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BREAST TUMOR;

COMPARISON OF ULTRASOUNOGRAPHY AND MAMMOGRAPHY IN PREOPERATIVE ASSESSMENT OF BREAST TUMOR SIZE

Rakhshanda Jabbar[1], Bushra Riaz[2], Fatima Imran[3]

1. MBBS, FCPS (Diagnostic Radiology) Senior Registrar Department of Radiology DHQ Hospital, Faisalabad.
2. MBBS, FCPS (Diagnostic Radiology) Senior Registrar Department of Radiology DHQ Hospital, Faisalabad.
3. MBBS, FCPS (Radiology) Associate Professor Department of Radiology Aziz Fatima Medical & Dental College, Faisalabad.

Correspondence Address:
Dr. Rakhshanda Jabbar
House#7, Noor Fatima Block,
Amin Town, West Canal Road,
Faisalabad.
rakhshandajabbar@gmail.com

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ABSTRACT: Accurate preoperative assessment of tumor size in breast cancer is important for choosing appropriate treatment. Mammography & sonography both have been used to predict tumor size but there have been conflicting reports about their accuracy. Some studies have mentioned ultrasound to be more accurate than mammography in the preoperative assessment of breast tumor size. **Objectives:** The objective of the study was to determine the correlation of mammography and ultrasound in the preoperative assessment of breast tumor size in patients with breast cancer taking pathological tumor size as gold standard. **Study Design:** It was a cross-sectional survey. **Setting:** Radiology department SKMCH & RC Lahore. **Period:** Study was completed over a period of 6 months from Nov 09, 2008 to May 08, 2009. **Subjects and Methods:** Eighty cases fulfilling the inclusion criteria were selected. After informed consent, bilateral mammography and breast ultrasound were done in all the patients. Pathological measurements were done after surgery in the longest diameter of the specimen. Mammographic and ultrasonographic measurements were correlated with pathological measurements using Pearson's correlation coefficient. **Results:** Ultrasonographic measurements correlated more accurately with the pathological measurements as compared to mammographic measurements. Correlation coefficient "r" was 0.944 for ultrasound measurements versus 0.898 for mammographic measurements. Correlation was higher for lesions of 20 mm or less in there largest diameter than for larger tumors. **Conclusion:** Ultasonography is a more accurate tool for preoperative assessment of breast tumor size especially for small sized tumors of less than 20 mm.

Key words: Breast Carcinoma, Breast Self-Examination, Mammography, Pathology, Ultrasonography.

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INTRODUCTION

The incidence of breast cancer has increased all over the world in recent past. According to American Cancer Society (ACS), the increase in female breast cancer rates may be due to better screening tools like mammography, increased use of hormone replacement therapy and increasing obesity.[1]

Breast cancer is more common in white women than African American or Asian women. It is one of the leading causes of all cancer related deaths in women, exceeded only by lung cancer.[2] The incidence increases proportionately with age and the risk is especially high for women over age 60. Seventy percent females presenting with breast cancer have no definite risk factors. More than 20% breast lumps are malignant according to ACS.[2] The incidence of malignancy in female patients presenting with lumps was 24.2% in Pakistan.[3] Therefore, early detection and early treatment is essential to decrease the mortality rates.[4]

The advancement in mammographic techniques and the development of breast screening programs have resulted in earlier diagnosis of breast cancer. Screening programs help in early detection of small cancers which can be treated with conservative breast surgery. This, in turn, relies on the accurate measurement of the pre-operative cancer size.[5,6]

It is mandatory practice to stage the disease before proceeding to surgery, because therapeutic decisions are based on preoperative staging.[7] Tumor size is the most important prognostic factor.[8] Underestimation of pre-surgical tumor size may lead to incomplete margins and hence, re-excision. On the other hand, over-estimation of the tumor size could lead to a change in treatment plan and prognosis.[9-10]

Tumor size is commonly measured clinically by palpation, but this method is very crude and variation among different observers is common. It is influenced by many factors such as skin thickness, edema and obesity.[11] Mammography is more accurate than palpation; however, it is influenced by distance between the tumor and the film. Moreover, measurements are usually taken in standard projections that do not always express the largest dimension. Sonography, in contrast, is a dynamic technique that allows tumors to be assessed in their greatest dimensions without increase in size. It seems to be an accurate way of determining breast tumor size before surgery.[11-12]

