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ORIGINAL RESEARCH

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Comparison of the clinical efficacy of body surface mapping plus wire-guided localization and body surface mapping plus methylene blue-guided localization in occult breast lesions

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Abstract

Accurate preoperative and intra-operative localization of occult breast lesions is important. We aimed to compare the clinical efficacy of body surface mapping plus wire-guided localization (BWL) and body surface mapping plus methylene blue-guided localization (BML) in occult breast lesions. Patient samples were obtained from the Xuzhou Central Hospital from 01 January 2018 to 31 December 2020. A total of 315 patients with a single occult breast lesion were included, comprising 225 cases in the BWL group and 90 cases in the BML group, were eligible for this study. We found that the average localization time in the BWL group was significantly greater than in the BML group (2.9 min *vs.* 1.6 min), while no significant difference was observed in the degree of pain, which was mild, between the two groups (average score, 1.3 *vs.* 1.5, respectively). The localization success rate and surgical resection rate were 100% in both groups. In addition, no significant difference was observed between the BWL group and BML group in terms of the average time of surgery (8.5 min *vs.* 9.8 min), the subjective difficulty of surgery, which was easy in both groups (average score, 2.1 *vs.* 2.4), and the average volume of surgical specimens (1.8 mL *vs.* 2.4 mL). Further, in the follow-up 3 months after surgery, the resection rate of lesions was 100%, and both groups demonstrated similar cosmetic effect scores. These findings indicated that both BWL and BML have the advantages of accurate localization, high resection rate, few adverse reactions, and excellent cosmetic effects in patients with occult breast lesions. Although both localization methods might be suitable for hospitals in remote areas, our results indicated that BML might be relatively simpler and more economical.

Keywords

Body surface mapping; Wire-guided localization; Methylene blue-guided localization; Occult breast lesions; Treatment

1. Introduction

Occult breast lesions are often detected by color Doppler ultrasound and molybdenum-target mammography, and account for 25% of all visible breast lesions on imaging [1]. In clinical practice, the Breast Imaging Reporting and Data System (BI-RADS) is used to evaluate the nature of breast lesions. BI-RADS 0, 1, 2 and a large proportion of BI-RADS 3 lesions are often monitored without any treatment, while a minority of BI-RADS 3 and BI-RADS 4 and above lesions necessitate biopsy for pathological examination. Ultrasound-guided fine needle aspiration biopsy (FNAB) or FNAB guided by molybdenum-target is preferred as the examination method of breast lesions. However, their diagnostic accuracy is often hindered by several factors that limit their widespread application in clinics. For instance, imaging examinations may not provide a complete representation of the lesions, and inadequate sampling may lead to incorrect pathological diagnosis [2]. Consequently, excisional biopsy is still required for a proportion of occult breast lesions to achieve a definitive pathological diagnosis.

Accurate preoperative and intra-operative localization of occult breast lesions is important. Currently, the common localization methods include body surface mapping, metal wire-guided localization, dye localization, nucleolin localization, and radioactive seed localization [3, 4]. However, nucleolin localization requires specialized equipment and nuclear medicine specialists, restricting their application in remote demographic areas [5]. It may also fail for tumors of size <5 mm, central quadrant breast lesions, or inexperienced physicians [6]. Additionally, although the radioactive dose has minor effects on patients and physicians [7], they may still pose

significant concerns about nucleolin localization. Radioactive seed localization, despite its advantages in localization and operation time, does not exhibit a significant difference in localization accuracy compared to other localization techniques. However, the safety of this technique requires further evaluation, as studies have demonstrated that prolonged waiting times before surgery can still result in radiation damage despite the seed's relatively limited tissue penetration [8]. Therefore, the current investigation aims to compare the clinical efficacy of body surface mapping plus wire-guided localization (BWL) and body surface mapping plus methylene blue-guided localization (BML) for occult breast lesions.

2. Materials and methods

2.1 Patient data

The data of patients with a single occult breast lesion who underwent surgical resection at the Xuzhou Central Hospital between 01 January 2018 and 31 December 2020, were retrospectively retrieved. The study inclusion criteria were: (1) occult breast lesions only detected by ultrasound and molybdenum-target; (2) BI-RADS 3 and above; (3) willingness to undergo surgery after imaging-guided localization. The exclusion criteria were: (1) palpable breast lesions; (2) presence of breast implant; (3) a recent history of breast surgery or chemoradiotherapy; (4) surgery is not performed or recommended following imaging examination and/or FNAB; (5) inability to tolerate the breast surgery for systemic diseases; (6) inability to cooperate with the breast surgery due to cognitive impairment or mental illness.

