

Comparative study of multiple breast cancer screening methods in the evaluation of breast non-mass-like lesions

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Abstract

Objective: To compare multiple breast cancer screening methods for evaluating breast non-mass-like lesions (NMLs) and to investigate the best screening method for breast non-mass-like lesions (NMLs).

Methods: This retrospective study examined 253 patients aged 24 to 68 years who were diagnosed with breast NMLs from April 2017 to December 2019. All lesions were evaluated by MG, HHUS, and ABUS to determine BI-RADS classification, underwent pathological examination within six months or at least 2 years of follow-up. The sensitivity, specificity, accuracy, positive predictive values (PPV), and negative predictive values (NPV) of MG, HHUS, and ABUS features in the prediction of malignancy were compared. Independent risk factors for malignancy were assessed using non-conditional logistic regression.

Results: MG, HHUS, and ABUS findings significantly differed between benign and malignant breast NML, including internal echo, hyperechoic spot, peripheral blood flow, internal blood flow, catheter change, peripheral change, coronal features of ABUS, and structural distortion, asymmetry, and calcification in MG. ABUS was superior to MG and HHUS in sensitivity, specificity, PPV, NPV, as well as in evaluating the necessity of biopsy and accuracy in identifying malignancy. MG was superior to HHUS in specificity, PPV, and accuracy in evaluating the need for biopsy. HHUS was distinctly superior to MG in sensitivity and NPV in determining malignancy; however, specificity, PPV, and accuracy were similar. Moreover, internal blood flow, calcification, and coronal plane feature were independent risk factors in distinguishing benign and malignant lesions.

Conclusions: ABUS was superior to HHUS and MG in evaluating the need for biopsy and differentiating benign and malignant in breast NMLs. Compared to each other, HHUS and MG had their own relative advantages. Internal blood flow, calcification, and coronal plane feature were independent risk factors in identifying benign and malignant lesions.

Introduction

Mammographic screening, as an effective method for early detection of the breast cancer, can reduce mortality rate of breast cancer [1]. Ultrasound and automated breast ultrasonography (ABUS) are considered to be important complementary means for breast cancer screening by mammography, especially dense breast [2-6]. However, at least 25% of detectable breast cancer would be missed by Mammographic screening [7], including some cases of non-mass-like lesions (NMLs). Although mammographic screening cannot diagnosis breast non-mass-like lesions (NMLs), it can detect the features of NMLs which include structural distortion, asymmetry and calcification. On ultrasonography (US) , NMLs refer to lesions that have no clear boundaries ,no spatial mass effect on two or more different scanning directions[8].NMLs account for 9.21% of all breast abnormalities[9], and lesions that show ambiguous hypoechoic characteristics and architectural distortion without duct-like structure are usually defined as NML[10].

Ultrasonography and mammography can detect mass-like abnormalities as standardized by the American College of Radiology Breast Imaging Reporting and Data System atlas (BI-RADS) [11]. Currently, breast BI-RADS classification using ultrasound is not considered for detection of NML, and there are no standard NML guidelines. Recently, studies based on B-mode, color Doppler flow imaging (CDFI), and strain or shear-wave elastography to distinguish benign from malignant NMLs have demonstrated their diagnostic performance. Similar to non-mass-like enhancement on breast MRI, with the enhanced image quality of high-resolution ultrasonography and widespread use of bilateral whole-breast examinations, it is possible to detect the hypoechoic regions (NMLs) that do not meet criteria for space-occupying lesions defined by BI-RADS [12,13]. NMLs reflect a wide range of breast lesions, including benign, high-risk, and malignant lesions. High-risk lesions presenting as an NML include atypical ductal hyperplasia, lobular carcinoma in situ, papillary tumor, and squamous epithelial atypia. Squamous epithelial atypia is observed in NMLs, although absent squamous epithelial atypia has been reported [13].

In breast ultrasound, our understanding of the specific pathological features that predict malignancy is incomplete. It is true that the methods used to evaluate breast US findings vary across practices and have been somewhat intuitive. In addition, there have been few studies on the relationship between US, NML lesion and their pathological importance [10,14]. Ko KH et al.[10] classified breast NMLs into four categories based on calcification and architectural distortions, which are correlated with different BI-RADS categories. However, overlapping features make it difficult to accurately categorize breast NMLs, so tissue biopsy is required for classification. Thus, ultrasound features are helpful in reducing biopsies of benign lesions [13].