Ultrasound technology and its ability to demonstrate breast anatomy and pathology have developed dramatically. Ultrasound can be used to measure tumor size, its nature (benign or malignant) and possible axillary lymph node involvement.[13] Sonographic findings suggestive of cancer can be confirmed by fine needle aspiration cytology of the primary tumor and the axillary lymph node metastases.[13-14]

Due to the major advancements observed in ultrasound systems, radiology specialists, these days, are having increased reliability on the ultrasound to determine pre-operative breast tumor size. Breast ultrasound is also being increasingly used by breast surgeons as part of their basic clinical evaluation.[15] But the accuracy of this modality as compared to mammography is not well documented and there have been conflicting reports. Some studies have proven ultrasonography to be significantly more accurate in determining tumor size. [12,15]

This prospective study aims to determine the most valid imaging method (mammography or ultrasound) to predict the gold standard pathological breast tumor size preoperatively. This study will help the clinicians for choosing an appropriate imaging method as an accurate adjunct to clinical examination in outpatient breast clinics.

OBJECTIVE

The objective of the study was to determine the correlation of mammography and ultrasound in the preoperative assessment of breast tumor size in patients with breast cancer taking pathological tumor size as gold standard.

OPERATIONAL DEFINITIONS

Malignancy

Diagnosis of malignancy was based on fine needle aspiration cytology (FNAC).

Pathological Tumor Size

It was measured in millimeters (mm) by making cross section of the gross specimen in its maximum dimension.

Mammographic Size

It was measured in mm along the maximum diameter of the tumor. A value of $\pm$ 2 mm from the gold standard was considered as accurate.

Ultrasonographic Size

It was measured in mm along the maximum dimension of the tumor. A value of $\pm$ 2 mm from the gold standard was taken as accurate.

MATERIALS AND METHODS

Study Design

It was a cross-sectional survey.

Setting

Study was conducted at Radiology Department of Shaukat Khanum Memorial Cancer Hospital & Research Center Lahore, Pakistan.

Duration

Study was completed in one year from 09-11-2008 to 08-11-2009.

Sample Size
The study included 80 cases of early breast cancer fulfilling the inclusion criteria.

Sampling Technique
It was a non probability, purposive sampling.

Sample Selection

Inclusion Criteria
1. All female patients, 25-75 years of age, with palpable breast masses proved to be malignant on FNAC.
2. Patients with early breast carcinoma. i.e.
- Tumor ≤ 2cm in greatest dimension (T1).
- Tumor > 2cm but < 5cm in greatest dimension (T2).

Exclusion Criteria
1. Breast tumor not detectable on ultrasound or mammography.
2. Patients with history of recent surgery or excision biopsy.
3. Patients with fungating breast mass. (assessed by clinical examination)
4. Recurrent tumors. (assessed by history & clinical examination)
5. Diffuse / multiple lesions. (assessed on clinical examination & ultrasound)

Data Collection Procedure
Eighty patients fulfilling the inclusion criteria were taken from out-patient department. Demographic profile (age, weight, marital status and socioeconomic status) was recorded. All the patients were reassured regarding confidentiality and expertise. Informed consent was obtained and clinical examination was carried out to localize the site of tumor. All patients first underwent bilateral mammography. Mammography was performed on MAMMOMAT 3000 machine and routine craniocaudal and mediolateral oblique views of the breast(s) were taken. Findings were recorded according to the Breast Imaging Reporting and Data System, or BI-RADS, lexicon by an expert radiologist. All the measurements were multiplied by a factor of 0.94 to minimize confounding due to magnification error. Other confounding factors which can affect image quality and size on mammography were X-ray exposure, noise and contrast. They were controlled by daily sensitometery and optical density testing. Motion artifact was controlled by compression of breast tissue. Bilateral whole-breast ultrasound of all those patients undergoing mammography was performed by a senior radiology fellow, using a 7-10 MHZ linear probe on Toshiba aplio 500 scanner. The observers were kept blind about the results of mammography to avoid equivocal results. The size measured from ultrasonography and mammography was calculated in millimeters. Surgical resection of the breast tumors was done in all the patients. Pathological size will be measured in mm by making cross section of the gross specimen in its maximum dimension. Measurements of breast tumor sizes were recorded in tabulated form and finally were correlated to pathologic size (gold standard). Specially designed proforma was used as data collection tool.

