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Accuracy of different sonomammographic imaging modalities in assessment of breast tumor size

Nour Mohamed Mahmoud Kandil^{1*} , Lamiaa Mohamed Bassam Hashem², Sherihan W. Y. Gareer³ and Aya Mohamed Bassam Hashem¹

Abstract

Background: Accurate breast cancer size is crucial for staging and an important prognostic factor in patient management. Therapeutic decisions heavily depend on tumor size detection by radiological imaging. The purpose of our prospective comparative study is to compare the diagnostic accuracy of different sonomammographic breast imaging modalities, namely DM, DBT, CESM, 2D US and 3D US in the preoperative tumor size measurement.

Results: CESM, 3D US and 2D US achieved moderately strong correlation with the pathological size measurements, while (DM) and (DBT) showed fair correlation with the pathology. CESM showed the highest correlation coefficient (0.789), while (DBT) showed the lowest correlation coefficient (0.411). Regarding the agreement, there was good agreement of the size measured by CESM, 3D US and 2D US with the pathology as the ICC was (0.798), (0.769) and (0.624), respectively. The highest agreement with the pathology was achieved with CESM. The agreement of the size measured by (DM) and (DBT) with the pathology was moderate as the ICC was (0.439) and (0.416), respectively. The lowest agreement was achieved with the size measured by (DBT).

Conclusions: CESM and 3D US are more superior to DM, 2D US and DBT regarding preoperative size measurement. 3D US can be used as preoperative noninvasive technique, especially in patients with impaired renal function who cannot tolerate CESM.

Keywords: Sonomammography, Imaging modalities, Breast, Tumor size

Background

Globally, breast cancer is the most common female malignancy. It was responsible for 24% of new cancer cases and 15% of cancer deaths in 2018. Africa shows the highest case fatality ratio [1].

Tailoring individualized treatment strategies for each patient is the current standard level of care. To help the treating physician and the patient reach an optimum decision regarding treatment, the tumor load and biology

(pathology, biomarkers and gene expression) should be thoroughly evaluated. The tumor load is assessed through loco-regional and systemic extent. The loco-regional extent includes size, multifocality/centricity and lymph node status [2].

Accurate size measurement of cancerous breast lesions is crucial, especially when breast cancer pathology is proven. Precise lesion size measurement is important for optimal management decisions and essential for the detection of patient's response to neoadjuvant chemotherapy and a relevant prognostic factor [3].

According to European society of Medical Oncology, digital mammography (DM) and ultrasound (US) are the standard preoperative imaging modalities for breast

*Correspondence: dr.n.kandil@hotmail.com

¹ Lecturer at Radiology Department, Faculty of Medicine, Cairo University, 1 Kasr ELainy Street Fom Elkalig, Cairo, Egypt
Full list of author information is available at the end of the article

cancer. They are used to measure the tumor size which is an important diagnostic and prognostic factor in disease management. However, the inevitable problem of tissue overlap in mammography prevents the accurate estimation of tumor size especially in dense breasts. This can be partly rectified using two-dimensional ultrasonography (2D US). But again, the size measurement could be affected by the background parenchymal echotexture resulting in over- or underestimation of the tumor size [4, 5].

By visualizing the breast lesions in the axial and coronal planes, three-dimensional ultrasonography (3D US) allows an increased accuracy in size assessment. Moreover, it produces a tumor volume that can be saved and revisited at any time by any radiologist not just the operator. This feature overcomes the operator dependency that is encountered with 2D US examination [6].

Digital breast tomosynthesis (DBT) is a three-dimensional (3D) modification of DM. It overcomes the problem of tissue overlap by producing multiple slices of the breast that allow thorough examination of the lesions, thus allowing better assessment of tumor size and margins [7].

Contrast-enhanced spectral mammography (CESM) uses contrast material to highlight the lesions on mammography. The images are processed to produce an image with suppressed parenchymal enhancement and emphasized pathological enhancement. Therefore, it can be used, to measure tumor size, as well as to assess tumor multiplicity. It has also been proven to be especially useful in the assessment of edematous breasts [8, 9].

