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OMISSION OF INTRAOPERATIVE FROZEN SECTION OF SENTINEL LYMPH NODES IN EARLY BREAST CANCER: A SAFE APPROACH GUIDED BY PREOPERATIVE AXILLARY ULTRASOUND

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Abstract

Background: *Axillary staging guides treatment in early breast cancer. In low-risk patients, routine intraoperative frozen section may be unnecessary, and preoperative axillary ultrasound could help identify those who can safely avoid it.*
Objective: *To evaluate whether axillary ultrasound findings, particularly cortical thickness and nodal morphology, predict sentinel lymph node metastasis and support selective omission of intraoperative frozen section.*
Methods: *This prospective pilot feasibility study included 26 patients with early-stage breast cancer from August 2025 to January 2026. Preoperative axillary ultrasound assessed cortical thickness and nodal morphology. Nodes with cortical thickness ≥0.3 cm underwent ultrasound-guided core biopsy; those <0.3 cm were considered benign. All patients underwent SLNB with intraoperative FS. Associations between clinicopathologic variables and FS positivity were analyzed using Fisher's exact test. Diagnostic performance of cortical thickness was calculated.*
Results: *Sentinel lymph node metastasis was detected in 3 patients (11.5%). Loss of fatty hilum on AUS was significantly associated with FS positivity (p = 0.009), whereas cortical thickness alone was not. Cortical thickness ≥0.3 cm showed 66.7% sensitivity, 69.6% specificity, 22.2% positive predictive value, and 94.1% negative predictive value. Most tumors were invasive ductal carcinoma and hormone receptor positive.*
Conclusion: *Preoperative axillary ultrasound of nodal morphology may help identify early breast cancer patients at minimal risk of sentinel lymph node metastasis. A cortical thickness <0.3 cm demonstrated a high negative predictive value in this pilot study. These findings suggest that selective omission of intraoperative frozen section may be feasible in carefully selected patients; however, larger studies are required to confirm these observations.*

INTRODUCTION

Sentinel lymph node biopsy (SLNB) has become the standard method for axillary staging in patients with early breast cancer and clinically negative axillae, replacing routine axillary lymph node dissection (ALND) in most cases.[1,2] This shift has significantly reduced morbidity, including lymphedema, pain, and shoulder dysfunction, while providing accurate staging information to guide adjuvant treatment decisions.[3,5]

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Traditionally, intraoperative frozen section (FS) analysis of sentinel lymph nodes has been used to identify metastasis during the primary surgery so that completion ALND can be performed immediately if required, thereby avoiding a second operation.[6]

However, the role of intraoperative FS has been increasingly questioned. Several studies have reported a relatively low rate of SLN positivity in early-stage, clinically node-negative breast cancer, particularly in patients with favorable tumor biology.[7,8] Furthermore, landmark trials such as ACOSOG Z0011 have demonstrated that omission of ALND in selected patients with limited SLN involvement does not compromise oncological outcomes when appropriate systemic therapy and radiotherapy are administered.[9]As a result, the clinical value of routine intraoperative FS has diminished in many scenarios, while its drawbacks including increased operative time, cost, and the risk of tissue loss or interpretive errors remain.[10]

In parallel, advances in breast imaging have improved preoperative assessment of axillary lymph nodes. High-resolution axillary ultrasound, combined with morphological criteria such as cortical thickness, shape, and presence or absence of fatty hilum, has shown reasonable performance in predicting nodal metastasis. A thin cortex and preserved fatty hilum are strongly associated with benign nodes, whereas cortical thickening and loss of hilum raise suspicion of metastatic involvement.[11] Incorporating these ultrasound features into preoperative evaluation may allow clinicians to better stratify patients according to their risk of nodal disease.

These developments raise an important question: in patients with early breast cancer and normal or low-risk axillary findings on preoperative ultrasound, is intraoperative FS of sentinel lymph nodes still necessary? If preoperative axillary ultrasound can reliably exclude significant nodal metastasis, selective omission of FS may be a safe and efficient strategy, reducing operative time, workload on pathology services, and healthcare costs without compromising oncological safety.

The present prospective study was designed to evaluate whether omission of intraoperative FS could be safely considered in early breast cancer patients with negative or low-risk axillary findings on preoperative ultrasound. Specifically, we assessed the diagnostic performance of ultrasound cortical thickness and nodal morphology in predicting sentinel lymph node metastasis and explored their potential role in guiding a more selective use of intraoperative FS.

MATERIALS AND METHODS

A prospective pilot feasibility study was performed in Surgical Unit I, Dow University Hospital, Ojha Campus, Dow University of Health Sciences, Karachi, from August 2025 to January 2026. The study adhered to institutional ethical standards; ethical approval was obtained from the Institutional Review Board of Dow University Hospital (Ref: IRB-3956/DUHS/Approval/2025/313).

