Diagnostic Accuracy of Resistive Index of Doppler Ultrasound in Differentiating Malignant from Benign Breast Lesions Taking Histopathology as Gold Standard

[1*]Dr. Sobia Kaleem, [2]Dr. Zainab Qayyum, [3]Dr. Farah Aslam, [4]Dr. Sonia Nisar, [5]Dr. Mahwish Shoaib, [6]Dr. Saira Saeed

Article Details

Dr. Sobia Kaleem
Post Graduate Resident of Radiology PINS, Lahore. Email: Sobiakaleem9449@gmail.com
Dr. Zainab Qayyum
Post Graduate Resident of Radiology PINS, Lahore.
Dr. Farah Aslam
Post Graduate Resident of Radiology PINS, Lahore.
Dr. Sonia Nisar
Senior registrar radiology PINS, Lahore.
Dr. Mahwish Shoaib
Assistant Professor of Radiology PINS, Lahore.
Dr. Saira Saeed
Professor of Radiology PINS, Lahore.

ABSTRACT

Introduction: Breast cancer remains one of the most prevalent and fatal malignancies in women worldwide, underscoring the need for diagnostic methods that are both rapid and accurate. Ultrasound, favored for its safety and accessibility, has become a primary tool for evaluating suspicious breast lesions. The addition of Doppler imaging, particularly the Resistive Index (RI), offers valuable insights into tumor vascularity, with elevated RI values often indicative of malignancy. Despite its potential, RI is underutilized in many clinical settings, where conventional grayscale ultrasound and mammography dominate. This study evaluates the diagnostic accuracy of RI against histopathological findings, aiming to reduce unnecessary biopsies and enhance the efficiency of breast cancer screening. Objective: To determine the diagnostic accuracy of the Resistive Index (RI) on Doppler ultrasound in distinguishing benign from malignant breast lesions. Methodology: This cross-sectional validation study was conducted at the Department of Radiology, Punjab Institute of Neurosciences, Lahore, over a six-month period from July 20, 2023, to January 20, 2024. A total of 209 female patients aged 25–60 years with clinically diagnosed breast lesions were enrolled. Patients were positioned supine oblique with the arm placed above the head during Doppler ultrasound examinations to assess lesion vascularity. For each lesion, three resistive index (RI) measurements were obtained, and their mean was recorded. Histopathological analysis served as the gold standard for diagnostic confirmation. Exclusion criteria included patients with comorbidities, those who had undergone mastectomy, and uncooperative individuals. Results: All patient information was entered into SPSS Version 20 for detailed examination. Continuous variables, like patient age, are reported as mean ± standard deviation (SD) to show the average and how spreads out the ages are. Categorical factors-parity, lactation status, smoking, oral contraceptive use, and family history of breast cancer-are presented as counts and percentages so readers can see how common each one is in the group. To test how well the Resistive Index (RI) from Doppler ultrasound spots cancerous breast masses, several classic metrics were calculated. These included sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy. Each figure came from simple 2x2 tables that matched Doppler results against the final tissue diagnosis made by a pathologist. We considered results statistically significant when the p-value dropped below 0.05, meaning there is less than a 5% chance the findings happened by random fluctuation. To guard against confounding and examine test performance in patient subgroups, we divided the data by age, number of pregnancies, oral contraceptive therapy, smoking, family breast-cancer history, and whether the patient breast-fed. This step revealed how the relevance index varied from one demographic cluster to another.