The objective of our study was to compare the diagnostic performance of different sonomammographic breast imaging modalities, namely DM, 2D ultrasound, DBT, CESM and handheld 3D US, in the assessment of preoperative tumor size which can alter the patient management. A preoperative evaluation of the size by imaging can help to decrease the incidence of residual and recurrent lesions.

Methods

This is a prospective comparative study comparing the role of digital mammography (DM), two-dimensional ultrasound (2D US), contrast-enhanced spectral mammography (CESM), three-dimensional ultrasound (3D US) and digital breast tomosynthesis (DBT) in the detection of the size of breast malignant lesions using postoperative histopathological analysis as the gold standard.

The study included 147 patients with 149 breast lesions (two cases have bilateral unifocal breast lesions) attended our breast imaging unit during the period from January 2020 to August 2021 with symptomatic (135) breast

lesions as well asymptomatic (14) breast lesions. Breast lesions classified as BIRADS 6 were included. No specific age group selection was applied.

Patients with impaired renal functions, with multicentric or multifocal breast lesions, known allergic reaction to contrast material, and pregnant women, were excluded from our study, as well as patients receiving preoperative neoadjuvant chemotherapy.

All patients initially underwent digital mammography (DM), two-dimensional ultrasound (2D B mode US) and ultrasound-guided biopsy as the baseline imaging. Afterward, breast lesions classified as BIRADS 6 were subjected to 3D US examination followed by DBT and finally CESM. The breast lesions were assessed regarding the size measured in cms in the greatest dimension including tumor spicules. The results were compared to the postoperative pathology as the reference standard.

Ultrasound technique

2D B-mode ultrasound

2D B-mode US was performed using Philips iU22 xMatrix ultrasound system with L 12–5 transducer. The breast quadrants examination was done in a radial pattern, and skin to pectoral fascia depth was fully examined. Axillary lymph nodes were then examined.

The examination criteria included the lesion size and presence of spicules, desmoplastic reaction or calcifications if present.

3D ultrasound

3D US was performed (targeted on the affected breast) using Philips iU22 xMatrix ultrasound system twice, first using L 12-5 probe by manually sweeping the lesion for surface rendering. After that, MPR images and volume acquisition were performed using X6-1 pure wave xMatrix transducer. Lesions were viewed in the axial, sagittal and coronal planes.

Technique of DM and DBT

Patients were examined by Senographe 2000 D full-field digital mammography Essential GE Healthcare. Standard two projections (CC and MLO) views were obtained for digital mammography. Similar views were acquired for DBT in a step-and-shoot tube motion, a complete stop for each of the nine exposures per each view. SenoClaire uses ASiRDBT, an iterative reconstruction algorithm that yields full-field digital mammography (FFDM)-like images. Images are then seen through tomosynthesis planes and slabs where dedicated tools to review tomosynthesis data sets such as cine loop and V-Preview reconstructed images were used.

