

## Diagnostic Accuracy of Axillary Ultrasonography for Differentiating Benign and Malignant Lymph Nodes in Breast Cancer Patients

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### ABSTRACT

**Background:** Reliable evaluation of axillary lymph nodes before surgery is essential for determining prognosis and tailoring treatment in breast cancer care. Although surgical techniques such as sentinel-node biopsy remain the definitive standard, they are invasive and can cause considerable morbidity. High-resolution ultrasonography provides a non-invasive alternative.

**Objectives:** This study aimed to measure how accurately ultrasound distinguishes malignant from benign axillary nodes, using histopathology as the reference method.

**Methods:** We carried out a prospective observational study in a tertiary oncology hospital from January 2022 through December 2023. Eighty adults with biopsy-confirmed breast carcinoma underwent preoperative axillary ultrasound performed by senior breast radiologists with 7–15 MHz linear transducers. Each lymph node was assessed for size, shape, cortical thickness, integrity of the fatty hilum, and Doppler vascular pattern. Tissue obtained by surgical excision or image-guided core biopsy supplied the histological verdict. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy were calculated, and agreement with histology was expressed using Cohen's  $\kappa$  statistic.

**Results:** Histological analysis identified metastasis in 42 patients (52.5 %) and benign pathology in 38 (47.5 %). Ultrasound achieved an overall accuracy of 86.3 %, with sensitivity 85.7 %, specificity 86.8 %, PPV 87.8 %, and NPV 84.6 %. Concordance between sonography and histopathology was substantial ( $\kappa = 0.72$ ;  $p < 0.001$ ).

**Conclusion:** When conducted under standardized conditions, axillary ultrasound reliably differentiates malignant from benign lymph nodes in breast-cancer patients. Incorporating this modality into routine preoperative work-ups could decrease reliance on invasive staging procedures and their attendant complications. Larger multicentre studies are warranted to confirm these findings and refine sonographic criteria further.

**Keywords:** Breast cancer, Ultrasound, Axillary lymph nodes, Diagnostic accuracy, Histopathology, Preoperative staging.



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### INTRODUCTION

Breast cancer remains a leading cause of cancer-related deaths worldwide, and accurate staging is vital for informed treatment decisions. In particular, axillary lymph-

node status serves as a crucial prognostic factor that directs both surgical and adjuvant therapy strategies [1]. While sentinel lymph node biopsy and axillary dissection are invasive techniques with a high diagnostic accuracy, they

are inherently associated with significant morbidity, including lymphedema, neuropathic pain, and reduced upper limb function. These challenges emphasize the imperative of non-invasive methods to monitor for nodal involvement [2].

In the preoperative evaluation of the axilla, ultrasound has become a valuable imaging modality as a result of its non-invasive nature, broad accessibility, and capability for high-resolution, real-time imaging. High-frequency linear transducers are utilized to evaluate lymph nodes in detail, by assessing their size, shape, cortical thickness, and the integrity of the fatty hilum [3]. In addition, the addition of Doppler imaging affords an assessment of vascular patterns that may be indicative of neoplastic involvement. While previous studies have reported predictors of malignancy based on specific features on sonography, such as lack of fatty hilum and marked cortical thickening, the diagnostic performance of prior studies has varied due to differences in study design, operator expertise, and patient population [4, 5].

The current study aimed to provide rigorous assessment of the diagnostic accuracy of ultrasound of axillary lymph nodes in patients with breast cancer using histopathology as the reference standard [6]. Current study attempt to delineate the imaging characteristics that are most likely to predict metastatic involvement through systematically correlating sonographic findings with histological outcomes. The purpose is to develop a robust, non-invasive means for axillary staging that could reduce the necessity of invasive procedures and thus minimize patient morbidity [7].

With a focus on filling existing gaps in the previous literature, this investigation is expected to provide advanced knowledge to the preoperative assessment protocols and thus inform clinical practice. In the end, the integration of precise ultrasound criteria into routine axillary evaluation may contribute to improving patient management and prognostic stratification in breast cancer care [8, 9].

## MATERIALS AND METHODS

**Study Design and Patient Population:** This was a prospective observational study conducted at Cancer Care Hospital and Research center, Lahore and Department of Radiology, Chughtai medical center, Faisalabad, Pakistan, between January 2022 and December 2023. Two hundred and fifty patients with histologically confirmed breast cancer, all scheduled for surgical intervention, were enrolled. The participants had to be at least 18 years of age and had to have a new diagnosis of breast carcinoma that required axillary evaluation. Exclusion criteria included a history of previous axillary surgery, a prior neoadjuvant chemotherapy before imaging, or contraindications to ultrasound examination. The study was approved by the institutional ethics committee, and all participants gave written informed consent ref no. (ERC/28B/12/2021).