Automated breast ultrasonography, also known as automated breast volume scanning, is a new imaging technology that can provide standardized image acquisition and coronal images of the entire breast. This system received FDA clearance as an auxiliary means to screening mammography in 2008[14]. By examining the breast continuously in transverse sections, ABUS can automatically perform three-dimensional breast reconstruction and simultaneously obtain morphologic and coronal images [6]. ABUS enhances the sensitivity, specificity and accuracy of breast lesion discrimination [15]. However, few studies have examined the value of hand-held ultrasonography (HHUS) or ABUS in diagnosing breast NMLs. As we all know, different screening methods have their own advantages. However, there are few studies on the relationship among different screening methods, NML lesion findings and their pathological significances. This study compared and analyzed the evaluation of breast NMLs by three different breast cancer screening methods: mammography, HHUS, and ABUS. Our findings will make contributions to selecting effective screening methods for the detection of NMLs, and assist in reducing the incidence of misdiagnosis and NML biopsy rate.

Materials And Methods

Participants

This retrospective study examined 253 patients aged 24 to 68 years who were diagnosed with breast NMLs from April 2017 to December 2019. All patients underwent MG, HHUS, and ABUS before breast surgery or biopsy. We excluded those who did not undergo all 3 imaging studies or pathological examination or did not receive at least 2 years follow-up. Patients who had previously undergone surgery and pathological examination were also excluded.

Only patients diagnosed with breast NML were enrolled. NMLs included ill-defined geographic hypoechoic or clustered hyperechoic spots without mass and tubular hypoechoic duct-like structural or architectural distortions on HHUS. These lesions exhibited suspicious calcification, distorted structure, asymmetry, and dilated ducts on mammography. The study was carried out in accordance with the Declaration of Helsinki and approved by the Ethical committee of the first affiliated hospital, Jinan University (ZE2020-232).

NML was first detected by ultrasonography in 17 patients younger than 35 years of age who had a family history of cancer or a personal high risk of cancer. Two hundred and forty patients also underwent surgery and pathology within six months. Thirteen patients had benign NMLs, of which 5 were diagnosed according to breast MRI criteria (BI-RADS category 1, 3 cases; BI-RADS category 3, 2 cases) and 8 were diagnosed by ultrasonography and ABUS (BI-RADS category 3). No change was found at 2-year follow-up in all 13 patients after multiple reexaminations.

Imaging analysis

Mammography (MG) was performed using the Hologic-Lorad M-IV (Bedford, MA, USA). HHUS and ABUS were performed using the GE logiq E9 (GE, USA) with an ML6-15 liner probe at 10–14 MHz, Apollo 500 (CANON, JPN) with a PLT-1005BT liner probe at 10–12 MHz, and GE invenia ABUS (GE, USA) with a C15-6XW arc probe at 10 MHz. Preset ultrasonic instrument scanning conditions were used. Depth, gain and focus point were adjusted according to the thickness of the breast lesion area. The field of view was adjusted to include the area from the subcutaneous fat to the pectoral muscle layer.

The NML was located in the central region of the ultrasonography image, and two-dimensional longitudinal and transverse sections and CDFI were stored. All NML features were evaluated and recorded, including location, maximum diameter, echo pattern, structural distortion, ductal changes, microcalcification (hyperechoic, <2 mm in diameter [16]), and posterior echo. To describe the distribution of microcalcification more accurately, scattered and aggregated point hyperechoic were used.

All NMLs were classified according to BI-RADS categories [8]. CDFI was evaluated according to Adler's grade. The category in two-dimensional sonography was used as the reference for ABUS classification. However, if the coronal appearance of ABUS was consistent with mass, the lesions were classified according to the lexicon of ACR BI-RADS. All mammography and MRI feature were evaluated using the lexicon of ACR BI-RADS. (Fig. 1).

Asymmetry (MG): Female, 48 years old. Fig A: Large irregular block shadow with fuzzy and rough boundary and a large number of burr like shadows of different lengths can be seen in the right upper

breast area of MG, ACR BI-RADS 4A. Fig B: HHUS showed a patchy heterogeneous echo area in the right breast with irregular thickened duct structure. The thickened duct was hypoechoic. CDFI showed a little color blood flow signal in this area, Adler grade 2, IA grade (k.o), ACR BI-RADS 4B. Fig C: The coronal plane of ABUS in the right breast showed patchy and uneven echo area with irregular shape, fuzzy edge and uneven internal echo. ACR BI-RADS 4B. Pathology: Intraductal carcinoma.