INTRODUCTION

Breast cancer ranks as the most prevalent cancer worldwide and the leading cancer-related mortality cause among women, with 2.3 million new diagnoses and 685,000 deaths documented in 2020 (World Health Organization, 2021). Timely identification markedly enhances prognosis; the five-year survival rate exceeds 90% when disease is confined to the breast, plummeting once malignant cells have disseminated (Arshad et al., 2022; Catalano et al., 2023). Accurate characterization further spares patients from superfluous invasive procedures—such as needle biopsies—that entail pain, risk of infection, and substantial psychological distress. Mammography continues to serve as the benchmark screening modality, excelling in the detection of microcalcifications and small opacities (Amin et al., 2019; Azhar &Candrawinata, 2023). Nonetheless, its diagnostic performance wanes in women who exhibit dense breast parenchyma, a prevalent characteristic among younger South Asian populations, with reported sensitivity falling to 30%–48% (Devkota et al., 2021). To mitigate this shortfall, ultrasonography has gained recognition as an effective adjunct. It is non-invasive, avoids ionizing radiation, and demonstrates superior sensitivity for visualizing abnormalities in dense breast tissue; additionally, real-time imaging facilitates the accurate localization of suspicious lesions for subsequent biopsies (Dhir et al., 2023). Tumor perfusion patterns, central to the angiogenic cascade, are evaluated by Doppler ultrasound, which visualizes neovascularization—an accepted malignant angiogenic signature (Feliciano et al., 2023). Folkman (1971) first articulated that neovessel sprouting from pre-existing networks supplies tumor cells in developing hypoxic microenvironments. Employing both Color Doppler and Spectral Doppler modalities, the technique yields complementary qualitative and quantitative data, revealing that elevations in both the resistance index (RI) and the pulsatility index (PI) are significantly associated with malignant behavior (Firdous et al., 2021; Farhana et al., 2024). Meta-analyses demonstrate that Doppler ultrasound can stratify lesions, with 71% of malignant neoplasms manifesting a central perfusion pattern; the positive predictive value for malignancy climbs to 92% when Doppler data are integrated with B-mode imaging (Koutras et al., 2023; Li et al., 2021). An RI threshold of 0.73 serves as a quantitative surrogate for malignant transformation, whereas heightened vascular flow operates as an independent risk factor for axillary lymph node involvement (Stanzani et al., 2023; He et al., 2023). Although variability among studies persists, the technique bolsters overall diagnostic precision, especially in dense glandular breast tissue when coupled with artificial intelligence–driven decision-support algorithms (Iqbal et al., 2022).

The differentiation of hypervascular benign breast lesions from malignant counterparts underlines the utility of an integrated grayscale and Doppler imaging strategy to mitigate false-positive rates (Jain et al., 2021). This multimodal approach further facilitates the identification of patients who may benefit from neo-adjuvant chemotherapy (Jesrani et al., 2024). Nevertheless, spectral Doppler capability remains sparse in many ultrasound platforms, particularly in low-resourced settings. This research therefore assesses the diagnostic performance of the resistive index in Pakistani women exhibiting dense breast parenchyma and constrained access to sophisticated imaging. The objective is to enhance detection of early-stage malignancy and to decrease the rate of non-indicated biopsies, with a special focus on rural health care delivery.

METHODOLOGY

This observational cross-sectional validation study was carried out from 20th July 2023 to 20th January 2024 at the Department of Radiology, Punjab Institute of Neurosciences, Lahore General Hospital, Pakistan. Utilizing non-probability consecutive sampling, 209 female patients between 25 to 60 years, previously diagnosed with breast lesions and within the inclusion and exclusion criteria, were recruited. Sheer sample size determination was conducted using the WHO sample size calculator with a 95% confidence interval, 13%

margin of error, 16.2% prevalence, and projected 82% sensitivity and specificity. Exclusion criteria incorporated patients with comorbidities, uncooperative patients, and patients with a history of mastectomy. Each subject received a complete clinical history and examination followed by a Doppler ultrasound with a 5–50 MHz linear transducer on a GE LOGIQ S8 ultrasound machine performed in the supine oblique position. The resistive index (RI) values were computed via averaging three readings taken from the periphery or center of each lesion. After ultrasound examinations, all participants underwent core needle biopsies (CNB). Thus, histopathologic evaluations were performed to validate the diagnosis, which served as the gold standard for the comparisons. The data were analyzed using SPSS software version 20. The evaluation of performance for diagnostics such as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the cumulative diagnostic precision were computed with the employment of a 2 by 2 contingency table. Further stratification was done on age, parity, oral contraceptive pill (OCP) usage, smoking history, familial history of breast cancer, and lactation to evaluate the gaps in performance across different subgroups.

