Assessment of lesions suspected calcifications in breast cancer patients through mammography and ultrasound images

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ABSTRACT

Background: Imaging plays a key role in modern medicine. It helps doctors assess the condition of tumours, thereby effectively supporting diagnosis and providing appropriate treatment regimens.

Objectives: This study aimed to describe some ultrasound and mammography characteristics of suspected calcified breast lesions; and determine the extent of breast lesions according to BIRADS-5 classification.

Methods: A cross-sectional prospective study was conducted with 71 women diagnosed with breast cancer at the Vietnam National Cancer Hospital from August 2022 to August 2023. All participants underwent mammography and breast ultrasound to assess the stage of cancer lesions based on BIRADS-5 criteria and to identify clinically suspected calcified lesions. The data were analysed using descriptive statistics and Chi-square tests, with a significant level set at p-value <0.05.

Results: The study showed that breast tissue density was mainly type C (90.1%), and the most common suspected calcification was polymorphic calcification (45.1%). Lobular distribution was the most common (49.3%) while asymmetric lesions (6.2%) and structural inversion (4.2%) were rare. Mass lesions accounted for the majority (60.6%). The distribution of mass lesions, non-mass lesions, and histopathological types was statistically significant (P=0.001). Malignant lesions often had increased density on mammography (71.8%), decreased echogenicity on ultrasound (60.6%), irregular shape (95.3%), and spiculated edges (53.4%). In addition, most tumours were classified as BIRADS 5 (40.8%), and BIRADS 4C (39.4%), and there was a difference in the proportion of BIRADS classification and histopathological lesion type (P=0.003).

Conclusion: The preliminary results of the study revealed a distinct difference in the imaging features observed in mammography and ultrasound for diagnosing breast lesions. Consequently, utilizing a combination of mammography and ultrasound is essential for accurate BIRADS classification, which in turn facilitates tailored prognosis and treatment plans for each patient.

Keywords: Breast cancer, Calcifications, Lesions, Mammography, Ultrasound

1. Introduction

Breast cancer is the most prevalent cancer and one of the leading causes of cancer-related deaths among women globally [1-2]. In 2020, there were over 2.3 million new cases of breast cancer worldwide [1]. In Vietnam, breast cancer is the most common cancer among women, accounting for 25.8% of cases [2].

Various imaging techniques are used in diagnosing breast cancer, with mammography considered the gold standard for early detection, capable of reducing mortality by 15-26% [3]. One key feature, microcalcifications, can indicate malignancy even without symptoms, accounting for 35–45% of non-palpable cancer lesions detected by mammography [4]. Ultrasound, while not effective for detecting microcalcifications, can help distinguish between cystic and solid masses and is useful in dense breast tissue [5].

However, it is operator-dependent and may underestimate malignancy, as up to 50% of cancers appear benign on ultrasound [6]. Studies show that calcifications visible on both mammography and ultrasound are more likely malignant and should be biopsied [7]. The detection rate of calcifications via ultrasound ranges from 23% to 49%, lower than mammography due to image noise and limited contrast resolution [8-9]. Recent studies suggest that combining both methods improves diagnostic performance. For instance, combined imaging increased accuracy from 87% to 94% in Japan [10], and improved cancer detection by 1.9 per 1,000 women in Korea while reducing unnecessary biopsies [11]. Thus, integration of mammography and ultrasound enhances breast cancer screening outcomes.

In Vietnam, most breast cancer patients are diagnosed using a combination of mammography and ultrasound imaging, typically guided by specific indications. Consequently, this study was conducted to 1) describe various ultrasound and mammography characteristics of suspected calcified breast lesions; and 2) assess the extent of breast lesions according to the BIRADS 5 classification.

2. Methods

2.1. Study Design

A cross-sectional prospective study was conducted in the Diagnostic Imaging Centre, Vietnam National Cancer Hospital (Tan Trieu establishment) from August 2022 to August 2023, and this study was in accordance with the STROBE

(Strengthening the Reporting of Observational Studies in Epidemiology) checklist (https://www.strobe-statement.org).

