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Breast Cancer Detection Using Automated Breast Ultrasound in Mammographically Dense Breasts

SHERINE K. AMIN, M.D.; MOHAMED G. ABDEL MUTALEB, M.D. and LATIFA E. GAD, M.Sc.

The Department of Radiodiagnosis, Faculty of Medicine, Ain Shams University

Abstract

Background: Automated Breast Ultrasound technology (ABUS) allows the radiologist to interpret ultrasonography images in a separate time after acquisition. Different interpretation times have been reported, ranging from 5 to 10min, probably according to differences in readers' experience and complexity of each case.

Aim of Study: To detect the impact of ABUS technique's advantages, pearls and pitfalls combining with mammography compared with mammography alone, significantly improved detection of breast cancers in women with dense breast tissue without substantially affecting specificity.

Patients and Methods: This cross-sectional study was conducted on of 20 women at Radiodiagnosis Department, Shoubra General Hospital referred from surgery clinic during a period of about one year. The study was limited to only females who were willingness to undergo additional investigations after being diagnosed as dense breast on mammography.

Results: We found that cases with ABUS study shows sensitivity about (60%) which is more than that of mammogram (30%) but less than HHUS (80%); while ABUS (70%) was less specific than both mammogram (100%) and HHUS (90%). Accuracy of HHUS (85%) was more than that of both mammogram (65%) and ABUS (65%), with p-value (0.257) to both mammogram and ABUS, and (0.008) to HHUS.

Conclusion: Adding automated breast ultrasound to mammography is of great value in detection of breast cancer in mammographically dense breasts. It increases the detection rate of breast lesions mostly cancer. It is important as screening tool to decrease doses of radiation that female exposed to while mammogram screening.

Key Words: *Breast cancer – Automated breast ultrasound – Dense breasts.*

Introduction

BREAST cancer is the most commonly diagnosed malignancy in women worldwide and is the second leading cause of cancer death in women in the United States. Early detection of breast cancer improves outcomes. Screening strategies for detecting early stage breast cancer are now stratified [1].

Mammography has been proven in randomized controlled trials to be a sensitive screening tool for the detection of early breast cancer. The reported sensitivity of screening mammography varies from 65% to 91% [2].

The performance of mammography is reduced for cancer detection in dense-breasted women as mammograms are summation images, with all breast tissue overlapping in each view. Cancers may not be visualized because of overlying dense breast tissue. Mammography can miss far posterior cancers in the retro-mammary space because of inadequate positioning of deep tissue [3].

Ultrasonography is currently considered the first-line examination in the detection and characterization of breast lesions including the evaluation of breast cancer. In spite of mammography consider as the primary method for screening especially the noteworthy ability of microcalcifications detection. US is good in mass or mass-like lesion detection, especially in the dense breast population [4].

Like traditional ultrasound, Automated Breast Ultrasound (ABUS) uses high-frequency sound waves targeted at the breast, but the scans provide physicians with a 3-D volumetric image of the entire breast. These 3-D images are more beneficial to women within the dense breast population because they give radiologists the ability to check the breast from a variety of angles and offer a better interpretation [5].

Automated Breast Ultrasound System is a comfortable, non-ionizing alternative to other supplemental screening options for women with dense

Correspondence to: Dr. Sherine K. Amin, The Department of Radiodiagnosis, Faculty of Medicine, Ain Shams University

breast tissue. When used in addition to mammography, ABUS can improve breast cancer detection by 55 percent over mammography alone [6].

Patients and Methods

A cross-sectional study was performed at Radiodiagnosis Department, Shoubra General Hospital. The study population consisted of 20 women of mean age (35 to 55 years) referred from surgery clinic during a period of about one year (from November 2018 to January 2020). The study was limited to only females who were willing and give consent to undergo an additional investigations.

Inclusion criteria: Dense breast on mammography.

Exclusion criteria: Patients with fatty breasts.

The clinical presentation differ among the cases, most of them presented with palpable masses (variable size), some complained of pain, mass with axillary lymph nodes and one case presented with bloody discharge.

All patients were subjected to: Full history: Including positive family history, history of breast lesions and hormonal drug intake. Also any previous imaging investigation if present should be considered. Reassurance and explanation of the steps of the study in details to patients. Informed consents were taken from all cases. Mammography study, automated breast ultrasound, hand held ultrasound were done in all cases. Histopathology was done to all cases as a gold standard to confirm diagnoses.

