Comparison Between Mammography, Ultrasonography and Digital Breast Tomosynthesis in Breast Cancer Size Measurement Accuracy

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ABSTRACT

Background: Mammography, ultrasonography and digital breast tomosynthesis (DBT) may vary in determination of tumor size of breast tumors.

Objective: to assess the three imaging modalities (mammography, ultrasonography and DBT) regarding tumor size determination.

Methods: This study is a cross-sectional study from November 2019 to December 2021. Patients pathologically diagnosed with primary breast cancer who had available postoperative histopathological tumor measurement with preoperative examination with mammography, ultrasonography and DBT were enrolled in the study.

Results: Univariate analyses showed that the breast density (p=0.014) and tumor pathology (p=0.004) were significantly correlated with the accuracy of mammography measurements. Tumor pathology (p< 0.001) was significantly correlated with the accuracy of US and breast density (p=0.039) was significantly correlated with the accuracy of DBT measurements (less significant than mammography). The ICCs were above 0.90 Z Excellent agreement between three methods. The highest result was for DBT.

Conclusion: DBT might play an important role in the detection and measurement of breast cancer. Ultrasound and mammography tend to underestimate lesion size and mass measurements may be affected with pathological type of tumor.

Keywords: mammography, ultrasonography and digital breast tomosynthesis, breast cancer.

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INTRODUCTION

Treatment options for breast cancer are determined by a multidisciplinary team based on the tumor's staging, localization, and extent. Broad lines of treatment include surgical options, neoadjuvant treatment, endocrinal treatment, chemo and radiotherapy (1). Surgical options include mastectomy or

breast-conserving surgery. Breast cancer size is an important factor in local staging, choosing treatment strategy and influencing prognosis (2).

Breast conserving surgery is widely accepted as a treatment of choice, especially for early breast cancer. Accurate pre-therapeutic tumor size determination helps to achieve adequate surgical margins, which was found to reduce locoregional recurrence (3). Although histopathological size measurement is the gold standard, but it is not yet available. So preoperative imaging based exact tumor size measurement has a significant role in choosing patients eligible for breast preservation, enabling surgeons to acquire perfect margins, reduce the need for re-removal and also determine the need for neoadjuvant therapy, chemo and radiotherapy(4).

Multiple imaging modalities are used to examine breasts for screening and diagnostic purposes. Mammography and ultrasonography are widely available and accessible methods. Size estimation with mammography may be affected by multiple factors which hinder accurate size measurement (5). The main factors that affect accurate size determination are overlapping breast parenchyma obscuring exact margins of the tumor, compression of breasts during mammography and distance between the tumor and the film/detector (4).

Ultrasound is a helpful tool, especially in dense breasts, but its accuracy in size measurement is controversial. Multiple studies state that ultrasound tends to underestimate tumor size (6).

Digital breast tomosynthesis (DBT) outperforms mammography for accurate cancer size measurement as it can unravel parenchymal overlap and adequately visualize exact tumor margins (7). This study aims to assess the three imaging modalities (mammography, ultrasonography and DBT) regarding tumor size determination.

METHODS

This study is a cross-sectional study. Patients' archived files from November 2019 to December 2021 were reviewed. Patients pathologically diagnosed with primary breast cancer who had available postoperative histopathological tumor measurement with preoperative examination with mammography, ultrasonography and DBT were enrolled in the study. Patients preoperatively treated with neoadjuvant or chemotherapy, patients with a long interval between imaging examination and surgery (more than one month), and patients with postoperative histopathological results of imperfect resection margins were excluded from our study. 111 patients were enrolled in this study.

Mammogram evaluation;

One radiologist with experience in breast imaging evaluated basic mammographic views (craniocaudal and mediolateral oblique views). Breast density is determined according to American college of radiology (ACR) classification system. The reader measured the largest dimension of lesions using the electronic built-in ruler of the work station, being blind to other measurements of ultrasound, DBT and histopathology. The reader was free to determine the exact margins of lesions to obtain measurements. Lesions presented with long speculations and lesions presented as grouped microcalcifications were measured as follows: long speculations were excluded, including only the mass core. The area of grouped microcalcifications was measured to the widest extent, including calcifications. In six mammograms, the tumor size could not be estimated due to extremely dense breasts obscuring the lesion.

Ultrasonography evaluation;

Using logic F8 GE ultrasound machine's built-in measurement tool, the greatest dimensions, including the hypoechoic mass or lobulations, were used for study. Radiating hyperechoic desmoplastic speculations were excluded. Diffuse masses with areas of tissue distortion were measured from edge to edge of tissue distortion.

