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# Diagnostic Accuracy of Combining Sonoelastography with Mammography in Solid Breast Lesions Keeping Histopathology as Gold Standard

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## ABSTRACT

**Background and objective:** Breast cancer is the most common malignancy in females. Early diagnosis can help in reducing the morbidity and mortality associated with this disease. Sonoelastography has shown to be a valuable tool in early detection of breast cancer. The aim of the study was to evaluate the diagnostic accuracy of combining sonoelastography with mammography in diagnosing malignant solid breast lesions taking histopathology as a gold standard.

**Methods:** A descriptive cross-sectional study was carried out at the Department of Radiology, Shaikh Zayed Medical Complex/Federal Post-Graduate Medical Institute (FPGMI), Lahore, Pakistan during six months period from 1<sup>st</sup> September, 2018 to 31<sup>st</sup> March, 2019. Female patients > 35 years of age and presenting with suspected malignant breast masses were included. Mammography and sonoelastography of the lesions were done. Finally, the patients were referred for tru cut biopsy. Diagnostic accuracy was calculated for mammography, sonoelastography and their combination.

**Results:** A total of 200 female patients were enrolled with a mean age of 50.8 ( $\pm$  8.6) years. Mammographic findings suggestive of malignancy (BI-RADS category IV and V) were present in 96 (48%) cases. Elastography showed finding of malignancy (Score 4 and 5) in 96 (48%) cases. Combined sonoelastography and mammography diagnosed malignancy in 112 (56%) cases. Histopathologically confirmed malignancy was seen in 110 (55%) cases. The sensitivity and specificity of mammography (76.3 % and 77.7%) and sonoelastography (77.3% and 87.7%), were comparable. The combination of mammography and sonoelastography showed a higher sensitivity (90.9%) and specificity (86.6%). The combination showed a diagnostic accuracy of 89% followed by sonoelastography (82%) and mammography (77%) alone.

**Conclusion:** Combination of sonoelastography and mammography can significantly enhance the diagnostic accuracy of breast carcinoma. Females may be offered mammography or ultrasonography in combination with sonoelastography for routine testing.

**Keywords:** Sonoelastography, Breast carcinoma, mammography, ultrasonography, diagnostic accuracy.

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## Introduction

Breast cancer is the most common malignancy in females. It accounts for almost 25% of new cancer cases in females and 15% of the cancer related deaths worldwide.<sup>1</sup> It leads to more than 600,000 death annually.<sup>2</sup> As per the GLOBOCAN Cancer Tomorrow prediction tool the incidence of breast cancer is expected to rise by more than 46% by the year 2040.<sup>3</sup> High incidence of obesity, tobacco exposure, physical inactivity, high fat diet, late age at first pregnancy, increased use of hormonal therapies and oral contraceptives are the

main contributing factors for the rise in the incidence of breast cancer.<sup>4</sup>

Early detection of breast cancer can prevent significant morbidity and mortality associated with this condition. The common radiological evaluating methods include mammography, ultrasonography and sonoelastography. Breast sonoelastography is an emerging technique that helps in assessment of breast deformability by measurement of breast tissue elasticity.<sup>5</sup> The World Federation of Ultrasound in Medicine and Biology (WFUMB) has recommended the

addition of sonoelastography to other radiological modalities available for the diagnosis of breast lesions.<sup>6</sup>

Conventional mammography is primary imaging modality with a sensitivity of 71% and specificity of 75% in detecting breast lesions.<sup>7</sup> Ultrasonography is widely used due to its availability and its usefulness particularly in younger patients with dense breast tissue. The sensitivity and specificity of ultrasonography for detecting breast lesions is 80% and 88%, respectively.<sup>8</sup> Sonoelastography gives better details of the epithelial and connective tissue components based on elasticity, which is property of material to reform back to its original position after stress is removed. The strain ratio is higher for stiffer/malignant lesions and lower for softer/benign lesions.<sup>9</sup> In one of the local studies conducted in Combined Military Hospital (CMH), Rawalpindi, Pakistan, using a strain ratio cut-off of 4.8, a high sensitivity and specificity of 88.6% and 90.2%, respectively, was achieved for sonoelastography.<sup>10</sup> Thus, the use of sonoelastography in our population may be recommended. Although it may be used independently, but the addition of sonoelastography to the already existing mammography protocol can significantly enhance the diagnostic capabilities.<sup>11</sup>

Currently, routine use of sonoelastography is not widely practiced in Pakistan. Although literature exists but more local evidence is required to thoroughly understand the utility of sonoelastography in our population. This may be particularly useful in case of indeterminate lesions where sonoelastography can complement other modalities and provide better identification of lesions. This study was, therefore, designed with the aim to evaluate the diagnostic accuracy of combining sonoelastography with mammography in differentiating benign from malignant solid breast lesions taking histopathology as gold standard.