RESULTS

Out of the total sample population, 209 patients were included **(Table 1)**, of which 198 (94.7%) were in the 41-60 years age category and only 11 (5.3%) were aged 25-40 years. The average age of the study population was 46.84 ± 3.72 years, indicating the prevalence of middle aged South Asian women (more than half of South Asian women diagnosed with breast cancer are from this age group). This may be due to the hormonal shifts related to perimenopause and menopause which increases the likelihood of breast tissue undergoing neoplastic changes. Concerning family history, only 7.7% (n=16) reported the presence of breast cancer in their family while 92.3% (n=193) had no family history of the disease, suggesting limited screening programs in the country along with cultural factors that tend to underreport the disease. From the distribution of parity, it was also observed that most of the women were multiparous (84.2%, n=176) with grand multiparous women making 12.0% (n=25) and nulliparous women accounting for 3.8% (n=8). The observed high prevalence of multiparity is consistent with the regional demographic where family sizes are culturally larger.

Analysis of lactation status indicated that merely 1.9% (n=4) of participants were lactating, likely stemming from the fact that most participants had surpassed the age of childbearing. Similarly, the lifestyle smoking and usage of oral contraceptive pills (OCPs) were noted in just 3.8% (n=8) and 10.5% (n=22) of the study population, respectively. It is important to note that these figures may be influenced by cultural stigma and sub-reporting. Taken together, these results illuminate the demographic and clinical features of the patient cohort, demonstrating a practical clinical setting where Doppler ultrasound is utilized, and accentuating the need to assess diagnostic methods in populations with specific reproductive and lifestyle characteristics.

In this research, the use of Doppler ultrasound with the resistive index (RI) detected malignant lesions in breasts with a frequency of 78.5% (n=164) as illustrated in Figure 1. Figure 2 corroborates this finding using histopathological analysis which confirmed malignancy in 81.3% (n=170) of cases. This demonstrates a strong correlation between Doppler RI results and histopathological evaluation.
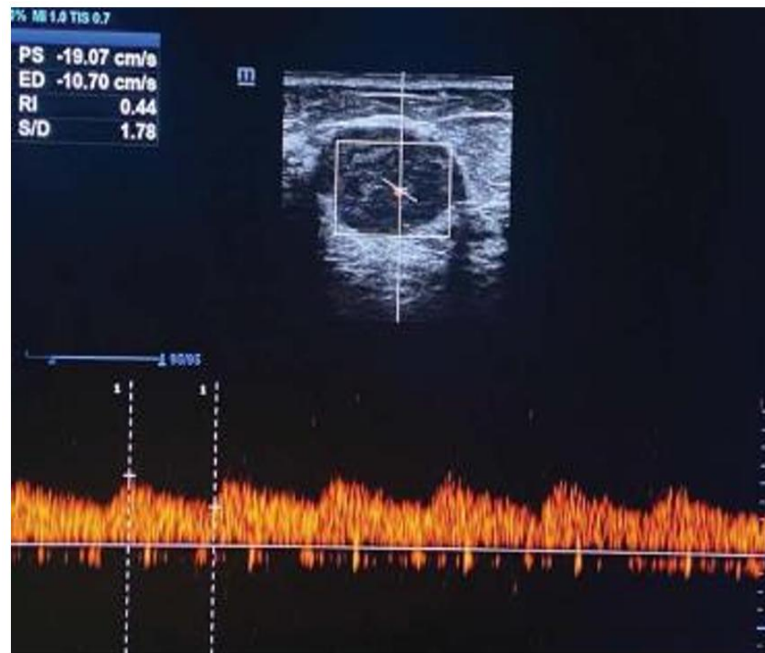
FIGURE 1 DOPPLER ULTRASOUND OF BREAST LESION SHOWING RI VALUE OF 0.4 SUGGESTING A BENIGN LOOKING LESION
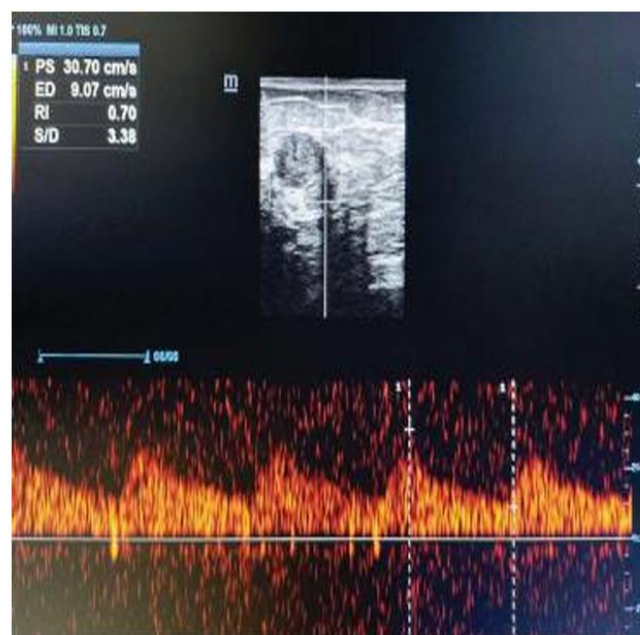
FIGURE 2 DOPPLER ULTRASOUND OF A BREAST LESION SHOWING RI VALUES OF 0.7 SUGGESTING A MALIGNANT LOOKING LESION

