

Evaluation of Acoustic Radiation Force Impulse Imaging in Differentiating Benign and Malignant Cervical Lymphadenopathy

Kamat Rohan¹, Ananthkrishnan Ramesh^{1*}, K. Nagarajan¹, K. M. Abdulbasith², Sathasivam Sureshkumar², Chellappa Vijayakumar², K. Balamourougan², B. H. Srinivas³

¹Department of Radio Diagnosis, Jawaharlal Institute of Post Graduate Medical Education and Research, Puducherry, India, ²Department of General Surgery, Jawaharlal Institute of Post Graduate Medical Education and Research, Puducherry, India, ³Department of Pathology, Jawaharlal Institute of Post Graduate Medical Education and Research, Puducherry, India

Abstract

Background: The aim of this study was to assess the diagnostic role of acoustic radiation force impulse imaging (ARFI) in differentiating benign and malignant cervical nodes. **Methods:** This was a diagnostic accuracy cross-sectional study. All patients who underwent ultrasound-guided fine-needle aspiration cytology (FNAC) of cervical nodes were included. Patients without FNAC/biopsy and patients in whom cervical nodes were cystic or completely necrotic were excluded. FNAC was used as reference investigation to predict the diagnostic accuracy. In all cases, FNAC was carried out after the B-mode, color Doppler and the ARFI imaging. In patients with multiple cervical lymph nodes, the most suspicious node based on grayscale findings was chosen for ARFI. ARFI included Virtual Touch imaging (VTI), area ratio (AR), and shear wave velocity (SWV) for each node, and the results were compared with FNAC/biopsy. **Results:** The final analysis included 166 patients. Dark VTI elastograms had sensitivity and specificity of 86.2% and 72.1%, respectively, in identifying malignant nodes. Sensitivity and specificity of AR were 71.3% and 82.3%, respectively, for a cutoff of 1.155. Median SWV of benign and malignant nodes was 1.9 [95% confidence interval (CI), 1.56–2.55] m/s and 6.7 (95% CI, 2.87–9.10) m/s, respectively. SWV >2.68 m/s helped in identifying malignant nodes with 81% specificity, 81.6% sensitivity, and 81.3% accuracy. ARFI was found to be inaccurate in tuberculous and lymphomatous nodes. **Conclusion:** Malignant nodes had significantly darker elastograms, higher AR and SWV compared to benign nodes, and SWV was the most accurate parameter. ARFI accurately identifies malignant nodes, hence could potentially avoid unwarranted biopsy.

Keywords: Acoustic radiation force impulse, acoustic radiation force impulse imaging, area ratio, cervical lymph nodes, shear wave velocity, Virtual Touch imaging

INTRODUCTION

Enlarged cervical lymph nodes (LNs) are routinely seen in clinical practice. The usual causes for their enlargement are tuberculosis, reactive lymphoid hyperplasia, lymphomas, and metastasis.^[1,2] Radiological differentiation of malignant nodes from the benign LNs is an essential part of clinical workup, as it influences the treatment and the prognosis.^[1,3,4]

Grayscale ultrasound has long been used to assess the LNs, and it provides useful information on the morphological characteristics of the cervical nodes such as size, shape,

borders, echogenicity, and the hilum.^[5] However, their predictive role in differentiating benign and malignant cause is relatively low. In 1991, Ophir *et al.* described elastography, an ultrasound technique which provides noninvasive means to assess the elastic properties of tissues.^[6,7] Two main variants of elastography, namely strain elastography (SE) and shear wave elastography (SWE) are helpful in the characterization of tissues.

Address for correspondence: Dr. Ananthkrishnan Ramesh, Department of Radiodiagnosis, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry - 605 006, India. E-mail: dr_rameshrad@yahoo.co.in

Received: 12-01-2021 Revised: 21-03-2021 Accepted: 04-06-2021 Available Online: 29-07-2021

Access this article online

Quick Response Code:



Website:
www.jmuonline.org

DOI:
10.4103/JMU.JMU_10_21

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Rohan K, Ramesh A, Nagarajan K, Abdulbasith KM, Sureshkumar S, Vijayakumar C, *et al.* Evaluation of acoustic radiation force impulse imaging in differentiating benign and malignant cervical lymphadenopathy. *J Med Ultrasound* 2022;30:87-93.