## Methods

A descriptive cross-sectional study was carried out at the Department of Radiology, Shaikh Zayed Medical Complex/Federal Post-Graduate Medical Institute (FPGMI), Lahore, during six months period from 1<sup>st</sup> September, 2018 to 31<sup>st</sup> March, 2019. Ethical approval was taken from the Institutional Review Board (IRB) of FPGMI, Sheikh Zayed Medical Complex (IRB # 1537, dated 01/08/2018). The study population included female patients more than 35 years of age and presenting with either breast lumps that on examination were suspected to be malignant or skin changes such as dimpling, peau d'orange appearance, nipple retraction or those with strong family history and were referred to the radiology department for further work-up. A non-probability consecutive sampling technique was used and 200 cases presenting during the study period and fulfilling the inclusion criteria were included. Lactating and pregnant females,

patients with palpable chest wall lesions and those refusing biopsy or not providing consent for the study were excluded. Informed consent was taken from all the participants. Mammography was performed using MAMMOMAT (Siemens electronics) with full field film-screen digital imaging system and two standard views in craniocaudal (CC) projection and mediolateral oblique (MLO) projections were taken. Breast Imaging-Reporting and Data System (BI-RADS) was used to classify lesions. BI-RADS category IV and V were regarded as malignant. All mammographic patients wore thyroid collar shielding around the neck.

Sonoelastography images were obtained using LOGIQ S7 EXPERT (GE Healthcare, Pittsburgh, PA, USA) with a 7.5 MHz linear transducer. Scanning was performed both in longitudinal and transverse planes first in B mode and then further acquisition of images with strain wave elastography. A chromatic scale was used to assign soft tissues, which can be compressed/strained, "green color" and hard tissues, which are not compressible, "blue color". Tsukuba University Scoring System<sup>12</sup>, that defines a lesion according to the color variation during compression in the region, was used to further categorize the lesions. A score of 1 to 3 were considered "benign" and a score of 4 and 5 was regarded as "malignant". Finally, the patients were referred for true cut biopsy. For biopsy confirmation of the lesion, core needle biopsy was performed using 14G needle with 20mm cutting length.

## Statistical Analysis

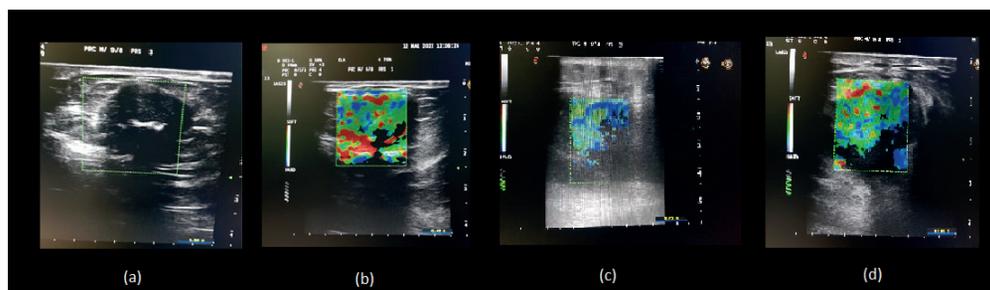
The data were entered into SPSS version 23.0 and was analyzed using its statistical package. Descriptive statistics were performed and presented as mean ( $\pm$ S.D) for quantitative variables and frequency and percentages for qualitative variables. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy were calculated using 2 x 2 tables. All the data were entered in to predesigned proforma and confidentiality of the data was maintained.

## Results

During the study period of six months, 200 female patients with suspicion of malignant breast lesions were enrolled in the study. The age characteristics of the patients are given in Table 1. Mammography results showed that highest number of patients belonged to of BI-RADS category II (29.5%), followed by category V (29%), category III (20%), category IV (19%) and category I (2.5%). The BI-RADS and sonoelastography characteristic of the patients are given in Table 1. Mammographic findings suggestive of malignancy (BI-RADS category IV and V) were present in 96 (48%) cases. Elastography showed finding of malignancy (Score 4 and 5) in 96 (48%) cases.

