Preoperative Ultrasound-Guided Marking, Mammogram, and Peroperative Use of Image Intensifier: A Cost-Effective Technique in Clipped Non-Palpable Breast Cancer Lesions to Achieve Adequate Surgical Margins

Amna Masud[1], Huma Majeed Khan[1], Eisha Tahir[2], Anam Waseem[1], Hafsa Ahmed[1] and Rabia Ikram[3]

[1]*Department of Breast Surgery, Ittefaq Hospital (Trust), Lahore, Pakistan*
[2]*Department of Radiology, Shalamar Hospital, Lahore, Pakistan*
[3]*Department of Breast Surgery, Rashid Lateef Medical College, Lahore, Pakistan*

ABSTRACT

Objective: To measure the effectiveness of localisation and removal of impalpable target lesions without compromising patient safety in a resource-limited setup using preoperative ultrasound and mammography with peroperative use of C-arm image intensifier.

Study Design: Descriptive study.

Place and Duration of the Study: Department of Breast Surgery, Ittefaq Hospital (Trust), Lahore, Pakistan, from 25th October 2011 to 17th February 2023.

Methodology: All the breast cancer patients who achieved complete clinical response after neoadjuvant systemic treatment and underwent breast conservation surgery during the study period were included. Tumour / clip localisation was done using preoperative ultrasound or image-guided marking, a 2-view mammogram in all cases and the use of an image intensifier to confirm the presence of clips in the excised specimen. The primary outcome was the accurate localisation and removal of the index lesion, while the secondary outcome included the reoperation rate for positive margins and early local recurrence.

Results: Data from 144 patients were reviewed. Successful localisation was done in all the patients; only one patient had a positive margin for ductal carcinoma-*in situ* (DCIS), achieving a 99.3% clear margin rate. Local recurrence within two years after primary operation was seen in one patient only.

Conclusion: By a combined approach of preoperative ultrasound-guided marking, a 2-view mammogram, and the use of image intensifier, successful localisation of an impalpable breast lesion is possible without compromising oncological and aesthetic principles.

Key Words: *Breast conservation surgery, Localisation, Non-palpable, Margins, Image intensifier.*

How to cite this article: Masud A, Khan HM, Tahir E, Waseem A, Ahmed H, Ikram R. Preoperative Ultrasound-Guided Marking, Mammogram, and Peroperative Use of Image Intensifier: A Cost-Effective Technique in Clipped Non-Palpable Breast Cancer Lesions to Achieve Adequate Surgical Margins. *J Coll Physicians Surg Pak* 2024; **34(11)**:1364-1368.

INTRODUCTION

Breast cancer is among the most prevalent cancers and a major contributor to cancer-related deaths.[1] In Pakistan the disease burden is steadily increasing and the majority of the cases are diagnosed when the tumour becomes clinically palpable.[2] Among these patients, a significant number become eligible for breast-conserving surgery (BCS) after tumour downsizing with neoadjuvant systemic therapy.[3] Breast Conserving Therapy (BCT) offers an improved survival rate as compared to mastectomy alone, with added cosmetic advantages and lesser psychological morbidities.[4]

Correspondence to: Dr. Amna Masud, Department of Breast Surgery, Ittefaq Hospital (Trust), Lahore, Pakistan
E-mail: amnamasud999@yahoo.com

Received: May 20, 2023; Revised: January 16, 2024; Accepted: May 13, 2024
DOI: https://doi.org/10.29271/jcpsp.2024.11.1364

The success of BCS depends on effective lesion localisation and removal without resecting healthy breast tissue.[5] Clipping of the tumour site before the start of systemic therapy is of prime importance as it will guide the surgeons in the removal of the tumour area with precision as in many cases the tumour will become impalpable after completion of the systemic therapy.[6]

Although the localisation of these areas has some limitations, it holds significant implications in the surgical resection of the tumour. Various methods have been developed for locating the tumour over time based on personal preference, skill, and available technology.[7] For any chosen method the goal is to successfully remove the target area achieving clear margins without resecting healthy tissue unnecessarily, providing an acceptable cosmetic outcome.[8] Various techniques developed so far include carbon marking, radioactive seed localisation (RSL), radio-guided occult lesion localisation (ROLL), non-radioactive radar localisation, magnetic seed localisation, intraoperative ultrasound, wire localisation, etc.[9-11]

