Original Article

Assessing the Utilization of Preoperative Ultrasound Guided Skin Marking for Tumor Localization in Post-Neoadjuvant Breast Cancer - A Single-Centre Study

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Abstract

Objective: To compare the cost-effectiveness of ultrasound-guided skin surface marking (USGSSM) and wire-guided localization (WGL) for tumor localization in patients undergoing breast cancer surgery following neoadjuvant therapy at Shalamar Hospital.

Methodology: This retrospective study was conducted at Shalamar Hospital, Lahore, between July 2023 and December 2023. Records of breast cancer patients including age, localization technique, sonographic and pathological tumor size, histologic type/grade, margin status, chemotherapy, and axillary dissection were included for analysis (27 WGL, 38 USGSSM). USGSSM involved preoperative surface marking in surgical position using ultrasound; WGL used ultrasound-guided wire insertion, confirmed with post-wire mammography. The data were entered and analyzed using SPSS version 25.

Results: The mean age of patients was 49 years, with invasive ductal carcinoma being most common. Mean ultrasound tumor size was 13mm in WGL group, 17.7mm in USGSSM group, and mean histopathological size was 15.7mm in WGL group and 27.7mm in USGSSM group. A significant correlation between ultrasound and pathological tumor sizes was noted ($p = 0.001$). Positive margins were involved in 6 cases (WGL: 2, USGSSM: 4), with no significant difference ($p > 0.05$).

Conclusion: USGSSM offers comparable efficacy to WGL for tumor margin clearance, making it a cost-effective option in breast-conserving surgery following neoadjuvant chemotherapy

Keywords: Wire-guided localization, Ultrasound-guided skin surface marking, Nonpalpable breast cancer, Localization techniques.

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Introduction

Breast cancer is the most frequently diagnosed cancer and a leading cause of cancer-related mortality among women throughout the world. Pakistan has the highest incidence of breast cancer in Asia, with approximately one in nine women at lifetime risk of developing the disease,[1] and the incidence continues to rise over recent decades.[2] Over the corresponding timeframe, advances in screening, imaging, pathology and systemic therapy have altered and enhanced its management. Population-based mammographic screening has enabled earlier detection and reduced breast cancer-related mortality.[3] Subsequently the neoadjuvant chemotherapy (NACT) is progressively used to downstage the primary tumor and axillary nodes, so numerous patients who would otherwise need mastectomy can now undergo breast-conserving surgery (BCS).[4]

The breast-conserving surgery followed by the radiotherapy provides survival at least equivalent to mastectomy in initial stage of disease, and recent registry data suggest a survival benefit.[5] Its success however, depends on complete tumor excision with negative margins (no tumor on ink). Marginal involvement requires re-excision or conversion to mastectomy, which increases the morbidity, cost and the anxiety among patients.[6] This challenge is greatest after NACT, because a good response can make a previously palpable tumor impalpable and difficult to

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locate during the surgical procedure.[4,7]

Numerous image-guided techniques have been developed to localize non-palpable breast tumors, including wire-guided localization (WGL), radioactive seed localization, radio-guided occult lesion localization (ROLL), intraoperative ultrasound, magnetic seed localization, and preoperative skin marking.[7] WGL has traditionally been the standard technique; however, it requires a separate radiological procedure on the day of surgery, causes patient discomfort, and carries a risk of wire displacement. Although wire-free localization techniques have been shown to reduce re-excision rates,[8] their use is often limited by the need for expensive equipment, radioactive material licensing, or advanced technical expertise, restricting their availability in low- and middle-income countries.[9] In contrast, ultrasound-guided localization offers a practical and potentially cost-effective alternative. A study involving 520 patients with non-palpable breast cancer reported fewer positive surgical margins and lower re-excision rates with ultrasound-guided excision compared with wire-guided localization.[10]

At the local level, the evidence on localization techniques remains very limited. A retrospective study from Karachi reported 100% successful retrieval with ultrasound-guided wire localization of clipped residual lesions after NACT, but it included only 39 patients, which limits the generalizability of its observations.[11] Another study from Lahore showed that preoperative ultrasound-guided marking, combined with mammography and an intraoperative image intensifier, achieved a 99.3% clear-margin rate in 144 patients after NACT.[12] Nevertheless, no local study has directly compared ultrasound-guided skin surface marking (USGSSM) with WGL in terms of margin outcomes and cost-effectiveness. The present retrospective study was therefore conducted to compare the cost-effectiveness of USGSSM and WGL for tumor localization in patients undergoing breast cancer surgery after neoadjuvant therapy, with a specific concern on achieving clear surgical margins. Its findings are expected to guide the choice of an effective and affordable localization strategy in resource-limited healthcare settings.