**Table 1: Baseline characteristics of the study participants (n=200)**

Age (years)	Mean ( $\pm$ S.D)	Minimum	Maximum
	50.8 ( $\pm$ 8.6)	35	70
Age Groups	Age (years)	No. of Patients (n)	Percentage (%)
	35-55	132	66%
	56-65	64	32%
	>65	4	2%
	<b>Total</b>	<b>200</b>	<b>100</b>
BI-RADS Category	Category	No. of Patients (n)	Percentage (%)
	I	5	2.5%
	II	59	29.5%
	III	40	20%
	IV	38	19%
	V	58	29%
	<b>Total</b>	<b>200</b>	<b>100%</b>
SONOELASTOGRAPHY SCORE	Category	No. of Patients (n)	Percentage (%)
	SCORE 1:	58	29%
	SCORE 2:	20	10%
	SCORE 3:	26	13%
	SCORE 4:	52	26%
	SCORE 5:	44	22%
	<b>Total</b>	<b>200</b>	<b>100%</b>



**Figure 1.** Sonoelastographic images of breast lesions showing, (a) & (b); a benign fibroadenoma with sonoelastography score of 2; red color coding signifies soft benign lesion (c); borderline intermix lesion with score of 3 and (d); a confirmed malignant lesion with sonoelastography score of 5.

Combined sonoelastography and mammography diagnosed malignancy in 112 (56%) cases. Histopathologically confirmed malignancy was present in 110 (55%) cases. Figure 1 shows results of sonoelastography in various patients with breast lesions. Table-2 shows the modality-wise diagnosis of all the patients.

Results from the histopathological examination of biopsy sample showed that 90 (45%) cases had benign pathology of which fibroadenoma (39%) was the most common. Among the malignant cases the most common pathology was invasive ductal carcinoma which was present in 95 (47.5%) cases. Table-3 shows the common pathologies diagnosed on histopathology.

Diagnostic accuracy of mammography, sonoelastography and combination was studied against the gold standard histopathology. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of mammography were 76.3%, 77.7%, 87.5% and 67.3%, respectively. The sensitivity, specificity, PPV and NPV of sonoelastography were 77.3%, 87.7%, 88.5% and 76%, respectively. The combination of mammography and sonoelastography showed a higher sensitivity, specificity, PPV and NPV of 90.9%, 86.6%, 89.3% and 88.6%, respectively. The diagnostic accuracy was highest in the combination of mammography and sonoelastography as compared to mammography and sonoelastography alone. The

**Table 2: Modality-wise diagnosis of patients with breast lumps (n=200)**

Mammography diagnosis	Category	No. of Patients (n)	Percentages (%)
	Benign	104	52%
	Malignant	96	48%
	Total	200	100%
Sonoelastography Diagnosis	Category	No. of Patients (n)	Percentages (%)
	Benign	104	52%
	Malignant	96	48%
	Total	200	100%
Sonoelastography + Mammography Diagnosis	Category	No. of Patients (n)	Percentages (%)
	Benign	88	44%
	Malignant	112	56%
	Total	200	100
Histopathology Diagnosis	Category	No. of Patients (n)	Percentages (%)
	Benign	90	45%
	Malignant	110	55%
	Total	200	100

**Table 3: Histopathological diagnosis of the patients with breast lumps (n=200)**

Diagnosis	No. of Patients (n)	Percentages (%)
<b>Benign Breast Lesions</b>		
Fibroadenoma	78	39%
Ductal Papilloma	4	2%
Lipoma	2	1%
Gynaecomastia	2	1%
Mastitis	2	1%
Granulomatous Mastitis	2	1%
<b>Total</b>	<b>90</b>	<b>45%</b>
<b>Malignant Breast Masses</b>		
Invasive Ductal Adenocarcinoma	95	47.5%
Lobular carcinoma	6	3%
Medullary Carcinoma	5	2.5%
Intra-ductal papillary carcinoma	4	2%
<b>Total</b>	<b>110</b>	<b>55%</b>

combination showed a diagnostic accuracy of 89% followed by 82% for sonoelastography and 77% for mammography. Table 4-6 show the diagnostic accuracy of the diagnostic modalities in patients with suspicious breast lumps.