DBT evaluation;

The reader used a workstation, examined both basic views, freely explored different sections to precisely determine tumor margins and measured the largest dimension of lesion using electronic built-in measurement.

The pathologic tumor size was also measured by a pathologist, and the largest lesion dimension was recorded in millimetres for analysis.

Satistical analysis;

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). The Kolmogorov- Smirnov was used to verify the normality of distribution of variables; Comparisons between groups for categorical variables were assessed using Chi-square test (Fisher or Monte Carlo). Paired t-test was used for normally distributed quantitative variables, to compare between two periods.. Bland Altman was used for agreement was used Bland Altman plot and one sample t test (between the difference and zero) (if significant then there is fixed bias). Intra class Correlation coefficient was used for the agreement between histopathology size and each other imaging. The ICCs were classified using a system suggested by Koo and Li (2016) as follows: less than 0.50 Z poor agreement; 0.50 to less than 0.75 Z moderate agreement; 0.75 to 0.90 Z Good agreement; Above 0.90 Z Excellent agreement. A P value less than 0.05 was considered statistically significant. Significance of the obtained results was judged at the 5% level.

RESULTS

111 patients' records with primary breast cancer were evaluated in a retrospective analysis. The median age was 57 years (range 28–87). Regarding density level of the breast tissue; mammographic density grade B was present in 44.1% and a density grade A in 23.4%. 12.6% of women had very dense glandular tissue (ACR D). IDC was present in 40.5% of the cases. 38.7% of the patients were allocated to the IDC + DCIS tumor group, and a DCIS alone or ILC alone were found in 4.5% and 16.2% respectively (table 1).

The mean of histological size of tumors was 25.28±8.11 mm (median: 23). The means of measured tumor sizes were 24.69±7.85 mm (median: 23), 23.06±7.06 mm (median: 23) and 25.09±8 mm (median: 23) in mammography, ultrasonography and DBT, respectively (table 2).

The number of concordant measurements were 93 (83.8%), 81 (73.0%) and 103 (92.8%) for mammography, ultrasonography and DBT, respectively. The numbers of concordant, underestimated and overestimated measurements for each imaging technique are represented in (Table 3).

The correlation between the accuracy of tumor size measurements by each of the three imaging modalities was evaluated for all variables included in the study. Accordingly, Tables 4, 5, and 6 present the results of these analyses for mammography, US, and DBT, respectively.

Univariate analyses showed that the breast density (p=0.014) and tumor pathology (p=0.004) were significantly correlated with the accuracy of mammography measurements. Tumor pathology (p< 0.001) was significantly correlated with the accuracy of US and breast density (p=0.039) was significantly correlated with the accuracy of DBT measurements (less significant than mammography).

The mean differences between histological sizes and mammography, ultrasonography, and DBT were 1.2 mm (-4.2 to 6.5), 2.4 mm (-3. 9 to 8.6), and 0.2 mm (- 3.3 to 3.6), respectively (Figure 1).

Paired test shows no significant difference between histopathology and DBT in mass measurement (table 7).

The ICCs were above 0.90 Z Excellent agreement between three methods. The highst result was for DBT.(Intra class Correlation coefficient excellent agreement between the three methods and histopathology(0.976) (Table 7).

Table (1): Distribution of the studied cases according to different parameters (n = 111)

	No. (%)
Age (years)	
Mean ± SD.	**54.85 ± 11.33**
Median (Min. – Max.)	**57 (28 – 87)**
<50	**25(22.5%)**
≥50	**86(77.5%)**
Family history	
Negative	**81(73.0%)**
Positive	**30(27.0%)**
Density	
Non dense	**75(67.6%)**
Dense	**36(32.4%)**
ACR	
A	**26(23.4%)**
B	**49(44.1%)**
C	**22(19.8%)**
D	**14(12.6%)**
Pathology	
DCIS	**5(4.5%)**
IDC	**45(40.5%)**
DCIS+IDC	**43(38.7%)**
ILC	**18(16.2%)**

Table (2): Descriptive analysis of the studied cases according to different parameters (n = 111)

	N	Min. – Max.	Mean ± SD.	Median
Histopathology size	**111**	**8.0 – 48.0**	**25.28 ± 8.11**	**23.0**
Mammography size	**105**	**8.0 – 54.0**	**24.69 ± 7.85**	**23.0**
Tomosynthesis size	**111**	**8.0 – 51.0**	**25.09 ± 8.0**	**23.0**
Ultrasound size	**110**	**6.0 – 42.0**	**23.06 ± 7.06**	**23.0**