Aggregated calcification (MG):42Y, Fig D: mammography showed multiple punctate and irregular calcification in the upper part of the right breast without distortion of local structure and obvious mass sensation. ACR MG BI-RADS 4B. Fig E: HHUS showed patchy heterogeneous echo area in the right breast with disorder of internal structure and multiple punctate hyperecho ; CDFI showed strip blood flow signal in the heterogeneous echo area, Adler grade 1.ACR US BI-RADS 4B. Fig. F: ABUS shows patchy heterogeneous echo area in the upper right breast, with irregular coronal plane shape, irregular edge, local angulation, uneven internal echo and multiple punctate hyperechogenicity. ACR US BI-RADS 5. Pathology: Breast invasive carcinoma (nonspecific type) with extensive intraductal carcinoma.

Structure distortion(MG)53Y, Fig G MG showed local structure distortion in the upper right breast without obvious mass and calcification, ACR BI-RADS 4A. Fig H Ultrasound showed focal heterogeneous hypoechoic area with thickened ductal structure, slightly increased blood flow signal, Adler grade 3, ACR BI-RADS 4C. Fig I ABUS showed hypoechoic mass on the coronal plane with irregular shape, irregular edge and convergence sign. ACR BI-RADS 5. Pathology: Invasive breast cancer (nonspecific type)

All examinations were performed and analyzed by two radiologists with more than 10 years of clinical experience. Based on BI-RADS guidelines, follow-up was recommended in NMLs classified as BI-RADS 1 to 3; pathological examination was recommended in those classified 4A to 5. BI-RADS 1 to 4A was considered suspicious benign; 4B to 5 was considered suspicious malignant.

Pathology analysis

According to the 2019 World Health Organization classification of tumors of the breast [16], ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS) are defined as breast precursor lesions. We included LCIS, DCIS, and other malignant tumors in the malignant and precursor lesions group. The benign lesions group included all other lesions, such as atypical ductal hyperplasia (ADH), flat epithelial atypia (FEA), and other benign lesions.

Statistical analysis

Quantitative data are expressed as means with standard deviation and categorical data as composition or rate ratios. Quantitative data were compared using the t-test or Kruskal–Wallis test as appropriate. Categorical data were compared using the chi-square test or Fisher's exact test. Influencing factors were analyzed by unconditional stepwise logistic regression. Sensitivity, specificity, and accuracy of mammography, HHUS, and ABUS for differentiating breast NMs were calculated using final pathologic

findings as the reference. Statistical analyses were performed using SPSS software version 22.0 (Chicago, USA). $P < 0.05$ was considered significant.

Results

Pathologic diagnosis of breast NML

Among the 253 study patients, 73 (28.9%) had lesions classified as malignant or precursor and 180 (71.1%) as benign. The pathologic diagnoses are presented in Table 1. Among the 73 malignant or precursor lesions, the pathologic diagnoses were invasive carcinoma in 12 (16.5%), invasive carcinoma with DCIS in 17 (23.3%), DCIS in 37 (50.7%), multiform lobular carcinoma in 3 (4.1%), multiform invasive lobular carcinoma in 1 (1.4%), and solid papillary carcinoma in 3 (4.1%). Among the 180 benign lesions, the diagnoses were hyperplasia of the breast with calcification in 38 (21.1%), hyperplasia without calcification in 23 (12.8%), hyperplasia with apocrine metaplasia in 3 (1.7%), ADH in 22 (12.2%), FEA in 7 (3.9%), sclerosing adenosis in 22 (12.2%), radial scar in 4 (2.2%), papilloma in 18 (10.0%), adenomatous hyperplasia in 21 (11.7%), stromal pseudoangiomatous hyperplasia in 1 (0.6%), adenosis with infection in 5 (2.8%), granulomatous lobular mastitis in 3 (1.1%), and 13 cases (7.2%) were considered benign after 2 years of follow-up (Fig. 2). Clustered punctate calcifications (hyperechoic punctate) were observed in 16 patients. The maximum lesion diameter was <10 mm in 68 patients and >20 mm in 64.