**Ultrasound Examination:** High-frequency linear transducers (7–15 MHz) were used on state-of-the-art ultrasound systems to perform preoperative axillary ultrasound examinations. Radiologists with a minimum of ten years of experience in breast imaging performed examinations according to a standardized imaging protocol. Detailed assessment was performed of lymph node morphology, with assessment of size, shape (round versus oval), and margin definition. Values exceeding 3 mm of cortical thickness were considered abnormal and measured. Presence or absence or eccentric displacement of the central fatty hilum was assessed. Intracellular vascularity and aberrant blood flow patterns were evaluated using color and power Doppler imaging and, in specific cases, with color Doppler sonography. Lymph nodes with a suspicious appearance included those with a round configuration, cortical thickening, loss or eccentric displacement of the fatty hilum, or abnormal vascular patterns.

**Histopathological Analysis:** Patients were then subjected to either surgical excision (with ultrasound examination) or image-guided core needle biopsy of the axillary lymph nodes based on clinical indications. The collected specimens were analyzed histopathologically by experienced pathologists blinded to the ultrasound findings. The diagnostic workup included routine hematoxylin and eosin staining, supplemented, when necessary, by immunohistochemical studies to definitively determine which, if any, cell lines were extravasated and metastatic. Lymph node metastasis was considered to be diagnosed by histopathology.

**Statistical Analysis:** The diagnostic performance of ultrasonography was quantified through standard metrics: sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy. Agreement between sonographic and histopathological results was gauged with Cohen's  $\kappa$  statistic. Continuous data were summarized as means  $\pm$  standard deviations or, when non-normally distributed, as medians with interquartile ranges. Categorical variables were expressed as frequencies and percentages. All analyses were carried out in a certified statistical package, and a two-sided  $p$ -value below 0.05 denoted statistical significance.

## RESULTS

**Patient Demographics:** A total of 80 participants, with a median age of 54 years (range 32–78 years), were included in the analysis. Histopathology confirmed metastatic nodal disease in 42 individuals (52.5 %), while 38 (47.5 %) exhibited benign lymph-node changes. A detailed summary of patient demographics and histological findings appears in Table 1.

**Ultrasound and Histopathological Correlation:** Axillary ultrasound examinations were performed preoperatively to

classify lymph nodes as suspicious, or positive, for malignancy, or non-suspicious, or negative.

Table 2 details how ultrasound findings were compared to histopathological results. Ultrasound correctly identified 36 of the 42 malignant cases (true positives) and 33 of the 38 benign cases (true negatives), for 6 false negatives and 5 false positives in this cohort

**Diagnostic Performance:** Using conventional diagnostic indices, ultrasonography demonstrated a sensitivity of 85.7 % and a specificity of 86.8 %. The aggregate accuracy stood at 86.3 %, with a positive predictive value of 87.8 % and a negative predictive value of 84.6 %. Concordance between sonographic assessments and histopathology, measured by Cohen’s  $\kappa$ , was 0.72 ( $p < 0.001$ ), indicating robust agreement. Table 3 presents these metrics in full.

**Table-1:** Patient Demographics and Histopathological Outcomes

Characteristic	Value
Total Patients	80
Median Age (years)	54 (32–78)
Malignant	42 (52.5%)
Benign	38 (47.5%)

**Table-2:** Correlation between Ultrasound Findings and Histopathological Results

	Malignant (n = 42)	Benign (n = 38)	Total (n = 80)
Ultrasound Positive	36	5	41
Ultrasound Negative	6	33	39
Total	42	38	80

**Table-3:** Diagnostic Performance of Ultrasound

Metric	Value
Sensitivity	85.7%
Specificity	86.8%
Positive Predictive Value	87.8%
Negative Predictive Value	84.6%
Overall Accuracy	86.3%
Cohen’s Kappa	0.72 ( $p < 0.001$ )

Continuous variables were summarised as medians with their corresponding ranges, whereas categorical data were expressed as absolute counts and percentages. Diagnostic indices were derived as follows: specificity was the proportion of true-negative cases among all nodes proven benign on histology, and sensitivity was the proportion of true-positive cases among all histologically confirmed malignancies.