Wire-guided localisation is considered cheap and effective and still remains the most commonly used method worldwide.[12] In Pakistan, only a few tertiary care centres are practising wire localisation method, whereas most hospitals lack these facilities,[13-16] consequently leading to a higher mastectomy rate. Moreover, wire-guided localisation has certain limitations including scheduling difficulties, patient discomfort, difficult localisation in dense breasts, peroperative difficulties such as wire tip localisation predisposing to excessive excision of healthy breast tissue, risk of wire migration, and inconvenience for surgeons in incision making.[17,18]

Use of 2-view mammogram along with preoperative ultrasound-guided marking of the lesion or clip followed by confirmation of the marker in the excised specimen using an image intensifier in the operating room, can be adopted specifically in resource-limited setups. It is more economical than wire localisation, feasible for the patient, does not have scheduling difficulties, has no risk of wire migration, and allows full access to the surgeon in planning an incision.

The objective of this study was to determine the effectiveness of localisation and removal of index lesions avoiding re-excision for positive margins.

METHODOLOGY

Consecutive patients with primary breast cancer of all types, who received neoadjuvant systemic therapy and underwent BCS at the Department of Breast Surgery, Ittefaq Hospital from October 2011 to February 2023, were included. Data were retrieved from the patient record system. Patients with palpable tumours were excluded from the study.

All the patients were diagnosed using bilateral mammograms and ultrasound breast followed by ultrasound-guided core biopsy of breast lesion. For suspicious-looking axillary lymph nodes, fine needle aspiration cytology (FNAC) was done. In the case of invasive lobular carcinoma (ILC), a breast MRI was also performed.

Prior to the start of systemic therapy, the tumour was clipped (Liga clip Lt 300, divided into two pieces) under ultrasound guidance, and post-clip 2-view mammograms (Figure 1) were obtained to make sure that the clips had been successfully placed. Number of marker clips varied depending on tumour size, multifocal disease, and presence of satellite lesions.

After the completion of systemic therapy, patients were again evaluated clinically for response and an ultrasound was done to check the residual disease. A 2-view mammogram was performed to exclude the migration of clips by comparing them with post-clipping mammograms.

All the markings were performed by an experienced breast radiologist 1-2 days before surgery. For accurate marking, proper positioning of the patient is important, similar to the position maintained during surgery, with the surgery side arm extended at 90 degrees. The residual tumour / marker clips were identified sonographically and residual tumour size was measured. The distance between tumour site and the skin was estimated by applying optimal probe pressure. The expected tumour site projected on the skin was marked using a permanent marker and covered with a waterproof dressing to avoid accidental erasure (Figure 2).

Before prepping and draping the patient, dressing was removed and mark was freshened. Incision was planned according to tumour site and skin flaps were raised going beyond target lesion as marked on skin surface. Once the flaps raised, wide local excision was performed considering the estimated depth and size assessed by ultrasound and a 2-view mammogram.

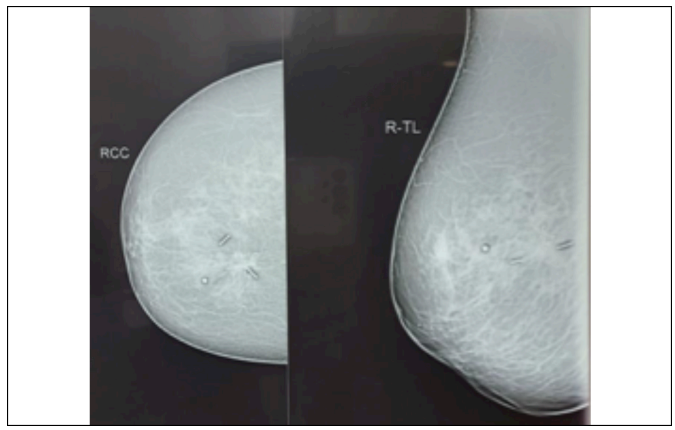

Figure 1: 2-view mammogram craniocaudal and true lateral with clips in lesion.