Table (3): Distribution of the studied cases according to US, Mammo and Tomo (n = 111)

	No. (%)
US	
Concordant	**81(73.0%)**
Underestimation	**25(22.5%)**
Overestimation	**5(4.5%)**
Mammography	
Concordant	**93(83.8%)**
Underestimation	**13(11.7%)**
Overestimation	**5(4.5%)**
DBT	
Concordant	**103(92.8%)**
Underestimation	**6(5.4%)**
Overestimation	**2(1.8%)**

Table (4): Relation Mammographic size measurement and different parameters (n= 111)

	Mammography				
	Concordant (n= 93)	Underestimation (n= 13)	Overestimation (n= 5)	p_1	p_2
ACR					
A	**21 (22.6%)**	**3 (23.1%)**	**2 (40.0%)**		
B	**46 (49.5%)**	**2 (15.4%)**	**1 (20.0%)**	$^{MC}p=$	$^{MC}p=$
C	**14 (15.1%)**	**7 (53.8%)**	**1 (20.0%)**	**0.511**	**0.014***
D	**12 (12.9%)**	**1 (7.7%)**	**1 (20.0%)**		
Pathology					
DCIS	**5 (5.4%)**	**0 (0.0%)**	**0 (0.0%)**		
IDC	**43 (46.2%)**	**1 (7.7%)**	**1 (20.0%)**	$^{MC}p=$	$^{MC}p=$
DCIS+IDC	**34 (36.6%)**	**6 (46.2%)**	**3 (60.0%)**	**0.474**	**0.004***
ILC	**11 (11.8%)**	**6 (46.2%)**	**1 (20.0%)**		

MC: Monte Carlo FE: Fisher Exact

p: p value for Chi square test for comparing between Underestimation and Overestimation
p: p value for Chi square test for comparing between concordant and discordant
***: Statistically significant at p ≤ 0.05**

Table (5):Relation between US size measurement and different parameters (n= 111)

	US				
	Concordant (n= 81)	Underestimation (n= 25)	Overestimation (n= 5)	p_1	p_2
ACR					
A	**20 (24.7%)**	**6 (24.0%)**	**0 (0.0%)**		
B	**41 (50.6%)**	**8 (32.0%)**	**0 (0.0%)**	$^{MC}p=$	**0.015***
C	**14 (17.3%)**	**7 (28.0%)**	**1 (20.0%)**	**0.052**	
D	**6 (7.4%)**	**4 (16.0%)**	**4 (80.0%)**		
Pathology					
DCIS	**4 (4.9%)**	**1 (4.0%)**	**0 (0.0%)**	$^{MC}p=$	^{MC}p
IDC	**40 (49.4%)**	**5 (20.0%)**	**0 (0.0%)**	**0.731**	**<0.001***

DCIS+IDC	**33 (40.7%)**	**8 (32.0%)**	**2 (40.0%)**
ILC	**4 (4.9%)**	**11 (44.0%)**	**3 (60.0%)**

MC: Monte Carlo FE: Fisher Exact

p: p value for Chi square test for comparing between Underestimation and Overestimation
p: p value for Chi square test for comparing between concordant and discordant
***: Statistically significant at p ≤ 0.05**

Table (6):Relation Tomosynthesis size measurement and different parameters (n= 111)

	DBT				
	Concordant (n= 103)	**Underestimation (n= 6)**	**Overestimation (n= 2)**	**p_1**	**p_2**
ACR					
A	**25 (24.3%)**	**1 (16.7%)**	**0 (0.0%)**		
B	**47 (45.6%)**	**1 (16.7%)**	**1 (50.0%)**	**^{MC}p=**	**^{MC}p=**
C	**17 (16.5%)**	**4 (66.7%)**	**1 (50.0%)**	**1.000**	**0.036***
D	**25 (24.3%)**	**1 (16.7%)**	**0 (0.0%)**		
Pathology					
DCIS	**5 (4.9%)**	**0 (0.0%)**	**0 (0.0%)**		
IDC	**43 (41.7%)**	**1 (16.7%)**	**1 (50.0%)**	**^{MC}p=**	**^{MC}p=**
DCIS+IDC	**40 (38.8%)**	**2 (33.3%)**	**1 (50.0%)**	**0.683**	**0.397**
ILC	**15 (14.6%)**	**3 (50.0%)**	**0 (0.0%)**		