Methodology

A retrospective cohort study was conducted among patients with biopsy-confirmed breast cancer who underwent tumor localization at Shalamar Hospital, Lahore, between July and December 2023. The study was initiated following approval from the Institutional Review Board (IRB No. SMDC-IRB/AL/40/2023).

Medical records of women aged 18 years or older with histologically confirmed breast cancer based on core needle biopsy were reviewed. Eligible patients had non-palpable or vaguely palpable breast lesions detectable on ultrasonography and had undergone wide local excision following preoperative localization using either ultrasound-guided skin surface marking (USGSSM) or wire-guided localization (WGL).

Patients with lesions visible exclusively on mammography, multicentric or multifocal disease, locally advanced or metastatic breast cancer, a history of recurrent disease in the ipsilateral breast, previous breast surgery, or prior radiotherapy to the affected breast were excluded. Additionally, patients who underwent localization using other techniques, such as radioactive seed or magnetic marker localization, those who received more than one localization technique during the same procedure, and those with missing essential outcome data, including histopathological margin reports or cost records, were excluded.

To ensure patient confidentiality, each medical record was assigned a unique study identification code. No patient names or other personally identifiable information were recorded.

Baseline demographic and clinical characteristics were extracted from medical records, including age, initial tumor size before neoadjuvant therapy, residual tumor size after treatment, residual tumor palpability, ultrasound visibility, and response to neoadjuvant therapy. Patients were subsequently categorized into two groups according to the documented preoperative localization technique: USGSSM or WGL.

In the USGSSM group, ultrasonography was used to identify the residual tumor or tumor bed, and its location was marked on the overlying skin before surgery. The procedure was performed using a high-frequency linear transducer (10–12 MHz), with the patient in the supine position and the ipsilateral arm abducted.

In the WGL group, the skin was sterilized and locally anesthetized using 1–2% lidocaine. Under imaging guidance, a 20-gauge needle containing a retractable hook wire (e.g., HS Hospital Service SpA or Cradles® Needle Localization Wire) was inserted to the target depth. The wire tip was advanced approximately 1 cm beyond the lesion to ensure appropriate positioning.

The needle was subsequently withdrawn, leaving the hooked wire anchored within the breast tissue.

For lesion localization and measurement, three orthogonal dimensions (x, y, and z axes) were recorded, along with lesion depth from the skin surface, distance from the nipple–areolar complex, and proximity to the pectoral fascia. The projected skin entry point was marked using a permanent marker and covered with a waterproof dressing.

Histopathological tumor size was obtained from the final histopathology report of the wide local excision specimen and defined as the largest tumor diameter, measured in millimeters. Ultrasonographic and histopathological tumor measurements were recorded for each patient to facilitate comparison of tumor size between the two localization groups and assess the agreement between ultrasonographic and histopathological measurements within each group.

All relevant data were entered and analyzed using IBM SPSS Statistics version 26.

Results

A total of 105 patients diagnosed with breast cancer underwent tumor localization at Shalamar Hospital. Of these 65 patients had complete health records therefore their data was analyzed. Twenty-seven patients had undergone wire-guided localization (WGL) while 38 underwent ultrasound-guided skin surface marking (USGSSM). The mean age of all patients analyzed was 49±9.8 years. Among patients who underwent WGL, the mean age was 46.8±8.1 years, while for those who underwent USGSSM, the mean age was 51±1.7 years. The most common histological type of the tumor amongst all patients was invasive ductal carcinoma (IDC) 26 and 36 in WGL and USGSSM. Other histological types identified were invasive lobular carcinoma in 2 patients and ductal carcinoma in situ in one patient. Histologically the most common grade of the tumor was 2 in both groups. Table I.

All patients in both groups underwent neoadjuvant chemotherapy except 4 patients, who underwent upfront surgery, 2 in each group (WGL and USGSSM). Axillary dissection was carried out in 23 cases in the WGL group and 32 cases in the USGSSM group. The rest underwent sentinel lymph node biopsy. Table II.

Table I: Patient Demographics & Tumor Characteristics.

Parameter	WGL (n=27)	USGSSM (n=38)	p-value
Mean age	46.8 ± 8.1	51 ± 1.7	0.829
BMI	27.30±3.74	25.78±3.99	0.127
Menopausal status			
Pre-menopausal	14 (51.9)	20 (52.6)	0.951
Post-menopausal	13 (48.1)	18 (47.4)	
Side			
Right	7 (25.9)	13 (34.2)	0.476
Left	20 (74.1)	25 (65.8)	
Most common histo type			
Invasive ductal carcinoma	26 (96.3%)	36 (94.7%)	0.314
Invasive lobular carcinoma	0 (0.0%)	2 (5.3%)	
Ductal carcinoma in situ	1 (3.7%)	0 (0.0%)	

