AMERICAN JOURNAL OF DIAGNOSTIC IMAGING
2024; 11(1): 1-8
10.5455/ajdi.20240826034244

WisdomGale

ORIGINAL ARTICLE

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Correlation of non-mass breast lesions on ultrasound with histopathology

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ABSTRACT

Background and Aim: Breast cancer is the most common invasive cancer among women worldwide. In Iraq, the incidence of new breast cancer cases significantly increased from 52.00 per 100,000 in 2000 to 91.66 per 100,000 in 2019. The goal is to develop standardized reporting criteria for Non-mass lesions (NMLs) on ultrasound to improve patient management.

Methods: A cross-sectional study at AL-Yarmouk Teaching Hospital in Baghdad included 55 female patients with NMLs. Participants underwent evaluations using ultrasound, with mammographic correlation when applicable. Lesion characteristics, such as size, location, echogenicity, and associated features, were documented according to BI-RADS lexicon. A tissue core biopsy was performed to obtain samples for histopathological analysis. Ethical approval and informed consent were obtained, ensuring data confidentiality and participant privacy.

Results: Among the 55 patients, 60% of NMLs were benign, 25.5% were malignant, and 14.5% had upgrade potential. Significant associations were found between ultrasound characteristics (e.g., distribution and echogenicity) and histopathological outcomes, with segmental distribution being more common in malignant lesions. Mammographic features such as calcifications and architectural distortion are also strongly correlated with malignancy.

Conclusion: The integration of advanced ultrasound technology has improved the detection of NMLs, crucial for early breast cancer detection. However, these lesions often mimic surrounding tissues, leading to potential false positives. Future research should focus on standardizing ultrasound interpretation of NMLs to enhance diagnostic accuracy and patient management.

ARTICLE HISTORY

Received August 26, 2024
Accepted September 22, 2024
Published October 05, 2024

KEYWORDS

Correlation; non-mass; breast lesions; ultrasound; histopathology

Introduction

Breast cancer is the most common invasive cancer among women worldwide. In Iraq, the incidence of new breast cancer cases significantly increased from 52.00 per 100,000 in 2000 to 91.66 per 100,000 in 2019. Breast cancer remains the leading cause of cancer-related mortality among Iraqi women, accounting for one-third of all cancer cases in 2019 [1]. Advances in detection methods, including mammography and ultrasound, have led to an increase in diagnosed cases and a subsequent decline in mortality rates. This improvement is attributed to a better understanding of breast cancer epidemiology, encompassing factors like reproductive history, genetics, and environmental influences [1]. The triple evaluation protocol, which includes clinical examination, radiological imaging, and biopsy procedures, is vital for the accurate diagnosis of breast abnormalities [2]. Breast ultrasound is particularly valuable for women under 40 due to its noninvasive nature and lack of ionizing radiation, while mammography is recommended for women over 40, especially in cases of less dense breast tissue [2]. Non-mass lesions (NMLs) in the breast pose a unique challenge in imaging, as they can be difficult to characterize and may represent a spectrum of pathologies ranging from benign to malignant. Accurate characterization of NMLs on ultrasound is essential for determining appropriate

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management and guiding biopsy decisions [3]. Correlating imaging findings with histopathological results is crucial for improving diagnostic accuracy and breast cancer management. Tru-cut biopsy is preferred over Fine Needle Aspiration Cytology for obtaining adequate tissue samples, as it allows for comprehensive histological analysis, including the differentiation between invasive and non-invasive diseases and the assessment of the tumor's hormonal receptor status [4,5]. This study aims to characterize breast NMLs using ultrasound and correlate the imaging findings with histopathological results to enhance diagnostic accuracy and guide appropriate management decisions. The findings may contribute to developing standardized reporting criteria for NMLs on ultrasound, ultimately improving overall patient management.

Materials and Methods

A cross-sectional study was conducted at AL-Yarmouk Teaching Hospital in Baghdad from February 2023 to 2024, involving 55 female patients aged 25–75 years with non-mass breast lesions visible on ultrasound according to prior study with no any missing data and if any missing data of patients, we delete and substitute by another patient with complete data.

Inclusion criteria

The study included women referred from the breast clinic for either screening mammograms followed by ultrasound evaluation of abnormal findings or for diagnostic evaluation due to symptoms like pain, palpable abnormalities, or nipple discharge. Women aged 35 years or younger began with ultrasound, while those older than 35 started with mammography, proceeding to ultrasound if necessary.