Technique:

Mammography was done with the (Fujifilm digital mammography system FDR MS-3500) using the small focal spot (nominal size, 0.09mm; measured size, 0.14mm) for all exposures. Patients were entered into the study only after completion of the mammography examination, which include: Contact cranio-caudal and medio-lateral oblique projection mammograms of both breasts, any additional films (magnification views) that are judged to be necessary. Mammograms were reviewed for the breast density, presence of masses with detailed analysis of its site, type, number, border, calcifications, and size. Then interpreted before selection for study. Breast sonography (Automated Breast Ultrasound) was done, after mammography examination, using the (Invenia ABUS system, GE healthcare) which consists of an automated scanner that produces serial 1.7-mm-thick high-resolution sonograms of both breasts, coupled with several efficient modes of image review. Examination of each breast with all sequences take about from 5mins (about one minute for the sweeping of the probe per view). Patient lies in the supine position, with the ipsilateral arm above the head. A lotion or gel and disposable membrane were used to aid as acoustic coupling.

Each breast was examined in three different positions, Antero-Posterior (AP), Lateral (LAT) including the pectoral muscle and medial (MED).

After scanning all quadrants of both breasts using ABUS, hand-held US was performed in all the patients. Hand held ultrasound also done using (GE ultrasound koreo, Ltd), using a 7-11MHz linear transducer. The technique performed for HHUS was done after exposure of the breasts with the patient lying supine and her ipsilateral hand raised above the head. The ultrasound probe was oriented perpendicular to the chest wall. Radial scanning technique, in a clockwise fashion, using the nipple as a center point was followed. Scanning of each breast quadrant in the sagittal and transverse planes was also performed and the examination time took about 20min for both breasts. Also scanning of axilla was performed using HHUS to detected lymph nodes, which is not available through ABUS scan.

Results of the breast history, physical examination, mammography examination, automated breast ultrasound, and hand held ultrasound were available.

Pathologic correlation was undertaken for all patients who had breast biopsy within about 7-15 days of study.

Statistical analysis:

Descriptive statistics were used in terms of frequencies (number of cases) and percentages when appropriate. Accuracy was represented using the terms sensitivity, specificity, positive predictive value, and negative predictive value. Analytic statistics using *t*-test and chi-square tests were used to compare the clinical and imaging findings obtained using pathological diagnosis as the gold standard of the detected masses.

Results

Of the 20 women included in our study, the mean patient age was 43.40 years (standard deviation, 6.19 years; range, 35-55 years) who underwent mammography, the both ABUS and HHUS followed by biopsy.

The clinical presentation differ among the cases, most of them presented with palpable masses (variable size), some complained of pain, mass with axillary lymph nodes and one case presented with bloody discharge.

Among the 20 patients studied, 10 women were found to have pathologically confirmed breast cancers.

On comparing the findings of breast biopsy and mammogram, only 10 cases were found negative by biopsy while 17 cases reported negative by mammogram.

Regarding positive cases, 10 cases were found positive by biopsy, while only 3 cases were suspected by mammogram with 30% sensitivity, 100% specificity, 100% PPV, 58.82% NPV and 65% accuracy (Table 3).

On comparing the findings of breast biopsy and HHUS, 10 cases found benign by biopsy, and 11 cases reported benign by HHUS.

Regarding malignant cases, 10 cases were found malignant by biopsy, and 9 cases were suspected by Hand Held Ultrasound (HHUS) with 80% sensitivity, 90% specificity, 88.89% PPV, 81.82% NPV and 85% accuracy (Table 4).

On comparing the findings of breast biopsy and ABUS, 10 cases were found benign by biopsy, and 11 were found benign by ABUS. Regarding malignant cases, 10 cases were found malignant by biopsy, and 9 cases were suspected by ABUS with 60% sensitivity, 70% specificity, 66.67% PPV, 63.64 NPV and 65% accuracy (Table 5).

We found that cases with ABUS study shows sensitivity about (60%) which is more than that of mammogram (30%) but less than HHUS (80%); while ABUS (70%) was less specific than both mammogram (100%) and HHUS (90%). Accuracy of HHUS (85%) more than that of both mammogram (65%) and ABUS (65%), with p-value (0.257) to both mammogram and ABUS, and (0.008) to HHUS.

Table (1): Distribution of the studied cases according to age (years) (n=20).

Age (years)	No.	%
<40	7	35.0
≥40	13	65.0
Min.-max.	35.0-55.0	
Mean ± SD.	43.40±6.19	
Median	42.50	

Table (2): Distribution of the studied cases according to clinical examination (n=20).

Clinical examination	No.	%
Mass	14	70.0
Pain	3	15.0
Mass + LNs	2	10.0
Bloody discharge	1	5.0

Table (3): Agreement (sensitivity, specificity and accuracy) for biopsy (n=20).

	Biopsy				Sensitivity	Specificity	PPV	NPV	Accuracy
	Benign (n=10)		Malignant (n=10)						
	No.	%	No.	%					
Mammogram:									
Negative	10	100.0	7	70.0	30.0	100.0	100.0	58.82	65.0
Positive	0	0.0	3	30.0					
χ_2 (FEp)	3.529 (0.211)								

Table (4): Agreement (sensitivity, specificity and accuracy) for biopsy (n=20).

