International Journal of Biology and Life Sciences
ISSN: 2957-9511 | Vol. 12, No. 2, 2025

Advances in Ultrasonic Characterization of Breast Masses for Predicting Sentinel Lymph Node Metastasis

Chunxiang Wei *

Youjiang Medical University for Nationalities, Baise, Guangxi, China
* **Corresponding author Email**: 958867056@qq.com

Abstract: Lymph node metastasis remains the predominant spread pattern of breast cancer. Accurate assessment of sentinel lymph node status through ultrasound examination is crucial for clinical decision-making regarding surgical approaches and patient prognosis. In non-invasive preoperative evaluation of sentinel lymph nodes, tumor characteristics in breast masses provide valuable diagnostic information. This review systematically examines current research advancements in assessing sentinel lymph node status using ultrasound imaging of primary lesions, provide crucial imaging support for precision treatment and prognosis management in breast cancer.

Keywords: Breast Cancer; Sentinel Lymph Node; Elastography; Contrast-enhanced Ultrasound; Artificial Intelligence.

1. Introduction

According to a study published in Nature Medicine by researchers from the International Agency for Research on Cancer (IARC) and Health Services Alberta, there were 2.3 million new breast cancer cases globally in 2022. By 2050, new cases are projected to increase by 38%, reaching 3.2 million [1]. The presence of metastasis in axillary lymph nodes (ALN) is a critical factor affecting recurrence, metastasis, and long-term survival in early-stage breast cancer patients. Sentinel lymph nodes (SLN), the first lymph nodes draining breast cancer to regional lymphatic systems, play a crucial role. Patients with sentinel lymph node-negative status can opt for breast tumor resection without lymph node dissection, which studies show does not affect survival time [2] and may reduce the need for subsequent radiotherapy. Therefore, clinical assessment of sentinel lymph node metastasis is essential. Conventional lymph node ultrasound remains the primary method for sentinel lymph node evaluation due to its non-invasive, radiation-free, and simple advantages. However, its low sensitivity and specificity often lead to missed or misdiagnoses. Currently, sentinel lymph node biopsy (SLNB) is recognized as the gold standard for assessing ALN metastasis in cN0 patients before neoadjuvant therapy. However, the lengthy procedure for SLNB biopsy hinders clinical diagnosis. Therefore, there is an urgent clinical need for more advanced technologies to overcome the limitations of sentinel lymph node detection in conventional imaging diagnostics, which would help clinicians better stage breast cancer and determine surgical approaches. While ultrasound is commonly regarded as the preferred method for breast cancer screening, analyzing the characteristics of breast masses to further investigate sentinel lymph node status could provide a more convenient diagnostic approach for clinicians while offering patients more cost-effective and accessible testing options. This article reviews recent research progress in evaluating sentinel lymph node status through assessment of primary tumor characteristics in breast cancer.

2. Predictive Features of Conventional Ultrasound (US) Findings in Primary Breast Cancer Lesions for Sentinel Lymph Node Metastasis

The gold standard for breast examination is conventional ultrasound, which includes grayscale and color Doppler modalities. Grayscale ultrasound utilizes high-frequency sound waves to produce non-invasive, high-resolution images of breast tissue. This technique provides comprehensive visualization of internal structures, enabling physicians to precisely locate tumors and measure their dimensions. As the cornerstone of ultrasound imaging, grayscale ultrasound serves as the foundation for clinical practice. Color Doppler ultrasound, a highly sensitive method for blood flow monitoring, allows real-time observation of vascular patterns in breast lesions and lymph nodes. When combined with hemodynamic parameters, it offers a promising diagnostic tool. Building upon grayscale ultrasound, color Doppler ultrasound enables detailed analysis of fine structures within breast masses, including borders, margins, internal echoes, microcalcifications, and peripheral blood flow, thereby addressing grayscale ultrasound's limitations and enhancing diagnostic accuracy. With advantages such as radiation-free safety, high sensitivity for dense breast tissue, excellent cystic-solid differentiation, real-time imaging capabilities, ease of guided procedures, and relative comfort, conventional breast ultrasound has become an indispensable diagnostic tool. Recent years have seen growing interest in predicting lymph node metastasis through ultrasound imaging of primary breast cancer lesions. International studies indicate that tumor characteristics—including location, margins, size, distance from the body surface [3], and spiculation—can serve as potential biomarkers for sentinel lymph node metastasis.