Table 1: Pathological findings in 253 breast non-mass-like lesions

Pathological diagnosis	
malignant or precursor	
Invasive carcinoma (non-special type)	12
Invasive carcinoma with DCIS	17
DCIS	37
Multiform lobular carcinoma	3
Multiform invasive lobular carcinoma	1
Solid papillary carcinoma	3
hyperplasia with calcification	43
benign	
hyperplasia without calcification	18
hyperplasia with apocrine metaplasia	3
Sclerosing adenosis	22
ADH	22
FEA	7
Radial scar	4
Papilloma	18
Adenomatous hyperplasia	21
Pseudoangiomatous hyperplasia of stroma	1
Adenosis with infection	5
Granulomatous lobular mastitis	2
Benign after follow-up	13

Association between imaging features and pathological diagnosis

As shown in Table 2, there were significant differences between benign and malignant breast NMLs in the following characteristics: hyperechoicity, peripheral change, ductal changes, microcalcification, posterior echo, peripheral CDFI, internal CDFI, coronal plane feature (ABUS), calcification (MG), and structural (MG). These findings indicate that these imaging features acquired by different techniques can effectively predict pathological diagnosis.

Table 2 Association between imaging features and pathological diagnosis

		Total n=253	Pathologically benign n=180	Pathologically malignant or precursor n=73		P
Internal echo	Homogeneous	24	21	3	3.454	0.063
	Heterogeneous	229	159	70		
Hyperechoic	Non	105	86	19	13.093	0.001
	Scattered spotty	83	48	35		
	Aggregated spotty	65	46	19		
Peripheral flow	Adler 0	163	139	24	67.550	<0.001
	Adler 1	50	33	17		
	Adler 2	23	5	18		
	Adler 3	17	3	14		
Internal flow	Adler 0	161	139	22	65.131	<0.001
	Adler 1	49	30	19		
	Adler 2	25	8	17		
	Adler 3	18	3	15		
Ductal change	Non	182	129	53	14.617	0.001
	Duct ectasia anechoic inside	29	28	1		
	Duct ectasia Low-echo inside	42	23	19		
Peripheral change	Non	216	167	49	29.008	<0.001
	Architectural distortion	36	12	24		
Structure distortion X-ray	Non	173	134	39	11.449	0.003
	Distortion	38	20	18		

	Disorder	42	26	16		
asymmetry	Non	223	167	56	12.826	<0.001
	Focal asymmetry	30	13	17		
Calcification	Non	53	48	5	14.107	0.001
	Scattered spotty	120	75	45		
	Aggregated spotty or cluster	80	57	23		
Coronal plane	Non	106	99	7	60.580	<0.001
	Obscure	103	67	36		

Indicative capability of different imaging techniques to evaluate the necessity of biopsy.

As shown in Table 3, MG, HHUS, and ABUS all showed significant differences in evaluating the need for biopsy in breast NMLs ($P < 0.01$). The sensitivities in evaluating the necessity of pathological examination for ABUS, HHUS, and MG were 98.6%, 95.9%, and 84.9%, respectively. Respective specificities were 53.9%, 30.6%, and 42.2%. Respective positive predictive values (PPVs) were 46.5%, 35.9%, and 37.3%. Respective NPVs were 99.0%, 94.8%, and 87.4%. Respective accuracies were 66.8%, 49.4%, and 52.2%.

ABUS was superior in sensitivity, specificity, PPV, NPV, and accuracy in evaluating the need for biopsy compared to MG and HHUS. MG was superior to HHUS in specificity, PPV, and accuracy; HHUS was superior to MG in sensitivity and NPV.

Table 3. Capability of different imaging techniques to evaluate the need for biopsy

		Total n=253	Pathologically benign n=180	Pathologically malignant or precursor n=73		P
Mammography	Follow-up	87	76	11	16.973	0.001
	Biopsy	166	104	62		
HHUS	Follow-up	58	55	3	20.558	0.001
	Biopsy	195	125	70		
ABUS	Follow-up	98	97	1	60.366	0.001
	Biopsy	155	83	72		

Diagnostic capability of different imaging techniques to determine malignant breast NML

As shown in Table 4, MG, HHUS, and ABUS all showed significant differences in determining malignant breast NML ($P < 0.01$). The sensitivities in evaluating the need for pathological examination for ABUS, HHUS, and MG were 93.2%, 89.0%, and 64.4%, respectively. Respective specificities were 77.8%, 67.2%, and 67.8%. Respective PPVs were 63.0%, 49.2%, and 44.8%. Respective NPVs were 96.6%, 93.4%, and 82.4%. Respective accuracies were 82.2%, 70.4%, and 66.8%.

