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Breast Screening Using 3D Automated Breast Ultrasound in Addition toConventional B Mode Ultrasound

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Abstract:

Background:Breast cancer is a major worldwide health problem. Many radiologists recognize that there are increasing incidence of breast cancer in the past decade.Automated three-dimensional (3D) breast ultrasound (ABUS) was developed for better diagnosis of architectural distortions.

Aim of work:evaluation of validity of ABUS in cancer breast detection in addition toHand Held Ultrasound (HHUS).

Subjects and methods:This prospective cross-sectional study was done at radiology department of Al Sheikh Zayed Aal Nahyan hospital and included105 female patients, aged >18 years old, presented with breast complaint or screening, they were referred from general surgery Department of Al Sheikh Zayed Aal Nahyan Hospital. They were evaluated by HHUS and ABUS individually. Each lesion was assigned an independent BIRADS score for each modality.diagnosis was confirmed by biopsy (56cases).

Results:HHUS and ABUS showed good substantial agreement regarding lesions classification (benign or malignant) with kappa (κ) 0. 789.with diagnostic accuracy and sensitivity of ABUS were higher than that of HHUS as for ABUS were 97.1% and 100% respectively, while for HHUS were 90.5% and 90.7 % respectively.

Conclusion:From our results ABUS may serve as an effective new screening tool in addition to HHUS.

Keywords:Breast Cancer, 3D Automated Breast Ultrasound, Hand Held Ultrasound (HHUS).

INTRODUCTION:

In recent years there has been an increase in the incidence of breast cancer. Worldwide there are more than 1 million new cases and more than 450,000 deaths annually **(19)**.

Hand Held Ultrasound (HHUS) is widely available, well-tolerated method which allows detailed evaluation of the breast and the axilla and has the availability of color Doppler and elastography modes **(1).** But it has several disadvantages as it is time consuming, operator-dependent, not reproducible, requires high level of experience and with small field of view. so, a new scanner device is designed to overcome these defects.

Automated three-dimensional (3D) breast ultrasound (ABUS) was developed to obtain an operator independent system **(2)**. It is reproducible and obtains three dimensional (3D) high resolution imaging with a large FOV. The new generation ABUS provides better detection of architectural

distortions and lesion localization **(2),**as it provides 3D reconstruction of volumes for better breast anatomy assessment, good observation of lesion margin, speculations and anatomical relations.
We aimed in this study to evaluatethe validity of ABUS in cancer breast detection in addition to Hand Held Ultrasound (HHUS).

SUBJECTS AND METHODS:

This prospective cross-sectional study was done at radiology department of Al Sheikh Zayed Aal Nahyan hospital, over the period between December 2019 and December 2020 and included105 female patients, aged >18 years old, presented with breast complaint or screening, they were referred from general surgery Department of Al Sheikh Zayed Aal Nahyan Hospital.
The study was applied on 105 female patients, aged >18 years old, presented with breast complaint or screening.

Patient inclusion criteria:

1**-** Adult females more than 18 years old.
2- Breast complaint or breast masses detected either clinically or by sonomammography.

Patient exclusion criteria:

1- Patient refuse to share in the study.
2- Pregnant female to avoid the hazards of ionizing radiation to the fetus.
3- Tender breast can't tolerate compression for long time.

They filled out a sheet including; (name, age, complaint, present history and family history), then underwent scanning by mammography, hand held ultrasound (HHUS), and automated breast ultrasound (ABUS).

Patients were subjected to the following:

1- Clinical assessment:

A.Complete history taking: about age of the patient, lactational history, detailed history of breast complaint (e.g: duration of breast mass, its consistency, nipple discharge or skin manifestations) and family history.
B.Full clinical examination: was performed by referring physician.

2-Radiological assessment

Methods:

Hand Held Ultrasound (HHUS):

Equipment: HHUS was performed using (Philips, affinity 50) machine with linear transducer at 10–15 MHz gray scale.
Technique: The patient lies in supine position with elevating the ipsi-lateral hand above the head and the ultrasound probe oriented perpendicular to the chest wall. The patient may be rolled to contralateral to facilitate flattening of the breast against her chest. radial scanning technique of the breast by (ductal anatomy plan). Examination starts at 12 o'clock of the breast and run on a clockwise direction**.**

Automated Breast Ultrasound (ABUS):

Equipment: examination wasperformedby an ABUS system (GE health care, Invenia ABUS).