MC: Monte Carlo FE: Fisher Exact

p: p value for Chi square test for comparing between Underestimation and Overestimation
p: p value for Chi square test for comparing between concordant and discordant
***: Statistically significant at p ≤ 0.05**

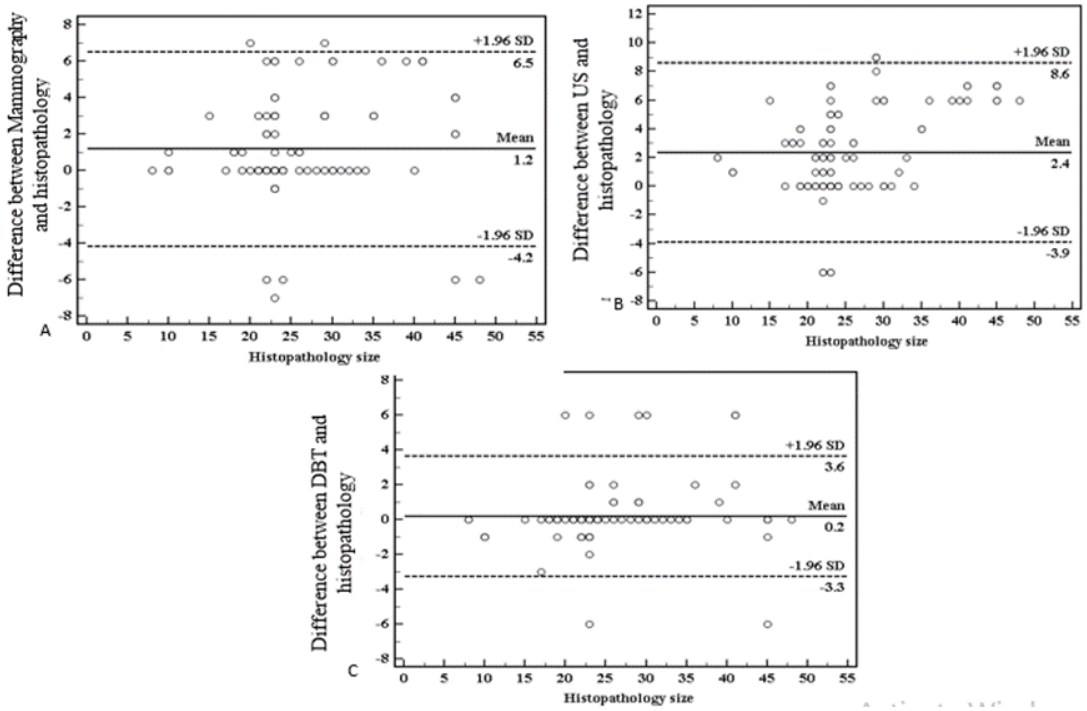

Figure (1) Deviation of mammography (A), Ultrasound (B) and tomosynthesis (C) measured breast cancer sizes from histopathology size. The mean of the difference in size estimation (thick dashed lines) and ±1.96 SD limits (thin dashed lines) are illustrated on each graph.

Table (7):Comparison between histopathology size and different imaging

	Histopathology (n = 111)	Mammography (n = 105)	DBT (n = 111)	US (n = 110)
Mean ± SD.	**25.28 ± 8.11**	**24.69 ± 7.85**	**25.09 ± 8.0**	**23.06 ± 7.06**
Median (Min. – Max.)	**23 (8 – 48)**	**23 (8 – 54)**	**23 (8 – 51)**	**23 (6 – 42)**
p		**<0.001***	**0.259**	**<0.001***
ICC		**0.940**	**0.976**	**0.911**
p_0		**<0.001***	**<0.001***	**<0.001***

p: p value for Paired t-test for comparing between histopathology size and each other imaging

p_0: p value for ICC for the agreement between histopathology size and each other imaging