ABUS was superior in sensitivity, specificity, PPV, NPV, and accuracy in determining malignant breast NML compared to MG and HHUS. HHUS was distinctly superior to MG in sensitivity and NPV but similar in specificity, PPV, and accuracy.

Table 4. Capability of different imaging techniques to determine highly suspicious malignant breast non-mass-like lesion

		Total n=253	Pathologically benign n=180	Pathologically malignant or precursor n=73		P
Mammography	Benign	148	122	26	22.128	0.001
	Malignant	105	58	47		
HHUS	Benign	121	113	8	55.890	0.001
	Malignant	132	67	65		
ABUS	Benign	145	140	5	106.799	0.001
	Malignant					

Independent risk factors predicting malignancy or precursor breast NML

Taking benign and malignant tumors as the dependent variable Y (malignant or precursor (Y=1), benign (Y=0)), possible influencing factors were considered the independent variable Xi: internal echo, punctate hyperecho, peripheral CDFI (HHUS), internal CDFI (HHUS), catheter change, peripheral change, structural distortion (MG), asymmetry (MG), calcification (MG), coronal plane feature (ABUS). The results were analyzed by unconditional stepwise logistic regression. As shown in Supplementary Table 5, the predictive coincidence rate of the regression model was 81.3%. The influencing factors, relative risk, and 95% confidence intervals (CIs) for breast malignancy or precursor lesions were CDFI (internal) for HHUS (odds ratio (OR) = 2.51, 95% CI:1.68–3.75), calcification for MG (OR = 2.21, 95% CI:1.34–3.65), and coronal plan feature for ABUS (OR= 3.90, 95% CI:2.23–6.82). These factors positively correlated with breast malignancy or precursor lesions and may be associated risk factors.

Table 5. Unconditional stepwise logistic regression analysis of factors influencing breast cancer

factor	B	S.E.	Wald	P	Exp(B)	95% CI	
						Lower	Upper
Internal flow	0.920	0.206	20.020	<0.001	2.508	1.677	3.753
Calcification	0.794	0.256	9.593	0.002	2.211	1.338	3.654
Coronal plane	1.361	0.285	22.730	<0.001	3.899	2.229	6.822
Constant	-6.782	0.950	50.973	<0.001	0.001	—	—

Discussion

Breast NMLs are usually characterized by non-oriented hypoechoic areas due to normal tissue deformation, absence of clear mass formation or layered duct-like structures. They can reflect a variety of pathological changes, such as fibrous cystic changes, fibrosis, mastitis, intraductal papilloma, ductal carcinoma in situ, invasive ductal carcinoma, and invasive lobular carcinoma.[12] Thus, further non-invasive examination is critical. Approximately 20%–25% of BI-RADS 4 breast NMLs with microcalcification are subsequently found to be malignant [18]. Although MG has been shown to reduce the incidence of breast cancer, its effect on biopsy rate is an ongoing debate [19]. In this study, we found that ABUS had the highest diagnostic sensitivity, specificity, PPV, NPV and accuracy. MG was superior to HHUS in evaluating the need for biopsy in specificity, PPV, and accuracy. However, in terms of determining malignancy, HHUS was superior to MG in sensitivity and NPV, but similar in specificity, PPV, and accuracy.

Conventional ultrasonography characteristics such as internal echo, hyperechoic spot, peripheral blood flow, internal blood flow, catheter changes, peripheral changes, as well as the coronal plane of ABUS are significant factors in the evaluation of breast NMLs and provide a theoretical basis for accurate ultrasonographic differentiation of benign and malignant lesions. MG is important in screening and diagnosing breast cancer. Its main aim is to identify densities, microcalcifications, and asymmetry [20]. Ultrasonography can assist in further characterization. Breast densities may be solid or cystic with smooth or irregular margins [21]. Microcalcifications may be focal or diffuse, and calcifications may be coarse or fine. Multifocal, fine calcifications are more likely to be malignant, whereas uniform, large, coarse calcifications are usually benign. Furthermore, they may be stable or increase over time [22], which is characteristic of NMLs. Proliferative NMLs with calcification are often classified as more dangerous and require biopsy. In this study, NMLs in 64 patients exhibited hyperplasia, including 43 cases of hyperplasia with calcification and 3 of hyperplasia with apocrine metaplasia and calcification. Among these, 23 were classified as more dangerous and biopsy was recommended.

