# ORIGINAL ARTICLES

## ACCURACY OF THE DOPPLER RESISTIVE INDEX IN THE DIAGNOSIS OF MALIGNANT BREAST MASSES

**Sadaf Aziz, Arfan-ul-Haq*, Asad Maqbool Ahmad**

Combined Military Hospital Khuzdar, *AFIRI Rawalpindi

## ABSTRACT

***Objective:*** To determine the accuracy of the resistive index in the diagnosis of malignant breast masses using histopathology as the gold standard.

***Study Design:*** Validation study.

***Place and Duration of Study:*** Radiology department, PNS Shifa Karachi from 2nd February to 8th August 2007.

***Methods:*** Appropriate technical and ethical approval for the study and patient consent were obtained. Fifty three adult female patients (selected by non-probability purposive sampling) with ages ranging from 14 to 58 years presenting with one or more breast lumps at Radiology department, PNS Shifa Karachi, who subsequently underwent biopsy were included in the study. All patients underwent doppler ultrasonography by an experienced consultant radiologist. Doppler spectral parameters including the Resistive Index (RI) were calculated on all tumor vessels more than 3 mm long visible on Pulsed Doppler Sonography. The resistive indices for each patient were compared with the histopathology result, which was considered as gold standard. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the RI was calculated.

***Results:*** Thirty five (35) patients were found to be having benign lesions whereas 18 patients were having malignant lesions on histopathology examination. In the group that had benign lesions, the mean RI was 0.60 with a range of 0.45 to 0.78 whereas the median was 0.61. In the group, that had malignant lesions the mean RI was 0.76 with a range of 0.64 to 0.93 and the median was 0.74. The ROC curve lies close to the top left corner of the ROC space and has a significant area under the curve (AUC) of 0.955 with a *p*-value of less than 0.001.

***Conclusion:*** The Resistive Index (RI) is an accurate diagnostic tool and may therefore be used in the diagnosis of carcinoma breast during evaluation of breast lumps in adult females. An RI of 0.675 is an adequate cut-off value that is both sensitive (94.4%) and specific (91.4%) enough to diagnose malignancy with a false positive rate of 8.6% and a false negative rate of 5.6%.

**Keywords:** Breast Imaging, Breast neoplasms, Doppler Resistive Index, Pulsed Doppler Ultrasonography.

## INTRODUCTION

Carcinoma of the breast in women is a major health burden worldwide. It is the most common cause of cancer among women in both high-income and low-income groups, and is responsible for over one million of the estimated 10 million neoplasms diagnosed worldwide each year in both sexes[1]. Imaging plays an important role in the diagnosis of breast diseases. With the advancement in technology, new diagnostic imaging modalities have been added to the arsenal of investigations for carcinoma of breast, which is showing a rising trend in the recent years. These include MRI, color Doppler ultrasound, contrast ultrasound and digital mammography[2]. Sonography (currently one of the main diagnostic methods) can help differentiate benign from malignant masses utilizing specific features[3]. The sensitivity of grey scale ultrasound for malignant lesions has been shown to be 95.24% and specificity 68.75% in our local population[4]. Since the introduction of high-frequency probes, this technique is commonly included in most routine procedures to detect and identify breast lesions[5].

Increasingly, tumor vascularization, particularly of breast tumors, is becoming the focus of scientific interest in prognostic, diagnostic, and possibly therapeutic terms. It

**Correspondence:** Maj Sadaf Aziz, Graded Radiologist, CMH Khuzdar
*Email: sadafaziz@yahoo.com*
*Received: 06 Feb 2013; Accepted: 18 Sep 2013*

plays an important role in the primary identification of a nonspecific breast lesion and in the diagnosis of a recurrence with MR imaging and duplex sonography[6]. Combining both color doppler analysis and 2D-US might remarkably increase the sensitivity and specificity of differential diagnosis of breast neoplasms[7]. Whereas the features of gray-scale sonography used to determine the nature of breast lesions are widely accepted, there is no such consensus regarding the use of doppler sonography. Several studies have used different doppler spectral parameters to differentiate between benign and malignant lesions of the breast[8]. One of these is the resistive index which is a quantitative measure of the resistance to arterial flow within a vascular bed. The use of the Resistive Index (RI) in conjunction with sonographic vascular characteristics of malignant and benign lesions holds promise of increasing the sensitivity of pulsed wave doppler in detecting malignant breast lesions in our population[9].