2.2. Sampling

All woman hospitalized at the Diagnostic Imaging Centre, Vietnam National Cancer Hospital (Tan Trieu establishment) with a new diagnosis of breast cancer.

Inclusion criteria: Female patients diagnosed with breast cancer; those who require mammography and ultrasound; and those with complete medical records.

Exclusion criteria include women with serious chronic illnesses and those who chose not to participate in the study.

2.3. Data collection process and methods

Equipment: Mammography machine, medical records, PACS system to store patient images; and Ultrasound machine with high-frequency linear probe (ideally higher than 10 MHz).

Data collection method: Characteristics of breast lesions assessed by mammography are described according to BIRADS 2013, including information on tumour density, tumour shape, border, presence or absence of structural inversion, and presence or absence of asymmetry. In addition, mammography results also assessed the shape and distribution of suspected calcifications.

Ultrasound evaluation results included whether the tumour forms a mass or not, echogenicity, size, border, and shape.

Based on the above results, the tumour was classified according to BIRADS 2013 regulations [19] (from grade 3 to 5) as follows:

BIRADS 3 (likely benign): 2% risk of malignancy

BIRADS 4A (low suspicion): risk of malignancy >2% to 10%

BIRADS 4B (moderate suspicion): risk of malignancy >10% to 50%

BIRADS 4C (high suspicion): risk of malignancy >50% to <95%

BIRADS 5 (likely malignant): ≥95% risk of malignancy [12].

2.5. Data Analysis

Data were analysed using SPSS version 20.0. Descriptive statistics were employed to summarize the variables, and the Chi-square test was utilized to compare proportions. For variables with small frequencies ($n < 5$), Fisher's Exact Test was applied to ensure the reliability of the analysis. For continuous variables, the Independent T-test was used to compare differences. A P-value of ≤ 0.05 was deemed statistically significant.

3. Results

3.1. Participants' characteristics

Among 71 patients, the mean age was 50.7±11 years. In each age group, the highest rate of malignancy was found in the group from 40 to 60 years old (52.1%). There were no benign lesions in the group > 60 years old. In addition, 54.9% of the lesions were on the left breast, and the malignant rate in the left breast was higher than that in the right breast (96.5%). The most common location of lesions was in the upper outer quadrant (57.7%), and the upper inner quadrant (22.5%). The upper outer quadrant had the highest rate of malignant lesions (53.5%) (Table 1).

Table 1: General characteristic of breast cancer women (n=71).

Contents	Benign n (%)	Malignant n (%)	Total n (%)
Age		**50.7±11**	
< 40	2 (2.8)	15 (21.1)	17 (23.9)
40 – 60	1 (1.4)	37 (52.1)	38 (53.5)
> 60	0 (0.0)	16 (22.6)	16 (22.6)
Tumor distribution			
Right breast	2 (2.8)	30 (42.3)	32 (45.1)
Left breast	1 (1.4)	38 (53.5)	39 (54.9)
Tumor location			
¼ upper outer	3 (4.3)	38 (53.5)	41 (57.8)
¼ upper inner	0 (0.0)	16 (22.5)	16 (22.5)
¼ lower inner	0 (0.0)	4 (5.6)	4 (5.6)
¼ lower outer	0 (0.0)	10 (14.1)	10 (14.1)

3.2. Characteristics of lesions and suspected calcified lesions on mammography and ultrasound

The results of Table 2 showed that among 71 patients, 64 had lesions belonging to density type C (90.1%), and the number of benign and malignant lesions was the highest in this density group. The most common suspected calcification lesion morphology was polymorphous (45.1%), and 32 (45.1%) malignant lesions were also in this group. Regarding tumour distribution, region, lobe and branching distributions were malignant lesions (84.4%). In the malignant lesion group, the lobular distribution had the highest number (49.3%). There were only 3 calcification lesions accompanied by structural inversion among the total 71 lesions (4.2%), and all 3 of these lesions were malignant. 95.8% of benign and malignant lesions were in the non-asymmetric group. Suspicious calcifications with increased density on mammography and all were malignant (71.8%). The proportion of mass lesions (60.6%) and malignant lesions (93.9%) was the majority. Of the 43 mass lesions, 41 were irregular in shape and all were malignant (95.3%). Regarding lesion size, lesions with a size of 20-50 mm accounted for the highest proportion (49.3%).