Breast symmetry is often the most difficult to characterize, as it shows great variation between individuals as well as between the left and right breasts of the same individual and even between different breast quadrants. As the primary screening tool for breast cancer, the sensitivity of conventional MG is approximately 70% [23], and the sensitivity decreases with the increase of the quality of breast tissue assessed. Moreover, 76% of cancers are missed in women with dense breast tissue, while the overlap of normal breast tissue can lead to false-positives [24, 25].

ABUS allows non-invasive imaging of tissue using real-time sonography with high sensitivity, specificity, and accuracy [26]. At different strain levels, ABUS acquires different sonographic features of fat, normal glandular tissue, fibrous tissue, DCIS, and infiltrating ductal carcinoma [27]. Moreover, vascular distribution by CDFI provides data regarding blood supply [28]. CDFI can depict microvasculature and allows continuous dynamic observation of microcirculation. In our study, abundant blood flow was more frequently observed in malignant NMLs, similar to existing studies [10]. These features allow ABUS to differentiate various mass lesions. In comparisons of HHUS and ABUS evaluation of breast NML malignancy, most studies have reported higher sensitivity for ABUS but higher specificity and accuracy for HHUS [29], which is consistent with our findings. ABUS can focus on a lesion from three orthogonal

sections at the same time and display the accurate spatial position of the lesion in real-time, which allows a thorough and detailed evaluation [30].

In previous studies, lower diagnostic sensitivity and specificity restricted the use of ABUS [31]. Therefore, it is critical to determine independent breast NML risk factors to enhance diagnostic capability. The logistic regression model that combined NML and internal flow and coronal surfaces detected by ABUS provided a more objective and accurate method for characterizing NML. However, age is also important (breast lumps), as shown by epidemiology [32].

There are several limitations to our study. First, the differences between observers and the standardization of image storage are well-known imaging limitations. To reduce these, all imaging was retrospectively analyzed by two experienced experts while standardizing the scanning. The concise definition of descriptors was discussed, and an evidence-based consensus was reached. However, it remains necessary to standardize an accurate and specific definition of NML. Second, the study was conducted in a single institution and involved a small number of subjects, so the disease distribution was not necessarily generally representative. Further large-scale multicenter studies are warranted.

In conclusion, conventional ultrasonographic (HHUS) characteristics, such as internal echo, hyperechoic spot, peripheral blood flow, internal blood flow, catheter change, and peripheral change, as well as coronal features (ABUS), structural distortion (MG), asymmetry (MG) and calcification characteristics (MG) are significant in evaluating the risk of malignancy and need for biopsy in breast NMLs. Internal blood flow (HHUS), calcification (MG), and coronal features (ABUS) may be risk factors for malignant or precursor lesions. ABUS evaluation significantly increased the diagnostic sensitivity, specificity, PPV, NPV, and accuracy. HHUS was distinctly superior to MG in sensitivity and NPV in determining malignancy; however, MG was superior in specificity, PPV and accuracy in evaluating the need for biopsy.

Declarations

Ethic approval and consent to participate

The study was carried out in accordance with the Declaration of Helsinki and approved by the Ethical committee of the first affiliated hospital, Jinan University (ZE2020-232). Informed consent to participate was obtained from all subjects.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analyzed during the current study are not publicly available due to patient privacy protection but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author contributions

JZ conceived the research and designed the study. LiCai, LingChen, SZ, YL and WH analyzed the imaging data. JZ, MC and DY drafted the manuscript. JZ, JL and YY conducted the statistical analysis. LL reviewed the final manuscript. All authors read and approved the final manuscript.

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1. Ultrasonographic features of HHUS are significant for differentiating benign and malignant breast NMLs.
2. ABUS evaluation was associated with the highest sensitivity, specificity, PPV, NPV, and accuracy in the diagnosis of breast NMLs.
3. MG was superior to HHUS in specificity, PPV, and accuracy in evaluating the need for biopsy.
4. HHUS was distinctly superior to MG in sensitivity and NPV in determining malignancy.
5. Internal flow (HHUS), calcification (MG), and coronal plan feature (ABUS) may be risk factors for malignant or precursor lesions.

