

Research Progress on Ultrasound Radiomics in Preoperative Prediction of Axillary Lymph Node Metastasis in Breast Cancer

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Abstract: Axillary lymph node (ALN) metastasis is a critical factor influencing prognosis and treatment strategies in breast cancer patients. However, traditional methods—ranging from physical examination to ultrasound—often lack the precision required for clinical decision-making. In recent years, ultrasound radiomics and deep learning have emerged as promising solutions, leveraging high-throughput quantitative features from ultrasound images to enhance detection accuracy. This review explores the development and application of radiomics and deep learning across multiple ultrasound modalities (grayscale, elastography, and contrast-enhanced ultrasound), as well as in multimodal imaging approaches that integrate ultrasound with MRI and PET/CT, underscoring the benefits of incorporating clinicopathological variables to boost predictive performance. These studies provide a vital foundation for personalized treatment and precision medicine in breast cancer management.

Key words: Lymphatic metastasis; Radiomics; Deep learning; Ultrasonography

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Breast cancer has become the most common malignant tumor among women worldwide and remains a major disease of global concern [1,2]. Early diagnosis and effective treatment are critical to reducing breast cancer mortality [3]. ALN metastasis is an important prognostic indicator and serves as a key basis for treatment decision-making; thus, accurate preoperative diagnosis is essential for de-escalating surgical interventions. Traditional methods for evaluating ALNs, such as physical examination and ultrasound, have not yet achieved the level of accuracy required in clinical practice. In recent years, ultrasound radiomics has emerged as a novel technique that extracts and analyzes a large number of features from ultrasound images, offering new insights and methods for the preoperative prediction of ALN metastasis in breast cancer.

Updates in the Concept of Diagnosis and Management of ALNs in Breast Cancer

In recent years, a series of high-quality clinical studies have continuously promoted the de-escalation of ALN surgery in breast cancer. The ACOSOG Z0011 study found that for T1-2 breast cancer patients undergoing breast-conserving surgery with whole-breast radiotherapy, those with 1-2 lymph node metastases who did not undergo ALN dissection did not show increased survival or local recurrence rates [4]. The SENOMAC study reported that for patients with T1-3 breast cancer, 1-2 SLN metastases, and postoperative axillary radiotherapy, there was no significant difference in local recurrence rates or overall survival [5]. The latest clinical guidelines indicate that for female patients with T1-3

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primary invasive breast cancer, if clinical examinations reveal negative ALN and only 1-2 SLN metastases, ALN dissection may be omitted in the context of breast-conserving surgery and whole-breast radiotherapy, thereby reducing the risk of complications [6]. The SOUND study further demonstrated that for T1 breast cancer patients with clinically negative axilla and normal ultrasound findings, omitting SLNB is also safe [7]. These shifts in clinical practice will greatly promote research into the accurate preoperative imaging identification of ALN metastasis. If high tumor burden can be identified preoperatively, patients could directly undergo ALN dissection without the need for SLNB; conversely, if patients without lymph node metastasis can be accurately identified, even the SLNB might be omitted.

Currently, ultrasound is the primary non-invasive imaging method used in clinical practice to evaluate the preoperative ALN status in breast cancer [8,9]. However, the diagnostic performance of ultrasound for detecting ALN metastasis varies significantly across studies, with reported sensitivity and specificity ranging from 0.185 to 0.871 and 0.395 to 0.980, respectively [8-12]. According to Ahmed et al. [13], among patients with ultrasound-suggested positive ALN metastasis, 43.2% actually have a low tumor burden in the ALNs (fewer than 3 SLN metastases). Based on the latest guidelines, this implies that nearly half of the patients with a positive ultrasound assessment might not require ALN dissection. However, given the limited ability of ultrasound to discern axillary tumor burden, there is an urgent need to develop a more accurate evaluation method.

The Application of Ultrasound Radiomics in Predicting ALN Metastasis in Breast Cancer

In recent years, two major technical directions have emerged in the field of breast cancer imaging analysis—radiomics and deep learning—both of which have attracted significant attention for their clinical application value. Both techniques can integrate multi-source clinical data (including basic patient information, laboratory test indicators, molecular biological features, etc.) to build predictive models that support clinical decision-making. The technical pathways and advantages of these two methods differ: Radiomics is a data-driven analytical approach focused on extracting deep-seated information from medical images that is difficult to discern by the naked eye. Through a systematic process—including image acquisition, preprocessing, feature engineering, and modeling—it converts visual information into a quantified feature matrix. This technique relies on expert-

designed feature extraction algorithms, primarily constructing a multi-dimensional parameter system based on image pixel distribution patterns and spatial topological relationships. In contrast, deep learning is an end-to-end feature learning paradigm that, by simulating the information processing mechanisms of neural networks, autonomously captures an abstract set of features that are highly relevant to the research objective. Its advantage lies in overcoming the limitations of manually designed features; however, the feature generation process lacks interpretability, and different models exhibit significant differences in feature expression.

It is noteworthy that a research team from Harvard Medical School has proposed a generalized radiomics framework that incorporates deep learning within its scope [14]. However, considering that the concept of radiomics was originally introduced specifically to refer to traditional feature engineering methods [15]. This paper adopts a narrow definition for clarity and discusses traditional radiomics and deep learning as parallel concepts. The term “radiomics” in the title of this paper still adheres to its broad concept, as clarified herein.

Figure 1 compares the workflows of radiomics - and deep learning-based model development and feature selection methods. Table 1 shows the summary of recent studies on ultrasound radiomics on predicting ALN status in breast cancer.

Radiomics research based on grayscale ultrasound

Early clinical predictive models were primarily constructed based on traditional clinicopathological parameters, including tumor size, histological grade, and hormone receptor status. Studies have shown that the predictive performance of these models is relatively limited, with the area under the receiver operating characteristic curve (AUC) generally ranging from 0.58 to 0.82 [16-19]. With the rapid development of radiomics technology, researchers have extracted high-throughput quantitative features—including texture features, morphological parameters, and dynamic enhancement characteristics—from ultrasound images of either the primary breast tumor or ALN to build predictive models, achieving AUCs in the range of 0.65 to 0.82. Notably, some studies have achieved predictive performance with an AUC exceeding 0.9 in optimized cohorts by rigorously screening enrolled cases (excluding those with atypical imaging features or ambiguous clinical diagnoses); however, such selective inclusion strategies may compromise the clinical generalizability of the models.

