ORIGINAL ARTICLE http://doi.org/10.3126/njr.v14i1.64625

Role of Sonoelastography in Differentiating Benign and Malignant Breast Lesions: A Prospective Study Comparing Elasticity Contrast Index and Tsukuba Score

Amlendu Kumar[1], Anamika Jha[2], Pradeep Raj Regmi[2], Ghanshyam Gurung[2]

[1]Department of Radiology, Anand Diagnostics, Sitamarhi, Bihar, India
[2]Department of Radiology, Tribhuvan University Teaching Hospital, Kathmandu, Nepal

Received: August 21, 2023 **Accepted:** February 20, 2024 **Published:** April 26, 2024

Cite this paper:
Kumar A, Jha A, Regmi PR, Gurung G. Role of Sonoelastography in Differentiating Benign and Malignant Breast Lesions: A Prospective Study Comparing Elasticity Contrast Index and Tsukuba Score. *Nepalese Journal of Radiology* 2024;14(1):16-21.
http://doi.org/10.3126/njr.v14i1.64625

ABSTRACT

Introduction: Breast cancer is the most common cancer occurring in women globally which is potentially curable if detected early. Ultrasound elastography is a dynamic technique that estimates tissue stiffness to differentiate between benign and malignant masses. Our study aimed to determine and compare the diagnostic accuracy of B mode Sonography, Elasticity contrast index, and Tsukuba score in differentiating malignant and benign breast masses.

Methods: This was a prospective cross-sectional study done including 110 lesions in 102 patients in the age group of 15-73 years. The solid breast lesions seen on sonography were categorized according to the American College of Radiology Breast Imaging Reporting and Data System (ACR BI-RADS) and further evaluated with elastography using both Elasticity Contrast Index (ECI) and Tsukuba score with pathological diagnosis taken as the gold standard. The cut-off value of ECI was obtained. The diagnostic accuracy of B-mode sonography, ECI, and Tsukuba score was compared.

Results: We found that B-mode sonography had a sensitivity of 85.7%, specificity of 100%, and accuracy of 96.9 %. The accuracy of Tsukuba scores for differentiating benign and malignant lesions was 81.2 %. The cut-off value of ECI obtained was 2.8 and the accuracy was 81.8%. A statistically significant correlation ($p < 0.05$) existed between sonographic diagnosis, ECI, and Tsukuba score.

Conclusions: B mode sonography had the highest diagnostic accuracy while ECI and Tsukuba scores were comparable. ECI can be used for breast masses using a cut-off of 2.8 to differentiate benign from malignant.

Keywords: *Breast; Elasticity; Elasticity Imaging Techniques; Sonoelastography; Ultrasonography*

Correspondence to: Dr. Anamika Jha
Department of Radiology
Tribhuvan University Institute of Medicine
Kathmandu, Nepal
Email: ***dranamikakasyap@gmail.com***

INTRODUCTION

Breast cancer is the most common malignancy occurring in women globally and the second most common malignancy overall, with a disparity in mortality, which is disproportionately higher in low-income countries. Though mammography is an established screening tool, masses may be obscured in dense breasts lowering its sensitivity. Ultrasonography (US) has several advantages including high sensitivity for breast imaging but is limited by low specificity and operator dependence. Histopathological diagnosis is the gold standard for the diagnosis of a mass. However, almost 75% of biopsied breast masses are benign suggesting a need to lower the number of biopsies in favor of follow-up for masses with a low index of suspicion.[1,2,3,4,5]

Ultrasound elastography is a non-invasive sonographic imaging technique that provides additional information based on tissue stiffness as malignant masses are stiffer, thus, increasing the specificity of conventional B-mode US to differentiate benign from malignant. There are several techniques for elasticity imaging based on strain elastography like Elasticity Contrast Index which is semi-quantitative and Tsukuba. In solid masses with borderline sonographic features, elastography may help defer biopsy in favor of follow-up by suggesting a benign nature. Elasticity contrast index (ECI) is a quantitative technique that is easy to obtain and reproducible with higher values for stiffer nodules, suggesting higher chances of malignancy. Tsukuba score, also based on strain elastography, has been verified by multiple studies to be more qualitative and subjective.[6,7]

In this study, we determined the cut-off of ECI value to differentiate benign and malignant breast lesions, determined the accuracy of the B-mode sonography with Tsukuba score and ECI, and compared them using histopathology diagnosis as the gold standard. To our knowledge, no previous study compares Tsukuba and ECI.

