ROLE OF 3D AUTOMATED BREAST ULTRASOUND AS A FUTURE BREAST SCREENING TOOL IN ADDITION TO MAMMOGRAPHY

Amal Mahmoud Mohamed¹, Khalid Ahmed Lakouz², Ahmed Abd Al Azim³, Mona Mohammed Refaat⁴
¹,²,³,⁴Radiology Department, Faculty of Medicine, Zagazig University Zagazig, Egypt
E-mailaddress: ramanoseery@gmail.com

ABSTRACT

Background: Breast cancer is the most common malignant tumor in females, diagnosed in approximately 1.4 million people each year. Mammography is considered the gold standard for breast cancer screening yielding 30% reduction in breast cancer mortality among women. Automated Breast Ultrasound (ABUS) is a new technique that was developed to obtain an operator independent system.

Aim of the study: evaluation of validity of ABUS in cancer breast detection in addition to Mammography.

Subject and Methods: This prospective cross-sectional study was done at radiology department of Al Sheikh Zayed Aal Nahyan hospital and included 105 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 mammography and ABUS individually. Each lesion was assigned an independent BIRADS score for each modality. diagnosis was confirmed by biopsy (56 cases).

Results: ABUS and Mammography showed fair substantial agreement regarding lesions classification (benign or malignant) with kappa (κ) 0.549. with diagnostic accuracy and sensitivity of ABUS were higher than that of mammography as for ABUS were 97.1% and 100% respectively, while for mammography were 83.8% and 67.4% respectively.

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

Keywords: 3D Automated Breast Ultrasound, Mammography.

I. 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 (1).

Mammography is considered the gold standard for breast cancer screening yielding 30% reduction in breast cancer mortality among women aged 50-74 years, but its low sensitivity in women with dense breasts, is considered as a limitation (14), which needs complementary scan to improve rate of detection of any breast masses.

Therefore, Automated three-dimensional (3D) breast ultrasound (ABUS) was developed to obtain an operator independent system (1). 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.

It also designed with wide linear transducer providing large scanned area in each separate volume as it cover the whole breast scan in three to five separate volume according breast size (2).

We aimed in this study to evaluate the validity of ABUS in cancer breast detection in addition to mammography.

II. STUDY DESIGN AND PARTICIPANTS

This study was performed in multicenter tertiary-care hospitals; Zagazig university Hospital Sharqia. 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 included 105 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:
- Adult females more than 18 years old.
- Breast complaint or breast masses detected either clinically or by sonomammography.
- Mammographically dense breast.

Patient exclusion criteria:
- Patient refuse to share in the study.
- Pregnant female to avoid the hazards of ionizing radiation to the fetus.
- 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:

Mammography:

Equipment: Mammographic examination was done using Fujifilm innovality digital mammogram and tomosynthesis.

Technique: (105) patients underwent mammography.

Standard views: mediolateral oblique (MLO) and craniocaudal (CC) views were obtained.

Then films were examined for:
Breast density was evaluated for each patient according to American college of radiology (ACR):
(A) Mostly fatty breast.
(B) There are scattered areas of fibro-glandular density.
(C) Heterogeneously dense breast, which may obscure small masses.
(D) Extremely dense breast, which decrease the sensitivity of mammography.

Absence or presence of mass: if mass is encountered we comment upon: Site, size, shape, margins, borders.

Focal or global asymmetry, parenchymal distortion and calcification.

Automated Breast Ultrasound (ABUS):

Equipment: examination was performed by an ABUS system (GE health care, Invenia ABUS).

Technique: The examination was performed in the supine position with elevation of the ipsilateral 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
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-ordination. 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.

III. RESULTS

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. (Figure 1,2).

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(Figure 3).

According to mammography examination among the studied cases there were 25 (23.8%) with BIRADS of 0, 20 (19.0%) with I, 28 (26.7%) with II, 7 (6.7%) with III, 16 (15.2%) with IV and 10 (8.6%) with V, according to lesion classification there were 80 (76.2%) benign and 25 (23.8%) malignant(Table 1).

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 proper assessment. (Table 2).

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(Table 3).

Using Mammography, it was shown that above BIRADS3, it can discriminate between benign and malignant lesions with AUC of 0.718, level of sensitivity 67.4%, specificity 95.2%, PPV 90.6%, NPV 80.8% and accuracy 83.8%.

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).
ABUS and Mammography showed fair substantial agreement regarding lesions classification (benign or malignant) with kappa (κ) 0.549 (Table 5).