In recent years, there has been a trend towards integrating radiomics features with clinicopathological parameters to construct joint predictive models. This multidimensional modeling strategy has significantly

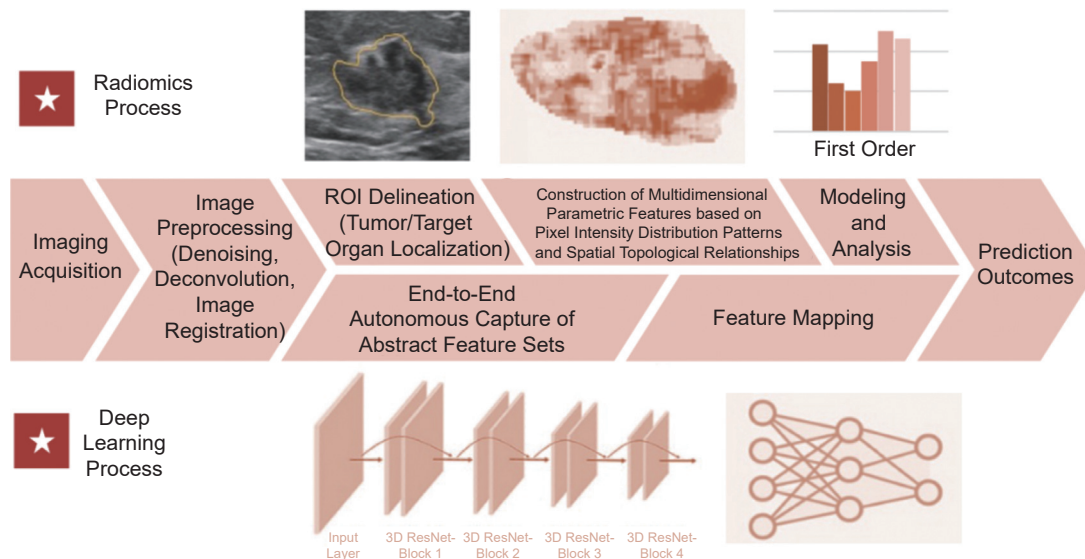


Figure 1 Two technical pathways for predictive modeling. The upper panel depicts the radiomics approach, comprising: Imaging acquisition; Image preprocessing; ROI delineation; Construction of multidimensional parametric features based on pixel intensity distribution patterns and spatial topological relationships; Modeling and analysis; Prediction outcomes. The lower panel shows the deep learning approach, comprising: Imaging acquisition; Image preprocessing; End-to-end autonomous capture of abstract feature sets; Feature mapping; Prediction outcomes.

improved predictive performance, with most studies reporting AUCs above 0.9. As more models are developed, researchers have found that existing models still struggle to address more complex clinical issues. Consequently, attention has shifted towards assessing the external validity of models in real clinical settings—either by developing targeted models for subgroups with atypical imaging features or by expanding sample sizes for multi-center validation. The following sections will sequentially introduce the "ultrasound imaging-only models" and the combined clinicopathological and ultrasound radiomics models.

Model Development Using Radiomic Features Derived Solely from Ultrasound Images Radiomic features extracted solely from primary breast cancer lesions can predict ALN metastasis. Qiu et al. [20], Yu et al. [21], and Zhou et al. [22] all utilized radiomic features derived from primary tumor images to predict ALN metastasis status, demonstrating that integrating these features with ALN ultrasound findings further enhances predictive accuracy.

Radiomic features of primary tumors also show potential in predicting ALN metastatic tumor burden. Gao et al. [23] pioneered this approach by developing a nomogram for prediction. Wu et al. [24] constructed 9 models using 3 feature selection methods and 3 machine learning classifiers, with SHAP (Shapley Additive Explanations) analysis explaining the contribution of individual radiomic features to ALN metastasis prediction. Zhang et al. [25] employed Pyradiomics and a pre-trained ResNet50 to extract radiomic features and deep learning features, respectively, for joint modeling.

Emerging evidence suggests that peritumoral regions may harbor predictive information for ALN metastasis. Lee et al. [26] found optimal model performance when incorporating a 3-mm-thick peritumoral zone around the tumor. Similarly, Wang et al. [27] extracted features from intratumoral and 1–5 mm peritumoral ultrasound regions, combined with clinical characteristics, and identified models integrating intratumoral and 3-mm peritumoral features as having superior diagnostic performance. Zhang et al. [28] corroborated these findings.

In addition to grayscale ultrasound images of primary breast tumors for predicting ALN metastasis, some researchers have attempted to directly utilize ALN ultrasound images to diagnose metastatic status. Coronado et al. [29] included normal ALNs and ultrasound-suspected lymph nodes confirmed as metastatic by biopsy. Ozaki et al. [30] developed models using lymph node images from healthy women and pathologically confirmed metastatic ALNs deemed clinically suspicious, demonstrating predictive performance comparable to that of a radiologist with 12 years of experience, with no statistically significant difference. Sun et al. [31] constructed a deep learning model using ultrasound images of biopsy-confirmed suspicious metastatic ALNs. Notably, these studies excluded lymph nodes that were both clinically and ultrasonographically negative but later found positive by sentinel lymph node biopsy (SLNB)—precisely the most diagnostically challenging cases. Tang et al. [32] incorporated ALNs from ultrasound-guided biopsies and non-metastatic ALNs confirmed by SLNB. After extracting shape and intensity-based radiomic features from ALN images, their feature selec-

Table 1 Summary of ultrasound radiomics studies in predicting axillary lymph node(ALN) status