	Biopsy				Sensitivity	Specificity	PPV	NPV	Accuracy
	Benign (n=10)		Malignant (n=10)						
	No.	%	No.	%					
Hand held U/S:									
Benign	9	90.0	2	20.0	80.0	90.0	88.89	81.82	85.0
Malignant	1	10.0	8	80.0					
χ_2 (FEp)	9.899* (0.005*)								

Table (5): Agreement (sensitivity, specificity and accuracy) for biopsy (n=20).

	Biopsy				Sensitivity	Specificity	PPV	NPV	Accuracy
	Benign (n=10)		Malignant (n=10)						
	No.	%	No.	%					
AB US:									
Benign	7	70.0	4	40.0	60.0	70.0	66.67	63.64	65.0
Malignant	3	30.0	6	60.0					
χ^2 (^{FE}p)	1.818 (0.370)								

Table (6): Comparison (sensitivity, specificity, accuracy and p-value) between Mammogram, HHUS and ABUS.

	Mammogram	HHUS	ABUS
Sensitivity	30%	80%	60%
Specificity	100%	90%	70%
Accuracy	65%	85%	65%
p-value	0.257	0.008	0.257

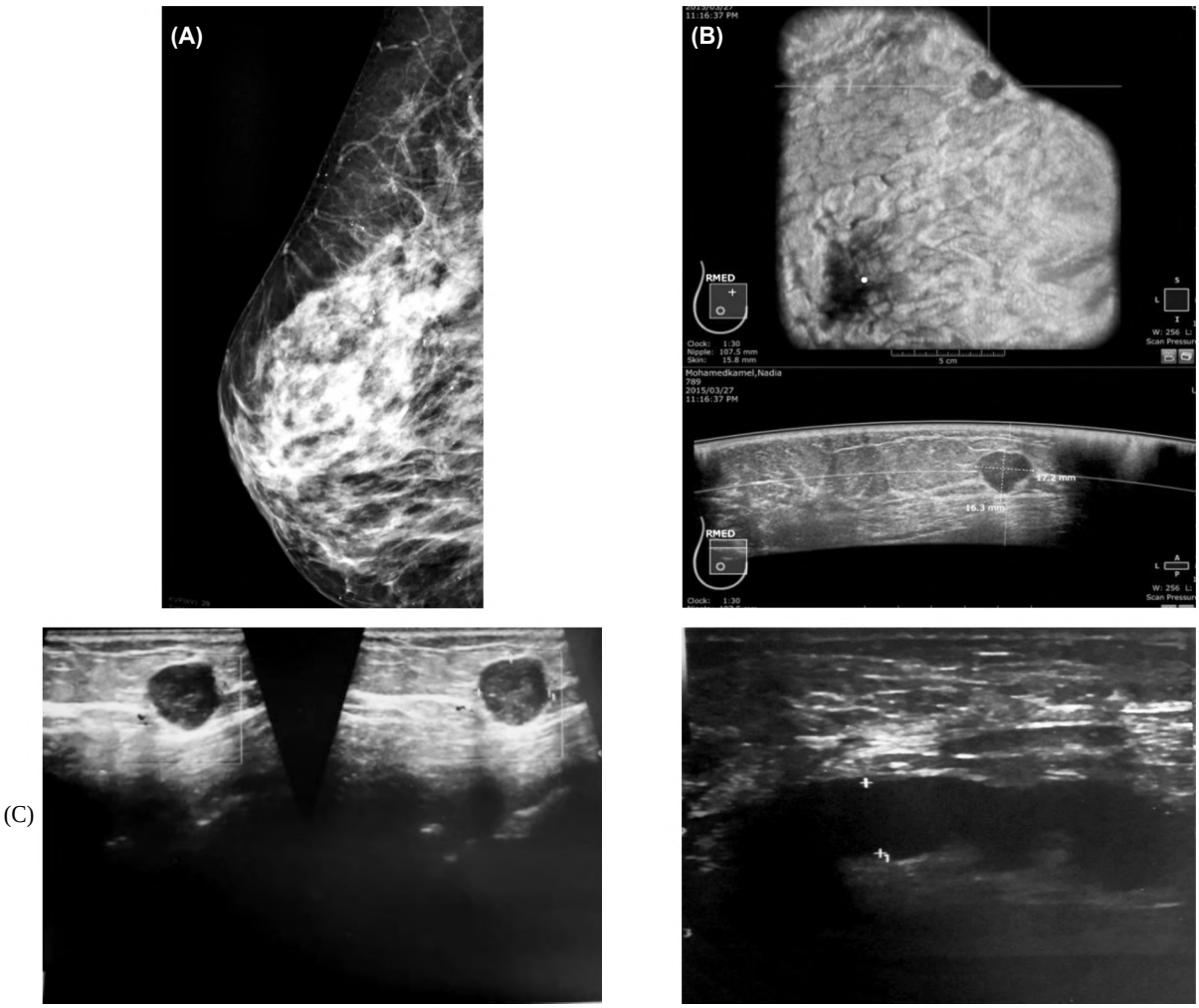


Fig. (1): A 39 year old female with right breast mass, (A) MLO view, ACR C right mammogram with tiny calcifications, (B) ABUS a: Coronal and b: Axial views show irregular hypoechoic lesion, (C) HHUS shows a: Round hypoechoic lesion with hyperechoic vascular lesion inside. b: Enlarged axillary lymph node with thick cortex. (Pathology: Ductal carcinoma insitu).

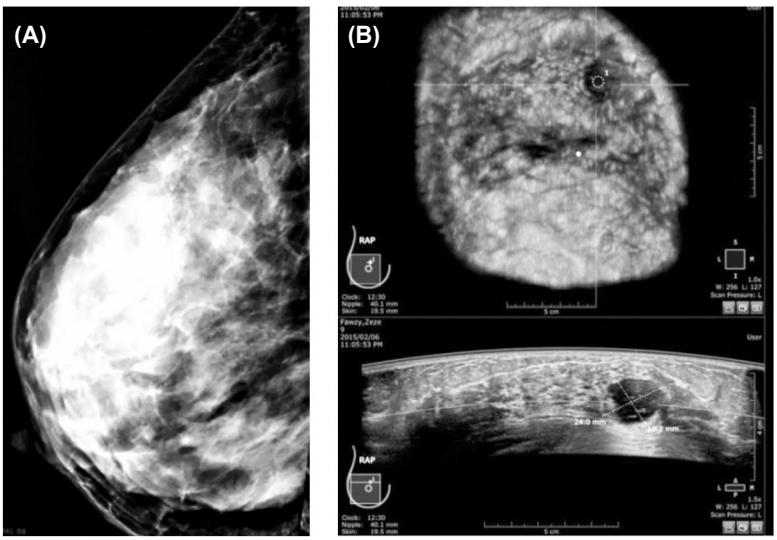
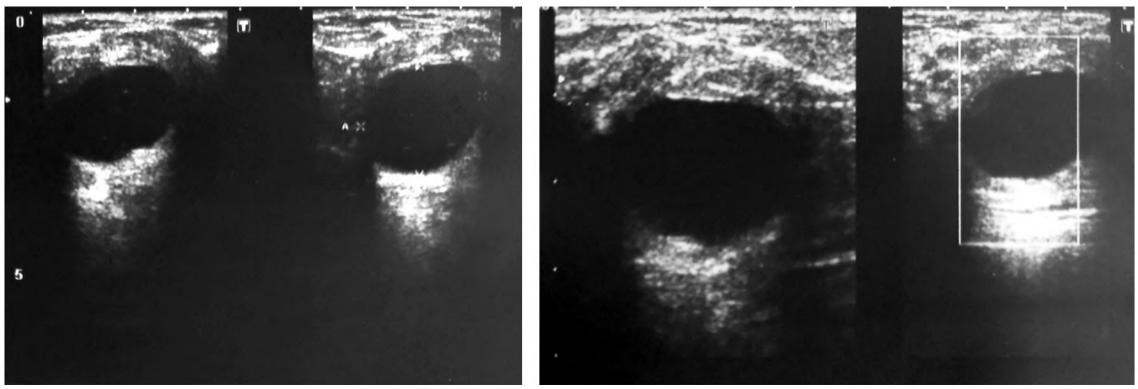


Fig. (2): A 37 year old female with breast mass, (A): MLO view, ACR D right mammogram, (B): ABUS a: Co-ronal and b, axial views show right breast hypoechoic lesion with internal echoes, (C): HHUS shows well defined hypoechoic lesion with free mobile internal echoes (pathology: Complicated Cyst (cyst with debris).