3. Contrast-enhanced Ultrasound (CEUS) of Breast Masses to Predict Sentinel Lymph Node Metastasis

Contrast-enhanced ultrasound (CEUS) is a diagnostic technique that significantly improves image quality and diagnostic accuracy by administering microbubble-containing contrast agents intravenously alongside standard ultrasound examinations [4]. This method is widely used to evaluate benign and malignant breast lesions, providing detailed information on lesion perfusion and microcirculation. CEUS has been extensively applied in clinical practice for breast cancer diagnosis, treatment efficacy evaluation, and prognosis assessment. It has also become a standard tool for differentiating benign and malignant breast cancers, as well as detecting axillary lymph node metastasis [5]. By leveraging CEUS' unique imaging properties, researchers can predict sentinel lymph node status to avoid unnecessary lymph node dissection in early-stage breast cancer cases. Studies by Yamaki et al. [6] have demonstrated a significant correlation between perfusion defects and lymph node metastasis.

4. Elastography (Ultrasound Elastography, UE) of Breast Masses Predicts Sentinel Lymph Node Metastasis

Ultrasound elastography (UE) is an advanced medical imaging technique that utilizes tissue mechanical properties to differentiate pathological conditions by assessing deformation levels (or "tissue stiffness") under stress. The core principle can be summarized as: tissue deformation decreases with increasing stiffness. Currently, strain elastography is the most widely used technique for breast disease evaluation. Studies have demonstrated that combining UE with conventional ultrasound enhances diagnostic accuracy in predicting sentinel lymph node metastasis. In China, research indicates that integrating UE with grayscale ultrasound significantly improves the predictive value for breast cancer lymph node metastasis. For instance, Chen Qingqing et al. identified SWVmin, SWVmean, and EI scores as prognostic factors for early-stage breast cancer axillary lymph node involvement [7].

5. Intelligent Prediction Model Predicts Sentinel Lymph Node Metastasis

5.1. Ultrasound Line Chart

The Nomogram model, as an intuitive graphical simulation tool, enables clinicians to rapidly and reliably obtain results through simple line segments [8]. Research on clinical prediction models plays a vital role in facilitating collaborative decision-making between clinicians and patients, with the visual clarity of Nomograms demonstrating significant practical value. In the era of precision medicine, clinical prediction models serve as essential tools for estimating risks and benefits, holding substantial scientific and clinical significance in medical decision-making and prognosis. For instance, Xue-Fei Wang et al. developed a Nomogram model using clinical data to evaluate the area under the curve (AUC) for predicting sentinel lymph node metastasis in breast cancer, achieving an AUC of 81.6%. Yang Sen et al. identified that the lesion aspect ratio, margins, axillary lymph node (ALN) status, and Ki-67 index significantly influence the prediction of sentinel lymph node (SLN) metastasis ($P<0.05$), constructing a nomogram with an AUC of 0.79 in the training dataset. This nomogram effectively predicts SLN metastasis risk in stage T1 breast cancer patients, serving as a reliable tool for identifying candidates exempt from sentinel lymph node biopsy, thereby guiding clinical decisions regarding axillary lymph node dissection and adjuvant therapy. Chen Qingqing's [9] nomogram model with a cutoff value of 0.171 achieved a predicted area under the curve (AUC) of 0.945 for high ALNM burden in stage T1 breast cancer, significantly outperforming single-factor models based on SWVmax (0.907), vascular invasion (0.794), and filling defects (0.733). However, these nomogram models have limitations, including small sample sizes, regional bias, and failure to account for primary breast tumor characteristics.

5.2. Ultrasound Imaging Omics

Ultrasound imaging omics, by extracting and analyzing quantitative features from ultrasound images through high-throughput methods, enables deep exploration of tumor-related heterogeneous information including morphology, structure, heterogeneity, invasiveness, immune activity, and tumor microenvironment. This provides a powerful new tool for non-invasive preoperative prediction of sentinel lymph node metastasis. In 1996, Naguib proposed the first imaging omics prediction model [10]. Tong et al. pioneered the use of ultrasound-based imaging omics (statistical models) for preoperative prediction of thyroid carcinoma lymph node metastasis [11]. Subsequently, Ali Abbasian Ardakani and colleagues developed the deep learning model "ClymphNet" and tested it in thyroid carcinoma patients [12,13], representing a paradigm shift in AI-driven lymph node metastasis prediction. Zha H. L. first utilized imaging omics to predict axillary lymph node metastasis in breast cancer [14]. Since then, an increasing number of ultrasound-based imaging omics models have demonstrated superior predictive performance compared to conventional ultrasound (with AUC values predominantly ranging between 0.75-0.90). For instance, the DeepLabV3+ deep learning model developed by Xuefei Wang achieved 85% validation accuracy for sentinel lymph node prediction, along with high specificity and positive predictive value [15]. Recent studies have demonstrated that integrating elasticity imaging stiffness characteristics [16] with Doppler [16] blood flow parameters can develop more robust multi-parameter models for comprehensive tumor evaluation across morphology, stiffness, and blood supply dimensions. The clinical-imaging omics hybrid model—combining ultrasound imaging features with clinical-pathological factors (tumor size, histological grade, Ki-67 index, molecular classification) [17]—has emerged as the gold standard in clinical practice. Yongliang Sha's groundbreaking research revealed that the predictive model combining ultrasound characteristics with primary tumor B3GALT4 staging achieved excellent accuracy and reliability in assessing breast cancer sentinel lymph node (SLN) status [17]. Recent studies indicate that combined models can achieve the highest area under the curve (AUC) values, with some exceeding 0.90. In 2021, Zha HL et al. pioneered the integration of imaging omics scores with nomogram models for breast cancer sentinel lymph node metastasis prediction, demonstrating superior diagnostic performance compared to standalone nomogram models [18]. Notably, the COMB model (Combining BMUS and CDUS Imaging) has been shown to achieve high negative predictive values, effectively reducing unnecessary invasive procedures.