Technique: The examination was performed in the supine position with elevation of the ipsi-lateral arm above the head. A towel or a sponge was placed under the shoulder of the patient to keep the breast stable with the nipple pointing to the ceiling. A hypoallergenic lotion was placed on the breast with an additional amount on the area of the nipple to avoid air bubbles.

A disposal membrane was used to apply gentle compression, enabling greater penetration,with respect to image quality and patient comfort. The ABUS scan was continuous and automated.

During the acquisition women were asked not to move and to breathe smoothly. Volume acquisitions were obtained in the axial plane starting from the inferior part of the breast with coronal and sagittal reconstruction.

Image data automatically acquired a 15.4 cm x 17.0 cm volume from the skin to the chest wall up to 5 cm deep with 0.2 mm thickness of each slice.

For each breast, three volumes were obtained: the central (antero- posterior) volume with the nipple in the center of the view, the lateral volume that included the upper outer part of the breast tissue with the nipple located in the inferior-medial corner and the medial volume that included the inner and inferior part of the breast tissue.

A nipple marker was placed in every examination for accurate co-ordinance. For optimal image quality a selection between three breast sizes was made. In women with larger breasts additional views were taken to avoid tissue exclusion. When the image data was completed, the volumes were transferred to a dedicated workstation for interpretation.

Statistical Analysis:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level. The used tests were: Receiver operating characteristic curve (ROC): The area under the ROC curve denotes the diagnostic performance of the test. Area more than 50% gives acceptable performance and area about 100% is the best performance for the test. The ROC curve allowed also a comparison of performance between two tests.Sensitivity: The capacity of the test to correctly identify diseased individuals in a population “TRUE POSITIVES”. The greater the sensitivity, the smaller the number of unidentified cases “false negatives”. Specificity:The capacity of the test to correctly exclude individuals who are free of the disease “TRUE NEGATIVES”. The greater the specificity, the fewer “false positives” have been included. Positive Predictive value (PPV): The probability of the disease being present, among those with positive diagnostic test results. Negative Predictive value (NPV): The probability that the disease was absent, among those whose diagnostic test results were negative. Kappa test (κ): For categorical variables, to determine agreement.

RESULTS:

Table (1)showed that the mean age of studied cases was 46.33 (±10.32 SD) with range (32-78), according to lactating history there were 68 (64.8%) with breast feeding and 37 (35.2%) non-lactating and there were 40 (38.1%) with positive family history for breast cancer and 65 (61.9%) with negative family history.

Among the studied cases there were 44 (41.9%) with breast lump, 33 (31.4%) with mastalgia, 21 (20%) came for screening, 6 (5.7%) for check-up and 1 (1%) nipple bloody discharge are demonstrated in**Table (2)**.

according to HHUS among the studied cases there were 0 (0%) with BIRADS of 0, 4 (3.8%) with I, 48 (45.7%) with II, 8 (7.5%) with III, 30 (28.6%) with IV and 15 (14.3%) with V, according to lesion classification there were 60 (57.1%) benign and 45 (42.9%) malignant and according to axilla there were 96 (91.4%) with non-significant lymphadenopathy, 2 (1.9%) right suspicious lymphadenopathy,5 (4.8%) with left suspicious lymphadenopathy and 2 (1.9%) with bilateral suspicious lymphadenopathy. **Table (3).**

According to ABUS among the studied cases there were 0 (0%) with BIRADS of 0, 2 (1.9%) with I, 40 (38.1%) with II, 17 (16.2%) with III, 27 (25.7%) with IV and 19 (18.1%) with V, according to lesion classification there were 59 (56.2%) benign and 46 (43.8%) malignant and according to axilla all the cases had no properly assessment.**(Figure 1).**

Among the studied cases there were 56 (53.3%) with biopsy and 49 (46.7%) with follow-up, according to lesion classification there were 62 (59.0%) benign and 43 (41.0%) malignant**(Figure 2).**