Author	Year	Image type	Number of participants	Number of Centers	AUC (dataset)←model name	ALN status		Parameters	Region of interest segmentation	Feature selection method	Model construction method
						>0 vs=0	≥3 vs. 1-2				
Only Grayscale US											
Qiu [20]	2020	Primary Lesion (PL)	196	1	0.73 (validation dataset (val))←radiomics (radiomics(RAD)) 0.76 (val)←RAD + US-reported ALN	✓	✓	RAD, US-reported ALN status	Manual	Elastic net logistic regression; univariate analyses	Logistic regression (LR)
Yu [21]	2019	PL	426	1	0.71(val) ← RAD 0.81(val) ← combined model	✓	✓	RAD + size + US-reported ALN status	Manual	Intra-class correlation coefficient (ICC); Least Absolute Shrinkage and Selection Operator (LASSO); variance inflation factor (VIF)	Multivariable LR
Zhou [22]	2021	PL	192	2	0.65 (External dataset (ex-test))	✓	✓	RAD	Manual	Max-relevance and min-redundancy (MRMR); LASSO	LASSO: leave group out cross-validation (LGOCV)
Gao [23]	2021	PL	343	1	0.73 (val)	✓	✓	RAD, size, age	Manual	LASSO	LR
Wu [24]	2024	PL	215	2	0.66 (ex-test) ← clinical model 0.72 (ex-test) ← RAD model	✓	✓	RAD/clinicopathological features	Manual	ICC; Mann-Whitney U test; LASSO; principal component analysis (PCA) and Boruta (final)	Extreme gradient boosting (XGB/XGBoost)(final); LR; support vector machine (SVM)
Zhang [25]	2023	PL	176	1	0.81(val)← Deep learning (DL)-RAD model 0.82 (val)←DL-nomogram	✓	✓	RAD + ResNet-50; size, clinicopathological features	Manual	ICC, Independent sample T-test; random forest recursive elimination; LASSO	Univariate/multivariate LR analysis
Lee [26]	2021	PL + peritumoral area	153	1	0.81 (val)	✓	✓	DL features or handcrafted features (shape, textural)	Mask R-Convolutional Neural Network (CNN)	\;	DenseNet-121 (final); LR; SVM; XGBoost
Wang [27]	2024	PL+ peritumoral area	321	1	0.78 (val)←clinical model 0.84 (val)←RAD model 0.91(val)←combined model	✓	✓	RAD + conventional ultrasound & immunohistochemical indicators	Manual	Correlation analysis; Univariate analysis; MRMR; LASSO	LR; Decision Tree; SVM; XGB (final); Random Forest(RF); K-Nearest Neighbors (KNN)
Zhang [28]	2024	PL+ peritumoral area	755	1	Combined model: 0.87(val) ←presence/absence 0.91(val)←high/low tumor burden	✓	✓	Conventional ultrasound & clinical indicators	Manual	MRMR; LASSO; Pearson's coefficient and VIF	Multivariate LR;
Coronado [29]	2019	ALN	105	2	0.94(train+val-k-fold*)	✓	✓	Computed ROI features	Manual	A variation of Fisher Vector Supervised machine learning	FV- CNN features
Sun [31]	2022	ALN	169	1	0.72 (test)	✓	✓	CNN features	Manual	Custom CNN	
Ozaki [30]	2022	ALN	300	1	0.97(val)	✓	✓	DL features	Deep Analyzer	GoogleNet Xception; Supervised learning	
Tang [32]	2023	ALN	147	2	0.92 (val)	✓	✓	RAD	Manual	ICC; Spearman correlation analysis; LASSO	

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Author	Year	Image type	Number of participants	Number of Centers	AUC (dataset)←model name	ALN status		Parameters	Region of interest segmentation	Feature selection method	Model construction method
						>0 vs=0	≥3 vs. 1-2				
Chen [33]	2023	ABUS	310	1	0.79(val)← ABUS RAD 0.74(val)← ABUS features 0.85(val)← RAD+retraction phenomenon+ US reported ALN status	✓	✓	RAD (ABUS) + ABUS imaging features +clinicopathologic features	Manual	Pearson correlation coefficient; Spearman's rank correlation coefficient; LASSO	Univariate & Multivariate LR
Li [34]	2023	ABUS	517	2	0.81(test)	✓	✓	RAD (ABUS) + size+ US-reported LN status +retraction phenomenon	Manual	ICC; LASSO	Univariate & Multivariate LR
Wang [35]	2023	ABUS	276	2	0.67(test)←RAD 0.83(test)←combined model	✓	✓	RAD (ABUS) + US-reported LN status + convergence + erythrocyte distribution width	Manual	ICC; LASSO	univariate LR
Li [36]	2023	US video	320	3	0.91(test)← video 0.86(test)← images	✓	✓	CNN features	Normalize the data	Video: CNN with R2+1D; Static images: ResNet50, InceptionV3, VGG19	ResNet-3D
Zha [37]	2021	PL	452	1	0.77(val) ← RAD 0.83(val) ← combined model	✓	✓	RAD+ MSKKCC nomogram	Manual	mRMR; LASSO Cox regression	LR
Ouyang [38]	2024	PL	212	1	0.85 (val)	✓	✓	RAD + size, tumor type, age, Ki67	Manual	Pearson correlation Coefficients; LASSO	SVM, naïve Bayesian (NB), optimization method
Yao [39]	2024	PL	278	1	0.92(val)← RAD 0.93(val)← combined model	✓	✓	RAD + high tumor grade & positive LVI	Manual	The synthetic minority oversampling technique; PCA, recursive feature elimination	linear discriminant analysis; SVM, RF, decision tree;
Zhao [40]	2023	PL	199	1	0.68 (val) ← RAD 0.69 (val) ← RAD+conventional US + peripheral blood T cell 0.79 (val) ← combined model	✓	✓	RAD + peripheral blood T-cell subsets	Manual	LASSO	NB; LR (final), classification decision tree, SVM
Qian [41]	2024	PL	364	1	0.89(val) ← RAD 0.74(val) ← clinical model 0.91(val) ← combined model	✓	✓	DL (DenseNet-201) features + RAD + clinical features	Manual rectangle ROI	DL: Spearman correlation coefficient; RAD: LASSO; ICC; mRMR	Univariate analysis; Stepwise multivariable LR
Zhou [42]	2019	PL	834	2	0.90(in-test) 0.89 (ex-test)	✓	✓	DL features	/	Inception V3 (final); Inception-ResNet V2; ResNet-101	
Wang [43]	2024	PL	266	1	0.80 (in-test)	✓	✓	DL features	DeepLabV3 + ResNet-101	CNN	
Liu [44]	2024	PL	883	4	0.91(ex-test1); 0.93 (ex-test2); 0.95 (ex-test3)	✓	✓	DL features (ResNet50) + RAD+ clinical parameters	Manual	ResNet50; ICC; LASSO	Univariate & multivariate LR
You [45]	2024	PL	792	3	Combined model: 0.83 (ex-test1); 0.83(ex-test2)	✓(received NAC)	✓	DL features; Clinicopathologic data	You Only Look Once Version 5	Progressive multi-granularity (PMG) classification network; Multivariable logistic regression; image super-resolution via iterative refinement (SR3)	
Guo [46]	2020	PL	937	2	0.84(ex-test) ← SLN 0.81(ex-test) ← non-SLN	✓	✓	Non-DL features + US-reported SLN ALN status metas tasis	Manual	DenseNet	