2.2 Body surface mapping

After identifying the breast lesions by ultrasound, their transverse, longitudinal, and multi-dimensional sections were recorded. The long diameter, short diameter, and distance from the skin were also measured. Briefly, the ultrasound probe was kept parallel to the long axis of the lesions, and the skin surface was pressed by a pen tip. When the pressure point was directly above the lesions, the point on the body surface was marked. The localization point was further confirmed by multi-dimensional sections.

2.3 Metal wire-guided localization

Following body surface mapping in the BWL group, patients received metal wire-guided localization under ultrasound guidance 20–180 min prior to surgery. A surgical incision was designed and disinfected around the localization point of the body surface. Then, the metal wire was penetrated from the surgical incision or its extended line into the lesion under ultrasound guidance. If the lesion was too hardy to be penetrated, the wire could be located 1 mm beyond the margin of the lesion. Following the localization, an ultrasound examination was performed to confirm that the metal wire was located in the lesion or immediately lateral to the lesion. For punctate calcifications or distorted glandular architecture shown in the molybdenum-target, which was not detected by ultrasound, the localization was performed under the molybdenum-target guidance. The time spent in either ultrasound-guided or molybdenum-target-guided localization was recorded. Wire-guided localization exhibited subtle deviation for coarse macrocalcifications because the wire could not penetrate macrocalcifications. However, the subtle deviation has no impact on the accuracy of the localization; thus, the choice of localization method was not affected by the type of lesions in this present study.

2.4 Methylene blue-guided localization

Following body surface mapping in the BML group, 0.2–0.4 mL methylene blue was injected into the lesion through a 26-gauge needle under ultrasound guidance 20–180 min prior to surgery. Since the methylene blue exhibited tissue diffusion, it was unnecessary to mark the channel between the body surface and the lesion in blue [9].

2.5 Surgical procedures

All the surgical procedures were performed under local anesthesia. Lidocaine was given layer by layer from the skin to the retromammary space. The designed surgical incision was used, and the length of the incision was recorded. In the BWL group, the incision was made down to the lesion along the metal wire using a scalpel, and the lesion and a few normal tissues surrounding the lesion were entirely removed. For punctate calcifications or distorted glandular architecture, the molybdenum-target was performed to confirm the completion of the resection of lesions. In the BML group, meticulous attention was paid to the dissection of the skin, progressing layer by layer until the site of the most intense staining was revealed, which typically corresponded to the location of the lesion.

The following data were recorded: localization time, pain severity (0: no pain, 1: mild pain, 2: moderate pain, 3: severe pain, and 4: extreme pain), adverse reactions associated with localization, operation time, the subjective difficulty of surgery (1: extremely easy, 2: easy, 3: moderately difficult, 4: difficult, 5: extremely difficult) [10].

2.6 Statistical analysis

Statistical analyses were performed using the SPSS v22.0 software (IBM, Chicago, IL, USA). Descriptive statistics are presented as percentage, means ± standard errors, or median. Measurement data were analyzed using the *t*-test, and categorical variables were compared using the Chi-square test. $p < 0.05$ was used to indicate statistical differences.

3. Results

A total of 315 patients with a single occult breast lesion, comprising 225 in the BWL group and 90 in the BML group, were eligible for this study. Schematical diagrams of the lesional localization are shown in Fig. 1 in reference to previous studies [11]. Of the lesions assessed, 163 were classified as BI-RADS 3, 46 as BI-RADS 4a, 40 as BI-RADS 4b, 37 as BI-RADS 4c, and 29 as BI-RADS 5 (Table 1). The resection rate of lesions was 100% in both the BWL and BML groups. The average localization time was 2.9 min in the BWL group and 1.6 min

in the BML group, but the difference was not statistically significant (Table 2, $p < 0.05$). In both the BWL group and the BML group, the degree of pain was mild (average score, 1.3 *vs.* 1.5), the subjective difficulty of surgery was easy (average score, 2.1 *vs.* 2.4), and the average operation time was 8.5 min and 9.8 min, respectively, with no significant difference observed between them.

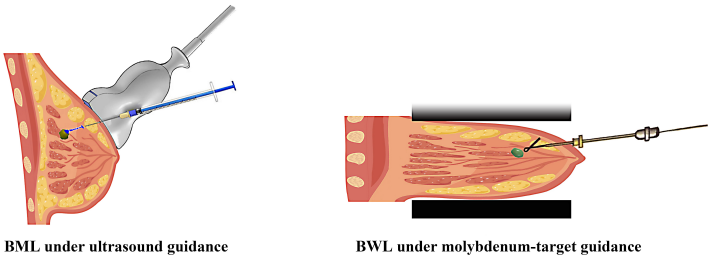

FIGURE 1. Schematical diagrams of lesion localization. BML: body surface mapping plus methylene blue-guided localization; BWL: body surface mapping plus wire-guided localization.

