withdrawn, 5-6 cm of the tail end of the positioning guide wire was left outside the skin, and this was covered with sterile gauze.

Localization needle placement under ultrasound: Patients were placed in the supine position, the upper limb was stretched outward, and the puncture point was determined. The skin underwent local disinfection, and local infiltration anesthesia was induced by 0.5% lidocaine. The needle was obliquely inserted from the probe side of the skin covering the tumor towards the tumor (45˚ to 60˚), and the movement of the high echo point of the needle tip to the scheduled location was dynamically displayed by ultrasound in real time. The guide wire was then pushed forward, the needle sheath was withdrawn, 5-6 cm of the tail end of the positioning guide wire was left outside the skin, and this was covered with sterile gauze.

Localization and needle placement under fiber-optic ductoscopy: Patients were placed in the supine position, local skin disinfection was performed, and 0.5% lidocaine was infused from the diseased breast duct for anesthesia. The breast-duct endoscope was inserted from the orifice of the primarily diseased breast duct to determine the location and depth of the lesions. The needle was inserted from the fiber-optic ductoscopy opening, the barb was fixed on the lesion site, and the endoscope was withdrawn. The tail end of the positioning guide wire was placed outside the nipple along the diseased breast duct, and this was covered with sterile gauze. For patients diagnosed with intra-ductal papillomatosis, methylene blue (0.5-1.0 ml) was injected slowly into the diseased breast duct along the positioning tail wire 5 minutes before surgery.

Surgical methods. Patients underwent local infiltration anesthesia and potentiated intravenous anesthesia with 0.5% lidocaine. A shuttle-shaped incision was made, along the skin where the guidewire was scheduled to puncture and be removed, and skin and subcutaneous tissues were cut off layer by layer. Local resection or selective segmental resection was performed according to the orientation of the needle, and the evaluation of the size and extent of the lesion before the operation. After resection, calcified lesions were prepared into specimens, and the patient underwent mammography to confirm the complete resection of the calcified lesions. During the excision of intraductal space-occupying lesions, an arc incision or radial incision was made at the edge of the mammary areola where the diseased breast duct traveled, and the sub-nipple and distal breast ducts were separated and ligated. For patients undergoing methylene blue staining, the distal ends and the range of the diseased breast ducts were determined by methylene blue staining, and segmental resection was performed. During the operation, the removed specimen was sent for frozen-section pathology. The surgical program was decided according to pathological results: segmental resection or quadrantectomy was performed for patients with severe dysplasia; quadrantectomy or simple mastectomy was performed for patients with carcinoma *in situ*; simple mastectomy plus sentinel lymph node biopsy (SLNB) or breast-conserving surgery were performed for patients with minimally invasive carcinoma; simple mastectomy plus SLNB, breast-conserving surgery, or modified radical mastectomy were performed for patients with invasive carcinoma.

Results

In 27 patient, calcified breast lesions were positioned under the guidance of mammography and surgically resected, and postoperative pathology confirmed that the lesions in all 27 patients were accurately resected. The localization needle was well-fixed near the lesion. All lesions were completely and surgically removed in a single procedure. Among three patients with BI-RADS grade 3, pathology confirmed cystic hyperplasia in two and sclerosing adenosis in the other. Among 19 patients with BI-RADS grade 4, pathology confirmed cystic hyperplasia in four, sclerosing adenosis in three, fibroadenoma in three, atypical hyperplasias in five, lobular carcinoma *in situ* in two, ductal carcinoma *in situ* in one, and invasive lobular carcinoma in one. Among five patients with BI-RADS grade 5, pathology confirmed severe atypical hyperplasia in one, ductal carcinoma *in situ* in one, invasive ductal carcinoma in two, and invasive lobular carcinoma in one

In 32 patients, breast lesions were positioned under the guidance of ultrasound and surgically resected, and postoperative pathology diagnosed lesions in 30 patients

(93.8%). In two patients, postoperative pathology revealed no clear lesions in these specimens. Among seven patients with BI-RADS grade 3, pathology diagnosed fibroadenoma in three and tumor-like hyperplasia in two, while no clear lesions were found in two patients. Among 22 patients with BI-RADS grade 4, pathology diagnosed fibroadenoma in 1, tumor-like hyperplasia and severe atypical hyperplasia in seven, ductal carcinoma *in situ* in one, and invasive ductal carcinoma in one. Among three patients with BI-RADS grade 5, pathology diagnosed severe atypical hyperplasia in one, lobular carcinoma *in situ* in one, and invasive ductal carcinoma in one.