(C)



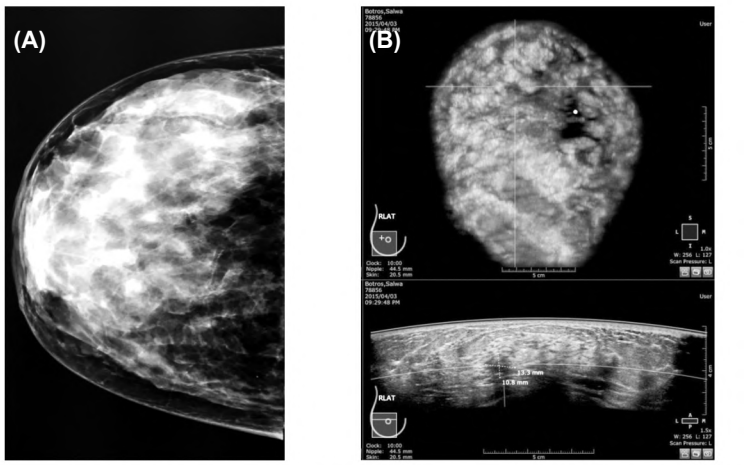
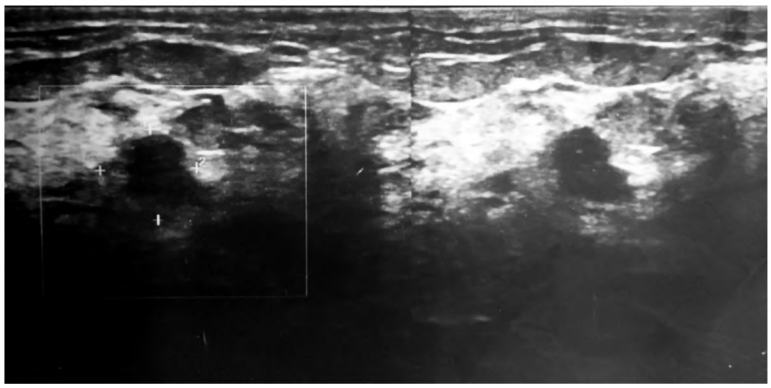


Fig. (3): A 40 year old female with right breast mass, (A): CC view, ACR D right mammogram, (B): ABUS a: Coronal and b: Axial views show ill defined lesion, (C): HHUS shows irregular hypoechoic lesion with multiple spiculations (pathology: Invasive ductal carcinoma).

(C)