Figure 2: Lesion marked with permanent marker under ultrasound. guidance.

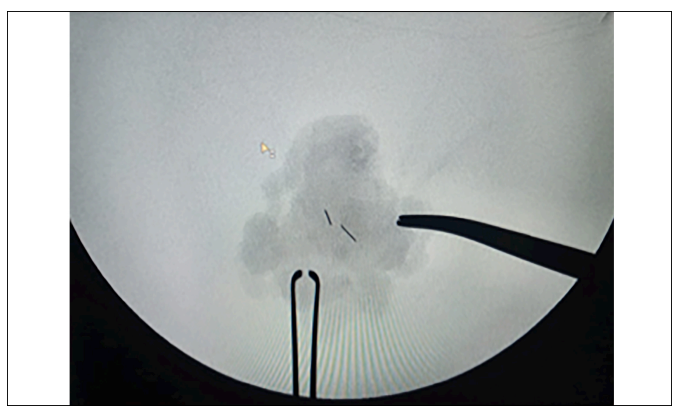

Figure 3: Clips with adequate margins confirmed in excised specimen image, under the image intensifier.

In a few cases, a lesion that was initially impalpable became palpable after raising the skin flap, making dissection easier, however, in most cases the excision had to be completed by re-evaluating the marked site on skin surface. After complete excision, the specimen was marked with instruments and placed under a C-arm image intensifier to check for the presence of clips in the resected specimen and its distance from the nearest margin (Figure 3).

If close margins were detected, further margins on the concerned site were cleared out per-operatively. In 3 patients, neither residual tumours nor the clips were identified under ultrasound so a C-arm image intensifier was used on the patient to mark the clipped area before prepping and draping the patient.

All the patients were seen after 2 weeks of operation with their histopathology report and then referred to an oncologist for radiation therapy. All the patients with hormone positive disease were given endocrine therapy. The patients were advised to have a monthly self-exam and follow-up at 6 months for the first five years and then annually for the next five years. Bilateral mammogram and ultrasound breast were advised annually. All the patients had access to the breast clinic outpatient department at Ittefaq Hospital for any concerns regarding locoregional recurrence, symptoms, or treatment-related side effects.

The primary outcome measure was to assess effectiveness by successfully identifying and removing the index lesion (residual tumour / fibrosis / clips), based on the margins status mentioned in the final histopathology report. Negative margins were defined as no tumour on the inked margin.[19] Secondary outcomes were re-excision rate and recurrence within two years.

Microsoft Excel 2010 was used to analyse the data. Categorical data were analysed for frequency and percentage.

RESULTS

A total of 144 patients were included in the study. Identification and removal of index lesion / clip was possible in all the cases. Only one (0.69%) patient had tumour margins (deep) involved by DCIS (ductal carcinoma-*in situ*).

In 3 (2.08%) cases, lesions were not picked on ultrasound, and a C-arm intensifier was used on patients. A close margin (tumour within 1mm of nearest margin) was found in 4 (2.77%) patients.

Additional margins peroperatively were taken (when the clipped lesion seen under the image intensifier was close to any specific margin) in 3 (2.08%) patients only.

Clinicopathological features were recorded. The mean age of the cohort was 46 (19 – 72) years.

Infiltrating ductal carcinoma (IDC) was the most commonly found type, present in 122 (84.72%) cases, 18 (12.5%) patients had both IDC and DCIU, one patient had IDC with metaplastic features, one had IDC with metaplastic features and DCIS, one had invasive lobular carcinoma, and one had metaplastic carcinoma.

Luminal type cancers were found in 99 (68.75%) patients, 35 (24.3%) were triple negative, and 10 (6.9%) patients had HER 2 enriched cancers.

Tumour size at presentation was recorded using ultrasound and classified as T1 (tumour size less than or equal to 2cm), T2 (tumour size greater than 2cm but less than 5cm) and T3 (tumour size greater than 5cm). One hundred and twenty (83%) cases were categorised as T2, 14 (10%) T3, and 10 (7%) T1.