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Author	Year	Image type	Number of participants	AUC (dataset)←model name	ALN status		Parameters	Region of interest segmentation	Feature selection method	Model construction method
					>0 vs=0	≥3 vs. 1-2				
Multimodal US (Combined with Grayscale US)										
Zheng [47]	2020	PL (shear wave elastography (SWE) & grayscale)	584	1	Combined model: 0.902 (in-test) ←presence/absence 0.91 (in-test) ←high/low tumor burden	✓	✓	DL features of (grayscale & SWE) + clinicopathological parameters	Manual rectangle ROI	ResNet50 (final), ResNet101, Inception V3, and VGG19
Jiang [48]	2022	PL (SWE)	433	2	C-index: 0.82(ex-test) ←presence/absence 0.81(ex-test) ←high/low tumor burden	✓	✓	RAD (grayscale/SWE) + molecular subtype + US-reported ALN status	Manual	Spearman's correlation; LASSO; MRMR
Wang [49]	2023	PL (strain elastography)	359	2	0.79(ex-test) ←PL (grayscale) 0.73 (ex-test) ←PL(color Doppler flow imaging (CDFI)); 0.88(ex-test) ←PL (elastography)	✓		DL (grayscale/CDFI/strain elastography)	Manual	ResNet-18
Gong [50]	2025	ALN (grayscale+SWE)	519	1	0.86 (in-test) ←ALN (grayscale) 0.83 (in-test) ←ALN (SWE); 0.93 (ex-test) ←ALN (SWE + grayscale)	✓		DAMF-former (grayscale/SWE)	Manual rectangle ROI	DAMF-former (core module: dual-modal adaptive fusion module)
Sun [51]	2024	PL (grayscale, Contrast enhanced ultrasound (CEUS))	111	1	0.82 (val)←US-reported ALN 0.89 (val)←US-reported ALN+RAD (grayscale) 0.90 (val)←US-reported ALN+RAD (grayscale+CEUS)	✓		RAD (grayscale/CEUS), US-reported ALN status	Manual (grayscale); computer vision algorithm (CEUS)	VIF; MRMR; LASSO
Yan [52]	2025	PL (grayscale, CEUS)	282	2	0.81 (ex-test)	✓		RAD (grayscale), histologic type (only for nomogram)	Manual	RF, LASSO
Other multimodal imaging (combined with grayscale US)										
Tang [53]	2025	PL (MRI + US)	588	2	0.81(ex-test) ←DL (MRI + US + clinical parameters)	✓		DL features (MRI/US), age, MRI-derived tumor size, MRI-derived ALN status	Manual rectangle ROI	ConvNeXt (final), ResNet18, VGG16 → US 3D-ResNet (final), C3D, R (2+1)D → MRI; multivariable LR
Li [54]	2023	(18F-FDG) PET/CT	124	1	0.87(val)←T-stage+US/PET reported ALN status+RAD(PET)	✓		RAD (PET), T-stage, US/PET reported ALN status	Manual	LASSO
										Univariate & multivariate LR

*means no separated validation dataset. (final) means finally chosen method to construct the model. Training dataset: Used for model training. Validation dataset: A dataset randomly split from the same source as the training set, used for parameter tuning and model selection. In-test: internal dataset or independent dataset. Partitioned from the same-source data that was never involved in training. External dataset: dataset from other hospitals: Independently sourced data (e.g., collected from other hospitals/equipment). PL, Primary lesion; ALN, Axillary lymph node; val, Validation dataset; RAD, Radiomics; LR, Logistic regression; ICC, Intra-class correlation coefficient; LASSO, Least Absolute Shrinkage and Selection Operator; VIF, variance inflation factor; MRMR, Max-relevance and min-redundancy; ex-test, External dataset; LGOVC, leave group out cross-validation; PCA, principal component analysis; XGB/XGBoost, Extreme gradient boosting; SVM, support vector machine; DL, Deep learning; CNN, Convolutional Neural Network; RF, Random Forest; KNN, K-Nearest Neighbors; NB, naïve Bayesian; SWE, shear wave elastography; CEUS, Contrast enhanced ultrasound.

tion process revealed that shape-related features were consistently eliminated, with models relying primarily on intensity-based features—contrary to clinicians' reliance on morphological criteria. This intensity-driven model outperformed radiologists across multiple institutions, achieving an AUC of 0.919 in the validation cohort without incorporating clinicopathological data and demonstrating robust performance in subgroup analyses with diverse clinicopathological characteristics. However, current studies using ALN images for metastasis diagnosis face critical limitations: (1) Pathology-image mismatch: The inability to precisely correlate pre-operative ultrasound images with post-surgical pathological results restricts training data to biopsy-confirmed cases or obviously non-metastatic lymph nodes. (2) Limited generalizability: Models derived from such selective cohorts exhibit poor external validity, failing to address the diagnostic challenges that radiologists encounter in ambiguous cases (e.g., SLNB-positive/ultrasound-negative nodes). (3) Clinical utility gap: While achieving high AUC values in controlled settings, these models lack practical adaptability to real-world clinical workflows where indeterminate cases dominate diagnostic uncertainty.

