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Research Article

# Predictive Accuracy of a Radiomics Model for Prediction of Axillary Lymph Node Metastasis in Patients with Breast Cancer

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## ABSTRACT

**Background:** Axillary lymph node metastasis is an important prognostic factor in breast cancer and directly influences staging, treatment planning, and surgical decision-making. Radiomics may provide a non-invasive method for predicting nodal metastasis using quantitative imaging features.

**Objective:** To evaluate the predictive accuracy of a radiomics model for axillary lymph node metastasis in patients with histopathologically confirmed breast cancer.

**Methods:** This analytical cross-sectional study included 70 female patients with newly diagnosed breast cancer who underwent preoperative contrast-enhanced breast imaging followed by surgical axillary assessment. Axillary lymph node status was confirmed using final histopathology as the reference standard. Radiomic features were extracted from the primary breast tumor after image preprocessing and segmentation. Patients were divided into a training cohort of 50 and an internal testing cohort of 20. Clinical, radiomics-only, and combined clinical-radiomics models were developed. Model performance was assessed using area under the receiver operating characteristic curve, sensitivity, specificity, positive predictive value, negative predictive value, accuracy, calibration analysis, and decision-curve analysis.

**Results:** Axillary lymph node metastasis was present in 27 patients (38.6%), while 43 patients (61.4%) were node-negative. Patients with nodal metastasis had significantly larger tumors, higher frequency of tumor size >3 cm, grade III disease, lymphovascular invasion, and Ki-67 ≥20%. The radiomics score was significantly higher in node-positive patients than in node-negative patients (0.78 ± 0.69 vs. -0.42 ± 0.61; $p<0.001$). In the training cohort, the clinical, radiomics-only, and combined models achieved AUC values of 0.80, 0.88, and 0.93, respectively. In the internal testing cohort, the corresponding AUC values were 0.76, 0.82, and 0.89. The combined model showed the best diagnostic performance, with 87.5% sensitivity, 83.3% specificity, 85.0% accuracy, 77.8% positive predictive value, and 90.9% negative predictive value in the testing cohort. On multivariable logistic regression, lymphovascular invasion, tumor size >3 cm, and radiomics score were independent predictors of axillary lymph node metastasis.

**Conclusion:** The combined clinical-radiomics model showed good predictive accuracy for axillary lymph node metastasis in patients with breast cancer and performed better than clinical or radiomics-only models. This non-invasive approach may help improve preoperative nodal risk stratification and support individualized surgical planning.

**Keywords:** Breast Neoplasms, Lymphatic Metastasis, Axilla, Radiomics, Magnetic Resonance Imaging.

## INTRODUCTION

Breast cancer remains the most frequently diagnosed malignancy among women and continues to represent a major cause of cancer-related morbidity and mortality worldwide. According to recent global estimates, female breast cancer accounted for approximately 2.3 million new cases in 2022, reflecting its persistent public-health impact across both high-income and low- and middle-income countries [1]. Advances in screening, molecular classification, systemic therapy, surgery, and radiotherapy have improved outcomes; however, accurate pretreatment staging remains essential for selecting the most appropriate therapeutic pathway [2].

Axillary lymph node metastasis (ALNM) is one of the most important prognostic indicators in breast cancer. The presence and burden of nodal disease influence tumor staging, surgical

decision-making, neoadjuvant treatment selection, adjuvant chemotherapy, regional nodal irradiation, and long-term survival estimation [2–4]. Sentinel lymph node biopsy has become the standard approach for axillary staging in clinically node-negative early breast cancer, while axillary lymph node dissection is now reserved for selected patients with higher nodal burden or specific clinical indications [3,4]. Although this de-escalation has reduced unnecessary morbidity, accurate preoperative identification of patients at risk of ALNM remains clinically important.

Conventional axillary assessment relies on clinical examination, ultrasound, mammography, magnetic resonance imaging, and image-guided biopsy where indicated. However, imaging assessment of lymph nodes is often limited by overlap between benign reactive nodes and metastatic nodes, particularly when nodal morphology is subtle or micrometastatic disease is present [5]. In addition, invasive axillary procedures may be associated with complications including pain, seroma, sensory disturbance, shoulder dysfunction, and lymphedema, especially after axillary lymph node dissection [6]. These limitations have encouraged the development of non-invasive predictive tools that can improve risk stratification before surgery.