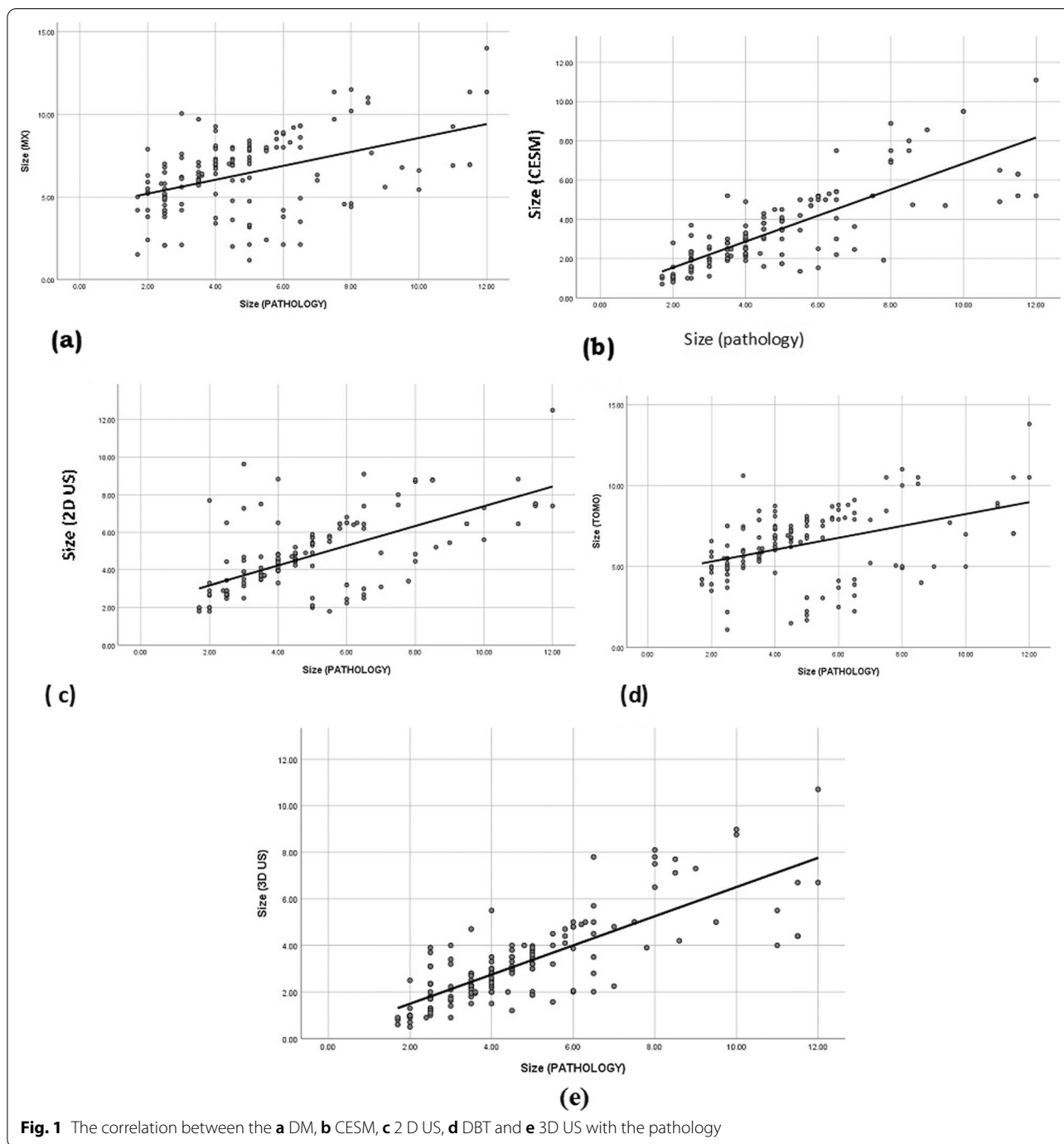


Fig. 1 The correlation between the **a** DM, **b** CESM, **c** 2 D US, **d** DBT and **e** 3D US with the pathology

Technique of CESM

The examination consists of an intravenous injection of an iodinated contrast agent (Omnipaque, 300 mg I/ml) at a dose of 1.5 ml/kg (maximum dose of 120 ml) through a catheter introduced in the ante-cubital vein. This is

followed by a 2-min wait, and afterward, both breasts are imaged in the standard mammographic views. Each view is obtained in low- and high-energy images. Low-energy images were acquired at peak kilovoltage values ranging from 26 to 31 kVp, which is below the k-edge of iodine,

and they resemble standard mammography. High-energy images were acquired at 45–49 kVp, which is above the k-edge of iodine. Subtraction of both high and low images suppresses the background parenchyma and highlights the areas of contrast uptake.

Image analysis

A subjective assessment using Image Diagnostic Mammography Workstation was done. The type of findings depicted on mammography, DBT were reported as regards the size of the pathological lesions, extension and calcifications.

The subtracted CESM images were reviewed using reading criteria based on the size of the mass/non-mass enhancement.

The ultrasound images were reviewed to detect the size of the lesions taking into consideration the long spicules as well as the extension and calcifications.