Tumour size after completion of chemotherapy was assessed on resected specimen's histopathology. T0 (no evidence of primary tumour), T1a (tumour size greater than 0.1 cm but not more than 0.5 cm), T1b (tumour size greater than 0.5 cm but not more than 1 cm), T1c (tumour size greater than 1 cm but not more than 2 cm), T2 (tumour size greater than 2 cm but less than 5 cm). Complete pathological response (T0) was seen in 69 (48%) patients.

Pathological staging of nodes showed N0 (no regional lymph node metastasis) in 116 (80%) patients, N1 (1-3 axillary lymph nodes metastasis) in 20 (14%), N2 (4-9 axillary lymph nodes metastasis) in 7 (5%), and N3 (>10 axillary lymph nodes metastasis) in only 1 patient.

Among 144 patients operated between October 2011 and February 2023, 84 patients completed 2 years of follow-up and local recurrence was found in only 1 (1.19%) patient. This patient had IDC with metaplastic features, high-grade DCIS, and TNBC (triple negative breast cancer). Initially, BCS with axillary lymph node dissection (ALND) was done in June 2016 followed by radiation. A complete pathological response was seen with 0/12 lymph nodes (ypT0N0). Local recurrence occurred in July 2017 for which completion mastectomy was done. The patients remained disease-free since then and were on routine follow-up. Among the 144 patients, six patients succumbed to metastatic disease.

DISCUSSION

Accuracy in localising the exact tumour site is mandatory for success in breast conservation. The selection of technique to be chosen largely depends upon the surgeon's preference, availability of specific equipment, the radiologist, and the surgeon's experience and skill directing toward the removal of the target lesion.[20]

This study describes a new technique to localise impalpable breast lesions and their accurate removal with readily available material taking into account minimal patient discomfort and reduced financial burdens. All the operative techniques described earlier are either costly or are not available in many centres in developing countries such as Pakistan, rendering a

greater trend towards mastectomy in patients who would have been good candidates for breast conservation. By using this technique, the authors were able to localise and remove targeted lesions / clips in all the patients and achieved negative margins in 99.3% of cases. In literature, clear margins rate with wire-guided localisation has been reported around 70.8 to 87.4%[21] and the failure rate of wire-guided technique is about 0.6%, achieving an identification rate of 99.4%[22] that is comparable with the present results.

With this technique, the authors suggest variable advantages over wire-guided localisation. Unlike wire-guided localisation, preoperative ultrasound marking can be planned 1-3 days before surgery. It is easy, non-invasive, has scheduling flexibility, and grants surgeons complete freedom in incision planning.[23]

When combined with a 2-view mammogram (true lateral and craniocaudal) it gives a precise assessment of targeted lesion depth. In the operating room, the excised specimen is placed under an image intensifier to confirm the position of the clips and their proximity to the excised specimen. Most of the lesions or clips were identified preoperatively on ultrasound, in only 3 (2.08%) cases, lesions were not picked on ultrasound and a C-arm intensifier was used on patients. An image intensifier also known as C-arm machine is a portable x-ray machine that is available in the majority of operating theatres. C-arms are routinely used for intraoperative imaging during orthopaedic and urological procedures but the use of image intensifier in breast surgery has not been documented before. By the use of fluoroscopy, the risk of occupational exposure to healthcare personnel is mainly from scatter radiation emitted by the patient, rather than from the primary beam itself. To minimise this risk, the triad of time, distance, and shielding should be considered.[24] To confirm clip in the excised specimen, image intensifier is used outside the operating room by an OT technician who wears lead apron and only single beam is used to take the image. Further to reduce radiation exposure, it is recommended to maintain a 2-meter distance from C-arm, as the intensity of radiation has an inverse relation to the distance from the C-arm.[25] In a few cases, image intensifier is used on the patient and beam is used for two or three times ensuring minimum fluoroscopy time to capture the image for localisation of clips.