The rationale of this study is to validate the RI as a potential diagnostic tool that would enable more accurate and non- invasive screening of malignant breast masses with high specificity and sensitivity.

## PATIENTS AND METHODS

The patients were divided into two groups on the basis of histopathology results i.e. benign and malignant groups. The mean, median, interquartile range and ROC curve of resistive indices in both groups were computed. Coordinates of the curve were used to determine sensitivity, specificity and true negative rate (1-specificity) of each RI value. The RI value with the most appropriate sensitivity and specificity was then selected as a potential cut off value for use as a diagnostic tool. Area under the curve (AUC) was obtained and *p*-value also computed.

**Table-1: Comparison of means and medians of Resistive Index.**

| | n | Minimum | Maximum | Range | Mean | Std. Deviation | Median | IQ range |
|---|---|---|---|---|---|---|---|---|
| Benign histology | 35 | 0.45 | 0.78 | 0.33 | 0.6017 | 6.789E-02 | 0.61 | 0.57–0.64 |
| Malignant histology | 18 | 0.64 | 0.93 | 0.29 | 0.7639 | 9.198E-02 | 0.74 | 0.69-0.81 |

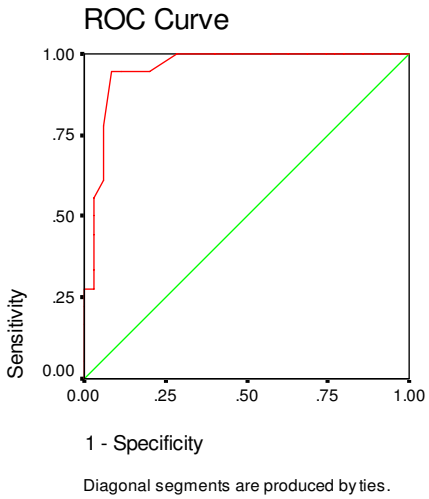


**Figure-1: ROC (receiver operating characteristic) curve.**

The study design was a cross sectional study carried out at PNS Shifa hospital Karachi from Feb to Aug 2007. All ladies presenting to Radiology department with one or more breast lumps were included in the study whereas those with history of ipsilateral breast surgery and fungating masses were excluded. Fifty three cases were selected by non-probability purposive sampling. After informed consent and detailed history, sonographic examinations were performed by an experienced consultant radiologist using a Toshiba Nemio-20 sonographic scanner with 7.5 MHz linear array transducer. B-mode study was performed to assess the size of the lesion. Power doppler study was performed to assess the vascularity of the mass. Examination was done carefully to apply as little pressure as possible with the probe on the lesion in order to prevent vessels from collapsing.

The detection of at least one vessel inside the lesion with power doppler sonography examination was considered sufficient for inclusion and further examination with other modalities/calculation of RI. Next, Pulsed doppler sonography was done. Doppler gain was decreased until clutter noise disappeared and the velocity range was adjusted to avoid aliasing. The sampling point of spectral analysis was placed over tumor vessels visible on Pulsed Doppler Sonography. The doppler angle was set by placing the cursor along the axis of the tumor vessel. The Resistive Index was calculated automatically by tracing the doppler spectrum in the tumor vessels using the Toshiba built-in software. All vessels were sampled both from within and from the margin of the lesion. When different velocities of the pulsatile flows were recorded, the highest resistive index (RI) was selected for statistical analysis.

The resistive indices for each patient were compared with the histopathology results, which were considered as gold standard. Computer package SPSS version 10.0 was used for computation and analysis of data.

## RESULTS

Out of 53 patients, 35 had lesions that proved to be benign on histopathology examination whereas 18 lesions were reported as malignant by the histopathologist. An assessment of age trends revealed that in the group that had benign lesions the age range was between 14 and 26 years whereas the age range in the group that had malignant lesions was between 34 and 58 years with a bimodal peak at 36 years and 55 years. A positive family history of carcinoma breast was found in 44.4% (n=8) cases in the malignant group and only 5.7% (n=2) cases in the benign group. The size of the lesion was larger in terms of width and anteroposterior diameter in the group that had malignant lesions.