Data Analysis Procedure
Data collected was entered into SPSS version 12 and analyzed through its statistical program. Qualitative variables like sex, marital status and socioeconomic status (lower class, middle class, high class) were presented as frequencies and percentages. Quantitative variables like age, weight and tumor sizes were presented as means and standard deviation. Correlation of ultrasonograhic & mammographic measurements (tumor size) with the gold standard pathological size was done by Pearson's correlation coefficient and tested for significance. A p-value of ≤ 0.05 was considered as significant.

RESULTS
Majority of cancer patients were between age ranges 45-65 years (62.4%). There were few patients at the extremes of age groups shown, with the minimum age of 26 years and maximum age of 75 years. Mean age was 51.59 years ± SD of 10.72. (Table-I)

Tables-II&III show the distribution of cases according to the marital status & socioeconomic status. Table-IV summarizes the minimum and maximum values for sonographic, mammographic and pathological measurements with mean value and standard deviation. Table-V & Table-VI, both show correlation of sonographic and mammographic measurements with the pathological measurements respectively. As shown in the table, both imaging modalities correlated very well with the gold standard pathological measurements. Correlation coefficient — r was 0.944 for ultrasound measurements and 0.898 for mammographic measurements. Correlation was stronger for small sized tumors T1 tumors (tumors ≤ 20mm) than T2 tumors (tumors >20mm). For T1 tumors "r" was 0.975 for ultrasound measurements and 0.949 for mammographic measurements. For T2 tumors "r" was 0.893 for ultrasound measurements and 0.685 for mammographic measurements.

Figure-1 is a scatter plot with regression line which shows graphically how the sonographic measurements correlate with the gold standard pathological measurements. Figure shows positive linear correlation with the pathological measurements. This positive relationship is very strong for ≤ 20 mm as most of the values are centered on the regress line. As the pathological size increases, correlation becomes less strong and the values become dispersed around the regression line.

Figure-2 is a scatter plot with regression line which shows graphically how the mammographic measurements correlate with the gold standard pathological measurements. Figure shows positive linear correlation with the pathological measurements. This positive relationship is very strong for ≤ 20 mm as most of the values are centered on the regression line. As the pathological size increases, correlation becomes less strong and the values become dispersed around the regression line.

On the whole, sonographic measurements showed a trend towards underestimation. Sixty six patients (82.5%) were underestimated and fourteen patients (17.5%) were overestimated. Thirty eight patients (47.5%) were diagnosed within 2mm of the pathological measurements.

Mammographic measurements showed a trend towards overestimation. Seventy five patients (93.8%) were diagnosed overestimated and five patients (6.3%) were underestimated. Twenty five patients (31.3%) were diagnosed within 2mm of pathological measurements.

Age groups	Frequency	Percentage
25-35	05	6.3%
36-45	20	25%
46-55	26	32.4%
56-65	24	30%
66-75	5	6.3%
Total	80	100.0
Mean Age = 51.59+/-10.72 years		

Table-I. Distribution of cases according to age groups (n=80)

Marital Status	Frequency	Percent
Married	73	91.2
Unmarried	7	8.8
Total	80	100.0

Table-II. Distribution of subjects according to marital status (n=80)

Class	Frequency	Percentage
Lower class	42	52.5
Middle class	30	37.5
High class	8	10.0
Total	80	100.0

Table-III. Distribution of cases according to socioeconomic status (n=80)

Statistics	Ultra-sound size	Mammo-graphic size	Pathological Size
N	80	80	80
Mean	24.3	31.3	25.6
Std. Deviation	11.3	12.5	9.5
Minimum	10	12	11
Maximum	49.9	49.9	44

Table-IV. Mean sizes of tumors by different modalities with Minimum & Maximum Measurements

Measurement	Number of Cases	Pearson's Correlation coefficient(r)	p-Value	Comments
Total	80	0.944	<0.001	Significant correlation
T1 Lesions (Lesions ≤20mm)	30	0.975	<0.001	Significant correlation
T2 Lesions (Lesions>20mm but <50mm)	50	0.893	<0.001	Significant correlation