TABLE 1. Basic clinical characteristics of breast occult breast lesions.

Clinical characteristics	No. of cases
BI-RADS	
3	163
4a	46
4b	40
4c	37
5	29
Pathologic types	
Adenosis	79
Fibroadenoma	94
Intraductal papilloma	47
Inflammatory mass*	48
Intraductal carcinoma	13
Invasive carcinoma	11
Others**	23

**including plasma cell mastitis and granulomatous lobular mastitis; **including atypical hyperplasia of duct epithelium, fat necrosis, and benign phyllodes tumor, etc. BI-RADS: Breast Imaging Reporting and Data System.*

TABLE 2. Comparisons of clinical parameters between BML and BWL.

Parameters	BWL	BML	*p* value
Localization time	2.9 min ($\sigma = 0.3$)	1.6 min ($\sigma = 0.2$)	<0.05
Degree of pain	Mild	Mild	>0.05
Subjective difficulty of surgery	Easy	Easy	>0.05
Operation time	8.5 min ($\sigma = 1.5$)	9.8 min ($\sigma = 1.9$)	>0.05
Specimen volume	1.8 mL ($\sigma = 0.4$)	2.4 mL ($\sigma = 0.7$)	>0.05

σ: standard deviation; BML: body surface mapping plus methylene blue-guided localization; BWL: body surface mapping plus wire-guided localization.

All occult breast lesions were completely resected in both groups. Representative images before and after excision are shown in Fig. 2. Except for malignant breast neoplasms, the average volume of surgical specimens was 1.8 mL in the BWL group and 2.4 mL in the BML group, and the difference between the two groups was not significant. Routine pathological examinations were performed on all occult breast lesions, including 79 cases of breast adenosis, 94 cases of breast fibroadenoma, 47 cases of breast intraductal papilloma, 48 cases of inflammatory mass, 13 cases of breast intraductal carcinoma, 11 cases of invasive breast carcinoma and 23 cases of other pathologic types. In particular, there were a total of 16 calcifications, whose pathological diagnosis were 11 adenosis, 2 intraductal papilloma and 3 intraductal carcinoma, respectively. Ten lesions morphologically described as distorted glandular architecture were pathologically confirmed as 8 adenosis and 2 invasive carcinomas, respectively.

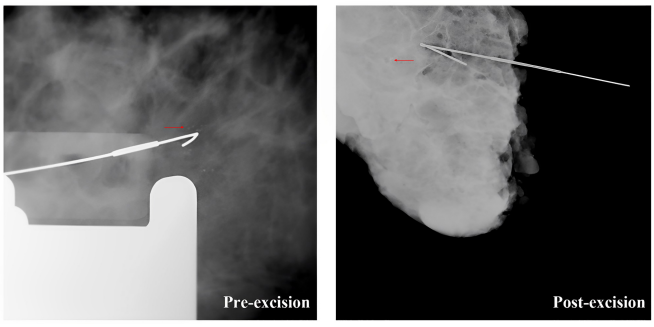

FIGURE 2. Representative image before and after excision.

In this present study, there were a total of 148 cases that underwent coarse/fine needle aspiration biopsy before the surgery, and the biopsy rate was 47.0% (148/315). The biopsy results were concordant with the postoperative pathological findings in 126 (85.1%) cases. Lesions with inconsistent outcomes were mainly manifested as densely calcifications or distorted glandular architecture, the proportion of which was about 14.9% (22/148). Cases with underestimated

pathological diagnosis accounted for 77.3% (17/22) of all patients with inconsistent outcomes, predominately due to sampling error and intratumor heterogeneity.

One patient in the study had local hematomas measuring 1.5 cm in diameter, but no extraordinary measures were needed.

4. Discussion

Radiographic grading is useful for differentiating benign and malignant breast lesions but has some limitations. Even if high radiographic grading is observed in some occult breast lesions, it may still be difficult to confirm the diagnosis through imaging-guided aspiration biopsy, and complete resections are thus necessary to obtain a definitive diagnosis. Dye localization, such as methylene blue-guided and carbon localization, is currently being clinically used. Carbon localization has the advantages of weak inter-tissue dissemination and lax temporal constraints between localization and surgery. However, it may contribute to an increased risk of granuloma formation and a physical imprint on the skin [9]. Moreover, carbon localization relies on trajectory tracing, making the accurate localization of deep lesions difficult [12].

