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# EVALUATION OF BREAST LESIONS WITH DOPPLER ULTRASOUND: DIAGNOSTIC ACCURACY OF RESISTIVE INDEX AS A PREDICTOR OF MALIGNANCY.

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**ABSTRACT… Objectives:** To evaluate breast lesions with doppler ultrasound and calculate the diagnostic accuracy of resistive index as a predictor of malignancy, taking histopathology as gold standard. **Study Design:** Cross-sectional study. **Setting:** Radiology Department, CMH Multan. **Period:** December 2015 to May 2016. **Material & Methods:** 150 female patients, having age between 20 – 60 years, with palpable breast lumps were admitted in the study. Doppler ultrasound of the lesion was performed with emphasis on the vascularity and resistive index was formulated. Categorization as malignant or otherwise was declared as established by doppler ultrasound. Patients then underwent biopsy followed by histopathology. Correlation of doppler ultrasound and histopathological findings was done with calculation of diagnostic accuracy of doppler ultrasound, keeping histopathology as gold standard. **Results:** The mean of age was 40.23 ± 5.75 years. In 81 breast doppler ultrasound positive patients, 73 (True Positive) showed malignant lesions in breast while 08 (False Positive) did not have malignancy on biopsy. Among 69 Breast Doppler Ultrasound negative patients, 06 (False Negative) demonstrated malignancy on biopsy whereas 63 (True Negative) did not have any malignant lesion. Overall specificity was 88.77%, sensitivity 92.40%, negative predictive value 91.30%, positive predictive value 90.12% and diagnostic accuracy of Doppler Ultrasound came out 90.67%. **Conclusion:** Angiogenesis in malignant lesions lead to formation of structurally abnormal and tortuous vessels with increased resistive index. Doppler ultrasound is a safe and effective modality which shows acceptable diagnostic accuracy for noninvasive characterization of malignant breast lesions. Therefore, it can be employed as an alternative to histopathology in patients who present with breast lesions.

**Key words:** Breast Carcinoma, Diagnostic Accuracy, Doppler Ultrasound, Histopathology, Resistive Index.

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## INTRODUCTION

Breast lesion is described as an area within breast parenchyma that differs from the surrounding breast tissue in appearance or consistency. It may vary in size from a small nodule to a large mass occupying almost the entire breast. Breast lump is the commonest symptoms of breast related disease with increasing number of patients reporting to the female OPD with this dilemma. Breast lumps may result from a number of reasons, broadly divided into benign and malignant causes, with majority of them being benign, such as fibrocystic disease, fibroadenoma, breast abscess or mastitis.[1] Fibroadenoma is the commonest cause of benign breast lump.[2]

Breast cancer comes second as the most frequent cancer worldwide (more than 1.6 million cases) and 5th most fatal malignancy (0.5 million, 6.4%).[3] Pakistan is a high risk area with regards to breast cancer[4] and its prevalence in Karachi is the highest in Asia.[5] Earlier it used to be considered a disease afflicting the older middle aged females; however its incidence is on the rise in younger population nowadays.[6] Even with major publicity and increasing awareness regarding breast carcinoma, there is a delay in seeking health care in Pakistan, with 88.8 % patients presenting late (more than 03 months) and 59 % presenting at an advanced stage (Stage III /IV).[7]

Ultrasonography is a non-invasive, widely available, affordable and easy to perform imaging modality, which is free from ionizing radiations, and can be used safely even in pregnant females. It can diagnose of breast lesions with specificity of 57% and diagnostic accuracy of ultrasound 80%.[8] However, as it is highly operator dependant, the quality assurance becomes more challenging due to human variability with the limitation that third parties are unable to scrutinize an earlier examination apart from the data and images provided by the operator.[9]