In addition, the study also found that the distribution of mass lesions, non-mass lesions, and histopathological types was statistically significant. Specifically, there was a difference in breast tumour morphology (P=0.008), tumour distribution (P=0.029), asymmetrical (P=0.025), intensity of lesions (P=0.02), type of lesions (P=0.001), the shape of mass lesions (P=0.001), and shoreline of mass lesions (P=0.002) and tumour histopathology (benign and malignant) (Table 2).

Table 2: Characteristics of lesions and suspected calcified lesions on mammography and ultrasound (n=71).

Contents		**Benign n (%)**	**Malignant n (%)**	**Total n (%)**	**P-value**
Breast tissue density[a]	B	0 (0.0)	6 (8.5)	6 (8.5)	0.261*
	C	3 (4.2)	61 (85.9)	64 (90.1)	
	D	0 (0.0)	1 (1.4)	1 (1.4)	
Morphology[a]	Coarse heterogeneous	2 (2.8)	0 (0.0)	2 (2.8)	0.008*
	Amorphous	1 (1.4)	21 (29.6)	22 (31.0)	
	Polymorphous	0 (0.0)	32 (45.1)	32 (45.1)	
	Straight	0 (0.0)	15 (21.1)	15 (21.1)	
Tumour distribution[a]	Cluster	3 (4.2)	8 (11.3)	11 (15.5)	0.029*
	Region	0 (0.0)	22 (31.0)	22 (31.0)	
	Lobe	0 (0.0)	35 (49.3)	35 (49.2)	
	Branching	0 (0.0)	3 (4.2)	3 (4.2)	
Structural inversion[a]	Yes	0 (0.0)	3 (4.2)	3 (4.2)	0.500*
	No	0 (0.0)	68 (95.8)	68 (95.8)	
Asymmetrical[a]	Yes	1 (1.4)	26 (36.6)	27 (38.0)	0.025*
	No	2 (2.8)	42 (59.2)	44 (62.0)	
Intensity of lesions[a]	Increase	0 (0.0)	51 (71.8)	51 (71.8)	0.02*
	Equal	3 (4.2)	17 (14.0)	20 (28.2)	
Type of lesions[a]	Mass	2 (4.7)	41 (55.9)	43 (60.6)	0.001*
	Unmass	1 (1.4)	27 (38.0)	28 (39.4)	
Tumour echogenicity[b]	Reduction	2 (2.8)	41 (57.8)	43 (60.6)	0.851*
	Mix	1 (1.4)	27 (38.0)	28 (39.4)	
Lesion shape *(only included in the mass group, with n=43)*[a]	Irregular	0 (0.0)	41 (95.3)	41 (95.3)	0.001*
	Oval	2 (4.7)	0 (0.0)	2 (4.7)	
Shoreline *(only included in the mass group, with n=43)*[a]	Clear	2 (4.7)	0 (0.0)	2 (4.7)	0.002*
	Unclear	0 (0.0)	8 (18.7)	8 (18.7)	
	Polyarches	0 (0.0)	10 (23.2)	10 (23.2)	
	Spinatus	0 (0.0)	23 (53.4)	23 (53.4)	
Lesion size[b]	**Classification by group**		**Classification by mass-forming properties (mm)**		
	≤ 20 mm	28 (39.4)	Mass	24.42±11.48	0.065**
	20-50 mm	35 (49.3)	Unmass	35.46±21.23	

Contents		Benign n (%)	Malignant n (%)	Total n (%)	P-value
	> 50 mm	8 (11.3)			

[a] resulted by mammography; [b] resulted by ultrasound.