Using HHUS it was shown that above BIRADS 3, it can discriminate between benign and malignant lesions with AUC of 0.902, level of sensitivity 90.7%, specificity 90.3%, PPV 86.7%, NPV 93.3% and accuracy 90.5%.Using ABUS it was shown that above 3, it can discriminate between benign and malignant lesions with AUC of 0.986, level of sensitivity 100%, specificity 95.2%, PPV 93.5%, NPV 100% and accuracy 97.1%.**(Table 4).**

HHUS and ABUS showed good substantial agreement regarding lesions classification (benign or malignant) with kappa (κ) 0.789.**(Table 5)**

Table (1): Demographic characteristics of the study population.

Demographic data		Cases (n = 105)
Age (Years)		
	Min. – Max.	32.0 – 78.0
	Mean ± SD.	46.33 ± 10.32
	Median (IQR)	43.0 (39.0 – 51.0)
	Lactating history	**No.** **%**
	Breast feeding	68 64.8
	Non lactating	37 35.2
	Family history for breast cancer	**No.** **%**
	+ve	40 38.1
	-ve	65 61.9

Table (2): Complaint of the study population.

Complaint	Cases (n = 105)	
	No.	**%**
Breast lump	44	41.9
Mastalgia	33	31.4
Screening	21	20.0
Check-up	6	5.7
Nipple bloody discharge	1	1.0

Table (3): Results of Hand-held ultrasound examination of the study population.

BIRADS	Cases	
	No.	%
0	0	0
I	4	3.8
II	48	45.7
III	8	7.6
IV	30	28.6
V	15	14.3
Lesion classification by Hand held ultrasound	**No.**	**%**
Probably benign (BIRADS I-III)	60	57.1
Probably malignant (BIRADS IV-V)	45	42.9
Axilla	**No.**	**%**
non-significant lymphadenopathy	96	91.4
Right suspicious lymphadenopathy	2	1.9
left suspicious lymphadenopathy	5	4.8
Bilateral suspicious lymphadenopathy	2	1.9

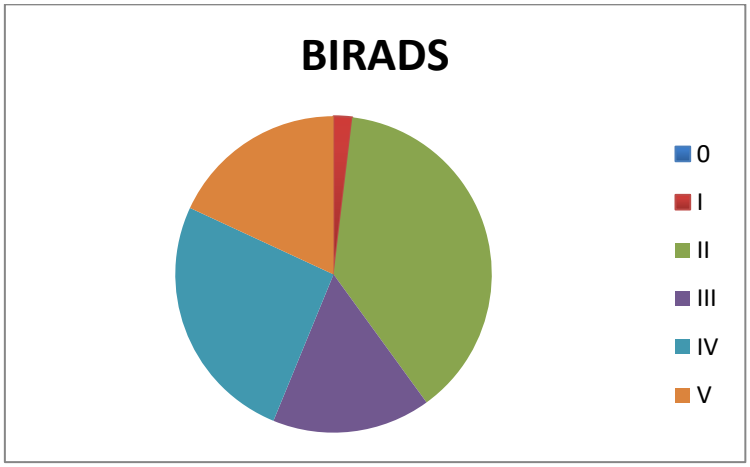

Figure (1): Results of ABUS examination of studied cases

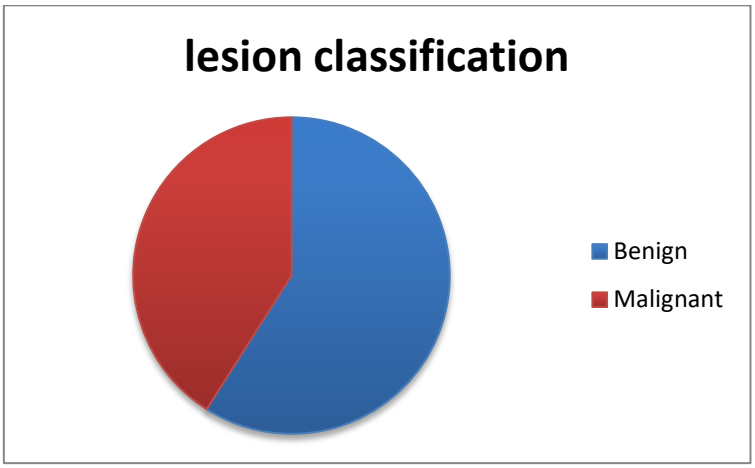

Figure (2): lesion classification of studied cases

Table (4): Roc curve analysis for the use of mammography, HHUS and ABUS examinations to discriminate between benign and malignant lesions.