Exclusion criteria

Patients were excluded if they had mass lesions, a recent history of breast surgery, ongoing radiotherapy, or breast implants.

After obtaining informed consent, patient history, clinical examination, and ultrasound evaluations were performed using a GE LOGIQ P7 R3 Ultrasound machine with a 7.5 MHz linear array probe. Ultrasound findings, including lesion size, location, distribution, echogenicity, and associated features, were documented based on BI-RADS lexicon. When applicable, mammographic correlation was established, focusing on asymmetry, calcifications, and architectural distortion. A tissue core biopsy was performed using the BARD MAXCORE biopsy instrument. Samples were collected under aseptic conditions after local anesthesia and analyzed histopathologically. The pathological outcomes were then compared with the ultrasound findings to classify lesions as benign or malignant.

Statistical analysis

Data were analyzed using SPSS version 25. Descriptive statistics were used for continuous variables, and categorical variables were presented as frequencies and percentages. The chi-square test was applied to examine the relationship between histopathological outcomes and various ultrasound features. This study's comprehensive evaluation strategy aims to enhance the accuracy of diagnosing non-mass breast lesions and guide effective clinical management.

Results

The study included 55 female patients with a mean age of 49 ± 13.5 years. The majority of patients (30.9%) were in the 41-50-year age group, followed by 23.6% of patients over 60 years old. The most common clinical presentations were breast pain (mastalgia) and palpable lesions, each reported by 29.1% of patients and 27.8%, respectively. 19.4% of patients were asymptomatic and underwent screening imaging, as shown in (Table 1).

No significant association was found between age group and histopathology results (Table 2).

Focal lesions were the most common ultrasound finding (38.2%), followed by segmental and regional

Table 1. Distribution of patients according to age groups and presentation.

Variables		Frequency (no.)	Percentage (%)
Age groups (years)	21–30	6	10.9
	31–40	10	18.2
	41–50	17	30.9
	51–60	9	16.4
	>60	13	23.6
Clinical presentation	Nipple discharge	5	9.1
	Asymptomatic (screening)	11	19.4
	Nodularity	8	14.5
	Pain	16	29.1
	Regional palpability	15	27.8

Table 2. Association between age group and histopathology result.

Variables			Histopathology result			
			Benign	Benign with upgrade potential	Malignant	*p*-value
Age Groups (years)	21–30		6	0	0	
			18.2%	0.0%	0.0%	
	31–40		6	2	2	0.2
			18.2%	25.0%	14.3%	
	41–50		12	1	4	
			36.4%	12.5%	28.6%	
	51–60		5	1	3	
			15.2%	12.5%	21.4%	
	>60		4	4	5	
			12.1%	50.0%	35.7%	
	Total		33	8	14	
			100.0%	100.0%	100.0%	
	Nipple discharge		3	2	0	
		9.1%	25.0%	0.0%		
	Asymptomatic (screening)		8	2	1	
		24.2%	25.0%	7.1%		
	Nodularity		7	0	1	
			21.2%	0.0%	7.1%	**0.0001**
	Pain		15	1	0	
		45.5%	12.5%	0.0%		
	Regional palpability		0	3	12	
		0.0%	37.5%	85.8%		
	Total		33	8	14	
			100.0%	100.0%	100.0%	

p-value ≤ 0.05 (significant).

lesions (23.6% each). Hypoechoic lesions were seen in 47.3% of patients, while 40% had mixed echogenicity lesions, as shown in (Table 3). Benign lesions were the most common histopathological diagnosis (60%), followed by malignant lesions (25.5%) and benign lesions with upgrade potential (14.5%) as shown in (Table 3).

Ultrasound lesion distribution was also significantly associated with histopathology (p = 0.0001). Segmental distribution was seen in 57.1% of malignant lesions, while 57.6% of benign lesions had a focal distribution as shown in. No significant association was found between ultrasound echogenicity and histopathology results (Table 5).

Significant associations were observed between mammographic features (calcifications, architectural distortion, asymmetry) and histopathology

Table 3. Distribution of NMLs according to their distribution and echogenicity on U/S and according to diagnosis.