*Fisher's Exact Test; **Independent sample T-test

The image demonstrated an iso-dense mass with poorly defined (ill-defined) margins. Internal calcifications are present, characterized predominantly by coarse and amorphous patterns distributed within the lesion (Figure 1).

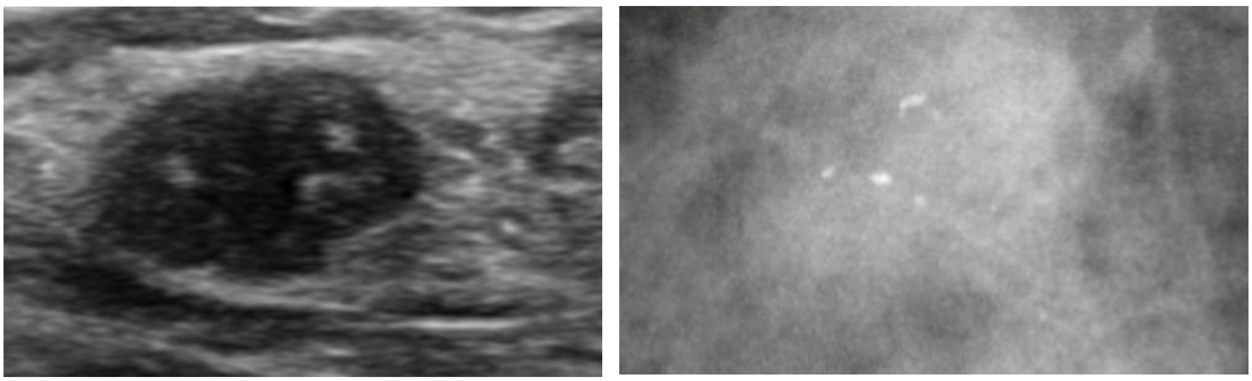

Figure 1: Calcification imaging results of patient NTN, 53 years old. Image: iso-density mass, unclear edges, calcification is mainly coarse and amorphous calcification within the mass

3.3. Classification of lesions according to BIRADS-5

Table 3 indicated that the majority of tumours were classified as BIRADS 5 (40.9%) and BIRADS 4C (39.4%). All three benign lesions were classified as BIRADS 4B. Notably, all lesions classified as BIRADS 4C and BIRADS 5 were found to be malignant. Additionally, there was a significant difference in the proportions of BIRADS classifications and the types of histopathological lesions, with a P-value of 0.003.

Table 3: Classification of lesions according to BIRADS-5 (n=71).

Classification of BIRADS	Benign n (%)	Malignant n (%)	Total n (%)	P-value
4A	0 (0.0)	0 (0.0)	0 (0.0)	0.003
4B	3 (4.2)	11 (15.5)	14 (19.7)	
4C	0 (0.0)	28 (39.4)	28 (39.4)	
5	0 (0.0)	29 (40.9)	29 (40.9)	

4. Discussion

4.1. Participants' characteristics

In our study, the mean age of the patients was 50.7 years, which is consistent with the mean age in studies of Asian women [13-14]. The most common age group was 40-60 years, which was also the age group with the highest number of malignant lesions.

In addition, 54.9% of the lesions were on the left breast, and the malignant rate in the left breast was higher than that in the right breast (96.5%). This difference is higher than that in the study of *Cheng SA et al.* with a rate of about 5% [15]. Amer's study showed that 343 (50.9%) patients had left breast cancer, 311 (46.1%) had right breast cancer, and 20 (3.0%) had bilateral malignancy [16]. According to *Perkins et al.,* breast cancer was about 5% more likely to be diagnosed in the left breast than in the right breast [17]. The left-sided predominance was evident in both young (<45 years) and older women, as well as in men with in-situ or invasive cancer. The difference in the proportion of left and right breast cancers in our study compared to other studies may be explained by our different sample sizes and the inclusion criteria for the type of lesions in our study including only lesions containing calcification.

