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Improving Multimodal Ultrasound Diagnostics In Non-Palpable Breast Lesions

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Abstract

Non-palpable breast lesions represent a significant diagnostic challenge in breast imaging due to their occult nature on clinical examination and variable presentations on conventional modalities. Multimodal ultrasound, integrating B-mode imaging with advanced techniques such as shear wave elastography (SWE), strain elastography, contrast-enhanced ultrasound (CEUS), and microvascular imaging, offers a promising non-invasive approach to enhance detection, characterization, and differentiation of benign and malignant lesions. This article explores advancements in multimodal ultrasound protocols, emphasizing their role in improving diagnostic accuracy, reducing unnecessary biopsies, and optimizing clinical management for non-palpable breast lesions. By combining morphological, vascular, and biomechanical data, multimodal ultrasound achieves superior sensitivity and specificity compared to conventional ultrasound alone, with reported areas under the curve (AUC) often exceeding 0.90 in combined approaches. Key innovations include quantitative stiffness measurements via SWE, perfusion pattern analysis through CEUS, and integration with artificial intelligence for automated feature extraction. These developments not only refine BI-RADS categorization but also support personalized diagnostic pathways, particularly in dense breast tissue where mammography sensitivity is limited. Future directions involve hybrid imaging, real-time fusion techniques, and machine learning models to further elevate precision and reproducibility. This comprehensive review underscores the transformative potential of multimodal ultrasound in early breast cancer detection and lesion characterization.

Keywords: Non-palpable breast lesions, multimodal ultrasound, shear wave elastography, contrast-enhanced ultrasound, breast cancer diagnostics, BI-RADS, non-mass lesions.

Introduction

Non-palpable breast lesions, often detected incidentally through screening mammography or ultrasound in asymptomatic patients, pose unique diagnostic difficulties because they lack tactile feedback and may exhibit subtle imaging features that overlap between benign and malignant processes. These lesions, including non-mass-like enhancements or small masses below clinical detection thresholds, frequently fall into BI-RADS category 3 or 4, where the risk of malignancy varies widely from less than 2% to over 50% depending on specific descriptors. Traditional reliance on grayscale ultrasound alone frequently results in indeterminate findings, leading to over-diagnosis, unnecessary interventions, or underestimation of malignant potential, particularly in women with dense breast parenchyma where acoustic shadowing and tissue heterogeneity complicate interpretation.

The evolution of ultrasound technology has introduced multimodal strategies that synergistically combine conventional B-mode imaging with functional and quantitative assessments. B-mode ultrasound provides essential morphological details such as shape, margins, orientation, echo pattern, and posterior acoustic features. Irregular shape, spiculated or angular margins, non-

parallel orientation, and hypoechoic patterns with posterior shadowing remain strong predictors of malignancy, yet these features alone lack sufficient specificity for non-palpable lesions, where microlobulated or indistinct margins often prove nonspecific. To address these limitations, elastography techniques evaluate tissue stiffness, a hallmark of desmoplastic reactions in malignant tumors. Shear wave elastography (SWE) quantifies elasticity in kilopascals or meters per second, with malignant lesions typically demonstrating higher values due to increased rigidity. Strain elastography offers qualitative or semi-quantitative scoring systems, such as the Tsukuba score, further aiding differentiation. Studies consistently demonstrate that adding SWE to conventional ultrasound elevates diagnostic performance, with improvements in sensitivity from approximately 86% to over 96% and corresponding gains in AUC. Contrast-enhanced ultrasound (CEUS) complements elastography by visualizing microvascular perfusion and neoangiogenesis, processes critical to tumor growth. Following intravenous administration of microbubble contrast agents, CEUS reveals enhancement patterns, timing, intensity, and washout characteristics. Malignant non-palpable lesions often exhibit rapid, heterogeneous, or penetrating vessel enhancement with higher peak intensities and prolonged retention compared to benign entities. Parameters such as mean contrast signal intensity, perfusion rate, and enhancement area at specific time points (e.g., 40 seconds) have proven particularly discriminative, achieving diagnostic accuracies nearing 90%. When integrated, conventional ultrasound plus CEUS yields AUC values around 0.885–0.917, with notable reductions in false positives for BI-RADS 4A lesions.

The true strength of multimodal ultrasound emerges from the concurrent or sequential application of these techniques. Combining B-mode, SWE, and CEUS provides a multifaceted profile encompassing morphology, biomechanics, and vascularity, significantly outperforming single-modality approaches. For instance, protocols incorporating all three modalities have reported sensitivities of 90–98%, specificities of 87–94%, and AUCs up to 0.96 for non-mass-like lesions. This integration is especially valuable for non-mass breast lesions (NMLs), which lack discrete borders and often manifest as architectural distortions, hypoechoic areas with calcifications, or ductal changes. In NMLs, multimodal ultrasound helps stratify risk more effectively than digital mammography, which struggles with non-calcified lesions, or even dynamic contrast-enhanced MRI in select contexts, offering comparable performance at lower cost and without ionizing radiation or gadolinium exposure.

Clinical implementation requires standardized protocols and operator training to minimize variability. Automated breast volume scanning (ABVS) combined with elastography reduces operator dependency by providing three-dimensional reconstructions and reproducible elastograms, enhancing lesion localization and characterization in dense breasts. Microvascular imaging techniques, such as superb microvascular imaging (SMI), detect low-velocity flows without contrast, adding another layer of vascular information. Artificial intelligence (AI) integration further refines this ecosystem: deep learning models trained on multimodal datasets automatically extract features, generate malignancy risk scores, and assist in BI-RADS downgrading or upgrading. Hybrid AI-ultrasound systems combined with mammography have shown potential to reduce unnecessary biopsies by up to 46% while maintaining high negative predictive values. Challenges persist, including inter-operator variability in handheld examinations, artifacts in elastography (e.g., from pre-compression or lesion depth), and variable contrast agent responses influenced by patient factors such as body mass index or vascular comorbidities. Non-mass enhancements on MRI may still require multimodal ultrasound correlation for better specificity, as ultrasound performance can be more limited in purely non-mass patterns. Standardization of acquisition parameters, quantitative thresholds, and reporting templates is essential for widespread adoption and reproducibility across centers. Cost-effectiveness analyses also support multimodal ultrasound as a first-line or problem-solving tool, particularly in resource-limited settings or for young patients where radiation avoidance is prioritized.

Advancements in probe technology, including higher-frequency transducers and fusion imaging with mammography or MRI, promise even greater precision. Real-time multimodal fusion allows simultaneous visualization of anatomical and functional data on a single display, facilitating targeted biopsies with improved yield. Longitudinal studies are needed to validate the impact on interval cancer rates, patient outcomes, and biopsy reduction in screening populations. Emerging techniques, such as contrast-enhanced elastography and photoacoustic ultrasound, may further expand the multimodal arsenal by linking mechanical and optical properties.

In summary, multimodal ultrasound represents a paradigm shift in the diagnostic approach to non-palpable breast lesions. By leveraging complementary data streams morphological, elastic, and vascular it enhances confidence in lesion characterization, supports more accurate risk stratification within the BI-RADS framework, and contributes to personalized, minimally invasive patient management. Continued research, technological refinement, and interdisciplinary collaboration will solidify its role in reducing breast cancer mortality through earlier, more precise detection while minimizing harm from overdiagnosis. The ongoing integration of AI and automated systems is poised to democratize expertise, ensuring high-quality diagnostics regardless of operator experience or clinical setting.

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