A total of 26 consecutive female patients aged ≥18 years with biopsy-proven early breast cancer (T1–T2, clinically N0) were enrolled during the study period. Patients who had received neoadjuvant chemotherapy, had prior axillary surgery or radiotherapy, had recurrent or metastatic disease, or had a positive preoperative axillary core biopsy were excluded.

All patients underwent preoperative axillary ultrasound using a high-resolution linear transducer (7–12 MHz). Examinations were performed by consultant radiologists in the women imaging department, each with more than five years of experience in breast imaging. The radiologists were not informed about the research objectives and performed ultrasound as part of routine clinical care. The most representative lymph node was evaluated for short-axis diameter, cortical thickness (measured at its thickest point), and nodal morphology including hilum status. The study investigators extracted ultrasound findings from documented radiology reports.

Lymph nodes with cortical thickness <0.3 cm were considered benign and were not biopsied. Nodes with cortical thickness ≥0.3 cm underwent ultrasound-guided 14-gauge core needle biopsy by the Radiologist expert in women imaging at Dow Radiology Department, DUHS. Only patients with negative biopsy results were included.

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All patients underwent sentinel lymph node biopsy using the standard dual-tracer technique. Excised sentinel nodes were subjected to intraoperative frozen section analysis. Axillary lymph node clearance was performed if frozen section was positive; otherwise, axillary dissection was omitted. Final paraffin-embedded histopathology of the sentinel and any additional axillary lymph nodes was reviewed for confirmation of nodal status.

Final histopathological assessment was performed according to standard institutional protocols. Pathologists were blinded to the specific aims of the study and reported findings as part of routine diagnostic practice.

Data were analyzed to assess the association between clinicopathological and ultrasound variables and sentinel lymph node frozen section positivity. Because of small, expected cell counts, Fisher's exact test was used to evaluate associations between categorical variables and frozen section results.

Diagnostic performance of ultrasound cortical thickness ≥0.3 cm for predicting sentinel lymph node metastasis was calculated in terms of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy. A p-value <0.05 was considered statistically significant.

Sample size was calculated using Open Epi Version 3 for estimation of a population proportion. Based on a hypothesized frequency of tumor-free sentinel lymph nodes of 91.5% in early-stage clinically node-negative breast cancer, with 95% confidence level and 5% margin of error, the required sample size was calculated to be 120 patients. However, during the study period (August 2025 to January 2026), the number of patients presenting with early-stage (T1–T2, N0) breast cancer who met the inclusion criteria was limited. Therefore, 26 consecutive eligible patients were enrolled. This study should therefore be considered a prospective pilot feasibility study intended to generate preliminary data and guide future adequately powered multicenter research.

RESULTS

Twenty-six patients with early-stage (T1–T2, clinically node-negative) breast cancer were included. Baseline clinicopathological characteristics are summarized in Table 1. Most tumors were invasive ductal carcinoma and hormone receptor positive and HER2 negative.

Preoperative axillary ultrasound findings are presented in Table 2. Most patients had benign-appearing lymph nodes on ultrasound, while a small proportion demonstrated suspicious morphology characterized by loss of fatty hilum. Cortical thickness ≥0.3 cm was observed in approximately one-third of patients, all of whom underwent ultrasound-guided core biopsy, and only those with negative biopsy results were included in the study.

Sentinel lymph node frozen section revealed metastatic involvement in 3 patients (11.5%), whereas the remaining patients had tumor-free nodes.

No statistically significant associations were found between frozen section positivity and tumor site, histological type, tumor grade, receptor status, Ki-67 index, TNM stage, lymph node size, cortical thickness, or type of breast surgery performed (Table 2).

However, suspicious nodal morphology on ultrasound, particularly loss of fatty hilum, was significantly associated with sentinel lymph node metastasis ($p = 0.009$).

The diagnostic performance of cortical thickness ≥0.3 cm for predicting sentinel lymph node metastasis is shown in Table 3. While sensitivity and specificity were moderate, the negative predictive value was high (94.1%), indicating that cortical thickness <0.3 cm reliably excluded nodal metastasis in most patients.

DISCUSSION

This prospective pilot feasibility study evaluated the predictive value of preoperative axillary ultrasound, specifically cortical thickness, and nodal morphology, for sentinel lymph node (SLN) metastasis in early breast cancer and explored whether these parameters could support selective omission of intraoperative frozen section (FS). Among 26 women with T1–T2 clinically node-

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negative disease, SLN metastasis was detected in 11.5% of cases, while 88.5% had tumor-free nodes. This low nodal positivity rate is consistent with previously reported outcomes in carefully selected early-stage populations.[1-8]