![Lactating history](image1.png)

**Fig (1):** Lactating history of studied cases

![Family history for breast cancer](image2.png)

**Fig. (2):** Family history for breast cancer of studied cases

![Complaint](image3.png)

**Fig (3):** Complaint of studied cases

| Table 1: Results of Mammography examination of the study population |
|-----------------|-----------------|
| BIRADS | Cases |
|        | No. | % |
| 0      | 25  | 23.8 |
| I      | 20  | 19.0 |
| II     | 28  | 26.7 |
| III    | 7   | 6.7 |
| IV     | 16  | 15.2 |
| V      | 9   | 8.6 |
|        |     |     |
| Lesion classification by mammography | Probably benign (BIRADS I-III) | 80 | 76.2 |
## Table 2: Results of ABUS examination of the study population

<table>
<thead>
<tr>
<th>BIRADS</th>
<th>Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>I</td>
<td>2</td>
<td>1.9</td>
</tr>
<tr>
<td>II</td>
<td>40</td>
<td>38.1</td>
</tr>
<tr>
<td>III</td>
<td>17</td>
<td>16.2</td>
</tr>
<tr>
<td>IV</td>
<td>27</td>
<td>25.7</td>
</tr>
<tr>
<td>V</td>
<td>19</td>
<td>18.1</td>
</tr>
</tbody>
</table>

Lesion classification by ABUS

<table>
<thead>
<tr>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>23.8</td>
</tr>
</tbody>
</table>

### Table 3: Reference Index of the study population

<table>
<thead>
<tr>
<th>Primary diagnosis</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
</tr>
<tr>
<td>Biopsy</td>
<td>56</td>
</tr>
<tr>
<td>Benign</td>
<td>49</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Lesion classification (final diagnosis)</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>62</td>
<td>59.0</td>
</tr>
<tr>
<td>Malignant</td>
<td>43</td>
<td>41.0</td>
</tr>
</tbody>
</table>

### Table 4: ROC curve analysis for the use of mammography, and ABUS examinations to discriminate between benign and malignant lesions

<table>
<thead>
<tr>
<th></th>
<th>AUC</th>
<th>Sens%</th>
<th>Spec%</th>
<th>PPV%</th>
<th>NPV%</th>
<th>Accuracy %</th>
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</thead>
<tbody>
<tr>
<td>Mammography</td>
<td>0.718</td>
<td>67.4</td>
<td>95.2</td>
<td>90.6</td>
<td>80.8</td>
<td>83.8</td>
</tr>
<tr>
<td>ABUS</td>
<td>0.986</td>
<td>100.0</td>
<td>95.2</td>
<td>93.5</td>
<td>100.0</td>
<td>97.1</td>
</tr>
</tbody>
</table>

### Table 5: Agreement between mammography and ABUS regarding lesion classification as probably malignant or probably benign

<table>
<thead>
<tr>
<th>ABUS</th>
<th>Mammography</th>
<th>Benign</th>
<th>Malignant</th>
<th>kappa (κ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammography</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td></td>
<td>56</td>
<td>53.3</td>
<td>24</td>
<td>22.9</td>
</tr>
<tr>
<td>Malignant</td>
<td>3</td>
<td>2.9</td>
<td>22</td>
<td>21.0</td>
</tr>
</tbody>
</table>
Figure 4: 47 years old patient, presented with bilateral breasts pain. A) Mammography CC and MLO views shows bilateral high density rounded lesions with benign macrocalcifications. B) ABUS image of right breast (sagittal and coronal views) shows multilocular cystic lesion.

IV. DISCUSSION

Of note, 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).

The aim of early detection of breast cancer is to reduce the morbidity and mortality rates (4).

Mammography has been established as the imaging modality for screening and early detection of breast cancer. The major disadvantage of mammography however is the relatively low sensitivity and specificity, especially in women with dense breasts, secondary to the low contrast between the density of tumor tissue and the surrounding breast tissue (5).

Automated breast ultrasound is new operator independent device (1). 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 volumes according breast size (5).

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 (6).

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

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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., (8) 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%.

In the present study, according to mammography examination among the studied cases there were 25 (23.8%) with BIRADS of 0, 20 (19.0%) with I, 28 (26.7%) with II, 7 (6.7%) with III, 16 (15.2%) with IV and 10 (8.6%) with V, according to lesion classification there were 80 (76.2%) benign and 25 (23.8%) malignant. In Brem et al. (8) study that included 15318 women presented for screening mammography, nearly all of the cancers detected with the additional ABUS screening were invasive cancers (51 of 82, 62.2%) for screening mammography with ABUS and 93.3% (28 of 30) for ABUS alone. In addition, cancers detected with ABUS were probably a lower stage (20 of 30, 66.7%) (stage IA or IB) at diagnosis. Of the 17 cancers detected by using screening mammography alone, 64.7% (11 of 17) were ductal carcinoma in situ, compared with 6.7% (two of 30) of the cancers detected by using ABUS alone.