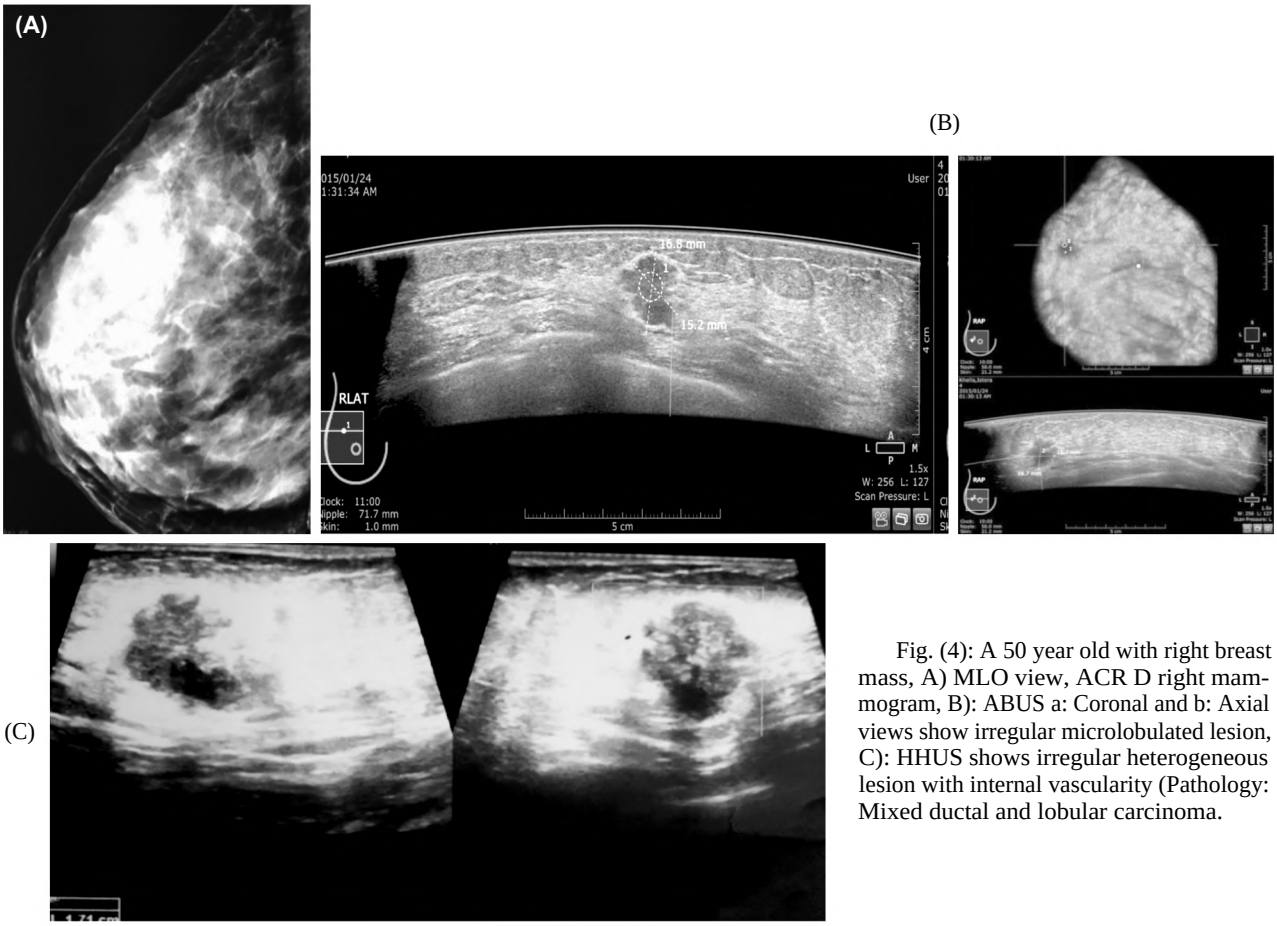


Fig. (4): A 50 year old with right breast mass, A) MLO view, ACR D right mammogram, B): ABUS a: Coronal and b: Axial views show irregular microlobulated lesion, C): HHUS shows irregular heterogeneous lesion with internal vascularity (Pathology: Mixed ductal and lobular carcinoma.

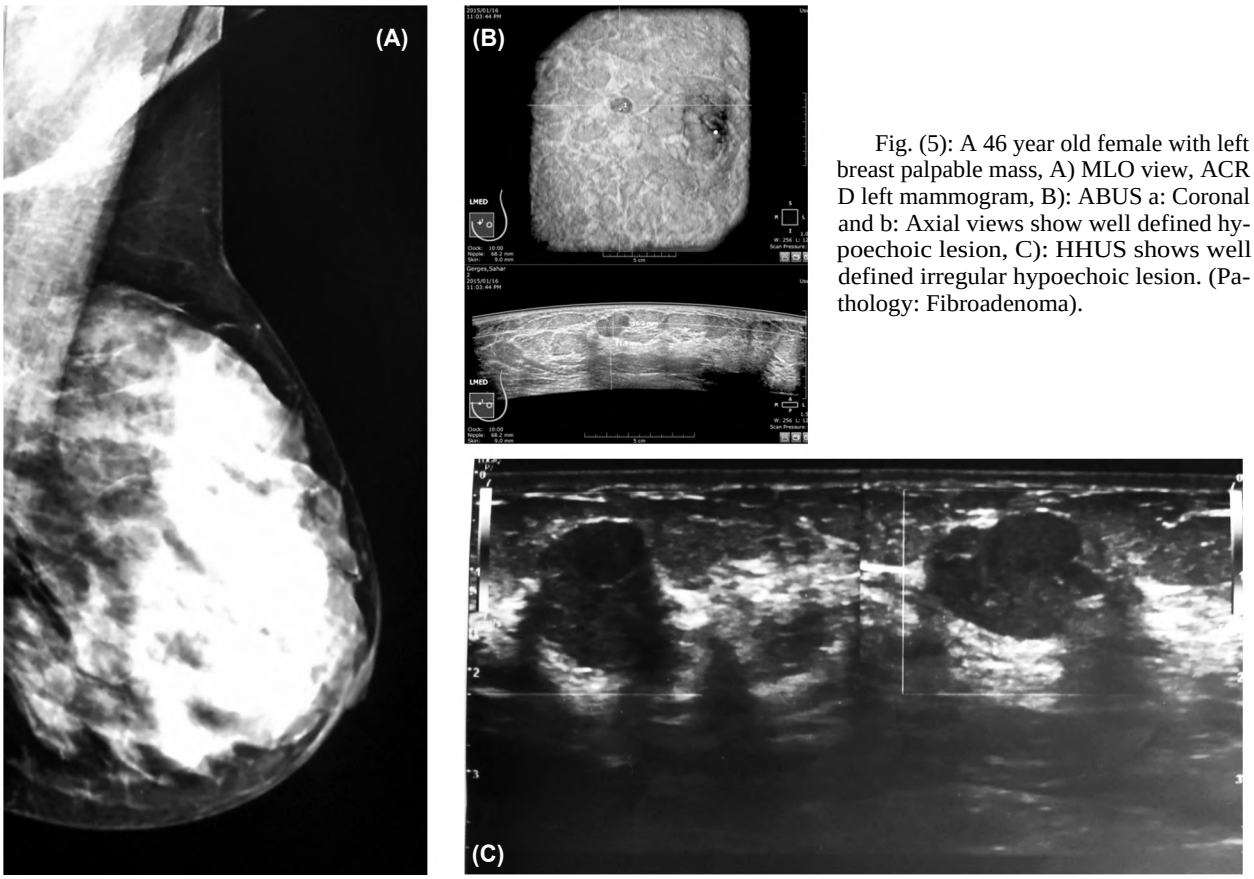


Fig. (5): A 46 year old female with left breast palpable mass, A) MLO view, ACR D left mammogram, B): ABUS a: Coronal and b: Axial views show well defined hypoechoic lesion, C): HHUS shows well defined irregular hypoechoic lesion. (Pathology: Fibroadenoma).