Both groups were compared in terms of measures of central tendency (i.e. means and median) in table-1. The ROC (Receiver Operating Characteristic) curve is shown as Figure 1 which shows an Area under the Curve (AUC) of 0.955 with a *p*-value of <0.001. The coordinates of the ROC curve are given in table-2 as calculated by SPSS. The highlighted RI of 0.675 shows a sensitivity of 94.4% and specificity of 91.4% (calculated from a 1-specificity of 0.086).

**Table-2: Coordinates of the curve.**

Test result variable: resistive index (RI)

| Positive if ≥ | Sensitivity | 1 - Specificity |
|---|---|---|
| 0.0000 | 1.000 | 1.000 |
| 0.4550 | 1.000 | 0.971 |
| 0.4800 | 1.000 | 0.943 |
| 0.5050 | 1.000 | 0.886 |
| 0.5200 | 1.000 | 0.857 |
| 0.5450 | 1.000 | 0.800 |
| 0.5650 | 1.000 | 0.771 |
| 0.5750 | 1.000 | 0.743 |
| 0.5850 | 1.000 | 0.686 |
| 0.5950 | 1.000 | 0.629 |
| 0.6050 | 1.000 | 0.571 |
| 0.6150 | 1.000 | 0.457 |
| 0.6250 | 1.000 | 0.400 |
| 0.6350 | 1.000 | 0.286 |
| 0.6450 | 0.944 | 0.200 |
| 0.6550 | 0.944 | 0.114 |
| **0.6750** | **0.944** | **0.086** |
| 0.6950 | 0.778 | 0.057 |
| 0.7050 | 0.611 | 0.057 |
| 0.7200 | 0.556 | 0.029 |
| 0.7400 | 0.500 | 0.029 |
| 0.7550 | 0.444 | 0.029 |
| 0.7650 | 0.333 | 0.029 |
| 0.7750 | 0.278 | 0.029 |
| **0.7850** | **0.278** | **0.000** |
| 0.8450 | 0.222 | 0.000 |
| 0.9100 | 0.167 | 0.000 |
| 0.9250 | 0.056 | 0.000 |
| 1.0000 | 0.000 | 0.000 |

## DISCUSSION

The above results show an evidently higher mean RI in the malignant group and are in keeping with the findings of other studies. A study by Hye-Young Choi and colleagues showed very similar mean RI (Benign: 0.62 ±

0.095; Malignant: 0.74 ± 0.097). These results are very comparable as is the percentage of malignant cases with an RI equal to or above 0.7 i.e. 88% compared to 80% in Hye-Young Choi's study[10]. Another study by Youssefzadah showed an RI of 0.7±0.08 (Range 0.56 to 0.9) in the malignant group[11]. A close study of table-2 reveals that the cut-off value of 0.675 carries a sensitivity and specificity high enough to warrant its routine use as a diagnostic tool. The sensitivity is the ability of a test to correctly identify those with the disease (true positive rate), whereas specificity is the ability of the test to correctly identify those without the disease (true negative rate). This sensitivity of 94.4% carries a false negative rate (type II error =1-sensitivity) of 5.6% whereas the specificity of 91.4% carries a false positive rate (Type I error =1-specificity) of 8.6 %. A recent study of similar methodology has identified a cutoff RI value of 0.69 to be significant[12]. The positive and negative predictive values have not been calculated as these values are prevalence dependent and must be evaluated on cross-sectional or population based samples in order to be reliable. Sensitivity and specificity are however prevalence independent and test specific.

Although the RI of 0.675 appears to be adequate as a cut-off value, it is necessary to examine it in the backdrop of the fact that the disease under consideration is malignant and also whether the RI can be used as a stand alone diagnostic test. In general, a highly specific test is unlikely to give a false positive result: a positive result (in this case RI ≥0.675) should thus be regarded as a true positive (i.e. malignant). A highly sensitive test rarely misses a condition, so a negative result (in this case RI < 0.675) should be reassuring i.e. the disease tested for is absent (i.e not malignant/benign). A close look at table-1 and 2 shows that the RI value of 0.785 has a specificity of 100% being higher than the maximum RI value of benign group (i.e. 0.78). The sensitivity however, is too low (27.5%). This would be very specific and would be pathognomonic of breast carcinoma if positive (i.e. RI ≥ 0.785) but would not be reliable enough alone as it would miss an unacceptable proportion of tumors (high false negative rate = 78%).