	AUC	Sens%	Spec%	PPV%	NPV%	Accuracy %
HHUS	0.902	90.7	90.3	86.7	93.3	90.5
ABUS	0.986	100.0	95.2	93.5	100.0	97.1

Table (5): Agreement between HHUS and ABUS regarding lesion classification as probably malignant or probably benign.

	ABUS				
HHUS	**Benign**		**Malignant**		**kappa (κ)**
	No.	%	No.	%	
Benign	54	51.4	6	5.7	0.787
Malignant	5	4.8	40	38.1	

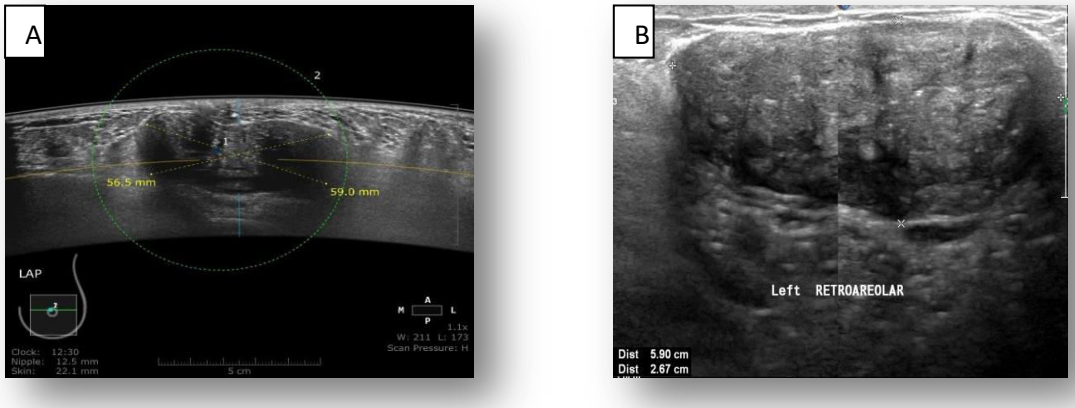

Figure 3: 37 years old female patient coming for screening with negative family history A)Well defined, oval shape, hypo-echoic solid mass lesion, parallel orientation seen at 11:30 o'clock ,measuring about (59 X 56 mm), 18.4 mm from skin & 13.3 mm from nipple (giant fibro adenoma by histopathology) (BIRADS III). B)Left breast shows large well defined hypo-echoic solid mass lesion with regular outlines noted at retro-areolar region measuring about (59 X 26 mm) and associated with bilateral inflammatory lymph nodes (BIRADSIII).

DISCUSSION:

Breast cancer is a major worldwide health problem as it is the most common cancer in women. It accounts for 22.9% of all new female cancers worldwide and in Egypt for 37.7% of total female cancers and 29.1% of cancer related death **(3).**

Hand Held Ultrasound (HHUS) is widely available, well-tolerated method which allows detailed evaluation of the breast and the axilla and has the availability of color Doppler and elastography modes. But it has several disadvantages as it is time consuming, operator-dependent, not reproducible, requires high level of experience and with small field of view. so, a new scanner device is designed to overcome these defects **(1).**

Automated breast ultrasound is new operator independent device **(2).** It is used to obtain three dimensional (3D) high resolution imaging with large field of view and provides better detection of architectural distortions and lesion localization **(2).** It also designed with wide linear transducer

providing large, scanned area in each separate volume as it covers the whole breast scan in three to five separate volume according breast size **(4).**
A few published studies showed the high reliability in detecting lesion and recording lesion location and size by ABUS while one report described low specificity and fair inter-rater reliability **(5).**