The combined use of preoperative ultrasound, a 2-view mammogram, and image intensifier in the operating room, gives favourable results regarding clear margins and patient safety in a resource-limited setup with a quick learning curve.

CONCLUSION

This technique is highly valuable in centres with minimum resources and in settings that lack expertise for wire-guided localisation. It does not need any new equipment and has a quick learning curve. With acceptable margin positivity, it provides an effective option for surgeons to perform breast conservation surgery.

ETHICAL APPROVAL:
Ethical approval was obtained from the Ethical Committee of the Ittefaq Hospital (Trust), Lahore (Approval No.: IHT/Adm/30).

PATIENTS' CONSENT:
Informed consent was taken from all the patients to publish the data concerning this study.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
AM, HMK: Conception and design of work, analysis and interpretation and critical revision of the manuscript for the important intellectual content.
ET: Design of work.
AW: Critical revision of the manuscript.
RI, HA: Drafting of work.
All authors approved the final version of the manuscript to be published.

REFERENCES

1. Lukasiewicz S, Czeczelewski M, Forma A, Baj J, Sitarz R, Stanislawek A. Breast cancer-epidemiology, risk factors, classification, prognostic markers, and current treatment strategies- An updated review. *Cancers (Basel)* 2021; **13(17)**:4287. doi: 10.3390/cancers13174287.
2. Khan NH, Duan SF, Wu DD, Ji XY. Better reporting and awareness campaigns needed for breast cancer in Pakistani women. *Cancer Manag Res* 2021; **13**:2125-9. doi: 10.2147/CMAR.S270671.
3. Rubio IT, Sobrido C. Neoadjuvant approach in patients with early breast cancer: Patient assessment, staging, and planning. *Breast* 2022 **62(Suppl 1)**:S17-24. doi: 10.1016/j.breast.2021.12.019.
4. Corradini S, Reitz D, Pazos M, Schonecker S, Braun M, Harbeck N, *et al.* Mastectomy or breast-conserving therapy for early breast cancer in real-life clinical practice: Outcome comparison of 7565 cases. *Cancers (Basel)* 2019; **11(2)**:160. doi: 10.3390/cancers11020160.
5. Fajdic J, Djurovic D, Gotovac N, Hrgovic Z. Criteria and procedures for breast conserving surgery. *Acta Inform Med* 2013; **21(1)**:16-9. doi: 10.5455/AIM.2013.21.16-19.
6. Shalaby LASED, Khallaf ESED. Moussa MM. Clip and wire localization of locally advanced malignant breast masses in patients undergoing neoadjuvant chemotherapy and breast conservation therapy. *Egypt J Radiol Nucl Med* 2019; **50**:96. doi: 10.1186/s43055-019-0066-z.
7. Sascha MD, Richard JG, Mohammed K. Strategies for localisation of impalpable breast lesions. *The Breast* 2011; **20(3**):246-53. doi: 10.1016/j.breast.2011.01.007
8. Moreira IC, Ventura SR, Ramos I, Fougo JL, Rodrigues PP. Preoperative localisation techniques in breast conservative surgery: A systematic review and meta-analysis. *Surg Oncol* 2020; **35**:351–3. doi: 10.1016/j.suronc.2020.09.004.
9. Franceschini G, Mason EJ, Grippo C, D'Archi S, D'Angelo A, Scardina L, *et al.* Image-guided localization techniques for

surgical excision of non-palpable breast lesions: An overview of current literature and our experience with preoperative skin tattoo. *J Pers Med* 2021; **11(2)**:99. doi: 10.3390/jpm11020099.