All techniques were performed by two experienced consultant's radiologists, with more than 10 years of experience in breast imaging. The definitions of the statistical terms provided in the ACR BIRADS glossary were adopted in this study.

Sample size and statistical methods

The software was used for sample size calculation: G*power version 3.0.10. According to Yamakanamardi and Hiremath (XX), the MMG combined with SMG had a sensitivity of 90.4% and specificity of 82.4%. Assuming a disease prevalence of 50%, an alpha error of 5% and an acceptable precision of 10%, the calculated sample size was 125 patients with accounting for 10% dropout rate.

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). Data were summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Correlations between quantitative variables were done using Spearman correlation coefficient [10]. Testing for agreement between size measured by pathology and by different methods was done using the intraclass coefficient (ICC) and Cronbach's alpha reliability coefficient with their 95% confidence interval (95%CI) [11]. *P* values less than 0.05 were considered as statistically significant.

Value of ICC	Strength of agreement
<0.20	Poor
0.21–0.40	Fair
0.41–0.60	Moderate
0.61–0.80	Good
0.81–1.00	Very good

Results

The current study included 147 patients with 149 suspicious unifocal breast lesions; two patients have bilateral unifocal breast lesions. Out of the 149 lesions, 80 lesions were in the left breast and 69 lesions were in the right breast.

Age of the patients ranged from 25 to 70 years with mean age 49.7 ± 11.5 SD. The most prevalent pathology was IDC ($n=123/149$, 82.6%), followed by ILC ($n=18/149$, 12.1%), mixed ($n=6/149$, 4%), and finally mucinous carcinoma ($n=2/149$, 1.3%).

Out of the 149 breast lesions in the 147 patients, ($n=14/149$, 9.4%) were incidentally discovered during screening and ($n=135/149$, 90.6%) were discovered during diagnostic study. [(127/149, 85.2%) were palpable masses, (2/149, 1.3%) were recurrent masses, and (6/149, 4.1%) were masses for follow-up.]

All the patients underwent digital mammography (DM), 2D and 3D ultrasound (US), contrast-enhanced spectral mammography (CESM) and digital breast tomosynthesis (DBT). Size of the breast lesion was measured in cms in the greatest dimension including tumor spicules and compared to the postoperative pathology.

The range, mean and SD of the size of the breast lesions as measured by the different imaging modalities compared to the postoperative pathology are shown in Table 1.

The mean of the size measured by DM was 6.37 ± 2.28 SD, the mean of the size measured by DBT was 6.31 ± 2.08 SD, the mean of the size measured by CESM was 4.64 ± 1.97 SD, the mean of the size measured by 2D US was 3.38 ± 1.96 SD, and the mean of the size measured by 3D US was 3.23 ± 1.89 SD. The mean of the postoperative pathology size was 4.78 ± 2.38 SD.

(See figure on next page.)

Fig. 2 A 64-year-old female patient presented with left breast lump. **a** and **b** Digital mammography of the left breast in CC and MLO views showed a LOQ spiculated mass with maximum dimension of 2.4 cm. **c** 2D US showed 3–4 O'clock spiculated, hypoechoic solid mass lesion, and maximum dimension of 1.53 cm. **d** 3D US in coronal plane revealed the irregularity and spiculations. Maximum dimension of the tumor was 1.57 cm. **e** and **f** DBT in CC and MLO views showed a spiculated lesion, and maximum dimension is 3.06 cm because of the extended spicules anteriorly and posteriorly. **g** and **h** CESM in MLO and CC views showed a single lesion of faint heterogeneous enhancement (the spicules did not show any enhancement) and maximum dimension of 1.8 cm. Postoperative pathology revealed IMC with maximum dimension of 1.5 cm