**Discussion**

The results from the current study show that the mean age of patients was 50.8 (±8.6) years with age range from 35 to 70 years. The majority of the patients were between 35-55 years of age (66%). In a study conducted on Pakistani population,

the mean age of patients was 38.20 (±10.63) years. The majority of the patients who had malignancy belonged to the 50-60 years age group.<sup>10</sup> Similarly, studies from India, South Korea and Japan have shown that the incidence of breast cancer peaks in the fifth and sixth decade of life.<sup>13-15</sup> A study from Srilanka reported breast cancer peak in even higher age group of 60-65 years.<sup>16</sup> Increasing age is a well-known risk factor for developing breast cancer. As per Pike’s model, breast tissue ageing is associated with increased cumulative exposure to growth factors, hormones and carcinogens.<sup>17</sup> In

**Table 4: Diagnostic accuracy of Mammography taking histopathology as gold standard (n = 200)**

		Histopathology Diagnosis Cross-tabulation		
		Malignant	Benign	Total
Mammographic Diagnosis	Malignant	84 (TP)	20 (FP)	96
	Benign	26 (FN)	70 (TN)	104
	Total	110	90	200

**Table 5: Diagnostic accuracy of Sonoelastography taking histopathology as gold standard (n = 200)**

		Histopathology Diagnosis Cross-tabulation		
		Malignant	Benign	Total
Sonoelastography Diagnosis	Malignant	85 (TP)	11 (FP)	96
	Benign	25 (FN)	79 (TN)	104
	Total	110	90	200

**Table 6: Diagnostic accuracy of combined Mammography + Elastography taking histopathology as gold standard (n = 200)**

		Histopathology Diagnosis Cross-tabulation		
		Malignant	Benign	Total
Mammography + Elastography Diagnosis	Malignant	100 (TP)	12 (FP)	112
	Benign	10 (FN)	78 (TN)	88
	Total	110	90	200

**Table 7: Diagnostic accuracy of Mammography, Sonoelastography and Combination in diagnosing malignant breast lesions taking histopathology as gold standard (n = 200)**

Parameters	Mammography	Elastography	Mammography + Sonoelastography
Sensitivity	76.3 %	77.3%	90.9%
Specificity	77.7%	87.7%	86.6%
PPV	87.5%	88.5%	89.3%
NPV	67.3%	76%	88.6%
Diagnostic Accuracy	77%	82%	89%

the current study the peak age group was 35-55 years, which is younger than that quoted in most of the studies from around the world. Literature is evident that recently much younger age groups are presenting with breast cancer in Pakistan due to rapid urbanization, western diets, inactivity and increased incidence of smoking.<sup>18</sup>

In the present study the results from the histopathological analysis showed that 45% of the tumors were benign and 55% were malignant. Fibroadenoma was the most common benign pathology and invasive ductal carcinoma was the most common malignancy. In one of the recent local studies conducted on the population of Lahore, Pakistan, fibroadenoma was the most common benign lesion which occurred in more than 50% of the cases. This was followed by fibrocystic disease, breast abscess, granulomatous disease,

lipoma and phylloides tumor.<sup>19</sup> A similar study from India also showed that fibroadenoma was most common benign condition (66.7%). This was followed by fibroadenosis, breast abscess and mastitis.<sup>20</sup> The study population of the current study only comprised of patients with clinically suspicious breast lumps. Therefore conditions like breast abscess, mastitis and lipoma were not included. Nevertheless, fibroadenoma, due to its discrete lump appearance which may resemble malignancy clinically, was referred for histopathology. This is the reason why fibroadenoma was solely the most common benign condition observed in the present study.

Among the malignant condition, invasive ductal carcinoma was the most common malignancy which occurred in 47.5% of all the cases. When considering the malignant

cases only, invasive ductal carcinoma was present in more than 86% of the cases, whereas, lobular, medullary and intraductal papillary carcinoma occurred in 3%, 2.5% and 2%, respectively. A review of literature shows that invasive ductal carcinoma is indeed the most common malignancy of breast.<sup>21,22</sup> In a study conducted in King Abdul Aziz Hospital in Riyadh, Saudi Arabia, ductal carcinoma was most common (85%) breast malignancy followed by lobular carcinoma (11%).<sup>21</sup> A study done in Muzaffarabad, Azad Kashmir, showed that in women with clinically palpable breast lumps, 35% were malignant. Among the malignant cases 95% were invasive ductal carcinoma.<sup>22</sup> In the present study, the percentage of malignancy appears higher than the studies quoted above due to the reasons pertaining to the inclusion criteria, as already mentioned earlier. However, among those with malignancy, the results are consistent with most of the studies mentioned in literature.