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Abbreviations

ABUS: automated breast ultrasonography; HHUS: hand-held ultrasound; NML: non-mass-like lesion; CDFI: color Doppler flow imaging; BI-RADS: Breast Imaging Reporting and Data System atlas; DCIS: ductal carcinoma in situ; LCIS: lobular carcinoma in situ

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Figures

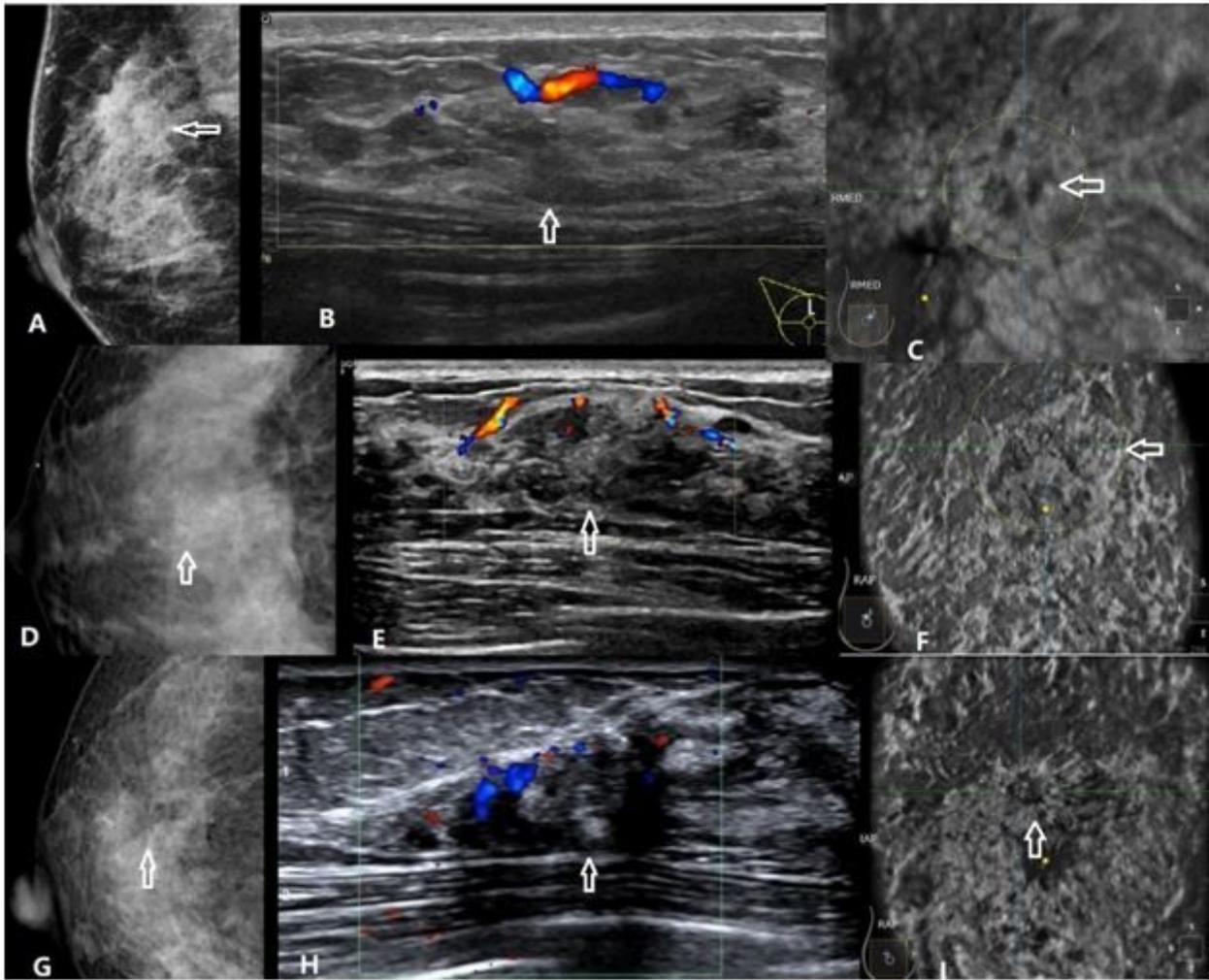
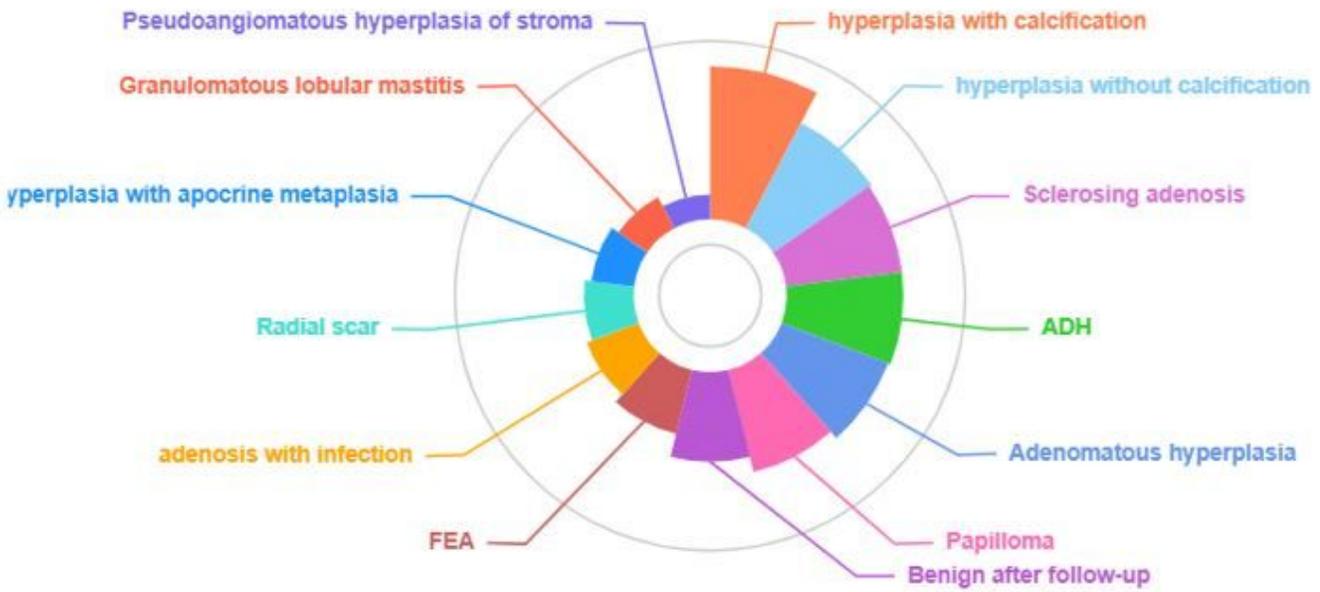