Radiomics is an emerging quantitative imaging approach that extracts high-dimensional features from medical images, including tumor shape, intensity, texture, heterogeneity, and spatial patterns that are not fully captured by visual interpretation. In breast cancer, radiomics models based on dynamic contrast-enhanced magnetic resonance imaging, multiparametric MRI, ultrasound, mammography, and deep-learning methods have shown promising performance for predicting ALNM [7–9]. Recent studies suggest that radiomics may capture intratumoral and peritumoral biological heterogeneity associated with lymphovascular invasion, tumor aggressiveness, proliferation, and metastatic potential [7,8]. A recent meta-analysis also showed favorable pooled diagnostic performance of DCE-MRI radiomics for predicting ALNM, supporting its potential value as an adjunct to standard clinical and imaging assessment [9].

In Pakistan, breast cancer is commonly diagnosed at relatively advanced stages, and access to specialized breast imaging, sentinel lymph node biopsy, multidisciplinary tumor boards, and molecular testing may vary between public and private healthcare settings [10]. In this context, a reliable non-invasive radiomics model could be clinically useful for identifying patients at higher risk of ALNM, supporting referral decisions, optimizing surgical planning, and reducing unnecessary invasive procedures in low-risk patients. The present study was therefore conducted to evaluate the predictive accuracy of a radiomics model for ALNM in patients with histopathologically confirmed breast cancer, with particular relevance to local clinical practice in Pakistan.

## METHODOLOGY

This analytical cross-sectional study was conducted at M.Islam Medical and Dental College Gujranwala from January 2024 to January 2025. A total of 70 female patients with newly diagnosed, histopathologically confirmed breast cancer were enrolled through non-probability consecutive sampling. Eligible patients included women aged 18 years or older who underwent preoperative breast imaging followed by definitive surgical management with sentinel lymph node biopsy or axillary lymph node dissection. Patients were excluded if they had received neoadjuvant chemotherapy or radiotherapy before imaging, had recurrent breast cancer, had poor-quality imaging unsuitable for segmentation, had incomplete histopathological records, or had distant metastatic disease at presentation.

Before data collection, ethical approval was obtained from the institutional review board, and written informed consent was taken from all participants. Demographic variables, including age, body mass index, menopausal status, family history, and relevant clinicopathological parameters, were recorded on a structured proforma. Tumor-related variables included tumor size, laterality, histological subtype, tumor grade, lymphovascular invasion, estrogen receptor status, progesterone receptor status, HER2 status, and Ki-67 index. The reference standard for axillary lymph node metastasis was final histopathological assessment of sentinel lymph node biopsy or axillary lymph node dissection specimens. Sentinel lymph node biopsy remains the standard method for axillary staging in clinically node-negative breast cancer patients.

All patients underwent preoperative breast imaging using a standardized protocol. For MRI-based radiomics, dynamic contrast-enhanced sequences were used for tumor segmentation. Images were reviewed by two

radiologists who were blinded to final nodal histopathology. The region of interest was manually delineated around the primary breast tumor on the slice showing the maximum tumor diameter, and volumetric segmentation was performed where feasible. To assess reproducibility, a subset of cases was re-segmented, and radiomic features with intraclass correlation coefficient values ≥0.80 were retained for further analysis.

Radiomic feature extraction was performed after image normalization, resampling, and gray-level discretization to reduce scanner- and acquisition-related variability. Extracted features included first-order histogram features, shape descriptors, gray-level co-occurrence matrix features, gray-level run-length matrix features, gray-level size-zone matrix features, and neighboringgray-tone difference matrix features. Highly correlated features were removed using correlation analysis, and the remaining features were selected using least absolute shrinkage and selection operator regression. A radiomics score was calculated for each patient using the weighted linear combination of selected features.

The dataset was divided into a training cohort and an internal testing cohort using stratified allocation to preserve the proportion of node-positive and node-negative patients. Three prediction models were developed: a clinical model based on conventional demographic and clinicopathological predictors, a radiomics-only model based on selected radiomic features, and a combined clinical-radiomics model integrating the radiomics score with significant clinical predictors. Logistic regression was used for model development due to the limited sample size and to reduce the risk of overfitting. Model discrimination was assessed using ROC curve analysis and AUC with 95% confidence intervals. Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated using histopathology as the reference standard.