In the current study, the mean age of included cases was 46.33 (±10.29SD) Years, ranged from 32 to 78 years old, and this was in agreement with **Mostafa et al., (7)**study that included 200 female patients studied for the added value of ABUS in the screening of women with suspected breast masses compared to conventional mammography and hand-held ultrasound, they aged between 19 and 61 years (mean 35.44 ± SD 10.83), but our documented age of patients was younger than **Brem et al., (6)** study that included 15318 women presented for screening mammography, the mean age was 53.3 ± 6.10 years, ranged 25–94 years.
In the recent study, among the most common complaint was breast lump representing 44 (41.9%) with breast lump, 33 (31.4%) with mastalgia, 21 (20%) came for screening, 6 (5.7%) for check-up and 1 (1%) nipple bloody discharge, while in **Mostafa et al., (7)**study, the most common patient complaint was pain in 140 patients representing 70% of the patient population and a lump in 32 patients representing 16%.
According to HHUS among the studied cases there were 0 (0%) with BIRADS of 0, 4 (3.8%) with I, 48 (45.7%) with II, 8 (7.5%) with III, 30 (28.6%) with IV and 15 (14.3%) with V, according to lesion classification there were 60 (57.1%) benign and 45 (42.9%) malignant and according to axilla there were 96 (91.4%) with non-significant lymphadenopathy, 2 (1.9%) right suspicious lymphadenopathy, 5 (4.8%) with left suspicious lymphadenopathy and 2 (1.9%) with bilateral suspicious lymphadenopathy, and according to ABUS among the studied cases there were 0 (0%) with BIRADS of 0, 2 (1.9%) with I, 40 (38.1%) with II, 17 (16.2%) with III, 27 (25.7%) with IV and 19 (18.1%) with V, according to lesion classification there were 59 (56.2%) benign and 46 (43.8%) malignant and according to axilla all the cases had no properly assessment.
In agreement with our findings, **Golatta et al. (8)**, which found good agreement between ABUS and HHUS (k = 0.34) in assigning a BIRADS value: in particular, this agreement increases (k = 0,68) if a lesion characterised by assigning it to two categories (non-suspect = BIRADS 1–2 or suspect = BIRADS 4–5). Similar results in terms of concordance of assignment of a BIRADS value were obtained in the studies of **Shin et al. (1)**(k = 0,64) and **Kim et al**.**(9)** (k = 0.773 ± 0.104). In **Kim's** study, the BIRADS descriptor that presented the best agreement was the 'orientation' (k = 0.608 ± 0.210) and the worst was the 'posterior echo feature' (k = 0.371 ± 0.225); **Kotsianos-Hermle et al. (10)** reported a good correlation for the descriptor 'margin'.
More recently, **Zhang et al. (11)** demonstrated a better diagnostic performance of ABUS versus HHUS, in particular in the detection of precancerous lesions or cancers (BIRADS 4-5). In this hospital-based multicentre diagnostic study, **Zhang et al.** have evaluated the clinical performance of the ABUS for breast cancer detection by comparing it to handheld ultrasound and mammography (MG) in 1973 women, from 30 to 69 years. The results not only shown a good diagnostic performance of ABUS but also that the ABUS results, compared to HHUS, were more consistent with the pathology results in the BIRADS 4–5 groups: 78.6% of women classified as BI-RADS 4–5 based on the ABUS were diagnosed with precancerous lesions or cancer, which was 7.2% higher than that of women based on HHUS. For BI-RADS 1–2, the false negative rates of the ABUS and HHUS were almost identical and were much lower than those of MG **(11).**

In this study, there were 56 (53.3%) with biopsy and 49 (46.7%) with follow-up, according to lesion classification there were 62 (59.0%) benign and 43 (41.0%) malignant, while in **Mostafa et al., (7)**study, 120/200 patients were found to have negative imaging and pathological findings. Eighty patients had different breast pathologies, 48 showed benign findings and 32 showed malignant disease. The most common benign finding was fibroadneoma in 36 patients, and the most common malignant finding was Invasive ductal carcinoma in 22 patients.