Table 1: Demographic and Clinical Characteristics of Study Participants (N = 209)

Characteristic	Category	Frequency (n)	Percentage (%)
Age Group	25–40 years	11	5.3
	41–60 years	198	94.7
	Total	**209**	**100.0**
Mean Age ± SD		—	46.84 ± 3.72
Family History of Breast Cancer	Yes	16	7.7
	No	193	92.3
	Total	**209**	**100.0**
Parity	Nulliparous	8	3.8
	Multiparous	176	84.2
	Grand multiparous	25	12.0
	Total	**209**	**100.0**
Lactation Status	Yes	4	1.9
	No	205	98.1
	Total	**209**	**100.0**
Smoking History	Yes	8	3.8
	No	201	96.2
	Total	**209**	**100.0**
OCP Use	Yes	22	10.5
	No	187	89.5
	Total	**209**	**100.0**

Benign lesions were diagnosed in 21.5% (n=45) of cases with RI, and in 18.7% (n=39) with histopathology. The overall diagnostic performance of resistive index was remarkable, attaining sensitivity and specificity of 94.11% and 89.74% respectively. This confirms the outstanding performance of RI in accurately diagnosing malignant lesions and controlling false positive results. The positive predictive value (PPV) reached 97.56%, while negative predictive value (NPV) was 77.77%. The resultant overall diagnostic accuracy was 93.30%, which is comparable, or slightly improved, to diagnostic accuracies reported in prior studies employing similar techniques **(Table 2)**.

Variations in the diagnostic performance in relation to different patient characteristics were further examined using stratified subgroup analysis**(Table 3)**. Among age groups, those belonging to the 25 to 40-year cohort showed the lowest sensitivity (88.88%) and specificity (50.00%) relative to those aged 41 to 60 years, who demonstrated sensitivity and specificity of 94.40% and 91.89%, respectively, with an overall accuracy of 93.93%.

Younger women may have the greatest impact from breast tissue density, which in turn adversely affects the quality of Doppler signals and the visualization of lesions. Nulliparous women achieved a sensitivity of 100%, although this came at a cost of low specificity of 50% as observed by multiparous women who showed strong performance with sensitivity and specificity values of 95.10% and 90.90%, respectively. Grand multiparous women exhibited slightly lower sensitivity of 85.71% but perfect specificity (100.0%). This suggests reproductive history may alter vascular features measured by Doppler ultrasound.