There were two studies validating the detection of BIRADS category 3 on screening US. The malignancy rate of category 3 lesions was 0.8%, and only 0.1% of the cases had suspicious changes at the 6-month follow-up (9).

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 fibroadenoma in 36 patients, and the most common malignant finding was Invasive ductal carcinoma in 22 patients.

In the current study, using Mammography it was shown that above BIRADS 3, it can discriminate between benign and malignant lesions with AUC of 0.718, level of sensitivity 67.4%, specificity 95.2%, PPV 90.6%, NPV 80.8% and accuracy 83.8%, where in Mostafa et al., (7) study, 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, they found that 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 = 0.0001. Using mammography alone, 20 out of 36 lesions were detected while with the addition of ABUS 34 out of 36 lesions were detected.

In Brem et al., (8) study, women with dense breasts who presented consecutively for routine screening mammography demonstrated improved detection of mammographically occult breast cancer by using ABUS over screening mammography alone. Breast cancer was diagnosed at screening in 112 women: in 82 women, by using screening mammography, and in an additional 30 women, by using ABUS. By using combined screening mammography and ABUS, 1.9 additional cancers per 1000 women screened were detected compared with the rate by using screening mammography alone.

Even Wilczek et al.(10), in a single-centre study, evaluated 1,668 asymptomatic women, with heterogeneously dense (50%–74% dense tissue) / extremely dense (>75% dense tissue) breast parenchyma. The combination of digital mammography plus ABUS determined an increase in cancer detection of 2.4 per 1,000 women screened. The increase in sensitivity was 36.4% for combined modalities versus mammography alone at study entry, while, including interval cancers, sensitivity increased by 25%. Specificity decreased by 0.7% when ABUS was added to mammography (10).

Giger et al. (11), in a multi-reader study on asymptomatic women with BIRADS C or D breast density, shown an improvement in detection of both mammography-negative and mammography-positive breast cancers with the use of ABUS. The improvement in sensitivity was 23.9%, for mammography-negative breast cancers (p = 0.004) and 5.9% for mammography-positive breast cancers (p=0.234); specificity decreased from 78.1% for mammography alone to 76.2% for the combined modalities. Combined ABUS-mammography compared to mammography alone, significantly improved reader’s detection of breast cancers in women with dense breast tissue without substantially affecting its specificity (11).
Brem et al. (8) stated an increased rate of cancer detection with the addition of ABUS to screening mammography in patients with dense breasts; however, there was an increase in the number of false positive results as well.

Kelly et al. (12), published a multicentre study based on 4,419 women with dense breasts and/or at elevated risk of breast cancer, compared the diagnostic performance of mammography alone versus that of ABUS plus mammography. The results showed that the mean sensitivity increased from 50% to 81%, an improvement of 63% in the number of cancer cases identified: all the researchers involved in the study found more cancers individually, and all found 16%–29% more cancers than the best mammography reader did with mammography alone. Specificity was 89.9% for ABUS, 95.15% for mammography and 98.7% for the combined modalities (12).

Kelly et al. (12), have also conducted another study on radiologists’ performance in detecting lesions in dense breasts using mammography alone versus automated whole breast ultrasound plus mammography: also, in this case the sensitivity increased by adding ABUS, from 50% to 81% (12).

Giuliano et al., (13) in a study performed in 3,418 asymptomatic women with mammographically dense breasts shows a detection of mammography plus ABUS of 12.3 per 1,000 breast cancers, compared to 4.6 per 1,000 by mammography alone (13).

Limitations of this study include the small number of patients, the relative bias in case selection as the researchers were still along the learning phase of this technique during the study, and that ABUS is a recently introduced imaging modality in Egypt with limited number of machines. Further studies incorporating this modality with the national screening program would definitely provide more information regarding the efficacy of the technique and the cost-benefit of its use on routine basis.

V. CONCLUSION

ABUS and Mammography showed fair substantial agreement regarding lesions classification (benign or malignant) with kappa (κ) 0.549. with diagnostic accuracy and sensitivity of ABUS were higher than that of mammography as for ABUS were 97.1% and 100% respectively, while for mammography were 83.8% and 67.4% respectively. So ABUS may serve as an effective new screening tool in addition to mammography.

REFERENCES