The most common location of lesions was in the upper outer quadrant (57.7%), and the upper inner quadrant (22.5%). The upper outer quadrant had the highest rate of malignant lesions (53.5%). This result was similar to the study of *Rummel et al.* [18]. The explanation for the frequency of tumours in different quadrants of the breast, Chan's study showed that the order of breast volume and density in the 4 quadrants was: upper outer quadrant > upper inner quadrant > lower outer quadrant > lower inner quadrant [19]. Breast cancers are most likely to occur in the upper outer quadrant, which is also the quadrant with the highest volume and density [18]. However, the amount of breast tissue in a particular quadrant cannot explain the predominance of breast cancers occurring there.

4.2. Characteristics of lesions and suspected calcified lesions on mammography and ultrasound

The study found that among 71 patients, 64 patients had lesions belonging to density type C (90.1%), and the number of benign and malignant lesions was the highest in this density group. This result is similar to the study of *Li et al. (2019)* in China [20] but is much higher than the study of *Sprague et al. (2014)* in the America [21]. This result showed that the difference in breast tissue density among different races is different.

The most common suspected calcification lesion morphology was polymorphous (45.1%), and 32 (45.1%) malignant lesions were also in this group. This result was similar to other studies [19, 22]. It can be explained that the polymorphic and linear calcification lesions in our study were mostly accompanied by mass lesions [19], calcifications were observed on both ultrasound and mammography, thus increasing the risk of the lesion being malignant [22].

Lobular calcifications are described as calcium deposits that conform to the expected distribution of one or more ducts and their branches, often radiating toward the nipple. Regarding tumour distribution, all 3 benign lesions belonged to the cluster distribution group (4.2%), and all the zonal, lobular, and branching distributions were malignant lesions (84.4%). In the malignant lesion group, the lobular distribution had the highest number (49.2%). However, regardless of their morphology, lobular or branching distributions of calcifications were twice as likely to be associated with malignancy as any other morphology [23].

Structural inversion is the third most common mammographic appearance of nonpalpable breast cancer lesions after microcalcifications and asymmetry, accounting for nearly 6% of abnormalities detected on mammography [24]. There were only 3 calcification lesions accompanied by structural inversion among the total 71 lesions (4.2%), and all 3 of these lesions were malignant. Besides, the non-asymmetric group had a higher proportion than the asymmetric group. 95.8% of benign and malignant lesions were in the non-asymmetric group. This proportion in our study was similar to *Hanafy et al. (2023)* [25]. Ultrasound is a valuable adjunct to radiography in diagnosing asymmetry. However, a normal ultrasound result does not exclude malignant lesions in cases of asymmetry on radiography [26].

Suspicious calcifications with increased density on mammography were the most common and all were malignant (71.8%). The malignant rates of the increased density and iso-density groups in our study were higher than *Woods et al. (2011)* [24]. The difference between Woods' study and ours was due to the criteria for selecting lesions. We selected lesions with calcification, Woods selected patients without calcification to evaluate the sole association of lesion density and malignancy risk. Woods' study showed that high lesion density was significantly associated with and was an important predictor of malignancy [27].

The proportion of mass lesions (60.6%) and malignant lesions (93.9%) was the majority, and the lesions were hypoechoic on ultrasound in the majority (60.6%). The study also showed that non-mass lesions were associated with malignancies [28]. *Lee et al. (2016)* reported that the malignant potential of non-mass lesions on breast screening ultrasound was >2% and they could be classified as BIRADS category 4A lesions [29]. According to *Uematsu et al. (2023)*, these lesions with calcification on ultrasound tend to be malignant and should be classified as suspicious and require biopsy [30].