This present study compared the clinical efficacy of BWL and BML in occult breast lesions to identify which one is simpler and more economical for potential application in remote demographic areas. Methylene blue is an easily available and inexpensive drug frequently used as a tracer of sentinel lymph nodes (SLNs) [13, 14]. The injection of methylene blue in breasts is considered safe and has no effect on hematoxylin-eosin (HE) staining and immunohistochemical examinations of the specimens [15]. Although methylene blue has the disadvantage of great inter-tissue dissemination, it allows easy lesion localization as long as the time interval between localization and surgery is controlled within a reasonable range. Additionally, the blue-stained site at the end of the needle can be clearly distinguished from the relatively shallow part. Thus, BML is used for selecting the optimal surgical incision to reach the localization point directly under local anesthesia. The volume of methylene blue used is usually 0.2–0.4 mL, as an excessive amount of methylene blue may lead to a wider range of staining, and too small volume may lead to severe tissue diffusion and inaccurate localization [16]. In our experience, it might be appropriate to control the volume of methylene blue to around 0.2 mL and the time interval between localization and surgery to 20–180 min. The width of tissue diffusion should be controlled between 0.8 and 1.5 cm to facilitate the identification of the localization point. It is important to note that the volume range of methylene is too small for SLN scintigraphy, even if occult breast lesions are confirmed as malignancies by pathology during the surgery. In such cases, breast-conserving therapy and SLN biopsy with a higher volume of methylene blue are recommended by clinical guidelines [17]. Due to the malignant nature of these lesions, a simple lumpectomy is not generally recommended.

Imaging-guided wire localization is the most common preoperative localization method with the advantages of simplicity and convenient operation [18]. However, wire localization may cause adverse events such as bleeding, metal wire displacement, fracture, and even pneumothorax [19, 20]. The success rate of wire localization alone is about 82.1%–93.7% [21, 22]. In this present study, BWL was applied to improve the localization success rate and complete resection rate. Further, accurate localization and minimal invasiveness are crucial in breast lesion surgery, as an imprecise localization or wire displacement may lead to the inadvertent removal of excessive tissue [23]. Thus, BWL, as a localization method, is useful for determining an optimal target area.

In the present study, we report a 100% localization success rate and complete resection rate in both the BML and BWL groups, demonstrating that a single operator can perform BML with a shorter localization time. In contrast, the process of BWL is more complex and time-consuming, requiring the operator to hold the trocar while an assistant feeds the metal wire and then removed by the operator. Notably, both the localization and surgery were performed under local anesthesia and well tolerated by all the patients, despite the risk of local anesthesia in causing local edema around occult breast lesions, which may significantly further increase surgical difficulty. In this study, we found that the lesions could be reached directly along the wire in the BWL group. In the BML group, blue-stained tissues were easily reached from the designed surgical incision under the guidance of body surface mapping. Therefore, there was no significant difference between the two groups regarding operation time and subjective difficulty of surgery.

Despite individual differences in pain perception, there was no significant difference in pain between the two groups, suggesting that both BML and BWL were well-tolerated by patients. In previous literature, it was reported that patients might present vasovagal syncope based on previous literature [24], but there have been few reports on related adverse events in the last decade. However, no such adverse events were observed in our study, which may be associated with familiarity with localization and surgical procedures. Overall, patient distress was effectively minimized through comprehensive communication and preoperative education.

One patient had local hematomas, possibly caused by abundant blood flow or punctured vessels of larger diameters. No extraordinary measures were needed, and the subsequent surgery was unaffected. However, in cases where electrocoagulation is required to manage bleeding, caution should be exercised to maintain a safe distance between the wire and electrotome, as an arc can be easily formed.

There were some limitations in the study. First, the sample size was small, with a very small proportion of malignant breast lesions. Second, this was a retrospective study, larger cohort, prospective and randomized controlled studies are needed to validate the reported findings.

5. Conclusions

In conclusion, both BWL and BML have the advantages of accurate localization, high resection rate, few adverse reactions, and excellent cosmetic effects in occult breast lesions. However, BML might be relatively simpler and more economical. Both localization methods are suitable for hospitals in remote areas.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

KL and CL—designed the research study. PW and SP—performed the research. PS, CT and KL—analyzed the data. CL and PW—wrote the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Written informed consent was obtained from all patients, and the study was approved by the Ethics Committee of Xuzhou Central Hospital (ID: XZXY-LJ-20220526).

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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