U/S distribution	Frequency (no.)	Percentage (%)
Focal	21	38.2
Linear	14.5	8
Segmental	23.6	13
Regional	23.6	13
Echogenicity on U/S.	**Frequency (no.)**	**Percentage (%)**
Mixed	22	40.0
Hyperechoic	9.1	5
Hypoechoic	47.3	26
Isoechoic	3.6	2
Variables	**Frequency (no.)**	**Percentage (%)**
Benign	33	60.0
Benign with upgrade	8	14.5
potential Malignant	14	25.5

Table 4. Distribution of NMLs according to associated mammographic features.

Variables		Frequency (no.)	Percentage (%)
Asymmetry	Focal	21	44.7
	Global	6	12.8
	Developing	5	10.6
	None	15	31.9
Architecture distortion	Absent	22	46.8
	Present	25	53.2
Calcification	Absent	35	74.5
	Present	12	25.5

Table 5. Association between ultrasound echogenicity, distribution, and histopathology result.

Variables	Histopathology result			
	Benign	Benign with upgrade potential	Malignant	*p*-value
Focal	19	1	1	
	57.6%	12.5%	7.1%	
Linear	3	2	3	
	9.1%	25.0%	21.4%	
Segmental	1	4	8	
	3.0%	50.0%	57.1%	**0.0001**
Regional	10	1	2	
	30.3%	12.5%	14.3%	
Total	33	8	14	
	100.0%	100.0%	100.0%	
Hypoechoic	13	3	10	
	39.4%	37.5%	71.4%	
Hyperechoic	5	0	0	
	15.2%	0.0%	0.0%	0.19
Isoechoic	1	1	0	
	3.0%	12.5%	0.0%	
Mixed	14	4	4	
	42.4%	50.0%	28.6%	
Total	33	8	14	
	100.0%	100.0%	100.0%	

p-value ≤ 0.05 (significant)

results (Table 6). Calcifications were present in 85.7% of malignant lesions, architectural distortion in 64.3%, and lack of asymmetry or focal asymmetry in 35.7% and 21.4%, respectively.

Table 6. Association between associated mammographic features (Calcification, Architecture distortion, and Asymmetry) and histopathology result.

Variable		Histopathology result			
		Benign	Benign with upgrade potential	Malignant	*p*-value
Calcification	**Absent**	17	3	2	
		68.0%	37.5%	14.3%	
	Present	8	5	12	**0.005**
		32.0%	62.5%	85.7%	
	Total	25	8	14	
		100.0%	100.0%	100.0%	
Architecture distortion	**Absent**	23	7	5	
		92.0%	87.5%	35.7%	
	Present	2	1	9	**0.0001**
		8.0%	12.5%	64.3%	
	Total	25	8	14	
		100.0%	100.0%	100.0%	
Asymmetry	**Focal**	15	3	3	
		60.0%	37.5%	21.4%	
	Global	4	0	2	
		16.0%	0.0%	14.3%	**0.049**
	Developing	0	1	4	
		0.0%	12.5%	28.6%	
	None	6	4	5	
		24.0%	50.0%	35.7%	
	Total	25	8	14	
		100.0%	100.0%	100.0%	

Associated sonographic features, including ductal changes, calcifications, architectural distortion, posterior shadowing, hypervascularity, and absence of cysts, showed significant associations with malignant histopathology (Table 7) (Figures 1 and 2).

Discussion

This study aimed to evaluate the characterization of breast NML on ultrasound and correlate these findings with histopathological results. The patient cohort, with a mean age of 47 ± 12 years, mirrors the demographic profile identified in literature, where middle-aged women are significant for breast cancer screening [6]. Advanced us machine

Table 7. Association between associated sonographic features and histopathology result.

Variables		Histopathology result			
		Benign	Benign with upgrade potential	Malignant	*p*-value
Ductal changes	**Absent**	20	4	2	
		60.6%	50.0%	14.3%	**0.014**
	Present	13	4	12	
		39.4%	50.0%	85.7%	
Calcification	**Absent**	31	2	2	
		93.9%	25.0%	14.3%	**0.0001**
	Present	2	6	12	
		6.1%	75.0%	85.7%	
Architecture distortion	**Absent**	30	8	8	
		90.9%	100.0%	57.1%	**0.007**
	Present	3	0	6	
		9.1%	0.0%	42.9%	
Posterior shadowing	**Absent**	28	8	6	
		84.8%	100.0%	42.9%	**0.002**
	Present	5	0	8	
		15.2%	0.0%	57.1%	
Hypervascularity	**Absent**	29	6	7	
		87.9%	75.0%	50.0%	**0.02**
	Present	4	2	7	
		12.1%	25.0%	50.0%	
Cysts	**Absent**	25	8	14	
		75.8%	100.0%	100.0%	**0.044**
	Present	8	0	0	
		24.2%	0.0%	0.0%	
	Total	33	8	14	
		100.0%	100.0%	100.0%	