Of the 43 mass lesions, 41 were irregular in shape and all were malignant (95.3%), while the spiny border group accounted for the largest proportion (53.4%). The high proportion of malignant lesions in the irregular-shaped group was due to the fact that the lesions were accompanied by many other features suggestive of malignancy, and the border was the most clearly distinguishing morphological criterion between benign and malignant masses. Regarding lesion size, lesions with a size of 20-50 mm accounted for the highest proportion at 49.3% and the mean diameter in the non-mass group was larger than that in the mass group. This result is similar to the study of *Avdan et al (2021)* according to which with tumours ≥ 19.5 mm, tumour size increased linearly as the distribution of microcalcifications changed from clusters to linear, lobular distribution ($P < 0.001$) [31].

4.3. Classification of lesions according to BIRADS 5

In our study, combining both mammography and ultrasound to classify BIRADS, the malignancy rate of BIRADS types 4B, 4C, and 5 was 78.6%, 100%, and 100% ($P = 0.003$), respectively, higher than the theoretical prediction value. This was due to our initial sample selection, the calcifications were observed on both mammography and ultrasound, and there were many other signs of malignancy. In the study of *Berg et al. (2012),* it was shown that when ultrasound was combined with mammography, the sensitivity increased to 76% compared to mammography alone (52%) or ultrasound (45%) [32]. Similarly, *Buchberger et al. (2018)* reported that the combination of mammography and ultrasound for the detection of breast cancer increased the sensitivity from 62% (mammography alone) to 81% in women with dense breast tissue [33]. In another study by *Lee et al. (2019),* ultrasound added to mammography increased the sensitivity from 74% to 79%, while the specificity decreased from 98% to 95%, although these differences were not significant [34]. One possible reason for the decreased specificity is that ultrasound may diagnose some lesions that mammography does not detect, especially in women with dense breast tissue. *Stavros et al. (1995)* reported that ultrasound had a high sensitivity and positive predictive value for the diagnosis of breast cancer, 98.4% and 99.5%, respectively [35]. However, the use of ultrasound as an adjunct to mammography for screening breast cancer remains controversial. One of the important reasons is the relatively low positive predictive value and/or high negative predictive value associated with the detection of lesions on ultrasound [33].

The study found some limitations. First, the study was conducted at a single site, which may reduce the generalizability of the findings to other populations or settings with different demographic characteristics, healthcare conditions, or organizational models. Second, the use of convenience sampling may lead to selection bias, as the sample was not randomly selected but based on the availability and accessibility of participants, potentially affecting the representativeness and reliability of the study results. Therefore, future studies consider conducting in multiple sites or institutions to enhance the representativeness and generalizability of the findings. Additionally, employing probability sampling methods, such as stratified random sampling, can help minimize selection bias and improve the reliability of the results.

5. Conclusion

The study found that most breast tissues were type C, with polymorphic calcifications being the most common. Lobular distribution was the most frequent calcification pattern, and both calcification morphology and histopathological type showed significant differences. Mass lesions predominated, while asymmetric and architectural distortions were less common. These lesion types and their distribution also showed statistical significance with histopathology. Malignant lesions often appeared as dense areas on mammography, hypoechoic on ultrasound, with irregular shapes and spiculated margins. Most tumours were classified as BIRADS 5 or 4C, with a notable correlation between BIRADS categories and histopathological types. Overall, the study highlighted distinct imaging features between mammography and ultrasound, reinforcing the need to combine both methods for accurate BIRADS classification, diagnosis, and treatment planning.

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Author Contribution

NDL: Conceptualization, data curation, formal analysis, methodology, writing - original draft, writing - review and editing.
PQL: Conceptualization, methodology, supervision, writing - original draft, writing - review and editing.

Declaration

Ethics approval and consent to participate

The study received approval from the Vietnam National Cancer Hospital (Tan Trieu establishment) under Decision No. 75/GCN-HDDD, dated July 22, 2023. All participants were informed about the study's purpose and content, and those who consented were asked to sign a consent form before completing the questionnaire. Participants were free to withdraw from the study at any time without consequences. The study was designed to ensure that it did not interfere with the participants' health or well-being.

Competing interests

There are no conflicts of interest in this study.

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