METHODS

This prospective cross-sectional observational study was performed in the Department of Radiology and Imaging and Department of Pathology, Institute of Medicine (IOM), Tribhuvan University Teaching Hospital (TUTH) from October 2018 to September 2019 after obtaining ethical approval. The study included 110 solid masses in 102 individuals (females) referred for ultrasonography. Patients who refused tissue diagnosis, masses with inconclusive/ no available cytologic/histopathologic diagnosis, anechoic lesions (clearly cystic), lesions larger than 30 mm in diameter on their shortest axis and less than 10 mm in diameter on their longest axis, and lesions positioned close to the skin or the rib cage were excluded from our study.

The patients were examined using optimal positioning and sonography technique for B-mode followed by strain elastography using a high frequency (7-12 MHz) probe. Tsukuba score was obtained in breast protocol while ECI was calculated in thyroid protocol available in the unit. The elastogram was displayed over the B-mode gray-scale ultrasound scan in a color scale. For obtaining the ECI value, the probe was kept at the surface with very light pressure to minimize variations. The ROI was placed to include the largest solid part of the lesion and the ECI value was computed interactively and displayed on the monitor. A minimum of two measurements were obtained for each lesion and the lowest value was recorded.[7,8]

Based on ultrasound features masses were categorized into ACR BI-RADS (American College of Radiology Breast Imaging Reporting and Data System) categories (Table 1).[8]

BI-RADS 2 and 3 lesions were categorized as benign, 4a and 4b indeterminate, and 4c, and 5 malignant. Cut-off ECI value was calculated using the ROC curve and lesions with higher values were categorized as malignant while those with lower values were benign. On the Tsukuba color score, hard tissue was blue and soft tissue red to green with masses categorized into scores 1 to 5. Score 1 or 2 was categorized as benign, lesions scored 3 were categorized as indeterminate and lesions scored 4 or 5 malignant. Histopathological diagnoses of all lesions were obtained with image-guided fine needle aspiration cytology or core needle biopsy. All findings were tabulated and statistical analysis was done using Statistical Package for the Social Science (SPSS), Microsoft Excel, Independent t-test, Man Whitney U test, and ROC curve.

RESULTS

There were a total of 110 masses in 102 patients with ages ranging from 15 to 73 years, mean age being 33. Most of the masses were in the left breast (51.8%, n=57) and 42.7 % (n=47) in the upper outer quadrant. The mean dimension of mass included in the study was 2.4 ± 0.8 cm (mean ± SD) and 1.6 ± 0.6 cm (mean ± SD) in the long and short axes respectively.

Based on the histopathology examination obtained by aspiration cytology or biopsy, 75.5 % (n=83) of the lesions were benign and 24.5% (n=27) malignant. Of the benign cases, fibroadenoma was the most common, accounting for 68.2% (n=75). Invasive ductal carcinoma was the most common malignancy (21.8%, n=24). Using a 95 % confidence interval, ROC curve analysis was performed and the ECI cut-off value obtained was 2.8 (figure 1 and Table 1).

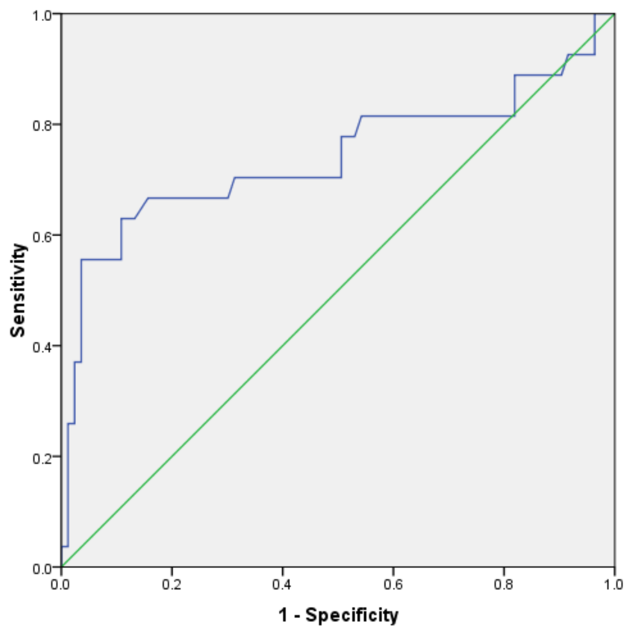

Figure 1: *ROC curve of the ECI values and tissue diagnosis.*

Table 1: Data about the area under the curve for ECI values.