has better resolution and image processing in addition to many tools that make the dx more easy and confident NML is a new Ultrasound descriptor for breast lesion found at ultrasound examinations and added to American College of Radiology breast. So when there is focal asymmetry or architectural distortion at mammography and do us show no detected mass instead show non-mass area at US. Good percentage of them diagnosed as proliferative fibrocystic changed and papilloma's and ductal ca in situ. The prevalence of breast lesions was highest in the 41–50 age group (30.9%), followed by those over 60 years (23.6%), which is consistent with data indicating increased breast pathology risk with age [7]. The study observed that 80% of the patients underwent diagnostic imaging due to clinical symptoms, such as palpable lesions (29.1%) and breast pain (27.8%), paralleling findings that the pain and discomfort levels during the mammography screening were higher than those observed pre- and post-screening. Post-screening, residual irritation persisted. Participants during the mammography examination reported that state anxiety was positively correlated with pain and psychoticism with unpleasantness [8]. Additionally, 18.2% of the participants were asymptomatic and engaged in screening, emphasizing the importance of routine breast cancer screening as in American Cancer Society state that all females must have breast screening [9]. Ultrasound findings showed that focal lesions were most prevalent (38.2%), with hypoechoic lesions being common (47.3%). Mixed echogenicity was observed in 40% of lesions, Alikhassi et al. [10] agreed and highlighting the need for a comprehensive diagnostic approach. Histopathologically, 60% of lesions were benign, 25.5% malignant, and 14.5% had upgrade potential, aligning with the established understanding that most breast lesions are benign but may require further investigation similar to Sickles et al. [11] stated that most of breast lesions are benign but must follow up regularly. This study found that focal asymmetry, architectural distortion, and the lack of calcifications in most breast lesions are common mammographic features. Focal and Global Asymmetry: 44.7% of patients had focal asymmetry on mammography, whereas 12.8% had global asymmetry, highlighting breast imaging's diagnostic problems. Focal asymmetry may signal disease but not cancer. This supports previous research showing localised asymmetry may indicate benign or malignant diseases and require further imaging or biopsy [12]. Though rare, global asymmetry may indicate broad pathogenic processes and requires thorough investigation [13]. Architectural Distortion: Malignancy is typically linked with architectural distortion, which is present in 53.2% of patients [14]. A biopsy may be needed to diagnose invasive cancer in architectural deformation without a recognized etiology, such as past surgery. This cohort's significant architectural distortion rate supports Sickles et al. [11]'s claim that it predicts breast cancer. Calcifications: Mammography detects a variety of breast abnormalities, since 74.5% of patients had no calcifications. Calcifications are typically linked with benign diseases and malignancies such as ductal carcinoma in situ (DCIS), but their absence does not preclude severe underlying pathology [15]. Calcifications vary across breast