6. Summary

While existing retrospective studies provide valuable clinical references, their single-center data often suffer from patient population homogeneity limitations, with results' extrapolability and generalizability requiring further validation. This makes it challenging to directly guide personalized decision-making across different medical scenarios. The combined application of multiple imaging technologies—such as the complementary features of ultrasound and MRI in lesion morphology, margins, and internal structures, or their integration with PET-CT for metabolic function information—can overcome the limitations of single-modal imaging. This approach enables more comprehensive capture of tumor biology-related imaging characteristics, thereby enhancing prediction accuracy and reliability. Additionally, integrating previously mentioned intelligent models like ultrasound contouring and imaging omics, along with multimodal imaging data and clinical-pathological parameters (e.g., tumor grading, hormone receptor status, HER2 expression), and molecular biomarkers to construct comprehensive predictive models, holds promise for transitioning from "morphological description" to "functional prediction." This could provide clinicians with more precise risk stratification tools. Future research should urgently focus on multicenter, prospective large-sample studies to establish standardized ultrasound examination protocols and feature quantification systems, incorporating long-term patient follow-up data to validate the clinical effectiveness of combined models. Furthermore, exploring synergistic effects between ultrasound and emerging technologies (e.g., elastography, contrast-enhanced ultrasound) and applying artificial intelligence in multimodal data fusion will expand possibilities for non-invasive prediction of sentinel lymph node status in breast cancer. These efforts not only reduce unnecessary invasive procedures and alleviate patient healthcare burdens but also provide crucial imaging support for precision treatment and prognosis management in breast cancer.

References

[1] Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries[J].

[2] Kast, K., Link, T., Friedrich, K., Petzold, A., Niedostatek, A., Schoffer, O., Werner, C., Klug, S. J., Werner, A., Gatzweiler, A., Richter, B., Baretton, G., & Wimberger, P. (2015). Impact of breast cancer subtypes and patterns of metastasis on outcome. Breast cancer research and treatment, 150(3), 621–629. https://doi.org/10.1007/s10549-015-3341-3.

[3] Li, N., Song, C., Huang, X., Zhang, H., Su, J., Yang, L., He, J., & Cui, G. (2023). Optimized Radiomics Nomogram Based on Automated Breast Ultrasound System: A Potential Tool for Preoperative Prediction of Metastatic Lymph Node Burden in Breast Cancer. Breast cancer (Dove Medical Press), 15, 121–132. https://doi.org/10.2147/BCTT.S398300.

[4] Bar-Zion, A., Yin, M., Adam, D., & Foster, F. S. (2016). Functional Flow Patterns and Static Blood Pooling in Tumors Revealed by Combined Contrast-Enhanced Ultrasound and Photoacoustic Imaging. Cancer research, 76(15), 4320–4331. https://doi.org/10.1158/0008-5472.CAN-16-0376.

[5] Xu, H., Xu, G. L., Li, X. D., Su, Q. H., & Dong, C. Z. (2021). Correlation between the contrast-enhanced ultrasound image features and axillary lymph node metastasis of primary breast cancer and its diagnostic value. Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico, 23(1), 155–163. https://doi.org/10.1007/s12094-020-02407-6.

[6] Yamaki, T., Sukhbaatar, A., Mishra, R., Kikuchi, R., Sakamoto, M., Mori, S., & Kodama, T. (2021). Characterizing perfusion defects in metastatic lymph nodes at an early stage using high-frequency ultrasound and micro-CT imaging. Clinical & experimental metastasis, 38(6), 539–549. https://doi.org/10.1007/s10585-021-10127-6.

[7] Wang, Y., Liu, W., Yu, Y., Liu, J. J., Xue, H. D., Qi, Y. F., Lei, J., Yu, J. C., & Jin, Z. Y. (2020). CT radiomics nomogram for the preoperative prediction of lymph node metastasis in gastric cancer. European radiology, 30(2), 976–986. https://doi.org/10.1007/s00330-019-06398-z.