In these 83 patients, 5 patients underwent resection of the mass, 50 underwent segmental resection, 11 underwent quadrantectomy, six underwent breast-conserving surgery, four underwent simple mastectomy with SLNB, 5 underwent modified radical resection, and two underwent simple mastectomy with primary breast reconstruction by flap transfer. Patients with severe atypical hyperplasia and papillomatosis underwent tamoxifen treatment for 6 months, and were reviewed every 6 months. Patients with malignant tumor were reviewed every 3 months for 2 years after surgery. All patients were followed up after the operation and no patient was lost to follow-up; the mean follow-up duration was 23 months (range=13-31 months), and no recurrence or metastasis occurred.

Discussion

Calcified breast lesions are often the specific sign of non-palpable breast cancer. The calcified granules of breast cancer are mostly caused by degeneration and necrosis of intraductal cancer cells, and may derive from the sedimentation and calcification of secretions caused by cancer cells blocking the lumen of the duct. The morphology of malignant calcifications have different forms, and often manifest as small pleomorphic calcifications (gravel-like or granular calcifications) and linear or linear branching calcifications (casting calcification). On X-ray, if the range of the clustered calcification is >5/cm^2, clinical vigilance should be raised. According to BI-RADS classification, breast calcification grades 0-3 mostly indicate benign lesions; grade 4 indicates possible malignancy, in which biopsy is considered; and grade 5 indicates highly suspected malignancy, and the possibility of malignancy is ≥95% (8). A study revealed that in patients with non-palpable breast cancer, 50-60% were diagnosed through detection of calcified lesions by imaging examination (9). In this study, the calcified breast lesions of 27 patients were positioned under mammography, and in all 27 patients, the calcified lesions were confirmed to be accurately resected after operation, and the localization needle was well-fixed near the lesion. Pathology diagnosed malignant lesions in eight patients.

Puncture localization and incisional biopsy guided by mammography are the routine diagnostic and treatment methods recommend by guidelines for calcified breast lesions. The traditional localization method guided by mammography can two-dimensionally determine the location of calcified lesions by adjusting the X and Y axes, and the puncture point and depth of needle insertion are determined according to the experience of the operator. Hence, the accuracy of puncture localization is closely related to the experience of the operator (10, 11). Mammography X-ray three-dimensional positioning system has been used at our hospital, and the Z-axis and depth of needle insertion were determined according to the data calculated by the positioning system. Thus, the error caused by the lack of experience of the operator was avoided, and the accuracy of the puncture localization of calcified breast lesions was greatly improved. Despite the development of technology, we have recognized some limitations of this technology in the clinic: (i) Puncture localization under mammography needs the localization needle to be vertically inserted. Hence, for patients with small breasts, superficial lesions, or lesions close to the chest wall or located in the axilla, this technology cannot be implemented. (ii) In order to ensure the accuracy of puncture localization, the pressure of the positioning compression plate exerted on the mammary gland is maintained at approximately 120-150 N, and the operation lasted for 15-30 minutes. Hence, elderly and weak patients, as well as patients with a low pain threshold, would often experience difficulties in tolerating this procedure. (iii) Since the placement of the localization needle is not in real time and non-dynamic, after the puncture, it should be confirmed and corrected by repeated mammography photographs, increasing the risk of exposure to radiation.