It may be possible to utilize both values of RI i.e. 0.675 and 0.785 in a graded approach to diagnosis. Values of RI ≥ 0.675 to ≤ 0.784 may be evaluated as highly suspicious for carcinoma breast whose further evaluation may include a biopsy whereas those with an RI ≥ 0.785 may be considered diagnostic of malignancy and managed accordingly. All those breast lumps with an RI <0.675 may be considered benign and biopsy not included as part of evaluation. To increase the diagnostic accuracy of non-invasive methods a combination of grey scale ultrasound and doppler ultrasound may be evaluated in further studies.

The strength of this study was the accuracy of the data and the comparison of cases with gold standard i.e. histopathology. The weakness of this study was the focus on RI alone instead of utilizing a number of parameters in unison which may have increased the overall non-invasive diagnostic accuracy.

## CONCLUSION

The Resistive Index (RI) is an important diagnostic tool in ruling out carcinoma breast during evaluation of breast lumps. An RI of 0.675 is an adequate cut-off value that is both sensitive and specific enough to diagnose malignancy. An RI of 0.785 has a specificity of 100% and may be considered diagnostic.

### Recommendations

Further studies using multiple non-invasive parameters may further increase diagnostic accuracy.

## REFERENCES

1. Bray F, McCarron P, Parkin DM. The changing global patterns of female breast cancer incidence and mortality. Breast Cancer Res. 2004; 6(6): 229–239.
2. Ahmed R, Ali M. Role of imaging in diagnosis of carcinoma of breast. J Coll Physicians Surg Pak 2005; 15:238-41.
3. Murad M, Bari V. Ultrasound differentiation of benign versus malignant solid breast masses. J Coll Physicians Surg Pak 2004; 14:166-9.
4. Shahid R, Ghaffar A, Bhatti AM. Role of grey scale ultrasound in benign and malignant breast lesions. J Coll Physicians Surg Pak 2005; 15: 193-5.

5. Del Cura JL, Elizagaray E, Zabala R, Legorburu A, Grande D. The use of unenhanced doppler sonography in the evaluation of solid breast masses. Am J Roentgenol 2005; 184:1788-94.
6. Stuhrmann M, Aronius R, Schietzel M. Tumor vascularity of breast lesions, potentials and limits of contrast enhanced doppler sonography. Am J Roentgenol 2000; 175:1585-9.
7. Lee SW, Choi HY, Beak SY, Lim SM. Role of color and power doppler imaging in differentiating between malignant and benign solid breast masses. J Clin Ultrasound 2002; 30: 459-64.
8. Mehta TS, Raza S. Power Doppler sonography of breast cancer: does vascularity correlate with node status or lymphatic vascular invasion? Am J Roentgenol 1999; 173: 303 –7.
9. Batool S, Shaukat A, Ahsan Z, Batool S, Siddiqa A, Qureshi A et al. Doppler evaluation of breast solid masses differentiation of benign and malignant masses role of resistive index. Ann King Edward Med Coll Jun 2006; 12(2):325-6.
10. Choi HY, Kim HY, Baek SY, Kang BC, Lee SW. Significance of resistive index in color doppler ultrasonogram: Differentiation between benign and malignant breast masses. The Korean Radiological Society 1999;23(5 ) 284-8
11. Youssefzadeh S, Eibenberger K, Helbich T, Jakesz R, Wolf G. Use of resistance index for the diagnosis of breast tumours. Clin Radiol. 1996 Jun; 51(6):418-20.
12. Schmillevitch J, Filho H A G, Nicola H, Gorski AC. Using vascular resistance index in differentiating between benign and malignant breast lumps. Radiol Bras [serial on the Internet]. Aug 2009 [cited 2013 Jan 08]; 42 (4): 241-244. Available at: http:/ / www.scielo.br /scielo.php?script = sci_arttext&pid=S010039842009000400010&lng=pt. http://dx.doi.org/10.1590/S0100-39842009000400010.