Ultrasound assessment focused on cortical thickness and hilum status. Using a cortical thickness threshold of ≥0.3 cm, sensitivity was 66.7% and specificity 69.6%, with a notably high negative predictive value (NPV) of 94.1%. Although the positive predictive value (PPV) was modest (22.2%), the high NPV indicates that cortical thickness <0.3 cm was reliable in excluding SLN metastasis in most patients within this study. These findings align with earlier studies demonstrating that thin cortex and preserved fatty hilum are typical of benign nodes, whereas cortical thickening increases the likelihood of metastatic involvement.[11]

Importantly, suspicious nodal morphology, particularly loss of fatty hilum, showed a statistically significant association with SLN positivity ($p = 0.009$). Patients with absent hilum had a higher rate of metastasis compared to those with preserved hilum. This supports evidence that morphological features, including hilum status and nodal shape, enhance diagnostic accuracy beyond size criteria alone. [2,12] Together, cortical thickness and hilum assessment provide practical and reproducible indicators of axillary risk.

In contrast, traditional clinicopathological variables such as tumor site, histological type, grade, receptor profile, Ki-67 index, and TNM stage were not significantly associated with FS positivity in this study. Within clinically node-negative early-stage disease, ultrasound morphology therefore emerged as a more immediate indicator of nodal status than tumor biology parameters, although the small sample size limits definitive conclusions and reduces statistical power.

The clinical relevance of these findings lies in the evolving role of intraoperative FS. Historically, FS enabled immediate axillary lymph node dissection (ALND), thereby avoiding a second surgery.[6] However, recent studies and updated recommendations suggest that many patients with limited nodal involvement can safely avoid further axillary surgery (ALND).[9] As surgeons increasingly aim to avoid unnecessary procedures when appropriate, routine intraoperative frozen section (FS) is no longer required in many cases. Frozen section may lengthen the operation, add to hospital costs, and sometimes affect tissue quality, which can make the final histopathological examination more challenging.[10]

In our study, patients with cortical thickness <0.3 cm and preserved hilum had a very low rate of SLN metastasis. While the limited sample size prevents firm conclusions, these findings suggest that omission of intraoperative FS may be reasonable in carefully selected low-risk patients. Final paraffin section remains available for confirmation. Given that many patients with limited nodal disease no longer require ALND, the clinical impact of occasional false negatives in this low-risk group may be limited when multidisciplinary treatment is appropriately delivered.[9]

Conversely, patients with suspicious ultrasound features, particularly hilum loss and/or significant cortical thickening, represent a higher-risk subgroup. In such cases, intraoperative FS may still influence immediate surgical decisions, or preoperative image-guided biopsy can clarify nodal status prior to definitive surgery.[11] In practical terms, ultrasound can guide the next step: patients with benign-appearing nodes may proceed to SLNB without frozen section, whereas those with suspicious findings may require closer evaluation.

Previous literature reports variable sensitivity and specificity for axillary ultrasound depending on criteria and patient selection.[2,12] When morphological features are combined with size thresholds, sensitivities of 60–80% and specificities above 70% have been described, often with particularly high NPVs in clinically node-negative populations.[11] In our study, sensitivity of 66.7% and specificity of 69.6% using a 0.3 cm cortical cutoff are consistent with these ranges. This reinforces that ultrasound appears more useful for ruling out nodal disease than for definitively confirming metastasis in early-stage breast cancer.

The low SLN positivity rate observed in this series mirrors contemporary experiences in early breast

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cancer management, where advances in systemic therapy and radiotherapy allow many patients with limited nodal disease to avoid ALND safely.[7-9] In this setting, routine intraoperative FS has been increasingly questioned, and selective omission has been explored without compromising oncological outcomes.[10] Our findings suggest that straightforward ultrasound features, including cortical thickness and hilum status, may help identify patients who are less likely to benefit from intraoperative frozen section.

Strengths of this study include its prospective design and standardized ultrasound evaluation using predefined cortical and morphological criteria. SLNB and FS were performed uniformly, and final histopathology served as the reference standard. Nonetheless, limitations must be acknowledged. The small sample size restricts statistical precision and may obscure associations with clinicopathological factors. Additionally, this single-center experience may not be generalizable to institutions with different patient demographics, tumor characteristics, or imaging expertise.

Although the number of patients with loss of hilum was small, the association observed suggests that nodal morphology remains an important indicator of metastatic risk. Overall, this study provides preliminary evidence supporting ultrasound based selection for frozen section omissions. However, the findings should be interpreted cautiously and considered hypothesis-generating. Larger, multicenter studies are necessary to validate these observations and to establish clear, standardized ultrasound-based criteria for guiding more conservative axillary management strategies.

CONCLUSION

Preoperative axillary ultrasound, particularly nodal morphology and cortical thickness assessment, may help identify early breast cancer patients at low risk of sentinel lymph node metastasis. A cortical thickness <0.3 cm demonstrated high negative predictive value in this pilot study. Selective omission of intraoperative frozen sections may be feasible in carefully selected patients; however, larger studies are required for validation.

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