In recent years, with the application of 40-100 MHz high-frequency probes and the improvement of ultrasound properties, the resolution of high-frequency ultrasound imaging has been greatly improved. Ultrasound can detect the size, shape and distribution of NPBL, as well as the presence of sound shadow and flash artifacts in the rear. It can also help understand the two-dimensional ultrasonic image manifestations of the lesions, and analyze the hemodynamics using color Doppler ultrasound, in order to infer the nature of the lesions. Puncture localization under ultrasound is a real-time and dynamic operation. In addition to its accuracy in positioning, it can be repeated many times in a short time. In this study, the breast lesions of 32 patients were positioned under the guidance of ultrasound and were surgically resected. Pathology confirmed that these lesions were accurately resected in 30 patients. Among these, malignant lesions were found in four patients. In addition to the accuracy of localization, puncture localization under ultrasound has the advantages of good patient compliance, being a simple operation and having a short operative time.

Differently from perpendicular needle insertion under the guidance of mammography, in localization under ultrasound, the needle is inserted from the base of the lesions, the puncture needle is parallel to the chest wall or skin and is not confined to the lesion site, and location of superficial lesions or lesions close to the chest wall is possible, which extends the application range of this technique in the clinic. Real-time and dynamic ultrasound guidance ensures the accuracy of puncture localization, and the puncture can be repeated many times in a short time interval. Puncture localization under ultrasound does not require the breast tissues to be clamped, and reduces the risk of bleeding and hematoma formation at the puncture site.

Intraductal space-occupying lesions include papillary epithelioma, papillomatosis and intraductal carcinoma, which account for 36-52% of patients with nipple discharge, who mostly need surgical treatment (12). Due to the absence of characteristic manifestations, ultrasound, mammography and other conventional examinations are difficult to guide localization. Previously, the injection of dyes through the discharging lactiferous duct and other indirect means were used to help localization, in which the operative area was large, and resection of often missed lesions. The application of fiber-optic ductoscopy has greatly improved the accuracy of diagnosis of intraductal space-occupying lesions, and made clear the indications for surgery. For single papillary carcinoma and intraductal carcinoma, a new technique was used in our Department, in which the resection of lesions was guided by localization needle placement under fiber-optic ductoscopy; and the accuracy of the surgical resection has been enormously improved (4). For papillomatosis usually found in multiple small ducts, since the localization needle can only be placed in one of the diseased lactiferous duct, it is difficult to locate all diseased ducts, which easily leads to missed resection of lesions. The technique of localization needle placement under fiber-optic ductoscopy combined with methylene blue staining was used in our Department, which can simultaneously locate large and small diseased ducts with papillomatosis, achieving a satisfactory clinical effect (13). In this study, in 24 patients, the localization needle was placed guided by fiber-optic ductoscopy or combined with methylene blue staining, and the lesions were surgically resected. Postoperative pathology confirmed that in all 24 patients, the lesions were accurately resected. Pathology diagnosed malignant lesions in five patients after the operation. Among these 24 patients, the square-frame head fell off in one patient, and the needles were well-fixed on the lateral wall of the lesions in the 23 patients (95.8%).

The placement of a localization needle is invasive, and the needle is difficult to remove under non-invasive conditions. Therefore, it is necessary for it to be placed on the day of surgery or one day before in order to avoid the displacement of the localization needle and secondary infection. It is difficult for intraoperative frozen-section examination to distinguish between severe atypical hyperplasia and carcinoma *in situ*, intraductal papillary epithelioma and ductal carcinoma *in situ*, sclerosing adenosis and invasive carcinoma and other diseases. Hence, blind surgery should be avoided. It is necessary to determine the operative plan after diagnosis by pathology using paraffin sections and immunohistochemistry.

Localization needle placement by mammography, ultrasound and fiber-optic ductoscopy for NPBL resection improves the accuracy of surgical resection of NPBL, reduces tissue damage, avoids placing great psychological pressure on the patient due to missed resection or blind expansion of the resection, contributes to the qualitative diagnosis of NPBL, promotes the early detection and early diagnosis of non-palpable breast cancer, and improves the diagnostic level.

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