Such analysis considering the use of oral contraceptive pills (OCPs) showed perfect diagnostic performance (100% sensitivity, specificity, PPV, NPV, and accuracy) in women with a history of OCP use, perhaps because of hormonal influence on breast tissue vascularity. Those without

OCP use showed lower metrics of sensitivity at 93.37% and specificity at 88.88%. These same trends were seen in subsets with positive smoking and family histories where patients achieved 100% diagnostic performance, although such subgroups were small and warrant caution. Among non-lactating women, however high diagnostic accuracy was preserved with sensitivity of 94.01%, specificity of 92.01%, PPV of 98.12%, NPV of 77.77%, and overall accuracy of 93.65%. These results reinforce the high diagnostic utility of Doppler RI in older, multiparous women and indicate that its utility may be solely driven by physiological and hormonal factors that modify breast tissue vasculature. Moreover, almost flawless performance in defined subgroups underscores the promise of using Doppler RI as an adjunct breast cancer diagnostic tool in breast cancer tailored diagnostics, particularly in sharply defined demographic and clinical populations.

DISCUSSION

Sonography is one of the main methods used to image and evaluate for breast diseases since it does not expose patients to radiation and is non-invasive. Distinction between malignant and benign breast lesions using ultrasound has been achieved through grayscale ultrasound; nonetheless, greater focus has been placed on assessing tumor vascularity as an additional criteria due to its possible prognostic, diagnostic, and therapeutic significance(Li et al., 2023). In any case, the use of both color and spectral Doppler ultrasound (DS) has remained controversial. Some researchers doubt its accuracy because of vascular feature overlap between benign and malignant lesions, while some others have been able to demonstrate DS's usefulness for integrating with grayscale imaging increasing diagnostic reliability(Li et al., 2023; Luo et al., 2025; Mehdikhani et al., 2024). Although mammography is still the primary method for screening breast cancer, its use is limited among younger women with dense breasts, particularly pre-menopausal. In such cases, the combination of mammography and ultrasonography is more useful for detecting and characterizing lesions.

TABLE 2: FINDINGS OF DOPPLER ULTRASOUND RESISTIVE INDEX (RI) AND HISTOPATHOLOGY (N = 209)

Modality	Malignant (n)	Benign (n)	Total (n)
RI Ultrasound	164	45	209
Histopathology	170	39	209

TABLE 3: DIAGNOSTIC PERFORMANCE OF DOPPLER ULTRASOUND RESISTIVE INDEX (RI) COMPARED TO HISTOPATHOLOGY

Parameter	Subgroup	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Overall Diagnostic Accuracy	–	94.11	89.74	97.56	77.77	93.30
Stratified by Age Group	25–40 years	88.88	50.00	88.88	50.00	81.81
	41–60 years	94.40	91.89	98.06	79.06	93.93
Stratified by Parity	Nulliparous	100.0	50.00	85.71	100.0	87.50
	Multiparous	95.10	90.90	97.84	81.08	94.31

	Grand multiparous	85.71	100.0	100.0	57.14	88.00
Stratified by OCP Use	Yes	100.0	100.0	100.0	100.0	100.0
	No	93.37	88.88	97.24	76.19	92.51
Stratified by Smoking History	Yes	100.0	100.0	100.0	100.0	100.0
	No	93.90	89.18	97.46	76.74	93.03
Stratified by Family History	Yes	100.0	100.0	100.0	100.0	100.0
	No	93.58	89.18	97.33	76.74	92.74
Stratified by Lactation Status	Yes	—	—	—	—	—
	No	94.01	92.01	98.12	77.77	93.65

The significance of angiogenesis in cancer biology highlights the importance of Doppler ultrasonography, first described by Folkman in 1971(Mohindra & Soni, 2024). Malignant neoplasms foster neovascularization to meet their metabolic needs within hypoxic microenvironments, giving rise to disordered, excessive, and fragile blood vessels. Such neovascularization can be detected and serves as a qualitative indicator of malignancy through color Doppler and other Doppler techniques. Contrastively, spectral Doppler provides quantitative vascular parameters such as resistive index (RI) and pulsatility index (PI), which have been suggested as secondary markers of malignancy. However, the presence of highly vascular benign lesions disguising malignant vascular patterns poses a challenge, diminishing the specificity of color Doppler alone. Despite this, research shows that using grayscale ultrasound in conjunction with color and spectral Doppler increases sensitivity and specificity when assessing suspicious breast masses(Nayab, 2023).