Table-V. Correlation of ultrasonographic measurements with pathological measurements. (n=80)

Measurement	Number of Cases	Pearson's Correlation coefficient(r)	p-Value	Comments
Total	80	0.898	<0.001	Significant correlation
T1 Lesions (Lesions ≤20mm)	30	0.949	<0.001	Significant correlation
T2 Lesions (Lesions>20mm but <50mm)	50	0.685	<0.001	Significant correlation

Table-VI. Correlation of mammographic size with pathological size (n=80)

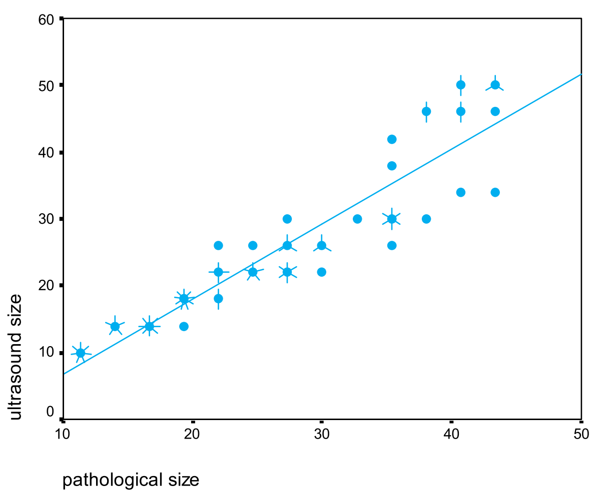

Figure-1. Scatter-plot showing correlation of ultrasonographic size with pathological size (size shown is in mm)

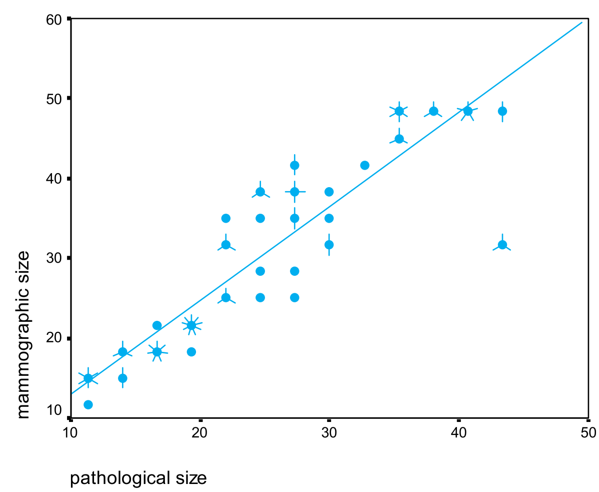

Figure 2. Scatter-plot showing correlation of mammographic size with pathological size (size shown in mm)

DISCUSSION

Both sonographic and mammographic measurements had good correlation with the gold standard pathological measurements but the ultrasound measurements correlated more strongly than mammographic measurements as shown in these results. Better size correlation with ultrasound might be due to the fact that there are two differences between ultrasound and mammography. Firstly in ultrasound it is possible for the operator to change the position of probe to find out largest diameter while mammograms are performed in standard projections, so it is possible to miss the largest diameter. Secondly in mammography images are enlarged slightly as the x-ray beams travel through the breast tissue. This is called magnification error. Although in standard practice we try to reduce this error by multiplying the mammographic size with magnification coefficient, but due to different nature of the breasts (e.g fatty breasts) and tumors (e.g irregular or lumpy tumors) it is not always possible to correct this error. Ultrasound is free from this error.