Beyond the predominant use of static grayscale images, researchers have explored radiomics applications in analyzing Automated Breast Volume Ultrasound (ABUS) and handheld ultrasound dynamic videos. For example, Chen et al. [33] and Li et al. [34] developed nomograms integrating ABUS radiomic features, ABUS retraction signs, and ultrasound-reported ALN status for preoperative evaluation of ALN tumor burden in early-stage breast cancer patients, both achieving robust predictive performance. Building on these features, Wang et al. [35] further incorporated serological biomarkers to enable risk probability assessment for ALN micrometastases (which typically lack definitive ultrasound characteristics).

Additionally, Li et al. [36] pioneered a dynamic video-based deep learning model using primary tumor ultrasound videos to predict ALN metastasis. Their results demonstrated that the video-driven model significantly outperformed static image-based deep learning models in AUC values. The temporal information and motion characteristics captured from dynamic video sequences enhanced prediction accuracy by revealing subtle functional and spatial-temporal patterns invisible in static frames.

Integration of Radiomic Features with Clinicopathological Characteristics Enhances Predictive Performance Early studies on predictive models for ALN metastasis often integrated radiomic features with established clinicopathological models to optimize per-

formance. Zha et al. [37] combined ultrasound-derived radiomic features with the Memorial Sloan Kettering Cancer Center (MSKCC) clinicopathological model [16]—a widely accepted clinical predictor—and demonstrated that the combined model achieved superior predictive accuracy compared to either modality alone.

Similarly, Ouyang et al. [38] integrated radiomic features extracted from primary tumors with clinicopathological variables including tumor type, size, patient age, and proliferation markers such as the Ki-67 antigen. Yao et al. [39] further enhanced their model by incorporating histologic grade and lymphovascular invasion status. Zhao et al. [40] developed a multimodal framework that fused radiomic features from breast lesions, conventional ultrasound characteristics, and peripheral blood T-cell subset analyses (reflecting systemic immune status) to predict ALN metastasis.

Enhancing Model Generalizability and Clinical Adaptability Breast cancer is a highly heterogeneous disease with substantial variability in treatment responses and prognoses across subtypes. Elderly breast cancer patients often present distinct clinical characteristics, including larger tumor size at diagnosis yet lower ALN metastasis rates, coupled with limited life expectancy, necessitating tailored therapeutic strategies distinct from general populations. Research focusing on this subgroup is critical for personalized management. Qian et al. [41] developed a predictive model for ALN metastasis in patients aged > 75 years by integrating deep learning features from primary tumor ultrasound images with histopathological grade and radiologists' subjective assessments of ALN status, demonstrating significant predictive improvement in this specific cohort.

Recognizing the diagnostic challenges in clinically node-negative ALN cases, researchers have targeted this subgroup for model optimization. Zhou et al. [42] constructed a deep learning model using primary tumor images from clinically node-negative patients, achieving an AUC of 0.89 in independent testing, comparable to radiologists' performance. Wang et al. [43] focused on patients with ultrasonographically suspicious ALNs but negative clinical palpation, developing a model with 100% specificity and positive predictive value.

As multiple models emerge, the field increasingly prioritizes generalizability validation. Liu et al. [44] not only validated their primary tumor-based deep learning model on a single test set but also conducted external validation across three independent medical centers, confirming robust generalizability. You et al. [45] further addressed real-world heterogeneity by incorporating data from three centers with varying image quality. Their model, enhanced with iterative refinement super-resolution techniques, showed superior performance,

underscoring the critical impact of image resolution optimization on clinical applicability.

While most studies use SLNB as the diagnostic gold standard for primary tumor-based predictions, clinical observations reveal potential non-sentinel lymph node metastases. Guo et al. [46] addressed this gap by developing a deep learning model that achieved high sensitivity (98.4% for both SLN and non-SLN) in identifying metastasis-free patients, thereby effectively avoiding overtreatment.

In summary, although substantial progress has been made in enhancing predictive accuracy and model robustness, further research should explicitly address limitations regarding clinical generalizability. Prospective, multicenter, large-sample studies are urgently needed to validate these promising predictive models across diverse clinical settings. Additionally, the clinical integration of advanced imaging methodologies—such as AI-driven enhancements, multimodal imaging, and high-resolution technologies—should be prioritized to improve model performance in complex and heterogeneous clinical populations. Such integrated approaches will ultimately facilitate tailored treatment decisions and better patient outcomes.

Radiomics with multimodal ultrasound imaging

Radiomic Studies Combining Grayscale Ultrasound and Elastography Shear wave elastography (SWE) quantifies tissue stiffness by measuring elastic modulus. Strain elastography evaluates tissue deformability by analyzing strain ratio under manual compression. These techniques offer novel insights for ALN metastasis prediction. Zheng et al. [47] developed a deep learning model integrating grayscale ultrasound and SWE images of primary breast tumors with clinicopathological factors to simultaneously predict ALN metastasis presence and tumor burden. Jiang et al. [48] extracted radiomic features from grayscale and SWE images of primary lesions, combined with ultrasound-reported ALN status and molecular subtypes, to predict both ALN metastasis and metastatic load. Wang et al. [49] compared deep learning models based on grayscale ultrasound, color Doppler flow imaging, and strain elastography, finding elastography-derived models exhibited superior diagnostic performance in differentiating metastatic lymph nodes.

Radiomic models can also be constructed using ALN-specific grayscale and elastographic images. Gong et al. [50] designed the DAMF-former model, which employs adaptive mid-fusion techniques to synthesize grayscale ultrasound and SWE images of axillary regions, mimicking radiologists' integrative analysis of target ALNs. This approach not only improved diagnostic accuracy

but also addressed a critical gap in prior AI research—the lack of clinical utility for sonographers. Implementation of this model significantly enhanced diagnostic capabilities for less-experienced clinicians: junior radiologists achieved an AUC increase from 0.807 to 0.883, while inter-observer agreement among clinicians of varying expertise reached near-perfect levels. These results suggest that human-AI collaboration could enable junior practitioners to attain diagnostic proficiency comparable to seasoned experts.