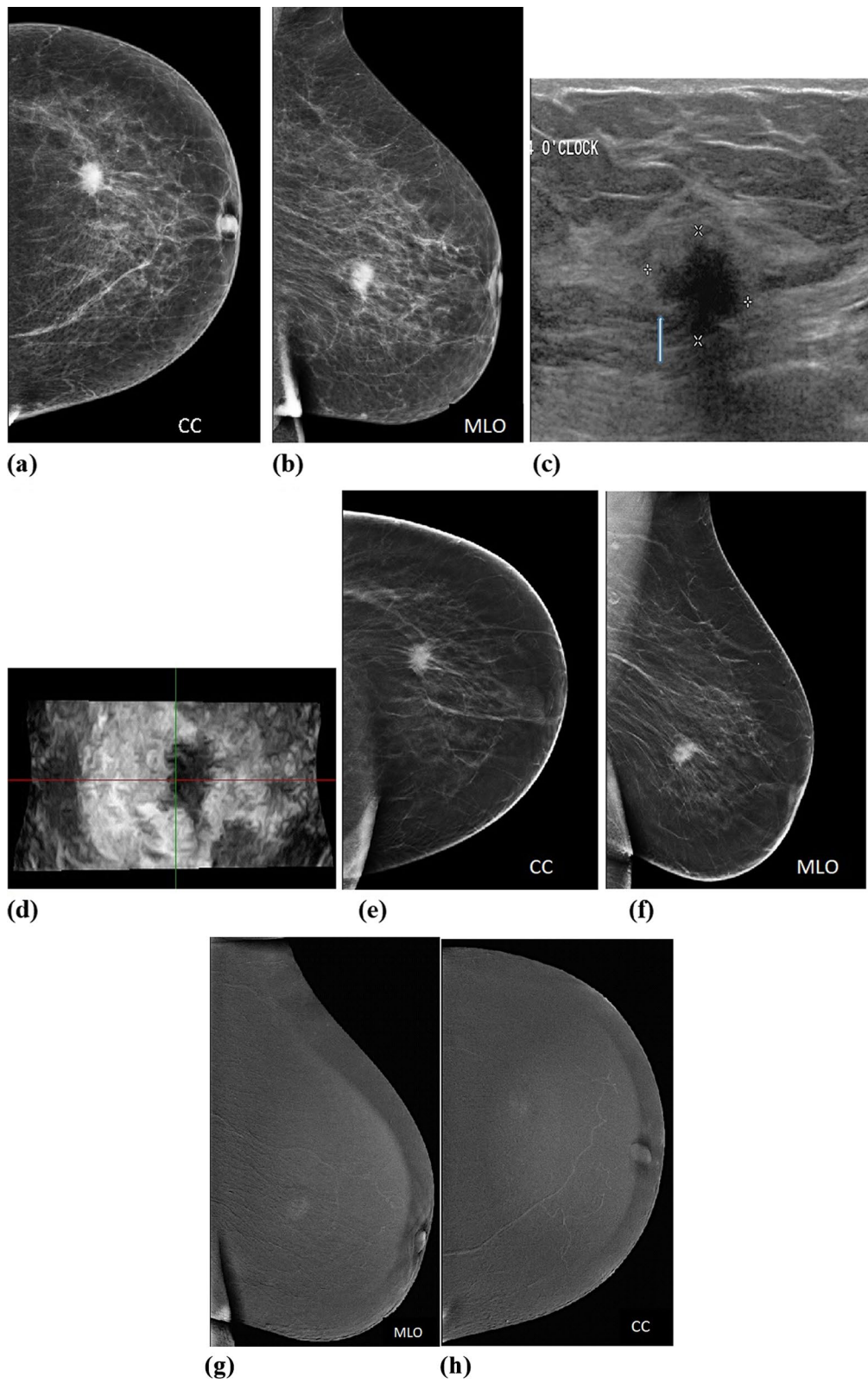


Fig. 2 (See legend on previous page.)