The results on the diagnostic accuracy of mammography, sonoelastography and the combination showed that the combination had a higher diagnostic accuracy for labeling breast carcinoma. The diagnostic accuracy for the combination was 89% followed by 82% for sonoelastography and 77% for mammography alone. The sensitivity of the combination was markedly increased; however, the specificity was lower than that of elastography alone. In one study conducted in China on eighty nine females with breast lesions, the combination of sonoelastography and mammography showed a high sensitivity of 95.5% and specificity of 94.6%. This was considerably higher than either of the modalities alone and thus it was concluded that compared to the mono detection of either technique, the combination has a superior diagnostic accuracy.<sup>23</sup> A study conducted in Romania showed that sonoelastography, when added to mammography, enhanced the detection of smaller lesion which were 17.9% more likely to be missed on mammography alone. Thus the study concluded that elastography can provide value addition to mammography for breast cancer detection.<sup>24</sup>

Mammography is a widely used screening tool for detection of breast cancer. It has a good diagnostic accuracy for breast lesions. Studies have shown that some limitations such as poor image quality, inappropriate reporting, breast positioning, quality control and equipment related issues, particularly in older analog machines, can adversely affect the accuracy.<sup>25,26</sup> Sonoelastography provides information on tissue elasticity, which when combined morphological findings of mammography can lead to enhanced detection of breast cancer.<sup>27</sup> In a study conducted at Baskent University Hospital, Turkey showed that the diagnostic accuracy of the combination of sonoelastography and mammography was

higher but the specificity was similar to elastography alone.<sup>28</sup> The present study has shown similar trends in which the specificity of combination is lower than that of elastography. Sonoelastography is operator dependent and subjective assessment of diverse sonoelastographic images can be a possible limitation for any ultrasonographer. Additionally various brands of sonoelastographic devices can have different cutoff values. These limitations may count towards the difference observed in various studies.<sup>29</sup> Nevertheless, results from studies mentioned above show that literature is evident in support of the combined use of sonoelastography with either ultrasound or mammography. Further research in this area can help in formulating local and regional guidelines for screening and diagnosis of breast cancer in our part of the world.

## Conclusion

Early and accurate diagnosis of breast cancer can reduce the morbidity and mortality. Results from this study show that addition of sonoelastography to mammography can significantly enhance the diagnostic capabilities of mammography. Thus it is recommended to complement mammography or ultrasonography with sonoelastography in routine breast screening in order to improve the diagnostic accuracy and thus the clinical outcome for the patient.

## Limitations of the study

The study is a single center study. A multi centric study involving various cities of Pakistan may provide more generalizability to the result. Additionally, the inclusion criteria of the study included clinically suspicious nodules. Impalpable lumps and locally advanced conditions were excluded. Inclusion of these cases may provide a better depiction of the role of sonoelastography in various types of breast lumps.

## List of Abbreviations

BI-RADS	Breast Imaging-Reporting and Data System
CC	Cranio-caudal
GLOBOCAN	Global Cancer Observatory
IRB	Institutional Review Board
MLO	Mediolateral oblique
NPV	Negative predictive value
PPV	Positive predictive value
SD	Standard deviation
SPSS	Statistical Package for the Social Sciences
WFUMB	World Federation of Ultrasound in Medicine and Biology

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### Ethical approval

The study was approved by the Institutional Ethical Review Board of Federal Post-Graduate Medical Institute (FPGMI), Sheikh Zayed Medical Complex, Lahore Pakistan vide Letter No.IRB # 1537-2018 dated 01/08/2018.

### Conflict of interest

None to declare

### Grant Support and Financial disclosure

None to disclose

### Authors' Contribution

**MSK:** Concept of study, acquisition of data and drafting of manuscript.

**AA:** Acquisition and analysis of data, important intellectual input, drafting of manuscript.

**WSA:** Acquisition of data, important intellectual input.

**SS:** Concept and design of study, supervision of data collection and analysis.

**ALL AUTHORS:** Approval of the final version of the manuscript to be published.

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