SE yields qualitative information, in which images are obtained with the aid of repetitive minimal pressure to the target tissue by using the probe or by physiological pressure variations like vascular pulsations or respiratory movement.^[8] Strain ratio (SR) is a semi-quantitative technique which provides a relative stiffness of the target tissue with respect to the surrounding tissue. However, it has a limitation, as it is affected by the adjacent reference tissues. In addition, the SR is operator dependent as the magnitude of compression could alter the elasticity maps.

SWE, on the other hand, uses system-generated acoustic pulses to deform the tissues instead of manual compression. It gives superior image quality with reduced inter-operator variability, and hence, more objective than SE.^[9,10] Acoustic radiation force impulse imaging (ARFI) technique is a type of SWE where the displacement of target tissues is achieved by using acoustic radiation pulses generated by the ultrasound transducer without any external compression, followed by monitoring of the deformation response. The elastic response of the tissues can be expressed qualitatively as Virtual Touch tissue imaging (VTI) elastograms and quantitatively by Virtual Touch tissue quantification (VTQ).

Although ARFI has been well established in liver, breast, thyroid, and prostate lesions, its diagnostic role in the cervical nodes is not very well instituted.^[11] Recent studies on the role of SWE in the diagnostic evaluation of cervical LNs have shown promising diagnostic performance in differentiating malignant cervical nodes.^[12-16] Owing to the high specificity of ARFI, it could also aid in identification of suitable node for fine-needle aspiration cytology (FNAC), thereby limiting false-negative results.^[17-19] When the study was initiated, most of the published studies on the role of ARFI in cervical nodes were on the smaller group of population and to the best of our knowledge, there was no published Indian study comparing the ARFI parameters between benign and malignant cervical nodes. Hence, this study was carried to assess the diagnostic role of ARFI parameters (namely VTI elastogram, area ratio [AR], and shear wave velocity [SWV]) in differentiating benign and malignant cervical LNs.

METHODOLOGY

Study population

This was a diagnostic accuracy cross-sectional study conducted from October 2015 to April 2017 in a tertiary care hospital in South India. Ethics committee approval was obtained (Approval no: JIP/IEC/2015/17/676), and patients were enrolled after obtaining prior informed consent. All the patients referred to the department of radiodiagnosis for ultrasound-guided FNAC of cervical nodes during the study period were included in the study. Patients who had undergone FNAC/biopsy prior to the study and in whom the cervical nodes were cystic (focal/large), completely necrotic, or smaller than 0.5cm in short-axis diameter were excluded from the study. FNAC/biopsy was used as a reference gold

standard investigation to predict the diagnostic accuracy of ARFI. In cases where both were available, the biopsy result was used for the diagnosis. In all the cases, FNAC was carried out after documenting the B-mode ultrasound (BMUS), color Doppler, and ARFI imaging. In patients with multiple cervical LNs, the most suspicious node based on grayscale findings was chosen for ARFI. The grayscale parameters used for selecting the most suspicious node were (1) nodes which were round ($S/L < 0.5$), (2) nodes with absent or flattened echogenic hilum, (3) and nodes which showed predominantly peripheral vascularity. A LN with any one of these features was chosen for ARFI.

Study procedure

ARFI was performed using the Acuson S3000 ultrasound system (Siemens, Erlangen, Germany) by a radiologist (Register in designation) experienced in ultrasound and ARFI imaging. Later, the image was confirmed by the senior radiology faculty. A linear array transducer (9L4) with a 9MHz frequency was used for imaging. The patients were examined in a supine position with their necks extended. ARFI imaging was carried out to include VTI elastogram, AR, and SWV parameters.