Radiomic Studies Combining Grayscale Ultrasound with Contrast-Enhanced Ultrasound Contrast-enhanced ultrasound (CEUS) provides hemodynamic insights into tumor perfusion through intravenous contrast agents, enriching diagnostic information. Sun et al. [51] developed a predictive model by extracting radiomic features from both conventional grayscale ultrasound and CEUS images of tumor interiors and peritumoral regions, combined with ultrasound-reported ALN status, demonstrating superior performance. Yan et al. [52] further compared nomograms and machine learning models integrating clinicopathological characteristics, conventional ultrasound features, radiomic signatures, and CEUS enhancement patterns.

Multimodal models combining ultrasound with MRI and Pet-CT

Multimodal models incorporating non-ultrasound imaging modalities show promising clinical applicability. For instance, Tang et al. [53] developed a multimodal deep learning framework fusing ultrasound and MRI data to predict ALN metastasis in breast cancer patients. Li et al. [54] constructed a comprehensive predictive model incorporating T-stage, ultrasound- and PET/CT-reported ALN status, and PET radiomic features. This multimodal approach achieved a significantly higher AUC compared to models using clinicopathological-ultrasound or clinicopathological-ultrasound-PET data alone, highlighting the added value of cross-modal integration.

Numerous studies—whether incorporating ultrasound or not [55,56]—have demonstrated that multimodal approaches significantly outperform single-mode ultrasound in lesion characterization and diagnostic prediction. Yet clinical translation of these advances remains limited by three principal challenges: the lack of standardized protocols for heterogeneous, multi-source image normalization; the need for more robust, high-precision algorithms for cross-modal image registration; and the practical difficulties of acquiring multiple imaging modalities—namely, poor accessibility and increased logistical burden—resulting in substantially higher data collection and model training costs. More-

over, because the marginal gain in diagnostic accuracy from multimodal over single - modal studies is often modest, these elevated costs further impede widespread clinical adoption. Looking ahead, the establishment of large, standardized clinical imaging databases and the deployment of pretrained, large - scale multimodal models may effectively address these obstacles and accelerate the integration of multimodal predictive models into practice. At present, however, grayscale ultrasound remains the predominant imaging modality in diagnostics by virtue of its superior cost - effectiveness and seamless integration with established clinical workflows.

Conclusions

Ultrasound radiomics has demonstrated significant potential in preoperative prediction of ALN metastasis in breast cancer. The development of machine learning models and deep learning models based on radiomic features extracted from grayscale ultrasound, elastography, and contrast-enhanced ultrasound (CEUS), along with the application of multimodal models integrating other imaging modalities such as MRI, CT, and PET-CT, has provided critical evidence for personalized treatment and precision medicine in breast cancer management. The evolution from single-parameter models to multidimensional intelligent prediction systems reflects the deepening conceptual understanding of precision medicine in breast cancer diagnosis and treatment. Despite remarkable progress in current models, balancing predictive accuracy with clinical generalizability and enhancing discriminatory capability for complex cases remains pivotal challenges requiring resolution in future research. Multicenter, large-sample clinical validation and the in-depth application of novel imaging technologies will propel ALN assessment toward more precise and intelligent development.

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Authors' Contributions

YJG and QLZ conceived of and designed the study; YJG drafted the manuscript; ZHN, YWL, YXJ and QLZ revised the article. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Data Availability

All data generated or analyzed during this study are included in this article.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Conflict of interest

The authors declare that there is no conflict of interest relevant to this study.

References

- [1] Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. *CA Cancer J Clin* 2022;72:7-33.
- [2] Chen W, Zheng R, Baade PD, Zhang S, Zeng H, Bray F, et al. Cancer statistics in China, 2015. *CA Cancer J Clin* 2016;66:115-132.
- [3] Sechopoulos I, Teuwen J, Mann R. Artificial intelligence for breast cancer detection in mammography and digital breast tomosynthesis: state of the art. *Semin Cancer Biol* 2021;72:214-225.
- [4] Giuliano AE, Ballman KV, McCall L, Beitsch PD, Brennan MB, Kelemen PR, et al. Effect of axillary dissection vs no axillary dissection on 10-year overall survival among women with invasive breast cancer and sentinel node metastasis: the ACOSOG Z0011 (alliance) randomized clinical trial. *JAMA* 2017;318:918-926.
- [5] de Boniface J, Filtenborg Tvedskov T, Rydén L, Szulkin R, Reimer T, Kühn T, et al. Omitting axillary dissection in breast cancer with sentinel-node metastases. *N Engl J Med* 2024;390:1163-1175.
- [6] Lyman GH, Somerfield MR, Bosserman LD, Perkins CL, Weaver DL, Giuliano AE. Sentinel lymph node biopsy for patients with early-stage breast cancer: American society of clinical oncology clinical practice guideline update. *J Clin Oncol* 2017;35:561-564.
- [7] Gentilini OD, Botteri E, Sangalli C, Galimberti V, Porpiglia M, Agresti R, et al. Sentinel lymph node biopsy vs no axillary surgery in patients with small breast cancer and negative results on ultrasonography of axillary lymph nodes: the sound randomized clinical trial. *JAMA Oncol* 2023;9:1557-1564.
- [8] Valente SA, Levine GM, Silverstein MJ, Rayhanabad JA, Weng-Grumley JG, Ji L, et al. Accuracy of predicting axillary lymph node positivity by physical examination, mammography, ultrasonography, and magnetic resonance imaging. *Ann Surg Oncol* 2012;19:1825-1830.
- [9] Alvarez S, Añorbe E, Alcorta P, López F, Alonso I, Cortés J. Role of sonography in the diagnosis of axillary lymph node metastases in breast cancer: a systematic review. *AJR Am J Roentgenol* 2006;186:1342-1348.
- [10] Cools-Lartigue J, Meterissian S. Accuracy of axillary ultrasound in the diagnosis of nodal metastasis in invasive breast cancer: a review. *World J Surg* 2012;36:46-54.
- [11] Chen X, He Y, Wang J, Huo L, Fan Z, Li J, et al. Feasibility of using negative ultrasonography results of axillary lymph nodes to predict sentinel lymph node metastasis in breast cancer patients. *Cancer Med* 2018;7:3066-3072.
- [12] Zhu Y, Zhou W, Jia XH, Huang O, Zhan WW. Preoperative axil-