In this work, we evaluated the diagnostic performance of RI detected by Doppler ultrasonography for detecting benign and malignant breast lesions and compared the results with histopathology examinations taken as the reference standard. The sensitivity, specificity, PPV, NPV, and overall diagnostic accuracy of RI calculated were 94.11%, 89.74%, 97.56%, 77.77%, and 93.30% respectively. The findings are corroborated with other studies and emphasize the potential value of RI in characterizing breast lesions.

According to (Pallio et al., 2023)central blood flow was detectable in 71% of malignant and 6.6% of benign lesions, with a PPV of 92% for malignancy when grayscale and color Doppler findings were combined. Early high-flow signals in breast tumors and their association with axillary lymph node metastasis were further demonstrated by (Quarato et al., 2023). Some earlier researchers assumed that stronger Doppler signals were constant in malignant tumors, but some more recent work has shown the presence of tumor grade and cellularity dependent variability; for example, low-grade malignant tumors may be poorly vascularized while highly aggressive, cellular tumors tend to be densely packed with neovascular networks(Pugliese et al., 2025; Raza et al., 2025; Reghunath et al., 2021). (Slobodnikova, 2022) matched an RI threshold of 0.73 to significant predictability of malignancy, which was also in line with our analysis. His

findings were also supported by (Tabassum et al., 2024) who noted sensitivity, specificity, and PPV of 80%, 90%, and 93%, respectively, using Doppler parameters and with RI greater than 0.80 slightly improved specificity. Defining a cut-off value for RI was not possible in the study done by(Tanweer et al., 2025) which was, therefore, one of the contributing factors of variability between studies.

Regardless of such differences, the published literature highlights the advantages of spectral Doppler for differentiating malignant from benign breast lesions, especially for minimizing unnecessary biopsies and aiding in treatment decisions(Tavarozzi et al., 2025). Recognizing the vascularity of lesions is important for planning neoadjuvant chemotherapy and for subsequent evaluations of treatment efficacy. However, scanner dependence and variability between different ultrasound machines still pose some challenges(Wang et al., 2020; Yongfeng et al., 2016; Zhang et al., 2022). At present, many imaging facilities do not routinely incorporate spectral Doppler ultrasound into standard breast ultrasound protocols. Given its non-invasive nature and widespread availability, the addition of Doppler ultrasound to assessment of breast lesions—with particular emphasis on women with dense breast tissue or those residing in areas with limited access to advanced imaging technologies—had the greatest potential to improve diagnostic certainty and outcomes(Zhang et al., 2025).

CONCLUSION

This study demonstrated that Doppler ultrasound with resistive index (RI) measurement is a highly effective diagnostic tool for differentiating malignant from benign breast lesions, achieving a sensitivity of 94.11%, specificity of 89.74%, and an overall diagnostic accuracy of 93.30% when compared to histopathology. The findings highlight RI's potential to reduce unnecessary biopsies and enhance early detection of breast malignancies, particularly in middle-aged, multiparous women—a demographic highly represented in the study population. Its utility was further emphasized in certain subgroups, such as patients with positive family history and oral contraceptive use, where diagnostic performance approached perfection. Given its non-invasive nature, affordability, and widespread availability, RI Doppler ultrasound can serve as a valuable adjunct to conventional imaging, especially in regions where access to mammography and advanced imaging modalities remains limited.

RECOMMENDATIONS

This study recommends incorporating resistive index (RI) measurements into routine breast ultrasonography, especially for women with dense breast tissue where mammography is less effective. Training programs for radiologists and sonographers should focus on standardizing Doppler techniques to reduce operator variability. Larger multicenter studies are needed to validate these findings and establish universal RI thresholds. Additionally, the use of AI-assisted Doppler analysis could further enhance diagnostic accuracy, particularly in low-resource settings.

LIMITATIONS

The study's single-center design and modest sample size limit the generalizability of results. Operator dependency and equipment variability inherent to Doppler ultrasound may have influenced findings. The absence of comparisons with advanced imaging modalities such as MRI or elastography is another limitation. Furthermore, subgroup analyses in smaller cohorts (e.g., lactating women, smokers) may lack statistical strength and should be interpreted with caution.

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