Doppler ultrasound works on the principle that frequency of a pulse from moving particle is altered, giving Doppler frequency, depending on its speed with respect to its origin.[10] Thus, it can be used provides information regarding the blood flow in the vessels, the direction of flow and velocities around and inside breast lesions. Resistive index is an estimate of resistance offered by vessels to the flowing blood. Cancerous growths release vascular growth factors, which promote development of newer vessels.[11] However these vessels are tortuous with an abnormal structure, resulting in increased resistance to blood. Thus, doppler ultrasound of malignant masses reveals a higher Resistance Index (RI) as compared to benign growths or normal tissue. Thus, using these features, doppler ultrasound can be used to characterize breast masses in to benign or malignant. Malignant lesions also have features such as central vascularity, hypervascularity or tortuous vessels while benign lesions are predominantly usually have normal or reduced number of vessels.[11]

Histopathology is contemplated as investigation of choice to ascertain the nature of pathology, differentiation of benign from malignant tumors and determination of tumor grade.[12] However, apart from being invasive, it may result in an array of potential unpleasant side effects like bleeding, infection or damage to adjacent nerves, vessels and viscera. Furthermore, it can result in seeding of the tumor cells along the biopsy track, leading to metastatic spread. Another limitation is the inadequate availability of trained specialists who perform and interpret this procedure.

Aim of conducting this research study is to establish doppler ultrasound as an accurate investigation for reliable characterization of breast masses. Not much research has been performed in Pakistan on this topic. A few studies have been conducted internationally but have yielded contrasting results. Once proved, doppler ultrasound can be used accurately to segregate patients that would require further biopsy and histopathology. This would result in a decline in the number of unnecessary biopsies, causing less unwanted complications and also reducing the burden on our health system.

## METHODOLOGY

This cross-sectional study was conducted in Radiology Department, CMH Multan, from 1st December 2015 to 30th May 2016. 150 patients meeting the inclusion criteria were evaluated. Sample size was calculated with 95 % confidence level, taking expected prevalence of breast cancer as 47%[13] with sensitivity of 91.6%[14] and specificity 84.6%[14] of Doppler ultrasound in diagnosing malignant breast lesions. Permission was taken from the ethical review committee of the hospital.

Female patients, having age 20 - 60 years, diagnosed with breast lumps, participated in the study. Patients with diagnosed breast lesions, previous breast biopsy or surgery were not included in the study. Each patient was made clear the objective and written consent was obtained. Using a high- frequency linear probe, ultrasonography of the affected breast was performed. Doppler ultrasound of the lesion was carried out and the resistive index was computed (RI = peak systolic velocity - end diastolic velocity / peak systolic velocity). Each lesion was characterized as malignant or otherwise on the verdict of resistive index calculated. Feature suggestive of malignancy was Resistive Index (RI) more than or equal to 0.70 while a RI less than 0.70 favored a benign lesion. The results were kept secret. Biopsy followed by histopathological examination was carried out. Doppler ultrasound findings were compared with histopathology to establish the diagnostic accuracy.

Analysis of data was done through SPSS 22.

## RESULTS

The mean of age was 40.23 ± 5.75 years while the range of age was 22 to 59 years. Most of the patients incorporated in the study were in the 40 to 49 age group. Mean duration of disease was 13.23 ± 3.85 months. Mean size of lump was 4.83 ± 2.35 cm. Mean BMI was 29.74 ± 5.35 kg/m$^2$.

All the patients were subjected to Doppler Ultrasound. In 81 (54.0%) patients Doppler Ultrasound favored the diagnosis of malignant breast lesions. In 83 (52.67%) cases histopathology confirmed the diagnosis of malignancy. In 81 breast doppler ultrasound positive patients, 73 (True Positive) showed malignant lesions in breast while 08 (False Positive) did not have malignancy on biopsy. Among 69 Breast Doppler Ultrasound negative patients, 06 (False Negative) demonstrated malignancy on biopsy whereas 63 (True Negative) did not have any malignant lesion. Overall specificity was 88.77%, sensitivity was 92.40%, negative predictive value was 91.30%, positive predictive value was 90.12% while diagnostic accuracy of Doppler Ultrasound in characterizing lesions of breast was 90.67% as shown in Table-I. Characteristics of benign and malignant tumor are shown in Table-II.

| Doppler Ultrasound | Histopathology | |
|---|---|---|
| | Positive | Negative |
| Positive | 73 (True Positive) | 08 (False Positive) |
| Negative | 06 (False Negative) | 63 (True Negative) |