Table 1 The range, mean and SD of the size measured by each modality and the pathology

	Mean	Standard deviation	Median	Minimum	Maximum
Size (DM)	6.37	2.28	6.40	1.17	14.00
Size (CESM)	4.64	1.97	4.43	1.80	12.50
Size (DBT)	6.31	2.08	6.40	1.10	13.80
Size (3D US)	3.23	1.89	2.90	0.50	10.70
Size (2D US)	3.38	1.96	3.00	0.70	11.10
Size (PATHOLOGY)	4.78	2.38	4.00	1.70	12.00

Correlation with pathology

Comparison of the lesion size by different modalities of imaging versus pathology showed that CESM, 3D US and 2D US achieved moderately strong correlation with the pathological size measurements, while (DM) and (DBT) showed fair correlation with the pathology. CESM showed the highest correlation coefficient (0.789), while (DBT) showed the lowest correlation coefficient (0.411), and all the modalities showed statistically significant results with p value < 0.001 (Figs. 1, 2 and 3). The results are shown in Table 2.

Agreement with the pathology (Table 3)

There was good agreement of the size measured by CESM, 3D US and 2D US with the pathology as the ICC was (0.798), (0.769) and (0.624), respectively. The highest agreement with the pathology was achieved with CESM. The agreement of the size measured by (DM) and (DBT) with the pathology was moderate as the ICC was (0.439) and (0.416), respectively. The lowest agreement was achieved with the size measured by (DBT).

Discussion

Together with clinical examination, DM and 2D US are used as the basis for initial diagnosis and staging of breast cancer. Although very useful in fatty breasts, its results can be compromised in dense breasts where tissue overlap can mask an underlying lesion. Limiting factors of 2D US include operator dependency and difficulty of accurate size measurement in the AP plane especially in lesion with strong posterior acoustic shadowing [3, 12].

Table 2 The correlation between the different modalities and the pathology

	Size (PATHOLOGY)		
	Correlation coefficient	P value	N
Size (DM)	0.415	< 0.001	149
Size (2D US)	0.617	< 0.001	149
Size (DBT)	0.411	< 0.001	149
Size (3D US)	0.782	< 0.001	149
Size (CESM)	0.798	< 0.001	149

In the current work, we compared the diagnostic performance of five different breast imaging modalities in the preoperative tumor size measurement in 149 breast lesions. We compared the correlation and agreement of tumor size—as measured by DM, 2D US, 3D US, DBT and CESM—to the postoperative pathology.

Our results showed that highest correlation and agreement were achieved by CESM. It showed the highest correlation coefficient (0.798) and highest ICC (0.789). Several studies discussed the role of CESM in the preoperative staging of breast cancer especially in size measurement. In concordance with our results, Youn et al. [13] concluded that CESM achieved higher agreement with the size than MG, with ICC 0.907 compared to 0.820, respectively. This was especially highlighted in the CC view.

In agreement with this study's results, Lobbes et al. [14] and another study conducted in 2014 [15] achieved the highest pathology size correlation with CESM. Although other studies suggested that sizes measured by both CESM and MG were comparable, MG resulted in more overestimation of tumor size [16].

Bozzini et al. [17] suggested that both CESM and 2D US can measure tumor size in concordance with pathology 64.6% and 62%, respectively, and both were significantly better than MG (45.2%) in size measurement. These results are keeping with our work, where both CESM and 2D US performed better than MG.

Another small study performed on 22 patients came to the conclusion that CESM was more accurate than 2D US in preoperative tumor size measurement [18].

(See figure on next page.)

Fig. 3 A 53-year-old patient presented with right breast lump. **a** and **b** DM in CC and MLO views showed UIQ irregular mass and maximum dimension of 3.6 cm. **c** 2D US revealed a spiculated mass lesion with marked desmoplastic reaction and maximum dimension of 2.1 cm. **d** 3D US revealed spiculated lesion and maximum dimension of 2.7 cm. **e** and **f** DBT in CC and MLO views revealed spiculated lesion and maximum dimension of 4 cm. **g** and **h** CESM revealed heterogeneously enhancing mass lesion and maximum dimension of 2.7 cm. Postoperative pathology revealed a single tumor, IDC, with maximum dimension of 2.5 cm