***: Statistically significant at p ≤ 0.05**

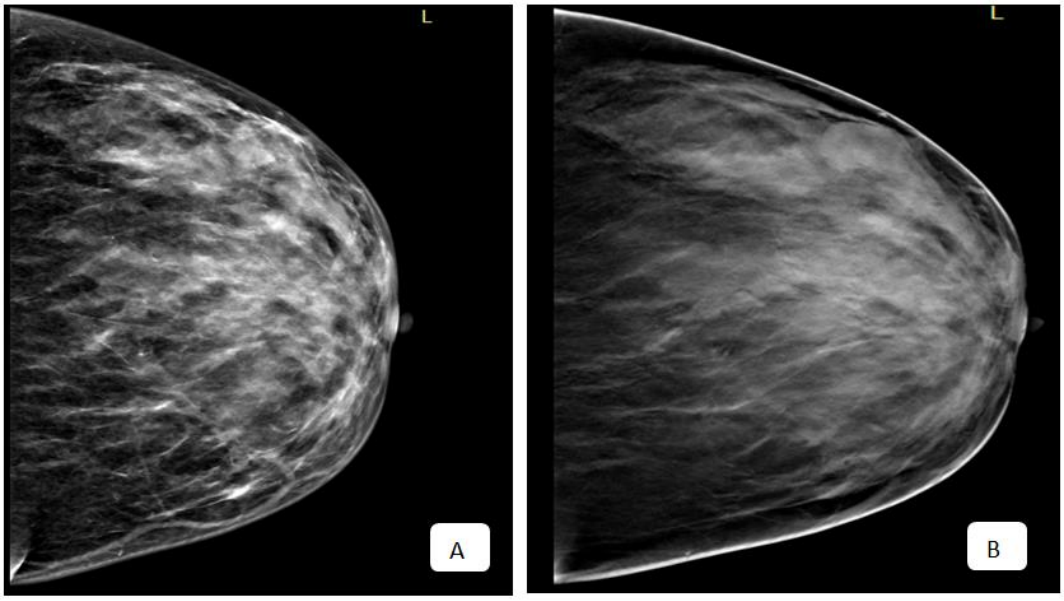

Figure 2; Mammogram (A) and DBT (B) of 32 years old female diagnosed with left breast ILC. The mass outlines were obscured with overlapping parenchymal density on mammogram, while tomosynthesis showed its outlines precisely. The mass size was concordant with histopathological size.

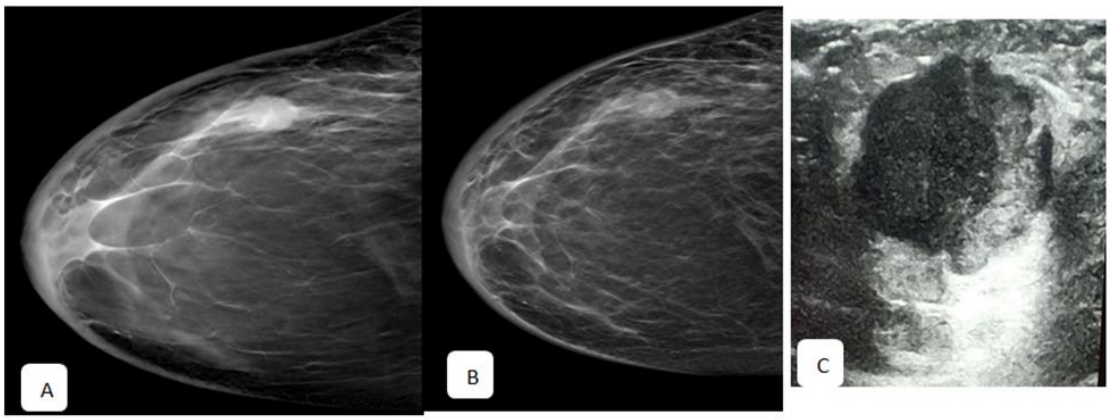

Figure 3; 40 years old female with right breast IDC+DCIS. Concordance between histopathology and DBT (A) regarding the mass size. It was measuring 35 mm.

Underestimation of lesion on mammogram (B) and ultrasound (C) was noted. The mass was measuring 30mm and 29 mm, respectively

DISCUSSION

In primary breast cancer, tumor size is one of the most essential factors to consider when making treatment decisions. Precise imaging based measurement is the available method for pre-therapeutic staging. This research is performed to measure accuracy of three widely available screening and diagnostic tests in breast cancer measurement compared to postoperative histopathological size as gold standard.

Multiple studies encourage DBT protocol to be utilized for mammography examinations for screening as well as diagnostic purposes. The current study provides a comparison between the already used imaging methods (mammography and ultrasound) in addition to DBT to understand their role in tumor size measurements.

Breast lesion sizing by ultrasound imaging, mammography and DBT in comparison to histopathological sizing

This retrospective analysis included 111 cases of primary breast cancer.

our results revealed that no statistical difference between tumor size assessment measured by DBT and histopathology. Also, showed excellent agreement between all three methods and histopathology with highest value for DBT , **Fornvik D (4)** stated that DBT is more accurate than mammography for tumor size assessment. Some studies have reported ultrasonography to be more accurate for mass size measurement than mammogram (9,10,11), whereas others have reported that mammogram is more accurate (8,12,13).