Discussion

Our results clearly show that it is feasible to implement ABUS into a high volume FFDSM center and increase the cancer detection rate in women aged 35-55 years.

It shows that addition of ABUS screening in women with dense breast tissue at FFDSM demonstrated an increase in detection rate of cancers in women screened despite of false positive and false negative cases by ABUS. The improved incremental cancer detection rate was comparable to the rates observed in studies of mammography screening supplemented by HHUS in women with dense breasts. Adding HHUS has also been shown to increase the cancer detection rate in women of ages ranges from 35-55 year.

ABUS showing no considered (wide) difference at lesion description from HHUS except for color Doppler and Axillary lymph node scanning that not available in ABUS.

Janie et al., [7] reported that of 121 women with complete follow-up, twenty-four women (19.8%) were recalled by at least one modality. Recalls increased from 5.0% to 13.2% (p=0.002) when ABUS was added to FFDM. Findings recalled by ABUS was more likely to result in a recommendation for short term follow-up imaging or tissue biopsy compared to findings recalled by only FFDM (100% vs. 42.1 %, p=0.041). The cancer detection rate was 8.3 per 1000 screens (1/121).

The agreement between ABUS and HHUS examinations in the BI-RADS categorization of suspicious breast masses was good, results of Yun et al., [8] found that their study analyzed 135 breast lesions in 135 patients (median age, 49 years; range, 35 to 82 years) who underwent both ABUS and HHUS followed by biopsy. The pathological analysis revealed 49 (36.3%) malignant lesions and 86 (63.7%) benign lesions. The overall agreement between ABUS and HHUS in all cases was 79.3% (kappa=0.61; p<0.001), while the agreement in confirmed malignancies was 55.1% (kappa=0.39, p<0.001).

Unlike our study, Abd Elkhalek et al., [9] according their results of a study of twenty-five female patients, age ranging 29-69 years complaining from breast pain or a palpable mass were submitted to ABUS and mammography. In their study, ABUS system was applied on 25 patients of mean age 43.4 with standard deviation of ±9.08. Eleven patients were below 40 years and 14 patients above 40 years. Thirteen patients (52%) with dense breasts were ACR C and D (9 and 4, respectively), while 12 patients (48%) were ACR A and B (4 and 8, respectively). The percentage of BIRAD II and BIRAD III detected lesions in mammogram was 28% and 12%, while, in ABUS, it increased to 32% and 20%, respectively thus, ABUS is a useful tool in detection of benign lesions and probably benign lesions compared to mammogram. While in our study, we noticed no significant difference at BIRAD IV and V between the two studies. The sensitivity of the ABUS is about 100%, and that means, in all the results of the mammogram study, ABUS can detect it without significant change, while the specificity of the ABUS was about 62% and was more evident in benign lesions. We found that the detected lesions by ABUS in the age group below 40 years was more than the mammogram (ABUS=7 cases and mammogram=5 cases), while in the age group above 40 years the ABUS found 1 case only more than the mammogram study.

Mostafa et al., [10] showed that there was a statistically difference between the number of patients with lesions detected by ABUS and HHUS with p-value of 0.012. There was no statistically difference between ABUS and HHUS in the detection of multiple lesions in the same patients with p-value of 0.16. Using mammography alone, lesions were detected in 24 out of 40 patients with positive findings, and addition of ABUS to mammography increased this number as lesions were detected in 38 out of 40 patients. A statistically significant difference was found with p-value=0.0001. The added value of ABUS to mammography in detection of breast lesions was most noted in patients with dense and extremely dense breasts (ACR C and D) as a statistically significant difference was found with p-value=0.000 1. Using mammography alone, 20 out of 36 lesions were detected while with the addition of ABUS 34 out of 36 lesions were detected. A statistically significant difference was found between ABUS and HHUS in the detection of lesions smaller than 5mm, when compared to HHUS. The number of lesions detected by ABUS smaller than 5mm was 10 compared to 4 by HHUS with a p-value of 0.002.

Also Giger et al., [11] reported an increase in sensitivity from 40% for mammography alone to 81 % with the addition of ABUS. In a recent study comparing FFDSM with a 3D ABUS to FFDSM alone for mammography negative cancers, the addition of 3D ABUS caused a 23.9% sensitivity increase.