Variables	P value	95% Confidence Interval		
		Lower Bound	Upper Bound	Cut-off
ECI	<0.001	0.607	0.873	2.8

Using an independent t-test for correlating ECI value (cut off 2.8) and histopathological diagnosis, a total of 85 lesions were found to be benign as per ECI, 74 were benign and the remaining 11 were malignant on histopathology. Out of 25 lesions labeled malignant, 16 were reported as malignant and 9 as benign on final diagnosis.

Table 2: Grayscale sonography, Tsukuba Score, and ECI (cut off 2.8) categorization of breast masses as benign, indeterminate, and malignant

	Gray scale sonography	Tsukuba	ECI (2.8 cut off)	Final HPE diagnosis
Benign	79 (71.8)	101 (91.9)	85 (77.3)	83 (75.5)
Indeterminate	13 (11.8)	5 (4.5)	-	-
Malignant	18 (16.4)	4 (3.6)	25 (22.7)	27 (24.5)
Total	110	110	110	

Of the 79 masses deemed benign on sonography, 76 were consistent while 3 were malignant on final diagnosis (table 2). All 18 masses that were diagnosed malignant on USG were confirmed so on histopathology. Out of 13 lesions labeled as indeterminate, 53.8% (n=7) were benign and

46.2% (n=6) were malignant on histopathology. Of 101 masses labeled benign on the Tsukuba score, 82 were confirmed while the remaining 19 were malignant. All 4 masses found to be malignant on the Tsukuba score were consistent in histopathology. Out of 5 indeterminate masses on the Tsukuba score, 80% (n=4) were reported as malignant (invasive ductal carcinoma) and 20 % (n=1) were benign (fibroadenoma) on final diagnosis.

Table 3: Sensitivity, specificity, and accuracy of sonography, Tsukuba, and ECI values for malignant breast masses

	Sensitivity	Specificity	PPV	NPV	Accuracy
Gray scale sonography	85.7	100.0	100.0	96.2	96.9
Tsukuba Score	17.4	100.0	100.0	81.2	81.9
ECI (cut off 2.8)	59.3	89.2	64.0	87.1	81.8

The sensitivity, specificity, accuracy, and negative and positive predictive values of B-mode, Tsukuba score, and ECI, are shown in Table 3. A significant correlation with a P value less than 0.001 was found between the Tsukuba score and sonography, ECI and Tsukuba score, and sonography and ECI using Mann Whitney and Independent t-tests.

DISCUSSION

Grey-scale sonography is known to have a high sensitivity but low specificity varying from 40-83% leading to higher false positives.[10,11,12,13] Various qualitative and semiquantitative elastography techniques like Tsukuba score, strain ratio, ECI, and Elasticity Index (EI)/B-mode size ratio have shown reasonable diagnostic accuracy in differentiating benign and malignant breast masses.[14,15] Our study aimed to evaluate the role of sonoelastography in differentiating benign from malignant breast lesions and compare the Tsukuba score, a qualitative elastography technique with ECI, a quantitative one.

In our study, all masses deemed malignant on sonography were confirmed so on histopathology, while three of the 79 benign-looking and six of the 13 indeterminate masses were malignant on histopathology, mostly being invasive carcinoma. The sensitivity, specificity, and diagnostic accuracy of sonography were 85.7, 100 and 96.9%, respectively. Our study compares well with others, values being higher than that determined in a study including 1203 patients in 2004 by Chen et al, where the sensitivity, specificity, and diagnostic accuracy values were 79.3, 89.3, and 86% respectively, and that by Evan et al including 175 patients, where the values were 95, 69 and 86% respectively.[16,17]

In our study, 101 (91.9%) cases were benign on Tsukuba score of which 82 were confirmed to be so on tissue diagnosis while 19 cases were malignant. All 4 (3.6%) lesions malignant as per Tsukuba score were confirmed as malignancy on histopathological. On comparing our Tsukuba score findings with other studies, we found that our sensitivity (17.4%) was low, with very high specificity (100%). However, the diagnostic accuracy is similar i.e., 81.9% in ours and 82.2% in a study done by Anil et al, including 90 patients.[18] A comparison of the values in different studies including ours is shown in Table 4.