The results in our study had considerable correlation with the studies conducted in the past. In this regard some of the studies are worth mentioning. Bosch et al included 96 women with invasive malignant breast tumors in their study. All patients were subjected to excision of the lump and the tumor size was measured on histology. Tumor size was measured by all three parameters in 73 cases. Correlation of tumor size with pathological size was calculated. The correlation coefficient between ultrasound and pathological size (r=0.68) was significantly better than the correlations between physical examination and pathological size (r=0.42) and mammographic and pathological size (r=0.44). Physical examination overestimated and ultrasound underestimated breast tumor size.[15]

Peritt et al measured tumor size in 138 female patients with palpable breast cancer, using all three modalities. i.e. palpation, mammography and ultrasonography. These measurements were correlated with the histological size. The correlation coefficients between clinical assessment, mammography, ultrasonography and histological size were 0.71, 0.65 and 0.80 respectively. Clinical assessment overestimated the tumor size, whereas mammography and ultrasonography slightly underestimated the size. Authors concluded ultrasonography to be most reliable method for pre-operative assessment of breast tumor size.[16]

In a recent study, Leddy *et al*. compared MRI, ultrasonography and mammography with pathological tumor size. They concluded that the MRI overestimates tumor size and measurements obtained with US and mammography are more accurate regardless of breast density. US proved to be superior to mammography to predict the tumor size.[12]

However some studies conducted in the past have reported mammography to be superior to ultrasonography. Among these is a study conducted by Golshan et al which measured breast tumor size in 202 patients with Stages I and II breast cancer. According to the authors, most accurate single modality to estimate tumor size was mammography with a correlation coefficient of 0.66, followed by ultrasound (r=0.48) and core biopsy (r=0.28). The combination of the three modalities underestimated 25% of the tumors >1 cm in size, and overestimated 10% of those <1 cm.[17]

Another important study worth mentioning is by Dummin et al. It is a retrospective study. They compared the sonographic and mammographic size with the histological measurements in 400 cases of invasive ductal carcinomas. The authors reported that mammography better correlated with the histological measurements, although it slightly overestimated the tumor size. The results in this study are different from our study. This might be due to the reason that authors in this study have used Altman-Bland (AB) bias plots to assess the agreement between both imaging modalities and the pathology. The AB test plots the difference between the measurements against the mean of the measurement. Secondly, measurements were recorded excluding the spicules in case of stellate or lobular lesions. Literature reviews report that mammographic measurements correlate better with pathological measurements when spicules are excluded in stellate or lobular lesions.[18]

As shown in the table 7 & 8 correlation of tumor sizes was stronger for small size T1 tumors (≤ 20mm) with both mammography and ultrasound. As the size of tumor increases, agreement between pathological size and imaging techniques decreases as the tumor loses its nodular shape and becomes stellate shaped or lobular due to invasion of surrounding parenchyma. This agrees with the work of Dummin et al. They reported that correlation of tumor size decreased for both modalities as the tumor size increased above 20mm and nodular lesions correlated more strongly than lobular lesions. Lobular cancers were underestimated significantly by sonography once over 30 mm in size. The breast surgeons should bear this fact in mind when planning for breast conservation or mastectomy in women with a larger tumor size.

The current study used the gross measurement of the cut section. This may have led to high observed agreement between imaging and the gold standard when compared to other studies. This is a fact that pathology will always see more under the microscope than on gross cut section. Therefore the studies using microscopic measurements as the gold standard would show less agreement then the studies using gross pathological measurements as gold standard.

Our study had two noticeable limitations. The first, study was conducted on small population but still the results are in accordance with the published international literature. Secondly, diagnosis of DCIS and its extension is quite difficult on sonography. This is an important limitation to use of this technique.

CONCLUSION

In view of our results and several other research workers, we conclude that ultrasound is a useful tool for preoperative staging of breast carcinoma. Assessment of tumor size by ultrasound is more accurate than mammographic measurements.

Ultrasound measurements have a general trend towards underestimation, while mammographic measurements have a general trend towards overestimation. Both techniques should be combined carefully to assess the pre-operative size of breast tumor size, to help the treating physician plan treatment options.

Correlation of both sonographic and mammographic measurements with the gold standard pathological measurements decreases as the tumor size increases, so another imaging method like magnetic resonance imaging can be used in case of large size tumors. The breast surgeons should keep this fact in mind when planning for breast conservation surgery or mastectomy procedure in order to avoid erroneous decisions.

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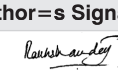
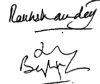
> *It's not what you look at that matters,*
> *It's what you see.*
>
> **– Henry David Thoreau –**

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Rakhshanda Jabbar	Data collection, Review of literature, Discussion.	
2	Bushra Riaz	Data analysis.	
3	Fatima Imran	Proof reading & Supervision