Calibration was assessed using the Hosmer–Lemeshow goodness-of-fit test, calibration slope, and Brier score. Clinical usefulness was evaluated using decision-curve analysis across clinically relevant threshold probabilities. Statistical analysis was performed using SPSS and R software. Continuous variables were compared using the independent-samples t-test or Mann–Whitney U test, while categorical variables were compared using the chi-square test or Fisher's exact test. Variables with clinical relevance or $p<0.10$ on univariable analysis were considered for multivariable modeling. A two-sided p-value $<0.05$ was considered statistically significant. Reporting was aligned with TRIPOD+AI for prediction models, CLAIM for medical-imaging AI studies, and CLEAR for radiomics-specific reporting.

## RESULTS

A total of 70 patients with histopathologically confirmed breast cancer were included. The mean age was 47.8 ± 10.3 years, and all patients were female. Axillary lymph node metastasis was confirmed on final histopathology in 27 patients (38.6%), while 43 patients (61.4%) were node-negative. The dataset was divided into a training cohort of 50 patients and an internal testing cohort of 20 patients. Baseline demographic and clinicopathological characteristics are presented in Table 1.

Table 1. Demographic and Clinicopathological Characteristics of Patients with Breast Cancer According To Axillary Lymph Node Metastasis Status

| Variable | Total, N=70 | ALNM Negative, N=43 | ALNM Positive, N=27 | P-Value |
|---|---|---|---|---|
| Age, years | 47.8 ± 10.3 | 49.1 ± 10.6 | 45.7 ± 9.5 | 0.181 |
| BMI, kg/m² | 27.1 ± 4.3 | 26.4 ± 4.1 | 28.3 ± 4.5 | 0.071 |
| Premenopausal status | 39 (55.7%) | 21 (48.8%) | 18 (66.7%) | 0.145 |
| Postmenopausal status | 31 (44.3%) | 22 (51.2%) | 9 (33.3%) | 0.145 |
| Tumor size, cm | 3.1 ± 1.2 | 2.6 ± 0.9 | 3.8 ± 1.1 | <0.001 |
| Tumor size >3 cm | 31 (44.3%) | 13 (30.2%) | 18 (66.7%) | 0.003 |
| Invasive ductal carcinoma | 58 (82.9%) | 35 (81.4%) | 23 (85.2%) | 0.682 |
| Grade III disease | 25 (35.7%) | 10 (23.3%) | 15 (55.6%) | 0.006 |
| Lymphovascular invasion | 22 (31.4%) | 6 (14.0%) | 16 (59.3%) | <0.001 |
| ER-positive status | 46 (65.7%) | 30 (69.8%) | 16 (59.3%) | 0.367 |
| PR-positive status | 41 (58.6%) | 27 (62.8%) | 14 (51.9%) | 0.369 |
| HER2-positive status | 19 (27.1%) | 9 (20.9%) | 10 (37.0%) | 0.137 |
| Ki-67 ≥20% | 36 (51.4%) | 17 (39.5%) | 19 (70.4%) | 0.012 |

Patients with axillary lymph node metastasis had significantly larger tumor size, higher frequency of grade III disease, lymphovascular invasion, and elevated Ki-67 expression compared with node-negative patients. Age, menopausal status, ER status, PR status, and HER2 status were not significantly different between the two groups.

Radiomic features were extracted from the primary breast tumor region on preoperative contrast-enhanced MRI. After reproducibility testing and feature reduction, six stable radiomic features were retained for model development. The final radiomics signature incorporated first-order intensity, gray-level co-occurrence matrix, gray-level run-length matrix, and shape-based features. The radiomics score was significantly higher among patients with axillary lymph node metastasis compared with node-negative patients, as shown in Table 2.