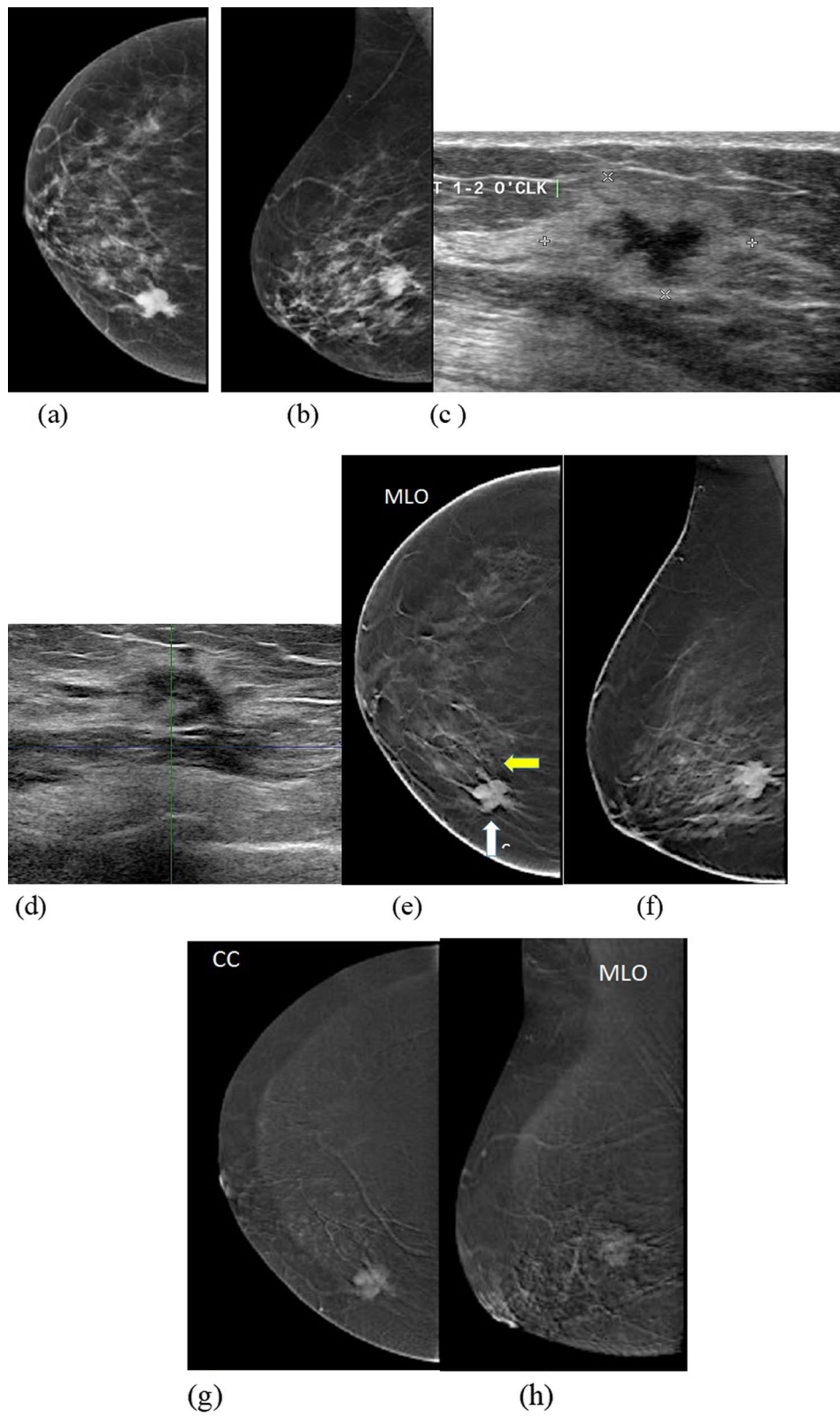


Fig. 3 (See legend on previous page.)