**Table-I. Calculation of diagnostic accuracy**

Sensitivity: TP / (TP + FN) x 100= 92.40%, Specificity: TN / (TN + FP) x 100= 88.77%, Positive predictive value: TP/ TP+ FP x 100=90.12%, Negative predictive value: TN / FN + TN x 100=91.30%, Accuracy: TP+ TN / TP+FP+FN+TN x 100=90.67%

| Diagnosis (Histo-Pathology) | Age (Yrs) | | | | BMI | | | Size of Lesion (cm) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 20 to 29 | 30 to 39 | 40 to 49 | 50 to 59 | ↓ 18.5 | 18.5 -24.9 | ↑ 25 | ≤ 1 | 1 – 2 | ≥ 2 |
| Benign | 17 | 20 | 18 | 12 | 12 | 21 | 34 | 13 | 21 | 33 |
| Malignant | 04 | 17 | 39 | 23 | 21 | 29 | 33 | 19 | 29 | 35 |

**Table-II. Characteristics of benign and malignant tumors**

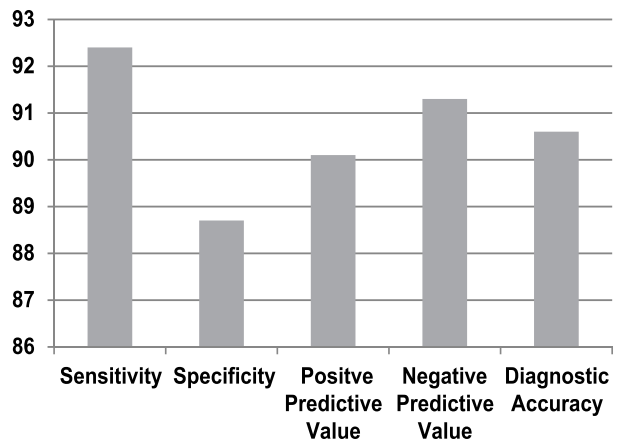


**Figure-1. Sensitivity, Specificity, PPV, NPV and Diagnostic Accuracy of Doppler ultrasound**

## DISCUSSION

Breast carcinoma is extremely notorious, being the most prevalent and lethal carcinoma in females globally.[15] Almost one woman in every eight will suffer from it in her lifetime while it will prove to be fatal in one in 30 women.[16] The role on a radiologist in patients with breast lumps is accurate differentiation of benign and malignant cases. This will not only comfort the patients with benign lesions but also result in early identification of the malignant cases, which will be of paramount importance in favorable prognosis of disease.

Doppler ultrasound utilizes the change in vascularity as the discriminating feature of malignancies. In our study, sensitivity was 92.40%,