- lary ultrasound in the selection of patients with a heavy axillary tumor burden in early-stage breast cancer: what leads to false-positive results? *J Ultrasound Med* 2018;37:1357-1365.
- [13] Ahmed M, Jozsa F, Baker R, Rubio IT, Benson J, Douek M. Meta-analysis of tumour burden in pre-operative axillary ultrasound positive and negative breast cancer patients. *Breast Cancer Res Treat* 2017;166:329-336.
 - [14] van Griethuysen JJM, Fedorov A, Parmar C, Hosny A, Aucoin N, Narayan V, et al. Computational radiomics system to decode the radiographic phenotype. *Cancer Res* 2017;77:e104-e107.
 - [15] Gillies RJ, Kinahan PE, Hricak H. Radiomics: Images are more than pictures, they are data. *Radiology* 2016;278:563-577.
 - [16] Bevilacqua JL, Kattan MW, Fey JV, Cody HS, 3rd, Borgen PI, Van Zee KJ. Doctor, what are my chances of having a positive sentinel node? A validated nomogram for risk estimation. *J Clin Oncol* 2007;25:3670-3679.
 - [17] Chue KM, Yong WS, Thike AA, Ahmed SS, Li HH, Wong CY, et al. Predicting the likelihood of additional lymph node metastasis in sentinel lymph node positive breast cancer: validation of the Memorial Sloan-Kettering Cancer Centre (MSKCC) nomogram. *J Clin Pathol* 2014;67:112-119.
 - [18] Rouzier R, Uzan C, Rousseau A, Guillot E, Zilberman S, Meyer C, et al. Multicenter prospective evaluation of the reliability of the combined use of two models to predict non-sentinel lymph node status in breast cancer patients with metastatic sentinel lymph nodes: the MSKCC nomogram and the Tenon score. Results of the NOTEGS study. *Br J Cancer* 2017;116:1135-1140.
 - [19] Barranger E, Coutant C, Flahault A, Delpech Y, Darai E, Uzan S. An axilla scoring system to predict non-sentinel lymph node status in breast cancer patients with sentinel lymph node involvement. *Breast Cancer Res Treat* 2005;91:113-119.
 - [20] Qiu X, Jiang Y, Zhao Q, Yan C, Huang M, Jiang T. Could ultrasound-based radiomics noninvasively predict axillary lymph node metastasis in breast cancer? *J Ultrasound Med* 2020;39:1897-1905.
 - [21] Yu FH, Wang JX, Ye XH, Deng J, Hang J, Yang B. Ultrasound-based radiomics nomogram: A potential biomarker to predict axillary lymph node metastasis in early-stage invasive breast cancer. *Eur J Radiol* 2019;119:108658.
 - [22] Zhou WJ, Zhang YD, Kong WT, Zhang CX, Zhang B. Preoperative prediction of axillary lymph node metastasis in patients with breast cancer based on radiomics of gray-scale ultrasonography. *Gland Surg* 2021;10:1989-2001.
 - [23] Gao Y, Luo Y, Zhao C, Xiao M, Ma L, Li W, et al. Nomogram based on radiomics analysis of primary breast cancer ultrasound images: prediction of axillary lymph node tumor burden in patients. *Eur Radiol* 2021;31:928-937.
 - [24] Wu J, Ge L, Guo Y, Xu D, Wang Z. Utilizing multiclassifier radiomics analysis of ultrasound to predict high axillary lymph node tumour burden in node-positive breast cancer patients: a multicentre study. *Ann Med* 2024;56:395061.
 - [25] Zhang H, Zhao T, Zhang S, Sun J, Zhang F, Li X, et al. Prediction of axillary lymph node metastatic load of breast cancer based on ultrasound deep learning radiomics nomogram. *Technol Cancer Res Treat* 2023;22:15330338231166218.
 - [26] Lee YW, Huang CS, Shih CC, Chang RF. Axillary lymph node metastasis status prediction of early-stage breast cancer using convolutional neural networks. *Comput Biol Med* 2021;130:104206.
 - [27] Wang SR, Cao CL, Du TT, Wang JL, Li J, Li WX, et al. Machine learning model for predicting axillary lymph node metastasis in clinically node positive breast cancer based on peritumoral ultrasound radiomics and shap feature analysis. *J Ultrasound Med* 2024;43:1611-1625.
 - [28] Zhang W, Wang S, Wang Y, Sun J, Wei H, Xue W, et al. Ultrasound-based radiomics nomogram for predicting axillary lymph node metastasis in early-stage breast cancer. *Radiol Med* 2024;129:211-221.
 - [29] Coronado-Gutiérrez D, Santamaría G, Ganau S, Bargalló X, Orlando S, Oliva-Brañas ME, et al. Quantitative ultrasound image analysis of axillary lymph nodes to diagnose metastatic involvement in breast cancer. *Ultrasound Med Biol* 2019;45:2932-2941.
 - [30] Ozaki J, Fujioka T, Yamaga E, Hayashi A, Kujiraoka Y, Imokawa T, et al. Deep learning method with a convolutional neural network for image classification of normal and metastatic axillary lymph nodes on breast ultrasonography. *Jpn J Radiol* 2022;40:814-822.
 - [31] Sun S, Mutasa S, Liu MZ, Nemer J, Sun M, Siddique M, et al. Deep learning prediction of axillary lymph node status using ultrasound images. *Comput Biol Med* 2022;143:105250.
 - [32] Tang YL, Wang B, Ou-Yang T, Lv WZ, Tang SC, Wei A, et al. Ultrasound radiomics based on axillary lymph nodes images for predicting lymph node metastasis in breast cancer. *Front Oncol* 2023;13:1217309.
 - [33] Chen Y, Xie Y, Li B, Shao H, Na Z, Wang Q, et al. Automated breast ultrasound (ABUS)-based radiomics nomogram: an individualized tool for predicting axillary lymph node tumor burden in patients with early breast cancer. *BMC Cancer* 2023;23:340.
 - [34] Li N, Song C, Huang X, Zhang H, Su J, Yang L, et al. 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 Med Press)* 2023;15:121-132.
 - [35] Wang H, Yang XW, Chen F, Qin YY, Li XB, Ma SM, et al. Non-invasive assessment of axillary lymph node metastasis risk in early invasive breast cancer adopting automated breast volume scanning-based radiomics nomogram: a multicenter study. *Ultrasound Med Biol* 2023;49:1202-1211.
 - [36] Li WB, Du ZC, Liu YJ, Gao JX, Wang JG, Dai Q, et al. Prediction of axillary lymph node metastasis in early breast cancer patients with ultrasonic videos based deep learning. *Front Oncol* 2023;13:1219838.
 - [37] Zha HL, Zong M, Liu XP, Pan JZ, Wang H, Gong HY, et al. 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. *Eur J Radiol* 2021;135:109512.
 - [38] Ouyang Q, Chen Q, Zhang L, Lin Q, Yan J, Sun H, et al. Construction of a risk prediction model for axillary lymph node metastasis in breast cancer based on gray-scale ultrasound and clinical pathological features. *Front Oncol* 2024;14:1415584.
 - [39] Yao J, Zhou W, Xu S, Jia X, Zhou J, Chen X, et al. Machine learning-based breast tumor ultrasound radiomics for pre-operative prediction of axillary sentinel lymph node metastasis burden in early-stage invasive breast cancer. *Ultrasound Med Biol* 2024;50:229-236.
 - [40] Zhao M, Zheng Y, Chu J, Liu Z, Dong F. Ultrasound-based radiomics combined with immune status to predict sentinel lymph node metastasis in primary breast cancer. *Sci Rep* 2023;13:16918.
 - [41] Qian L, Liu X, Zhou S, Zhi W, Zhang K, Li H, et al. A cutting-edge deep learning-and-radiomics-based ultrasound nomogram for precise prediction of axillary lymph node metastasis in breast cancer patients ≥ 75 years. *Front Endocrinol (Lausanne)* 2024;15:1323452.
 - [42] Zhou LQ, Wu XL, Huang SY, Wu GG, Ye HR, Wei Q, et al. Lymph node metastasis prediction from primary breast cancer us images using deep learning. *Radiology* 2020;294:19-28.