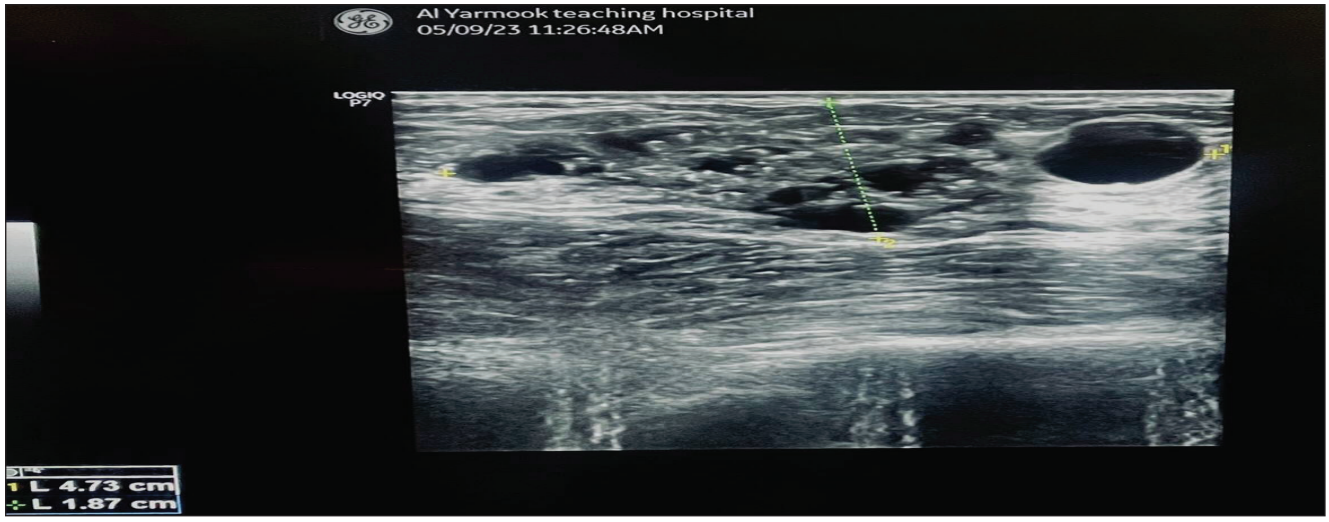


Figure 1. 30 years old patient presented with nodularity. Ultrasound showing heterogeneous non-mass finding with regional distribution and associated with multiple conglomerate cysts and calcific foci, histopathology result was (A proliferative fibrocystic changes).