Table 3 The agreement between the sizes measured by different modalities and the pathology

	value	95% confidence interval		P value
		Lower bound	Upper bound	
<i>CESM</i>				
Intraclass correlation coefficient	0.789	0.720	0.843	<0.001
<i>3D US</i>				
Intraclass correlation coefficient	0.769	0.695	0.828	<0.001
<i>2D US</i>				
Intraclass correlation coefficient	0.624	0.515	0.713	<0.001
<i>DM</i>				
Intraclass correlation coefficient	0.439	0.300	0.560	<0.001
<i>DBT</i>				
Intraclass correlation coefficient	0.416	0.274	0.540	<0.001

These results are also consistent with our work. We also suggest CESM performed better than 2D US regarding size measurement, showing better correlation and agreement with the pathology size.

In our study, the lowest correlation and agreement were noticed with DBT which tended to overestimate the size. These results may differ from previous studies that showed good correlation between DBT and pathology size [19–21]. A possible explanation in our study is that the tumor spicules—that are more evident on DBT—were included in size measurement.

A more recent study performed by Girometti et al. [22] compared the performance of CESM to DM + DBT in the preoperative setting. In concordance with our results, they concluded that although both CESM and DM + DBT showed comparable size performance, CESM still showed higher agreement with the pathology size, especially in less experienced readers.

In our study, the correlation coefficient and ICC by 2D US was (0.617) and (0.624).

On comparing 2D US to MG, our results showed better agreement with 2D US. Similar findings were suggested by Leddy et al. [12] who suggested US allowed more accurate tumor size measurement than DM and MRI.

In our study, close results to CESM were achieved by 3D US with correlation coefficient (0.782) and ICC (0.769). Few studies discuss the role of 3D US in the preoperative tumor size assessment.

Clauser et al. [23] measured the greatest dimension and the volume of the preoperative tumor using 2D and 3D US as well as MRI. Similar to our study, they concluded that both 2D and 3D US show good concordance with the pathology at 0.79 for 3D US and 0.82 for 2D US.

Helal et al. [24] compared the diagnostic performance of CESM and 3D US in preoperative staging including size, multiplicity and peritumoral stromal invasion.

According to their work, both CESM and 3D US were the most accurate regarding size measurement. However, 3D US showed the highest correlation.

Our study had few limitations. First is the small number of patients with the poor representation of different breast cancer pathologies, especially ILC. Second, the inter-reader variability was not measured.

Conclusions

Preoperative tumor size measurement is an important decision-making information. Although DM and 2D US are the baseline imaging modalities used to measure preoperative tumor size, better results could be reached through other modalities. CESM and 3D US are more superior to DM, 2D US and DBT regarding size measurement. 3D US can be used as preoperative noninvasive technique, especially in patients with impaired renal function who cannot tolerate CESM.

Abbreviations

ACR: American College of Radiology; BIRADS: Breast Imaging Reporting and Data System; CC: Craniocaudal; CESM: Contrast-enhanced spectral mammography; Cm: Centimeter; DBT: Digital breast tomosynthesis; DM: Digital mammography; ICC: Intraclass coefficient; IDC: Invasive ductal carcinoma; IMC: Invasive micropapillary carcinoma; MG: Mammography; MLO: Mediolateral oblique; SD: Standard deviation; 2D US: Two-dimensional ultrasound; 3D US: Three-dimensional ultrasound.

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Author contributions

NK and AH analyzed and interpreted the patient data regarding the breast lesions size measurement in the greatest dimension including tumor spicules. LH and SG revised all the data interpreted by other authors. All authors read and approved the final manuscript.

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Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations**Ethics approval and consent to participate**

The current study had been approved by Kasr El-Aini Hospital, Research and Ethical committee.

Consent for publication

The authors affirm that human research participants provided informed consent for publication of the images in the figures.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Competing interests

The authors have no relevant financial or non-financial interests to disclose.

Author details

¹Lecturer at Radiology Department, Faculty of Medicine, Cairo University, 1 Kasr ELainy Street Fom Elkalig, Cairo, Egypt. ²Assistant Professor at Radiology Department, Faculty of Medicine, Cairo University, 1 Kasr ELainy Street Fom Elkalig, Cairo, Egypt. ³Lecturer at Radiology Department, National Cancer Institute, Cairo University, 1 Kasr ELainy Street Fom Elkalig, Cairo, Egypt.

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