Figure 1

Hand-held ultrasonography and automated breast ultrasonography non-mass-like lesion findings with different types of mammography

Benign



Malignant

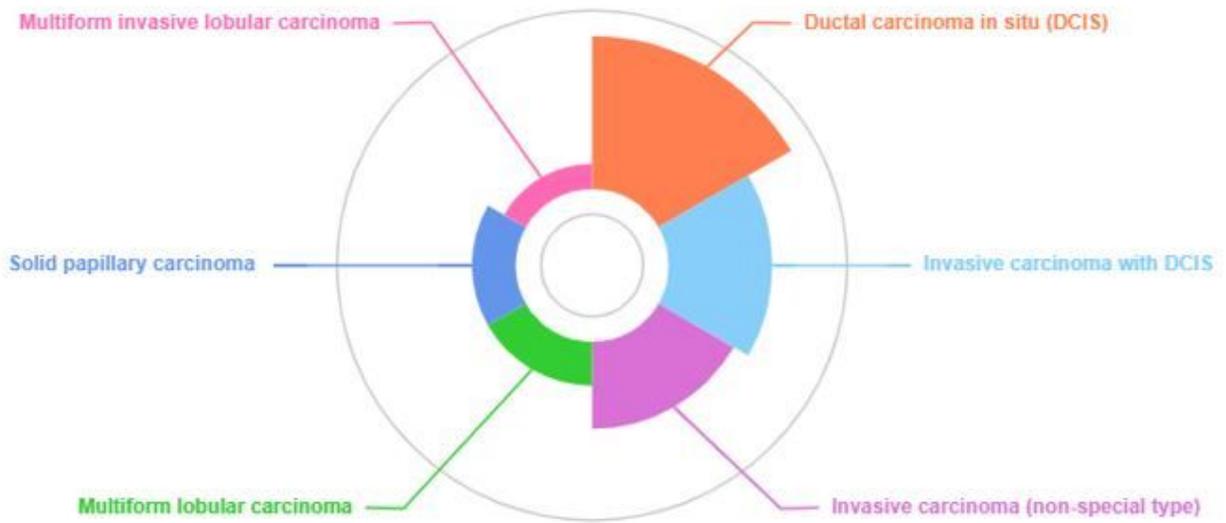


Figure 2

Nightingale rose graph of division of cases