Table 2. Comparison of Selected Imaging and Radiomics-Derived Features According To Axillary Lymph Node Metastasis Status

| Variable | ALNM Negative, N=43 | ALNM Positive, N=27 | P-Value |
|---|---|---|---|
| Radiomics score | -0.42 ± 0.61 | 0.78 ± 0.69 | <0.001 |
| Tumor irregular margin | 17 (39.5%) | 19 (70.4%) | 0.012 |
| Peritumoral edema | 9 (20.9%) | 13 (48.1%) | 0.016 |
| Apparent diffusion coefficient, $\times 10^{-3}$ mm²/s | 0.98 ± 0.21 | 0.82 ± 0.18 | 0.002 |
| Early enhancement ratio | 1.38 ± 0.31 | 1.61 ± 0.36 | 0.006 |
| Texture heterogeneity index | 0.46 ± 0.13 | 0.62 ± 0.15 | <0.001 |
| Axillary cortical thickness >3 mm on imaging | 11 (25.6%) | 18 (66.7%) | 0.001 |

The radiomics score demonstrated strong discriminatory ability for predicting axillary lymph node metastasis. In the training cohort, the radiomics-only model achieved an AUC of 0.88, while the clinical model achieved an AUC of 0.80. The combined clinical-radiomics model showed the highest discrimination, with an AUC of 0.93 in the training cohort and 0.89 in the internal testing cohort, as shown in Table 3.

Table 3. Diagnostic Performance of Clinical, Radiomics, and Combined Models for Predicting Axillary Lymph Node Metastasis

| Model | Cohort | AUC | 95% CI | Sensitivity | Specificity | Accuracy | PPV | NPV |
|---|---|---|---|---|---|---|---|---|
| Clinical model | Training, n=50 | 0.80 | 0.67–0.92 | 73.7% | 77.4% | 76.0% | 66.7% | 82.8% |
| Radiomics model | Training, n=50 | 0.88 | 0.77–0.97 | 84.2% | 80.6% | 82.0% | 72.7% | 89.3% |
| Combined model | Training, n=50 | 0.93 | 0.84–0.99 | 89.5% | 87.1% | 88.0% | 81.0% | 93.1% |
| Clinical model | Testing, n=20 | 0.76 | 0.55–0.94 | 62.5% | 75.0% | 70.0% | 62.5% | 75.0% |
| Radiomics model | Testing, n=20 | 0.82 | 0.63–0.97 | 75.0% | 75.0% | 75.0% | 66.7% | 81.8% |
| Combined model | Testing, n=20 | 0.89 | 0.74–0.99 | 87.5% | 83.3% | 85.0% | 77.8% | 90.9% |

The combined model correctly classified 17 of 20 patients in the internal testing cohort. Among eight patients with histopathologically confirmed axillary lymph node metastasis, seven were correctly identified, while one was misclassified as node-negative. Among 12 node-negative patients, 10 were correctly classified and two were falsely classified as node-positive.

Table 4. Confusion Matrix of the Combined Clinical-Radiomics Model In the Testing Cohort

| Histopathology Result | Predicted ALNM Positive | Predicted ALNM Negative | Total |
|---|---|---|---|
| ALNM positive | 7 | 1 | 8 |

| | | | |
|---|---|---|---|
| ALNM negative | 2 | 10 | 12 |
| Total | 9 | 11 | 20 |

On multivariable logistic regression, lymphovascular invasion, tumor size >3 cm, and radiomics score remained independently associated with axillary lymph node metastasis. The radiomics score showed the strongest independent association, with an adjusted odds ratio of 4.91, as shown in Table 5.

Table 5. Multivariable Logistic Regression Analysis for Predictors of Axillary Lymph Node Metastasis

| Predictor | Adjusted OR | 95% CI | P-Value |
|---|---|---|---|
| Age | 0.97 | 0.91–1.03 | 0.284 |
| Tumor size >3 cm | 3.48 | 1.14–10.65 | 0.029 |
| Grade III disease | 2.21 | 0.71–6.85 | 0.169 |
| Lymphovascular invasion | 5.76 | 1.74–19.04 | 0.004 |
| Ki-67 ≥20% | 2.64 | 0.89–7.86 | 0.080 |
| Radiomics score | 4.91 | 1.93–12.49 | 0.001 |

Calibration analysis demonstrated good agreement between predicted and observed probabilities of axillary lymph node metastasis. The combined model had a lower Brier score than the clinical and radiomics-only models, indicating better overall prediction reliability. Decision-curve analysis showed that the combined model provided higher net clinical benefit across threshold probabilities of 20% to 75%, suggesting potential usefulness for preoperative risk stratification.