[8] Naguib, R. N., Adams, A. E., Horne, C. H., Angus, B., Sherbet, G. V., & Lennard, T. W. (1996). The detection of nodal metastasis in breast cancer using neural network techniques. Physiological measurement, 17(4), 297–303. https://doi.org/10.1088/0967-3334/17/4/007.

[9] Abbasian Ardakani, A., Mohammadi, A., Mirza-Aghazadeh-Attari, M., Faeghi, F., Vogl, T. J., & Acharya, U. R. (2023). Diagnosis of Metastatic Lymph Nodes in Patients With Papillary Thyroid Cancer: A Comparative Multi-Center Study of Semantic Features and Deep Learning-Based Models. Journal of ultrasound in medicine: official journal of the American Institute of Ultrasound in Medicine, 42(6), 1211–1221. https://doi.org/10.1002/jum.16131.

[10] Tong, Y., Zhang, J., Wei, Y., Yu, J., Zhan, W., Xia, H., Zhou, S., Wang, Y., & Chang, C. (2022). Ultrasound-based radiomics analysis for preoperative prediction of central and lateral cervical lymph node metastasis in papillary thyroid carcinoma: a multi-institutional study. BMC medical imaging, 22(1), 82. https://doi.org/10.1186/s12880-022-00809-2.

[11] La Verde, N., Biagioli, E., Gerardi, C., Cordovana, A., Casiraghi, C., Floriani, I., Bernardin, E., Farina, G., Di Cosimo, S., Dazzani, M. C., & Gherardi, G. (2016). Role of patient and tumor characteristics in sentinel lymph node metastasis in patients with luminal early breast cancer: an observational study. SpringerPlus, 5, 114. https://doi.org/10.1186/s40064-016-1720-9.

[12] Zha, H. L., Zong, M., Liu, X. P., Pan, J. Z., Wang, H., Gong, H. Y., Xia, T. S., Liu, X. A., & Li, C. Y. (2021). Preoperative ultrasound-based radiomics score can improve the accuracy of the Memorial Sloan Kettering Cancer Center nomogram for predicting sentinel lymph node metastasis in breast cancer. European journal of radiology, 135, 109512. https://doi.org/10.1016/j.ejrad.2020.109512.

[13] Wang, X., Nie, L., Zhu, Q. et al. Artificial intelligence assisted ultrasound for the non-invasive prediction of axillary lymph node metastasis in breast cancer. BMC Cancer 24, 910 (2024). https://doi.org/10.1186/s12885-024-12619-6.

[14] Suo J, Zhang Q, Chang W, Shi J, Yan Z, Chen M. [Evaluation of Axillary Lymph Node Metastasis by Using Radiomics of Dual-modal Ultrasound Composed of Elastography and B-mode]. Zhongguo Yi Liao Qi Xie Za Zhi. 2017 Sep 30;41(5):313-316. Chinese. doi: 10.3969/j.issn.1671-7104.2017.05.001. PMID: 29862714.

[15] Li, S. Y., Li, Y. M., Fang, Y. Q., Jin, Z. Y., Li, J. K., Zou, X. M., Huang, S. S., Niu, R. L., Fu, N. Q., Shao, Y. H., Gong, X. T., Li, M. R., Wang, W., & Wang, Z. L. (2025). Contrast-enhanced ultrasound radiomics model for predicting axillary lymph node metastasis and prognosis in breast cancer: a multicenter study. BMC cancer, 25(1), 1315. https://doi.org/10.1186/s12885-025-14632-9.

[16] Viale, G., Zurrida, S., Maiorano, E., Mazzarol, G., Pruneri, G., Paganelli, G., Maisonneuve, P., & Veronesi, U. (2005). Predicting the status of axillary sentinel lymph nodes in 4351 patients with invasive breast carcinoma treated in a single

institution. Cancer, 103(3), 492–500. https://doi.org/10. 1002/ cncr.20809.

[17] Sha, Y., Ge, S., Wang, Y., Cai, S., Wang, C., Zhuang, H., Shi, J., He, S., Sun, X., Ma, L., Guo, H., & Cheng, H. (2025). Ultrasound-based radiomics combined with B3GALT4 level to predict sentinel lymph node metastasis in primary breast cancer. Frontiers in oncology, 15, 1570493. https://doi.org/ 10.3389/ fonc.2025.1570493.

[18] Yang, Z. Q., Zhang, Y., Lu, F., Yang, T., Shan, J., Jiang, Q., Lim, G. H., Bertucci, F., Du, H., & Zhu, Y. C. (2025). Integrating multimodal ultrasound imaging for improved radiomics sentinel lymph node assessment in breast cancer. Gland surgery, 14(7), 1348–1365. https://doi.org/10.21037/gs-2025-223.