Table II: Treatment characteristics of patients in both groups. (N = 65)

Variable	WGL (n = 27)	USGSSM (n = 38)	p-value
Treatment sequence, n (%)			
Neoadjuvant chemotherapy	25 (92.6)	36 (94.7)	1.000
Upfront surgery	2 (7.4)	2 (5.3)	
Axillary procedure, n (%)			
Axillary lymph node dissection (ALND)	23 (85.2)	32 (84.2)	1.000
Sentinel lymph node biopsy (SLNB)	4 (14.8)	6 (15.8)	
Fisher's exact test applied			

The overall mean tumour size on ultrasonography was 13.0 ± 6.4 mm in the WGL group and 17.7 ± 8.8 mm in the USGSSM group. According to the histopathology, the mean tumor size was 15.7 ± 7.3 mm in the WGL group and 27.7 ± 10.6 mm in the USGSSM group. Tumors were significantly larger in the USGSSM group on both ultrasonography and histopathology ($p < 0.05$). In both groups, the histopathological tumor size was larger than the ultrasonographic size, by 2.7 mm in the WGL group and 10.0 mm in the USGSSM group, as presented in table III.

Table III: Tumor Size Comparison (Ultrasound vs. Histopathology)

Men Tumor Size Measurement	WGL (n=27)	USGSSM (n=38)	P-value
Ultrasonographic Size	13 ± 6.4	17.7 ± 8.8	P = 0.001
Histopathological Size	15.7 ± 7.3	27.7 ± 10.6	P = 0.001

Majority of the cases in both groups received neoadjuvant chemotherapy, 25 (92.6%) in the WGL group and 36 (94.7%) in the USGSSM group, while only 4 cases (2 in each group) underwent upfront surgery. The axillary lymph node dissection was achieved in 23 (85.2%) cases in the WGL group and 32 (84.2%) patients in the USGSSM group, whereas the remaining 10 patients (4 and 6, respectively) underwent sentinel lymph node biopsy (SLNB). Positive margins were found in 2 (7.4%) patients in the WGL group and 3 (7.9%) in the USGSSM group, without significant difference across the techniques (p >0.05. Figure 1.

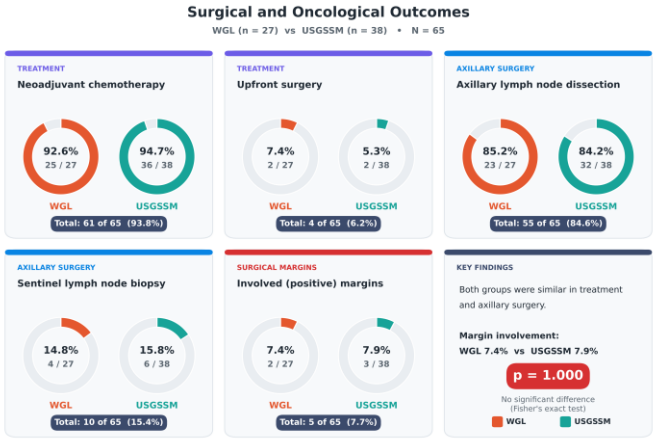


Figure 1. The surgical and oncological outcomes in WGL and USGSSM groups. (n = 65)

Discussion

The breast cancer remains a significant challenge in breast-conserving surgery (BCS) following neoadjuvant chemotherapy, specifically when localizing non-palpable lesions. The wire-guided localization required an extra radiology visit, resulting discomfort and increases cost, with higher margin and re-excision rates than wire-free methods, while ultrasound-guided skin marking is a simple, low-cost alternative with equivalent or the better margin outcomes. This retrospective study compared WGL and USGSSM procedures, nearly all performed after NACT and the most common finding was that involved margins were equally infrequent in both groups (7.4% vs 7.9%; P = 1.000), even though tumours in the USGSSM group were significantly larger on both ultrasound and histopathology. Furthermore, USGSSM is a non-invasive technique, which can be performed easily and quickly without utilization of any resources that are usually present within the breast radiology department, which may favor its utilization in resource limited settings.[13] A similar trend was documented by Franceschini et al, who compared the rates of achieving clear margins on histopathology among various localization techniques. It was seen that USGSSM had 95.9% clear margins rate, while WGL had a rate of 70.8 – 87.4%.[13,14] In comparison, our analysis showed a clear margin rate of 92.6% (2/27) and 91.6% (3/36) in WGL and USGSSM, respectively.