In the present study, there was statistically significant increase in the number of cases with lesions detected by ABUS compared to HHUS with increase in the accuracy 97.1% compared to 90.5%, sensitivity 100% compared to 90.5%, 95.2% specificity and negative predictive value 100% compared to 93.3%. The findings in this study are in agreement with those reported by **Choi et al.(12)** who reported a statistically significant difference between lesion detection by ABUS compared to HHUS and their diagnostic accuracy, sensitivity, and specificity were 97.70%, 77.78%, and 97.79% respectively. **Vourtsis et al. (13)** reported in their study that ABUS was comparable to HHUS; however, it outperformed HHUS in lesion detection of architectural distortion, though they did not report sensitivity or specificity of each technique.

In the recent study, HHUS it was shown that regarding BIRADS IV and V, it can discriminate between benign and malignant lesions with AUC of 0.902, level of sensitivity 90.7%, specificity 90.3%, PPV 86.7%, NPV 93.3% and accuracy 90.5%, and this was nearly similar to **Mostafa et al.,(7)**study, where the sensitivity of HHUS was 82.5 %, specificity was 100 %, positive predictive value was 100 %, and negative predictive value was 89.6 %, while in **Brem et al.,(6)** study, the rates of additional cancers identified by using HHUS range between 1.9 and 5.3 additional cancers per 1000 women screened compared with mammography alone .

In the present study, using ABUS it was shown that regarding BIRADS IV and V, it can discriminate between benign and malignant lesions with AUC of 0.986, level of sensitivity 100%, specificity 95.2%, PPV 93.5%, NPV 100% and accuracy 97.1%, and this was nearly similar to **Mostafa et al.,(7)**study, where the sensitivity of ABUS was 95 %, specificity was 100 %, positive predictive value was 100 %, and negative predictive value was 96.8 %, also a statistically significant difference was found between ABUS and HHUS in the detection of lesions smaller than 5 mm, when compared to HHUS. The number of lesions detected by ABUS smaller than 5 mm was 10 compared to 4 by HHUS with a p value of 0.002.

Mostafa et al., (7)proved that there was a statistically significant increase in the detection of lesions smaller than 5 mm by ABUS when compared to HHUS. These findings were in agreement with those reported by **Kelly et al.(14)** who reported a significant increase in the number of detected small invasive cancers measuring less than 20 mm in size when adding ABUS to mammography.

More recently, **Lin Niu et al.(15)** studied 599 breast lesions in 398 women comparing ABUS and HHUS with pathologic results or 1-year follow-up as a reference. The results shown that there was a significant difference between ABUS and HHUS in terms of sensitivity (92.23% versus 82.52%; $p < 0.01$) but not in terms of diagnostic accuracy, specificity, positive and negative predictive valu**(15).**

Wang et al. (18), in a study of 213 patients reported a sensitivity of ABUS versus HHUS of 95.6% versus 90.3% and a specificity of 80.5% versus 82.5%.

In the diagnostic setting, high reliability in recording lesion location and size by ABUS was reported in the prospective study of **Shin et al. (1)**

In preoperative setting, **Chae et al.(5)** evaluated diagnostic performance of ABUS as a replacement for a hand-held second-look US for MRI detected lesions. ABUS detected 85% (70/80) of suspicious lesions detected on MRI **(5).**

Li et al. (17) addressed in their prospective study that the size of pure ductal carcinoma in situ (DCIS) on ABUS shows a higher correlation coefficient with histopathology than that on conventional US **(17).**

Implementation of ABUS in the standard diagnostic work- flow requires radiologists to be familiar with the imaging features of breast cancer in ABUS. Image analysis in ABUS is essentially based on the evaluation of same features than for HHUS (shape, orientation, margins, echo pattern and posterior features as described in the BI-RADS lexicon). ABUS adds the possibility of three-dimensional analysis by generating a coronal view, with following improvement in accuracy **(18).**

Conclusionand recommendations:

HHUS and ABUS showed good substantial agreement regarding lesions classification (benign or malignant) with kappa (κ) 0. 789.with diagnostic accuracy and sensitivity of ABUS were higher than that of HHUS as for ABUS were 97.1% and 100% respectively, while for HHUS were 90.5% and 90.7 % respectively. So ABUS may serve as an effective new screening tool in addition to HHUS.

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