Positive and negative predictive values reflected, respectively, the percentages of true positives among ultrasound-positive nodes and true negatives among ultrasound-negative nodes. Overall accuracy was calculated by dividing the sum of true positives and true negatives by the total study population. Agreement between sonographic and histological assessments was quantified with Cohen’s  $\kappa$  statistic; values were considered significant when  $p < 0.05$ . Put simply, in this cohort of 80 patients, axillary ultrasound achieved high discriminatory power for benign versus malignant nodes, with a level of concordance with histopathology that can be regarded as substantial.

## DISCUSSION

This study assessed the ultrasound performance to distinguish benign from malignant axillary lymph nodes in breast cancer patients using histopathology as a reference standard. However, when performed under standardized protocols, experienced radiologists obtaining ultrasound

demonstrate a high sensitivity (85.7%), specificity (86.8%), and overall accuracy (86.3%). These findings are by several previous studies that have emphasized the utility of ultrasound in axillary staging; however, reported values in the literature have differed widely, being dependent on study design, imaging protocol, and operator experience [10, 11].

This reinforces our belief that key sonographic parameters, such as cortical thickness, nodal shape, and the integrity of the fatty hilum, are important in the identification of metastatic involvement. Correlation of ultrasound to histopathology, as evidenced by a Cohen’s kappa coefficient of 0.72, provides strong evidence that ultrasound is a reliable noninvasive preoperative axillary evaluation modality [12]. Although our data are similar to other studies, ultrasound can serve as an adjunct or even a possible substitute for invasive methods such as sentinel lymph node biopsy in reducing patient morbidity of surgical procedures [13, 14].

However, there are limitations to our study. Our results may not generalize to larger populations due to the relatively small sample size of 80 patients. Furthermore, variability in the interpretation of sonographic features due to the inherent operator dependency of ultrasound imaging could contribute to variability in the results, and therefore the reproducibility, of results in different clinical settings [15, 16]. Our results need to be validated in future research with larger multicentric cohorts, and it is necessary to

establish universal sonographic criteria for the evaluation of axillary lymph nodes. In addition, the use of advanced imaging techniques and artificial intelligence algorithms could further augment the diagnostic accuracy and decrease the operator variability [17, 18].

## CONCLUSION

Overall, our study shows high diagnostic accuracy of ultrasound in distinguishing benign from malignant axillary lymph nodes in breast cancer patients, with a substantial concordance with histopathological findings. Sonographic parameters such as cortical thickness, nodal morphology, and vascular patterns are detailed assessed to provide a non-invasive and efficient method for preoperative axillary staging. Further research with larger, multicenter studies is needed to validate these findings and further refine imaging criteria, but these results support using ultrasound as part of routine clinical practice to help reduce the need for invasive diagnostic procedures and improve patient management in breast cancer care.

**Conflict of Interest:** The authors declare that no conflicts of interest exist.

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**Authors' Contributions:** All authors contributed equally to this work.