In the study by Hu et al. on 520 patients with non-palpable breast cancer, observed that the ultrasound-guided excision gave significantly fewer positive margins compared to wire-guided localization (4.6% versus 19.4%), along with a lower intra-operative re-excision rate (11.1% versus 24.0%).[10] In contrast to the present finding Mendes et al[16] retrospectively reviewed 155 cases and reported the two techniques equivalent: negative margins were 92% versus 93%, re-excision 32% versus 33.3%, and repeat surgery 8% versus 7% (P = 1.000). Consistently, Chang et al[15] demonstrated an overall positive-margin rate of 7.2% among 143 patients, with no significant difference between non-wire and wire-guided localization (5.9% versus 11.5%; P = 0.33). The involved-margin rates of this study (WGL 7.4% versus USGSSM 7.9%; P = 1.000) are virtually identical to the equivalence shown by Mendes et al. and Chang et al.[15,16] Hamed et al[17] carried out a prospective controlled study using ultrasound-guided clip insertion with skin marking and achieved free margins in 47 of 50(94%) cases. A similar trend was documented by Gerrard et al[18], who reviewed 95 operations using surgeon-led intra-operative ultrasound skin marking, where each cancer was identified, and although 14 margins (14.7%) were positive, only 2 of the re-excised specimens contained residual tumour.[18] The some differences in the findings across the studies is most likely due to the experience of the operating team and the routine use of tumor-bed clips placed before chemotherapy.

In this study the IDC was noted to be a dominant histological type in both groups (WGL 96.3% versus USGSSM 94.7%), followed by two cases of invasive lobular carcinoma (ILC) in the USGSSM group, and one case of ductal carcinoma in situ (DCIS) in the WGL group, without significant difference across the groups (P = 0.314), along with moderately differentiated (grade 2) tumors as the dominant category. The findings were closely match to other relevant local studies, like Shah et al[19] conducted their study on 317 women and reported IDC in 91.2%, ILC in 7.9% and moderately differentiated (grade II) tumors in 67.2% of the patients. Comparable findings were observed by another local

cohort, where IDC reported in 91.7% cases and ILC in 7.2% patients.[20] The results are also broadly consistent with the studies of Ishaque and Asad, who reported IDC in 85.7% and ILC in 7.1% of premenopausal women.[21]

According to our findings, just over half of the patients in both groups were premenopausal (51.9% versus 52.6%) in WGL and USGSSM respectively (p = 0.951), shows that the two groups were well balanced for menopausal status and reflects the younger age profile of breast cancer in Pakistani population, which also supported by Shah et al who reported a mean age at presentation of 46.6 ± 11.5 years, with 42% of women premenopausal.[19] The proportion is somewhat lower than in this study, but it endorses that a large share of Pakistani women present before menopausal status.

Generally, the wire-guided localization is most widely utilized technique globally for the preoperative localization of breast cancer. Even though it is a safe and standardized technique, possess few draw-backs as well as: discomfort of the patient as it is an invasive procedure, risk of infection or wire migration, and scheduling the procedure as close to the surgery to mitigate the risk of wire migration and the infection.[22] On the other hand USGSSM has been used world over, but there is small number of data and literature limiting its implementation and a standardized approach. A study from Italy compared the utility of USGSSM to magnetic seed localization, and reported insignificant difference in achieving clear histopathological margins and re-excision rates.[17] Likewise, there is no exposure to ionizing radiation in USGSSM, as WGL needs post-wire insertion mammography to confirm the wire placement.

Collectively, the evidence and our data indicate that USGSSM achieves oncological adequacy comparable to the WGL technique. However, this study has several limitations, including its retrospective design, single-center setting, and limited sample size, making it susceptible to selection bias and limiting the generalizability of the findings. Additionally, the larger size of tumor size in the USGSSM group indicating a possible baseline imbalance, along with, the localization technique was selected by the surgeon rather than through randomization, potentially introducing selection bias and confounding.

Furthermore wire-associated morbidity did not observe, even in the more demanding post-NACT setting. To observe the finally conclusive evidence, further larger prospective and multicenter studies, ideally randomized controlled trials, with addition of re-excision rates, local recurrence, time of localization, volume of specimen, cosmetic outcome and patient satisfaction, are recommended to authorize whether USGSSM is as effective as WGL in post-neoadjuvant breast cancer.

Conclusion

Ultrasound-guided skin surface marking (USGSSM) appears to be an effective and safe alternative to wire-guided localization (WGL) for localizing non-palpable breast cancer lesions following neoadjuvant chemotherapy. It demonstrated comparable surgical margin outcomes to WGL, including in patients with larger residual tumors. Furthermore, preoperative ultrasonographic measurements showed good correlation with final histopathological tumor size.

In resource-limited settings, USGSSM may provide a practical, non-invasive, and potentially cost-effective approach to guide surgical planning and facilitate breast-conserving surgery. Its comparable margin outcomes suggest that it may be a suitable alternative to WGL in appropriately selected patients. However, larger multicenter prospective studies incorporating formal cost-effectiveness analyses and long-term follow-up are needed before its routine implementation can be recommended.

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