For evaluating the VTI elastogram using ARFI, an adjustable region of interest (ROI) box was placed completely enclosing the target LN, viewed on grayscale ultrasound. The section of the target LN without cystic areas or necrosis on BMUS is chosen for VTI. Three VTI elastograms were obtained for the LN and the VTI image in which the LN borders were best defined was chosen for the analysis.^[20] The patients were instructed to hold their breath at the time of image acquisition. On pressing the “update” button, an elastogram was generated besides the grayscale map. The elastogram obtained included varying proportions of dark/bright areas depending on the degree of nodal stiffness. More stiffer the tissue, more darker were the maps. The proportion of dark and bright regions were visually assessed, and the results were categorized into one of the following two grades: predominantly bright (>50% bright areas) and predominantly dark (>50% dark areas).

The AR is based on the principle that malignant nodes (known for their invasiveness and surrounding desmofibrotic reaction) lead to a larger area on the elastogram as compared to the corresponding grayscale map of benign nodes.^[8] The area of LNs on both elastogram and the corresponding B-mode images were measured using freehand callipers. AR was calculated by dividing the area of the elastogram map with that of its corresponding grayscale map.

For assessing the SWV, the ROI box measuring 5×5 mm size was placed entirely within the regions of the target LN, which were dark on the elastogram map. The size of the ROI box was set by the manufacturer and was not adjustable. Necrotic areas and calcifications were avoided while placing the ROI box. The patients were instructed to hold their breath during image acquisition. On pressing the “updat” button, an SWV was generated. As a low signal-to-noise ratio may result in aberration, five readings were obtained for all the LNs and

were studied to ascertain the result and the average value was recorded. The upper limit of SWV displayed on the ultrasound scanner used for the present study was 9.1 m/s. Values which were above this were displayed as X.XX (In Siemens ACUSON S3000 X.XX denotes SWV ≥ 9.1 m/s). Hence, a value of 9.1 m/s was assigned to the LNs which consistently showed X.XX in five consecutive measurements after ruling out the patient's respiration/movement/inappropriate placement of ROI.^[21,22] Elasticity values in kilopascal were not enabled in our ultrasonography scanner during the period of the study. Receiver operator characteristic (ROC) curve along with the area under the curve (AUC) was used to find the cutoff values. The cutoff was chosen by our team based on the best possible specificity that could be attained without causing an undiscerning drop in the sensitivity for each test.

Histopathological comparison

The LN of interest in each case was subjected to ultrasound-guided fine-needle aspiration. In cases where there was a clinical indication for a biopsy, it was carried out using an 18G \times 10 cm Bard Mission semi-automatic gun. In cases where both FNAC and core biopsy were performed, the results obtained by the latter were selected for reference diagnosis. All the FNAC/biopsies were reported by an experienced pathologist who was blinded to the ultrasound and ARFI findings.

Statistical analyses

The statistical analysis was carried out using the IBM SPSS Software (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp). Categorical data were expressed as frequencies and percentages and, continuous data as mean with standard deviation or median with the range depending on their distribution. The comparison of categorical and continuous data was carried out using the Chi-square test and the Mann–Whitney U-test/independent Student *t*-test, respectively. ROC curve along with the AUC was used to evaluate the diagnostic role of ARFI for malignant cervical LNs. Sensitivity and specificity along with predictive values were calculated for assessing the diagnostic role of ARFI parameters in detecting the malignant cervical LNs. All statistical analyses were carried out at a 5% level of significance and *P* < 0.05 was considered significant.