- [43] Wang X, Nie L, Zhu Q, Zuo Z, Liu G, Sun Q, et al. Artificial intelligence assisted ultrasound for the non-invasive prediction of axillary lymph node metastasis in breast cancer. *BMC Cancer* 2024;24:910.
- [44] Liu H, Zou L, Xu N, Shen H, Zhang Y, Wan P, et al. Deep learning radiomics based prediction of axillary lymph node metastasis in breast cancer. *NPJ Breast Cancer* 2024;10:22.
- [45] You J, Huang Y, Ouyang L, Zhang X, Chen P, Wu X, et al. Automated and reusable deep learning (AutoRDL) framework for predicting response to neoadjuvant chemotherapy and axillary lymph node metastasis in breast cancer using ultrasound images: a retrospective, multicentre study. *EClinicalMedicine* 2024;69:102499.
- [46] Guo X, Liu Z, Sun C, Zhang L, Wang Y, Li Z, et al. Deep learning radiomics of ultrasonography: Identifying the risk of axillary non-sentinel lymph node involvement in primary breast cancer. *EBioMedicine* 2020;60:103018.
- [47] Zheng X, Yao Z, Huang Y, Yu Y, Wang Y, Liu Y, et al. Deep learning radiomics can predict axillary lymph node status in early-stage breast cancer. *Nat Commun* 2020;11:1236.
- [48] Jiang M, Li CL, Luo XM, Chuan ZR, Chen RX, Tang SC, et al. Radiomics model based on shear-wave elastography in the assessment of axillary lymph node status in early-stage breast cancer. *Eur Radiol* 2022;32:2313-2325.
- [49] Wang C, Zhao Y, Wan M, Huang L, Liao L, Guo L, et al. Prediction of sentinel lymph node metastasis in breast cancer by using deep learning radiomics based on ultrasound images. *Medicine (Baltimore)* 2023;102:e35868.
- [50] Gong C, Wu Y, Zhang G, Liu X, Zhu X, Cai N, et al. Computer-assisted diagnosis for axillary lymph node metastasis of early breast cancer based on transformer with dual-modal adaptive mid-term fusion using ultrasound elastography. *Comput Med Imaging Graph* 2025;119:102472.
- [51] Sun C, Gong X, Hou L, Yang D, Li Q, Li L, et al. A nomogram based on conventional and contrast-enhanced ultrasound radiomics for the noninvasively prediction of axillary lymph node metastasis in breast cancer patients. *Front Oncol* 2024;14:1400872.
- [52] Yan M, He D, Sun Y, Huang L, Cai L, Wang C, et al. Comparative analysis of nomogram and machine learning models for predicting axillary lymph node metastasis in early-stage breast cancer: a study on clinically and ultrasound-negative axillary cases across two centers. *Ultrasound Med Biol* 2025;51:463-474.
- [53] Tang X, Zhang H, Mao R, Zhang Y, Jiang X, Lin M, et al. Preoperative prediction of axillary lymph node metastasis in patients with breast cancer through multimodal deep learning based on ultrasound and magnetic resonance imaging images. *Acad Radiol* 2025;32:1-11.
- [54] Li Y, Han D, Shen C, Duan X. Construction of a comprehensive predictive model for axillary lymph node metastasis in breast cancer: a retrospective study. *BMC Cancer* 2023;23:1028.
- [55] Guo F, Sun S, Deng X, Wang Y, Yao W, Yue P, et al. Predicting axillary lymph node metastasis in breast cancer using a multimodal radiomics and deep learning model. *Front Immunol* 2024;15:1482020.
- [56] Wang Q, Lin Y, Ding C, Guan W, Zhang X, Jia J, et al. Multi-modality radiomics model predicts axillary lymph node metastasis of breast cancer using MRI and mammography. *Eur Radiol* 2024;34:6121-6131.