Table 4: Comparison of Tsukuba color score with other studies

Study	Number	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Current study	110	17.4	100.0	100.0	81.2	81.9
Mohamed A Maaly et al[19]	30	69	86	85	71	
MAE Dawood et al[20]	40	93.7	70			
Anil Kumar et al[18]	90	95.6	68.1	75.8	93.7	82.2

ECI is a quantitative parameter based on strain elastography. Strain elastography requires compression which may be from exogenous palpation or endogenous like carotid artery pulsations.[8] The latter is used for obtaining ECI value for thyroid masses, and its use in breast masses has not been evaluated, with only one study regarding this application.[7] Higher ECI values suggest stiffer masses, thus increasing the likelihood of malignancy.[21] The ECI cut-off value was obtained to be 2.8 in our study with a sensitivity of 59.3%, specificity of 89.2%, and accuracy of 81.8%. In this study, the sensitivity of the Tsukuba score was low compared to grayscale USG, however, the specificity and PPV of both were 100 %.

In our study, both the elastography techniques showed a statistically significant correlation with each other and sonography. Sensitivity, specificity, PPV, and NPV of grayscale USG are highest as compared to ECI and Tsukuba. There was a good linear relationship between the Tsukuba color score and ECI values when correlated to histopathology findings. The sensitivity of ECI (59.3%) is significantly higher as compared to the Tsukuba color score (17.4%) with relatively less specificity and PPV. This supports the importance and utility of adding qualitative and/or quantitative strain elastography techniques to grayscale sonography. It also correlates with other similar studies which suggest that adding elastography in breast lesions can increase its specificity to 85-90 %.

Indeterminate solid masses with Tsukuba color score pattern 1 or 2 and with ECI Index < 2.8 may not need biopsy in favor of follow-up. Cases with Tsukuba color score patterns 3, 4, and 5 and ECI Score of >2.8 should be considered to increase the index of suspicion for malignancy, and hence such masses should be subjected to tissue diagnosis.

Our study suggests that Tsukuba color score pattern and ECI can be easily added to routine breast USG scans to facilitate evaluation of solid masses and categorize them avoiding unnecessary tissue diagnosis when elastography suggests benign features in an otherwise low suspicion indeterminate mass. Variability in compression which is subjective, is a limiting factor for elastography and can lead to inter and intra-observer differences. Masses which are posterior in location and large may also be difficult to evaluate with elastography. The major limitation of our study is the limited sample size. Elastography application is not commonly available in sonography units which may limit its widespread use.

CONCLUSION

B mode sonography had the highest accuracy for differentiating benign from malignant breast solid lesions compared to the Tsukuba score and ECI, which had similar diagnostic accuracies. We conclude that ECI can be used for breast masses using a cut-off of 2.8 to differentiate benign from malignant.

CONFLICT OF INTEREST

None

SOURCES OF FUNDING

None

REFERENCES

1. Malvia S, Bagadi SA, Dubey US, Saxena S. Epidemiology of breast cancer in Indian women. *Asia Pac J Clin Oncol 2017*;13(4):289-95. https://doi.org/10.1111/ajco.12661

2. Saarenmaa I, Salminen T, Geiger U, et al. The effect of age and density of the breast on the sensitivity of breast cancer diagnostic by mammography and ultrasonography. *Asian Pac J Cancer Prev* 2001;67(2):117-23. https://doi.org/10.7314/apjcp.2013.14.4.2277

3. Liberman L, Menell JH. Breast imaging reporting and data system (BI-RADS). *Radiologic Clinics* 2002;40(3):409-30. https://doi.org/10.1016/S0033-8389(01)00017-3

4. Athanasiou A, Tardivon A, Tanter M et al. Breast lesions: quantitative elastography with supersonic shear imaging-preliminary results. *Radiology* 2010;256(1):297-303. https://doi.org/10.1148/radiol.10090385

5. Hooley RJ, Greenberg KL, Stackhouse RM, Geisel JL, Butler RS, Philpotts LE. Screening US in patients with mammographically dense breasts: initial experience with Connecticut Public Act 09-41. *Radiology* 2012;265(1):59-69. https://doi.org/10.1148/radiol.12120621