Brem et al., [12] found that the relative increase in sensitivity for the 16 mammographic-negative

cancers that did not have any prior breast interventions to be of special interest. This finding shows that the confidence and performance of screening interpretations are improved with the use of supplemental screening ABUS.

ABUS can provide additional information in the differential diagnosis of a lesion. It has significantly higher sensitivity than mammography, but it is similar to manual US and cannot be preferred to a manual US examination. As Wang et al., **[13]** reported that detection rate, diagnostic accuracy and mammography sensitivity were significantly lower than those of each US method ($p<0.05$). There were no significant differences between manual US and ABUS. When combining ABUS, US and mammography, diagnostic accuracy, sensitivity and specificity reached 96.4%, 97.1% and 95.2%, respectively. A spiculated and stellate margin in the coronal plane has a high specificity in diagnosing malignant lesions.

Another agreement to our study by Kelly et al., **[3]** as reported that breast cancer detections doubled from 23 to 46 in 6,425 studies using AWBU with mammography, resulting in an increase in diagnostic yield from 3.6 per 1,000 with mammography alone to 7.2 per 1,000 by adding AWBU (an additional 3.6 per 1,000; 95% CI=2.3-5.4). Sensitivity for mammography alone was 40% (95%CI=27.5-54%; 23 out of 57 cancers), but increased to 81% (95% CI=68- 90%; 46 out of 57 cancers) with the addition of AWBU. Sensitivity of AWBU alone was 67% (95% CI=53-79%; 38 out of 57).

Conclusion:

According to our study, it shows that adding automated breast ultrasound to mammography is of great value in detection of breast cancer in mammographically dense breasts. It increases the detection rate of breast lesions mostly cancer. It is important as screening tool to decrease doses of radiation that female exposed to while mammogram screening.

But still hand held ultrasound is superior, it is of value in detection of breast lesions due to automated breast ultrasound pitfalls, and false positive and false negative cases.

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الكشف عن سرطان الثدى بإستخدام جهاز الموجات الفوق صوتية الآلى فى حالات الآثدية عالية الكثافة بالماموجرام

المقدمة: تسمح تقنية تصوير الثدى بالموجات فوق الصوتية لآخصائى الآشعة بتفسير صور الموجات فوق الصوتية فى وقت منفصل بعد الإكتساب. تم الإبلاغ عن آوقات تفسير مختلفة، تتراوح من ٥ إلى ١٠ دقائق، ربما وفقاً للإختلافات فى تجربة القراء ودرجة تعقيد كل حالة.

الهدف من الدراسة: للكشف عن تآثير مزايا تقنية الموجات فوق الصوتية الآلية وغيرها من تلك التى تتحد مع التصوير الشعاعى للثدى مقارنة مع التصوير الشعاعى للثدى وحده، تحسن الكشف بشكل كبير عن سرطانات الثدى لدى النساء المصابات بآنسجة الثدى الكثيفة دون التآثير بشكل كبير على الخصوصية.

المرضى والطرق: آجريت هذه الدراسة المستعرضة على ٢٠ سيدة فى قسم التشخيص بالآشعة، مستشفى شبرا العام واللاتى تم تحويلهن من عيادة الجراحة خلال فترة سنة واحدة. إقتصرت الدراسة على الإناث فقط اللاتى يرغبن فى الخضوع لفحوصات إضافية بعد تشخيص ثدى كثيف على التصوير الشعاعى للثدى.

النتائج: وجدنا آن الحالات الخاضعة للفحص بالموجات فوق الصوتية الآلية تظهر حساسية تصل إلى حوالى (٦٠٪) وهى آكثر من حساسية التصوير الشعاعى للثدى (٣٠٪) ولكن آقل من الموجات فوق الصوتية التقليدية (٨٠٪)، بينما كانت درجة خصوصية الموجات فوق الصوتية الآلية (٧٠٪) آقل من كل من تصوير الثدى الشعاعى (١٠٠٪) والموجات فوق الصوتية التقليدية (٩٠٪). وكانت دقة الموجات فوق الصوتية التقليدية (٨٥٪) آكثر دقة كل من التصوير الشعاعى للثدى (٦٥٪) والموجات فوق الصوتية الآلية (٦٥٪)، بقيمة دلالة إحصائية ٠.٢٥٧ لكل من التصوير الشعاعى للثدى والموجات فوق الصوتية الآلية، و (٠.٠٠٨) إلى الموجات فوق الصوتية التقليدية.

الخلاصة: إن لإضافة الموجات فوق الصوتية للثدى الآلى إلى التصرير الشعاعى للثدى قيمة كبيرة فى الكشف عن سرطان الثدى فى الثديين ذوى الآنسجة الكثيفة. ويزيد معدل الكشف عن آفات الثدى وخاصة فى حالات الكشف عن السرطان.