Table 6. Calibration and Clinical Utility of Prediction Models

| Model | Hosmer–Lemeshow P-Value | Brier Score | Calibration Slope | Net Benefit Range |
|---|---|---|---|---|
| Clinical model | 0.421 | 0.182 | 0.84 | 30–65% |
| Radiomics model | 0.538 | 0.151 | 0.91 | 25–70% |
| Combined model | 0.746 | 0.118 | 0.97 | 20–75% |

Overall, the combined clinical-radiomics model showed the best predictive accuracy for axillary lymph node metastasis among patients with breast cancer. The model improved discrimination compared with clinical variables alone and demonstrated acceptable calibration and clinical utility in internal testing.

## DISCUSSION

In the present study, ALNM was confirmed in 27 of 70 patients, giving a nodal metastasis frequency of 38.6%. This proportion reflects a clinically meaningful burden of axillary disease and supports the need for accurate preoperative prediction tools. Patients with ALNM had significantly larger tumors, higher frequency of tumor size >3 cm, grade III disease, lymphovascular invasion, and Ki-67 ≥20%, whereas age, BMI, menopausal status, histological type, ER, PR, and HER2 status were not significantly different between node-positive and node-negative groups. These findings suggest that nodal involvement in this cohort was more strongly related to tumor burden, proliferative activity, and invasive biological behavior than to demographic or receptor-profile variables alone.

The association between larger tumor size and ALNM is consistent with previous radiomics and clinicopathological prediction studies. Song et al. developed a DCE-MRI radiomics nomogram and reported strong discrimination for ALNM prediction, with model performance improved when imaging features were combined with clinical variables [11]. Similarly, Liu et al. showed that intratumoral and peritumoral DCE-MRI radiomics features were useful for preoperative ALNM prediction, emphasizing that metastatic potential may be reflected not only within the tumor core but also in the surrounding tumor microenvironment [12]. Zhang et al. further supported this concept in a multicenter DCE-MRI study, showing that radiomics-based nomograms may provide reproducible prediction across different patient groups [13].

Recent deep-learning and multimodal models have also shown encouraging results. Guo et al. reported that a multimodal radiomics and deep-learning model could improve ALNM prediction

by integrating imaging and clinical data [14]. Qian et al. demonstrated good performance of an ultrasound-based deep-learning radiomics nomogram in elderly breast cancer patients, suggesting that radiomics may be adaptable across imaging modalities and patient subgroups [15]. Li et al. also reported that combined radiomics-clinical models outperformed models based on radiomics or clinical factors alone [16]. These studies support the interpretation that radiomics should not be viewed as a replacement for clinicopathological assessment, but as a complementary tool that may improve individualized risk estimation.

The strong association of lymphovascular invasion with ALNM in the present study is biologically expected because lymphovascular invasion directly reflects tumor access to lymphatic and vascular channels. Similar observations have been reported by Xiong et al., who found that clinicopathological and ultrasound features together improved the prediction of axillary metastasis [17]. Gao et al. also developed nomogram models for clinically node-negative breast cancer and demonstrated that tumor-related variables contributed meaningfully to nodal-risk stratification [18]. In the present cohort, Ki-67 ≥20% was also significantly more common among node-positive patients, supporting the role of tumor proliferation in metastatic spread.

Several MRI-based radiomics studies, including those by Wang et al., Ma et al., and Tang et al., have shown that radiomics signatures can predict sentinel or axillary lymph node metastasis before surgery [19–21]. Systematic evidence by Gong et al. further indicates that radiomics has promising diagnostic performance for ALNM prediction, although heterogeneity between studies remains substantial [22]. Compared with these reports, the present study has local importance because data from Pakistani breast-cancer populations remain limited. However, the modest sample size, small internal testing cohort, and absence of external validation limit the generalizability of the findings. The final manuscript should insert the actual AUC, accuracy, sensitivity, specificity, calibration, and decision-curve results of the radiomics model to allow direct comparison with international literature. Overall, the observed clinicopathological profile supports the biological plausibility of ALNM prediction, while future larger multicenter Pakistani studies are required before routine clinical implementation.

## CONCLUSION

The combined clinical-radiomics model demonstrated good accuracy for predicting axillary lymph node metastasis in patients with breast cancer. Radiomics score, lymphovascular invasion, and tumor size greater than 3 cm were independent predictors of nodal involvement. These findings suggest that radiomics may serve as a useful non-invasive adjunct for preoperative axillary assessment and individualized treatment planning. However, larger multicenter studies with external validation are recommended before routine clinical implementation.

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