6. Itoh A, Ueno E, Tohno E, et al. Breast disease: clinical application of US elastography for

diagnosis. *Radiology* 2006;239(2):341-50. https://doi.org/10.1148/radiol.2391041676

7. Jha A. Ultrasonographic Elasticity Contrast Index of Palpable Breast Lumps. *J Nepal Med Assoc* 2018;56(212):787-90. https://doi.org/10.31729/jnma.3536

8. Kwak JY, Eun-Kyung K. Ultrasound elastography for thyroid nodules: recent advances. *Ultrasonography* 2014;33:75-82. https://doi.org/10.14366%2Fusg.13025

9. Rao AA, Feneis J, Lalonde C, Ojeda-Fournier H. A Pictorial Review of Changes in the BI-RADS Fifth Edition. *RadioGraphics* 2016;36(3):623-39. https://doi.org/10.1148/rg.2016150178

10. Thomas A, Kümmel S, Fritzsche F, et al. Real-time sonoelastography performed in addition to B-mode ultrasound and mammography: improved differentiation of breast lesions? *Acad Radiol* 2006;13(12):1496-504. https://doi.org/10.1016/j.acra.2006.08.012

11. Sheikh FA, Tinkoff GH, Kline TS, Neal HS. Final diagnosis by fine-needle aspiration biopsy for definitive operation on breast cancer. *Am J Surg* 1987;154(5):470-4. https://doi.org/10.1016/0002-9610(87)90254-6

12. Duncan III JL, Cederbom GJ, Champaign JL, Smetherman DH. Benign diagnosis by image-guided core-needle breast biopsy. *Am Surg* 2000;66(1):5-9. Available from: https://journals.sagepub.com/doi/abs/10.1177/000313480006600102 [Accessed 23rd October 2023]

13. Nowicki A, Dobruch-Sobczak K. Introduction to ultrasound elastography. *J Ultrason* 2016;16(65):113-24. https://doi.org/10.15557/jou.2016.0013

14. Garra BS, Cespedes EI, Ophir J et al. Elastography of breast lesions: initial clinical results. *Radiology.* 1997;202(1):79-86. https://doi.org/10.1148/radiology.202.1.8988195

15. Mutala TM, Ndaiga P, Aywak A. Comparison of qualitative and semiquantitative strain elastography in breast lesions for diagnostic accuracy. *Cancer Imaging* 2016;16(1):12. https://doi.org/10.1186/s40644-016-0070-8

16. Chen SC, Cheung YC, Su CH, Chen MF, Hwang TL, Hsueh S. Analysis of sonographic features for the differentiation of benign and malignant breast tumors of different sizes. *Ultrasound Obstet Gynecol* 2004;23(2):188-93. https://doi.org/10.1002/uog.930

17. Evans A, Whelehan P, Thomson K, et al. Differentiating benign from malignant solid breast masses: value of shear wave elastography according to lesion stiffness combined with greyscale ultrasound according to BI-RADS classification. *Br J Cancer* 2012;107(2):224-9. https://doi.org/10.1038/bjc.2012.253

18. Kumar A, Tanwar NS. Evaluation of breast lump using elastography, histopathology and its diagnostic accuracy. *Int Surg J* 2019;6(2):574-80. https://doi.org/10.18203/2349-2902.isj20190406

19. Maaly MA, Lattif HAA, Elsakhawy MM, Khallaf HM. Role of elastography in characterization of solid breast masses. *Menoufia Medical Journal*. 2019;32(1):101. Available from: https://go.gale.com/ps/i.do?id=GALE%7CA583343444&sid=googleScholar&v=2.1&it=r&linkaccess=abs&issn=11102098&p=AONE&sw=w&userGroupName=anon%7Ecf8fcaab&aty=open-web-entry [Accessed 12th December 2023]

20. Dawood MAE, Ibrahim NMA, Elsaeed HH, Hegazy NG. Diagnostic performance of sonoelastographic Tsukuba score and strain ratio in evaluation of breast masses. *The Egyptian Journal of Radiology and Nuclear Medicine.* 2018;49(1):265-71. https://doi.org/10.1016/j.ejrnm.2017.10.005

21. Di Z, Li Z, Tian J, Wang D, Liu L, Liu C. The Value of Elasticity Contrast Index in the Differential Diagnosis of Thyroid Solid Nodules. *Ultrasound Q* 2019;35(3):259-63. https://doi.org/10.1097/ruq.0000000000000457