10. Dave RV, Barrett E, Morgan J, Chandarana M, Elgammal S, Barnes N, *et al.* Wire- and magnetic-seed-guided localization of impalpable breast lesions: iBRA-NET localisation study. *Br J Surg* 2022; **109(3)**:274-82. doi: 10.1093/bjs/znab443.
11. Haloua MH, Volders JH, Krekel NMA, Lopes Cardozo AMF, de Roos WK, de Widt-Levert LM, *et al.* Intraoperative ultrasound guidance in breast-conserving surgery improves cosmetic outcomes and patient satisfaction: Results of a multicenter randomized controlled trial (COBALT). *Ann Surg Oncol* 2016; **23**:30-7. doi: 10.1245/ s10434-015-4906-4.
12. Khare S, Singh T, Santosh I, Laroiya I, Singh G. Wire- and ultrasound-guided localisation: A novel technique for excision of nonpalpable breast tumours. *Breast Cancer (Auckl)* 2020; **14**:1178223420938068. doi: 10.1177/ 1178223420938068.
13. Samreen UK, Syed AD, Zoona F, Sohaib A, Huma MK, Mohammad Z, *et al.* Outcome of wire localized lumpectomies for nonpalpable breast lesion following neoadjuvant chemotherapy. *J Clin Oncol* 2014; **32(26)**:96.
14. Masroor I, Afzal S, Shafqat G, Rehman H. Usefulness of hook wire localization biopsy under imaging guidance for nonpalpable breast lesions detected radiologically. *Int J Womens Health* 2012; **4**:445-9. doi: 10.2147/IJWH.S35280.
15. Anila R, Omema S, Ayesha W, Taqi P, Amjad S, Shirin J. Accuracy of ultrasound guided wire localization of the residual breast cancer lesion for breast conservation surgery: Experience at a tertiary care hospital in Pakistan. *Rawal Medical Journal* 2022; **47(2)**:358-61.
16. Shaista K, Midhat S, Naheed M, Farhana K. Needle Localization of Non Palpable Breast Lesions. *J Pak Med Assoc* 1996; **46(7)**:149-52.
17. Cheang E, Ha R, Thornton CM, Mango VL. Innovations in image-guided preoperative breast lesion localization. *Br J Radiol* 2018; **91(1085)**:20170740. doi: 10.1259/bjr.20170740.
18. Nanthesh K, Pasupathy K, Debasish D. Use of wire-guided and radio-guided occult lesion localization for non-palpable breast lesions: A systematic literature review and meta-analysis of current evidence. *Asian J Surg* 2022; **45(1)**: 79-88. doi: 10.1016/j.asjsur.2021.06.055.
19. Moran MS, Schnitt SJ, Giuliano AE, Harris JR, Khan SA, Horton j, *et al.* Society of Surgical Oncology/American Society for Radiation Oncology consensus guideline on margins for breast conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. *Int J Radiat Oncol Biol Phys* 2014; **88**:553-64. doi: 10.1200/ JCO.2013.53.3935.
20. Garzotto F, Comeretto IR, Michieletto S, Franzoso G, Mele ML, Gregori D, *et al.* Preoperative non-palpable breast lesion localization, innovative techniques and clinical outcomes in surgical practice: A systematic review and meta-analysis. *The Breast* 2021; **58**:93-105. doi:10.1016/j.breast.2021.04.007
21. Hayes MK. Update on preoperative breast localization. *Radiol Clin North Am* 2017; **55**:591-603. doi: 10.1016/j.rcl.2016.12.012.
22. Chan BK, Wiseberg-Firtell JA, Jois RH, Jensen K, Audisio RA. Localization techniques for guided surgical excision of nonpalpable breast lesions. *Cochrane Database Syst Rev* 2015; **2015(12)**:CD009206. doi: 10.1002/14651858.CD009206.
23. Carlino G, Rinaldi P, Giuliani M, Rella R, Bufi E, Padovano F, *et al.* Ultrasound-guided preoperative localization of breast lesions: A good choice. *J Ultrasound* 2019; **22(1)**:85-94. doi: 10.1007/s40477-018-0335-0.
24. Lakhwani OP, Dalal V, Jindal M, Nagala A. Radiation protection and standardization. *J Clin Orthop Trauma* 2019; **10(4)**:738-43. doi: 10.1016/j.jcot.2018.08.010.
25. Mahajan A, Samuel S, Saran AK, Mahajan MK, Mam MK. Occupational radiation exposure from C-arm fluoroscopy during common orthopedic surgical procedures and its prevention. *J Clin Diagn Res* 2015; **9(3)**:RC01-4. doi: 10.7860/JCDR/2015/10520.5672.