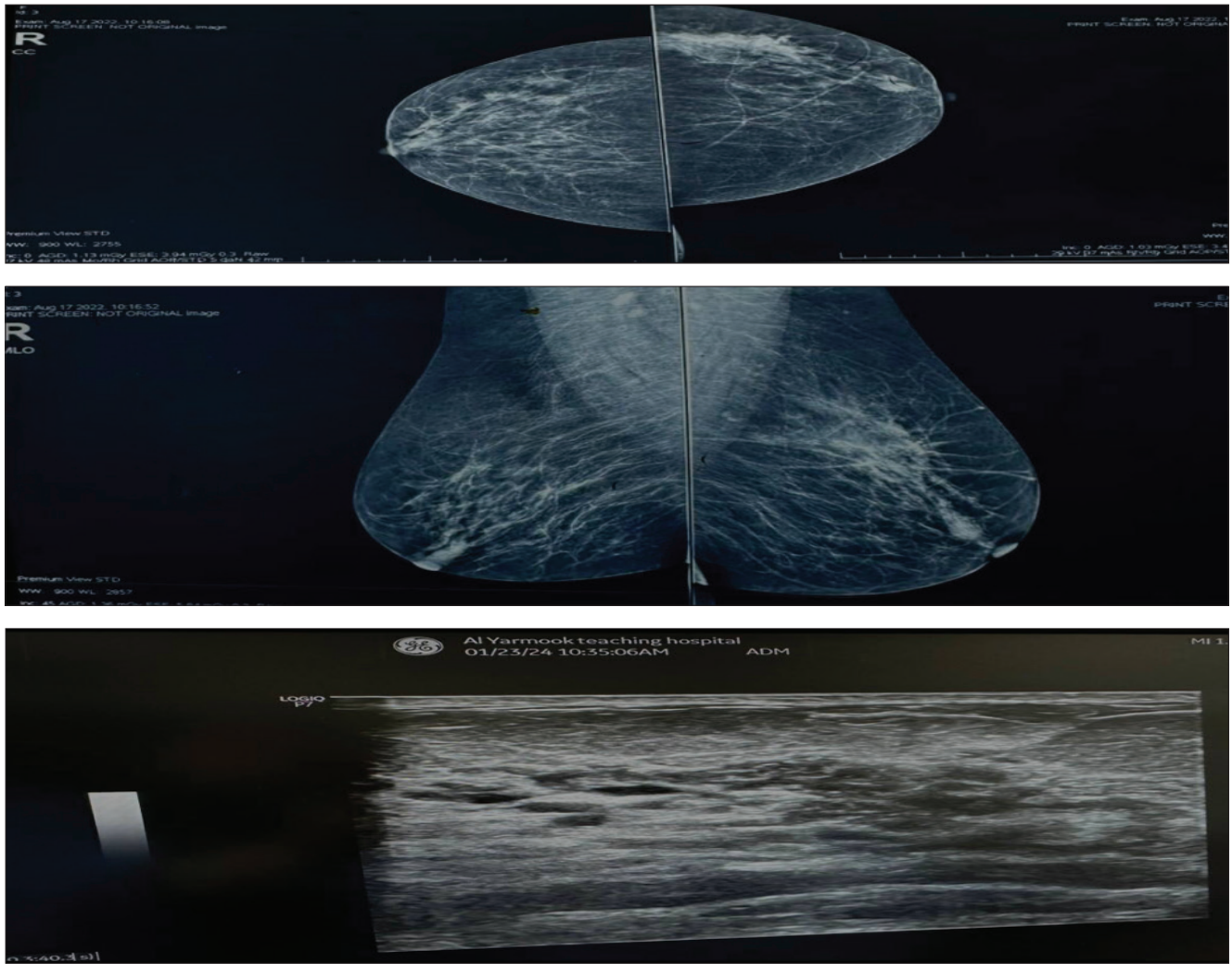


Figure 2. 63 years old patient presented with nipple discharge, mammography (CC and MLO views) (A) showing focal asymmetry at upper outer quadrant of left breast, ultrasound (B) showing heterogeneous non mass finding with segmental distribution consistent from multiple thick wall dilated ducts associated with multiple dilated retroareolar ducts showing thick internal contents, histopathology was [Atypical IDP with (DCIS)].

lesions, so a comprehensive diagnostic approach that includes mammography, ultrasound, and magnetic resonance imaging is necessary for a more accurate diagnosis. This study sheds light on patient age, clinical presentation, ultrasonography characteristics, and histological results in breast lesion assessment.

The lack of a significant correlation between age group and histopathological results may seem contradictory, considering the well-documented rise in breast cancer risk with age [16]. This highlights the variability of breast illnesses and the fact that benign and malignant tumors can arise at any age. It implies that while age is a risk factor for breast cancer, other specific features influence a breast lesion's histological type. Clinical History and Histopathology: Regional palpability strongly predicts histopathological results. Clinical examination is crucial in breast lesion assessment, since 92.9% of malignant lesions had regional palpability [17]. Ultrasound Lesion Distribution and Histopathology: The significant correlation between ultrasound lesion distribution and histopathology, with segmental distribution predominantly seen in malignant lesions, reinforces the value of ultrasound imaging characteristics in predicting lesion pathology. The significance of asymmetry, particularly focal asymmetry, as a potential indicator of malignancy, supports the need for vigilant analysis of mammographic images [11]. Conversely, the predominance of focal distribution among benign lesions aligns with the localized nature of many benign entities such as fibroadenomas or simple cysts. Segmental distribution suggests ductal involvement, which is consistent with the growth patterns of many breast cancers, including DCIS and invasive ductal carcinoma (IDC) [18]. The substantial relationships between sonographic characteristics and malignant histology demonstrate ultrasound's subtle ability to detect and characterise malignant breast lesions. Identification of sonographic indicators including ductal changes, calcifications, architectural deformation, posterior shadowing, hypervascularity, and cyst absence are critical to breast cancer diagnosis and decision-making. Ductal alterations and Calcifications: Breast ductal alterations and calcifications on sonography suggest intraductal processes like DCIS and IDC. These results support studies that have linked ductal changes and calcifications to malignancies, emphasising their relevance in cancer detection [15,19]. Architectural distortion, posterior shadowing: Invasive breast tumours are associated with sonographic features such as architectural distortion and posterior shadowing. These traits indicate an aggressive pathology that may alter tissue planes [20]. Architectural deformation and posterior shadowing may indicate cancer, necessitating additional diagnosis [21]. The relationship between ultrasonography hypervascularity and malignant histology is congruent with cancer biology, which commonly exhibits increased blood flow due to angiogenesis. Since cancers have a richer vascular network, this helps distinguish them from benign lesions [22]. The lack of cysts in malignant lesions reflects the solid nature of most breast cancers. Malignant lesions, which are solid, require closer inspection [11]. The study reinforces the importance of a multimodal imaging approach in the accurate characterization and diagnosis of breast lesions. The limitations of the current study. Include biases such as the ultrasound machine's limitations, the tiny sample size, and the single-center study.

Conclusion

The integration of advanced ultrasound technology into breast screening has led to more frequent detection of NMLs, which are subtle but potentially significant in early cancer detection. However, the increased identification of NMLs raises concerns about false positives, highlighting the need for standardized interpretation methods. Future studies should focus on correlating NML ultrasound findings with histopathology to refine diagnostic accuracy. End with the key findings, especially which ultrasound features (e.g., segmental distribution) were the most predictive of malignancy.

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