Regarding mammographic measurement of tumor size; mean size difference between histological size and mammographic mass size was 1.16 mm. Concordant measurements were 83.8%. Exact mass demarcation was difficult in 6 cases considered under estimated cases with total cases of mammographic mass size underestimation 13 cases (11.7%) and overestimation of 5 cases (4.5%). Our results showed that the discordant measurements with mammography have a tendency for underestimation rather than overestimation. **Şendur et al.(14)** included 71 cases in their study. Mammographic size estimation was concordant for 52.1% of cases. Underestimation and over estimation percentages were (33.8%) and (14.1%), respectively**. Luparia et al (7)** reported that the concordance between histological sizes and DM were 65.9%.

In our study discordance between mammographic tumor size was significantly affected by breast density ($p=0.015$) and histopathologic tumor type ($P< 0.001$).

80% of discordant cases were detected at dense breasts (ACR B& D). in agreement with **Fasching et al.(15**) Their study cohort included 434 patients with primary breast cancer. They stated that the size estimation difference the histological tumor size and mammographic size was greater at dense breast. Conversely, **Khalayleh et al (16)** included 197 breast cancer cases, they reported that breast density had no influence on the accuracy of tumor size measurements with mammography.

Regarding pathologic tumor type; ILC and DCIS+IDC showed 88% of discordant cases. **Hilleren et al (17)** reported that about 33% of ILCs visualized on MM appeared as an ill-defined opacity or an area of architectural distortion or vague asymmetry. in turn lead to discordance of tumor size measurement

with tendency to underestimate ILC. In our study also; out of 7 cases of mammographically discordant ILC estimated size; 6 cases were underestimated.

Our study showed underestimation of the histological tumors size with sonography in 25% of cases with a mean difference of 2.35 mm, only one case could not be detected on ultrasonography. This underestimation increased with histological result of ILC in 44% of under estimated cases followed by DCIS+ IDC. The investigations by **Hieken et al. (9)** , **Shoma et al. (10) and Bosch et al (18).** confirmed the sonographic underestimation of the histological tumors size.

Congruent with previous studies **Gruber et al. (8)** and **Pritt et al. (19)** who stated that the greatest mean difference between the sonographically measured tumor size and the actual histological tumor size was found for invasive lobular carcinoma. In our analysis we attributed that to that the demarcation of the lesion is more difficult because of the diffuse, infiltrative and multifocality growth pattern of ILC. Also, in agreement with **Yang et al (5)** and **L.J. Dummin et al.(3)** for the chosen method for US estimation for exclusion of hyper echoic desmoplastic speculation including only the hypoechoic core, **Madjar H et al.(11**) and **Ohlinger R et al.(20**) stated that this method of ultrasound measurement results in underestimation in addition to the dorsal acoustic attenuation and the blurred margin of ILC.

One study; **Skaane P et al. (21)** has suggested that ultrasonographic measurements need to include the hyperechoic desmoplastic halo around the hypoechoic lesion and that US was significantly more accurate in predicting size. However, infiltrating lobular carcinomas.

In agreement with **Hieken et al. (9)** who attributed the under-estimation results for DCIS + IDC histological type this is attributed to the unclear extensive intraductal in-situ components.

Regarding DBT measurement of tumor size; mean size difference between histological size and DBT mass size was 0.2 mm. Concordant measurements were (92.8%) . Discordant mass size estimation was (5.4%) for size underestimation and (1.8 %) for size overestimation.

Şendur et al. (14) results showed size estimation was concordant for 67.6 % of cases. Underestimation and over estimation percentages were (23.9%) and (8.5%), respectively. **Luparia et al** reported that the concordance between histological sizes and DM were 65.9%.

Although, DBT measurement is not statistically affected by pathologic type of the tumor, 50% of disconcordant measurements were ILC. D. **Förnvik et al. (4)** stated that multifocal, diffusely infiltrative of architectural distortion growth patterns of ILC result in ill-defined tumor outlines which hinders imaging-based measurements.

Breast density is also noted to affect DBT based tumor measurement with statistical significance (P=0.036). This significance is less than observed in mammography results. In agreement with **Förnvik et al.(4)** the disturbance effect of the parenchymal background is substantially reduced in DBT.

In conclusion: DBT might play an important role in the detection and measurement of breast cancer. Ultrasound and mammography tend to underestimate lesion size and mass mesurements may be affected with pathological type of tumor.

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