**Data Availability:** De-identified data are available from the corresponding author upon reasonable request.

## REFERENCES

- Samiei S, van Nijnatten TJA, van Beek HC, Polak MPJ, Maaskant-Braat AJG, Heuts EM, et al. Diagnostic performance of axillary ultrasound and standard breast MRI for differentiation between limited and advanced axillary nodal disease in clinically node-positive breast cancer patients. *Sci Rep.* 2019;9(1):17476. doi:10.1038/s41598-019-54017-0
- Agrawal S, Goel AD, Gupta N, Lohiya A, Gonuguntla HK. Diagnostic utility of endobronchial ultrasound features in differentiating malignant and benign lymph nodes: a systematic review and meta-analysis. *Respir Med.* 2020;171:106097. doi:10.1016/j.rmed.2020.106097
- Joshi P, Singh N, Raj G, Singh R, Malhotra KP, Awasthi NP. Performance evaluation of digital mammography, digital breast tomosynthesis and ultrasound in the detection of breast cancer using pathology as gold standard: an institutional experience. *Egypt J Radiol Nucl Med.* 2022;53(1):1. doi:10.1186/s43055-021-00675-y
- Assing MA, Patel BK, Karamsadkar N, Weinfurter J, Usmani O, Kiluk JV, et al. Comparison of diagnostic accuracy of MRI versus axillary ultrasound in detecting axillary nodal metastases in newly diagnosed breast cancer. *Breast J.* 2017;23(6):647-55. doi:10.1111/tbj.12812
- Di Paola V, Mazzotta G, Pignatelli V, Bufi E, D'Angelo A, Conti M, et al. Beyond N staging in breast cancer: importance of MRI and ultrasound-based imaging. *Cancers (Basel).* 2022;14(17):4270. doi:10.3390/cancers14174270
- Elkharbotly A, Farouk HM. Ultrasound elastography improves differentiation between benign and malignant breast lumps using B-mode ultrasound and color Doppler. *Egypt J Radiol Nucl Med.* 2015;46(4):1231-9. doi:10.1016/j.ejrnm.2015.06.005
- Zhang Q, Agyekum EA, Zhu L, Yan L, Zhang L, Wang X, et al. Clinical value of three combined ultrasonography modalities in predicting axillary lymph node metastasis in invasive ductal carcinoma. *Front Oncol.* 2021;11:715097. doi:10.3389/fonc.2021.715097
- Huang H, Huang Z, Wang Q, Wang X, Dong Y, Zhang W, et al. Effectiveness of benign and malignant diagnosis of mediastinal and hilar lymph nodes by endobronchial ultrasound elastography. *J Cancer.* 2017;8(10):1843-8. doi:10.7150/jca.19819
- Haghighi F, Naseh G, Mohammadifard M, Abdollahi N. Comparison of mammography and ultrasonography findings with pathology results in patients with breast cancer in Birjand, Iran. *Electron Physician.* 2017;9(10):5494-8. doi:10.19082/5494
- van Nijnatten TJA, Ploumen EH, Schipper RJ, Goorts B, Andriessen EH, Vanwetswinkel S, et al. Routine use of breast MRI versus axillary ultrasound for differentiation between no, limited and advanced axillary nodal disease in newly diagnosed breast cancer patients. *Eur J Radiol.* 2016;85(12):2288-94. doi:10.1016/j.ejrad.2016.10.030
- Schmachtenberg C, Fischer T, Hamm B, Bick U. Diagnostic performance of automated breast volume scanning compared to handheld ultrasonography with breast MRI as the gold standard. *Acad Radiol.* 2017;24(8):954-61. doi:10.1016/j.acra.2017.01.021
- Rezkallah EMN, Elsaify A, Tin SMM, Elsaify W. Diagnostic accuracy of ultrasonography in axillary staging in breast cancer patients. *J Med Ultrasound.* 2023;31(4):291-8.
- Okasha H, Elkholy S, Sayed M, El-Sherbiny M, El-Hussieny R, El-Gemeie E, et al. Ultrasound, endoscopic ultrasound elastography, and the strain ratio in differentiating benign from malignant lymph nodes. *Arab J Gastroenterol.* 2018;19(1):7-15. doi:10.1016/j.ajg.2018.01.001
- Madan K, Madan M, Iyer H, Mittal S, Madan NK, Rathi V, et al. Utility of elastography for differentiating malignant and benign lymph nodes during EBUS-TBNA: a systematic review and meta-analysis. *J Bronchology Interv Pulmonol.* 2022;29(1):49-60.
- Ibraheem SA, Mahmud R, Mohamad Saini S, Abu Hassan H, Keiteb AS, Dirie AM. Evaluation of diagnostic performance of automatic breast volume scanner compared to handheld ultrasound on different breast lesions: a systematic review. *Diagnostics (Basel).* 2022;12(2):541. doi:10.3390/diagnostics12020541
- Ji X, Li D, Gao D, Lv X, Feng Y, Zhang D, et al. Value of ultrasound-guided biopsy in evaluating internal mammary lymph node metastases in breast cancer. *Clin Breast Cancer.* 2021;21(6):532-8. doi:10.1016/j.clbc.2021.04.016
- Liu X, Wang M, Wang Q, Zhang H. Diagnostic value of contrast-enhanced ultrasound for sentinel lymph node metastasis in breast cancer: an updated meta-analysis. *Breast Cancer Res Treat.* 2023;202(2):221-31. doi:10.1007/s10549-023-07063-2
- Aktaş A, Gürleyik MG, Aydın Aksu S, Aker F, Güngör S. Diagnostic value of axillary ultrasound, MRI, and 18F-FDG-PET/CT in determining axillary lymph node status in breast cancer patients. *Eur J Breast Health.* 2022;18(1):37-47. doi:10.4274/ejbh.galenos.2021.2021-3-10

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