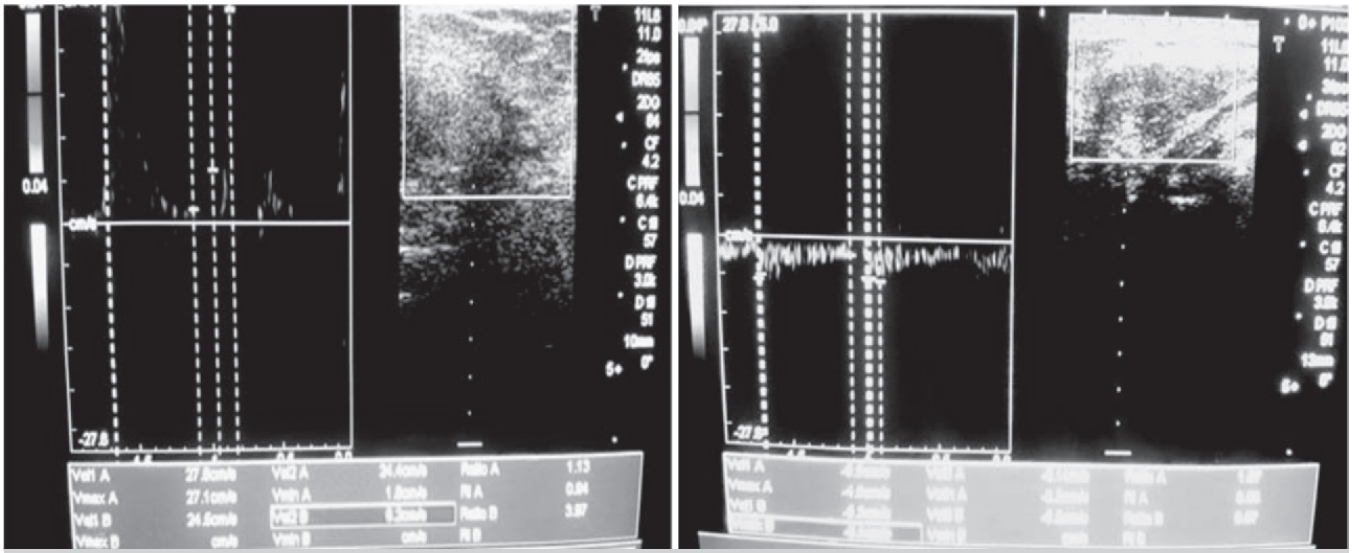

**Figure-2. Malignant lesion with RI of 0.9 and benign lesion with RI of 0.5 on Doppler ultrasound**

specificity was 88.77%, positive predictive value (PPV) was 90.12%, negative predictive value (NPV) was 91.30% while diagnostic accuracy was calculated as 90.67%. Only limited studies are found using doppler ultrasound alone for diagnosis of malignant breast lesions based on the RI values. del Sirous M et al[17] evaluated the role of doppler ultrasound in characterization of breast masses and concluded that resistive index (RI) value showed sensitivity of 75 % and high specificity of 97 % for diagnosing breast carcinoma at a threshold value of 0.83

Cura JL et-al[18] performed a study regarding application of doppler ultrasound for assessment of breast masses. The study shows that any breast mass may be established as malignant, if there is a vessel having RI value more than 0.99 inside, irrespective of other ultrasound features.

Choi HY et al[19] organized research regarding the role of doppler ultrasound in discrimination of benign from malignant breast masses. They formulated that mean of RI seen in benign breast masses was 0.62 +/- 0.095 (range 0.44-0.86) while that for malignant lesions was 0.74 +/- 0.097 (range, 0.50-0.92). The value of resistive index was more than 0.7 in about 80% cases of malignancies. The difference of the RI proved to be significant statistically for threshold value of 0.7 ($P < 0.001$) and resistive index exceeding 0.7, signified a malignant lesion.

Recent innovations in breast ultrasound, such as elastography, contrast enhanced ultrasonography and automated whole-breast ultrasound, are newer avenues that need to be explored. Elastography is a newer procedure that assesses the extent of elasticity of breast tissue and differentiates lesions into benign or malignant based on these findings.[20] Contrast-enhanced ultrasound is an innovative modality producing quantifiable measures of vascularity that could assist in evaluation of breast lesions.[21] Automated whole breast US is a recent technique that allows acquisition of a volumetric three-dimensional breast dataset and shows promising results in accurate characterization of breast masses.[22] However more studies are needed to validate these techniques.

The number of studies using resistive index as the discriminating criteria for breast lesions are scarce. The effort to find any national study on this topic was futile. Few international studies, mentioned above, were found and were consistent with our results.

## CONCLUSION

Angiogenesis in malignant lesions lead to formation of structurally abnormal and tortuous vessels with increased resistive index. Doppler

ultrasound is a safe and effective modality which shows acceptable diagnostic accuracy for noninvasive characterization of malignant breast lesions. Therefore, it can be employed as an alternative to histopathology in patients who present with breast lesions. Consequently, there will be a decline in morbidity and complications caused by biopsies as well as reduced burden on the health delivery system.

## CONFLICT OF INTEREST

Nil



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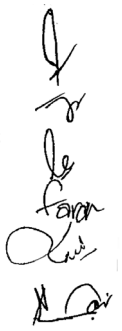
| 1 | Ishrat Parveen | Principal Author, Proposed topic, Basic study design. |  |
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