RESULTS

During the study duration, a total of 200 eligible patients were enrolled. Thirty-four patients were excluded due to invalid/inconclusive FNAC/biopsy results. Among the 166 patients included in the study, 24 patients had additionally undergone a biopsy due to the clinical indication. The final analysis included 166 patients, of which 95 were men and 71 were women. The age of the study population ranged from 18 to 80 years, with a mean age of 42.51 ± 18.88 years. The mean age of the patients with benign and malignant LNs was 34.06 ± 17.57 years and 50.18 ± 16.71 years, respectively. In the final FNAC/biopsy report of 166 cervical LNs, 87 (52%) were found to be malignant and 79 (48%) were

benign [Table 1]. The median SAD with IQR for benign and malignant nodes was 1.1 cm (0.78–1.30) and 1.6 cm (1.0–2.40), respectively.

Virtual Touch tissue imaging elastogram

As mentioned in Table 2, majority of the LNs with predominantly dark elastograms (86.2%) and predominantly bright elastograms (72.2%) were malignant and benign, respectively. Figure 1 shows ARFI parameters in malignant cervical LN. Furthermore, the proportions of malignant nodes were statistically significant in the predominantly dark elastograms (*P* < 0.001) [Table 2].

Area ratio

The median AR of malignant node was significantly higher than that of the benign node (1.3 [1.14–1.40] vs. 1.07 [0.98–1.13]; *P* < 0.001). The cutoff point of AR for cervical LN was calculated to be 1.155 using the ROC curve [Figure 2a].

Table 1: Results of fine-needle aspiration cytology/biopsy from the cervical lymph nodes

Etiopathological diagnoses	Frequency
Reactive nodes	53
Metastatic squamous cell carcinomas	35
Tuberculous/granulomatous nodes	24
Metastatic adenocarcinomas	17
Hodgkin and non-Hodgkin lymphomas	17
Metastatic thyroid carcinomas	8
Metastatic undifferentiated carcinomas	5
Chronic lymphoid leukemia	2
Necrotizing lymphadenitis	1
Lupus lymphadenitis	1
Metastatic anaplastic carcinoma	1
Metastatic sarcoma	1
Metastatic mucoepidermoid carcinoma	1
Highly suspicious of malignancy	1
Total	166

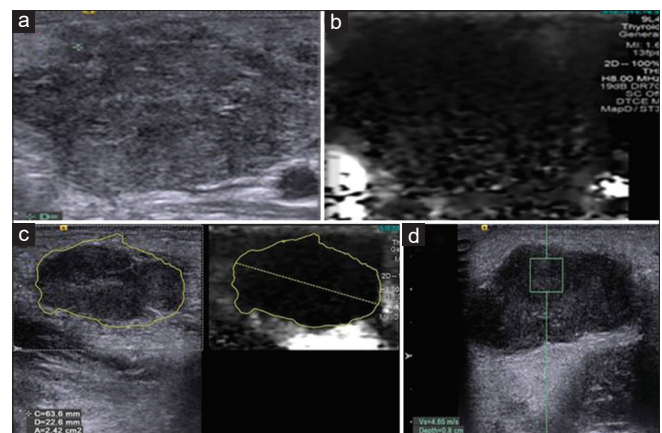


Figure 1: A 50-year-old woman with a metastatic papillary thyroid carcinoma of a cervical lymph node. (a) Grayscale ultrasound image (b) Predominantly dark elastogram on Virtual Touch imaging. (c) Area ratio – 1.3 (d) Shear wave velocity – 4.65 m/s (obtained from another cervical lymph node from the same patient)

Table 2: Results of acoustic radiation force impulse

Parameters	Features	Malignant (87) (%)	Benign (79) (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	AUC
VTI (two grades)	Predominantly dark	75 (86.2)	22 (27.8)	86.2	72.1	79.5	-
	Predominantly bright	12 (13.8)	57 (72.2)				
Area ratio (cutoff: 1.155)	≥1.155	62 (71.3)	14 (17.7)	71.3	82.3	76.5	0.842
	<1.155	25 (28.7)	65 (82.3)				
SWV (m/s)	≥2.68	71 (81.6)	15 (19.0)	81.6	81.0	81.3	0.856
	<2.68	16 (18.4)	64 (81.0)				

VTI: Virtual Touch imaging, SWV: Shear wave velocity, AUC: Area under the curve

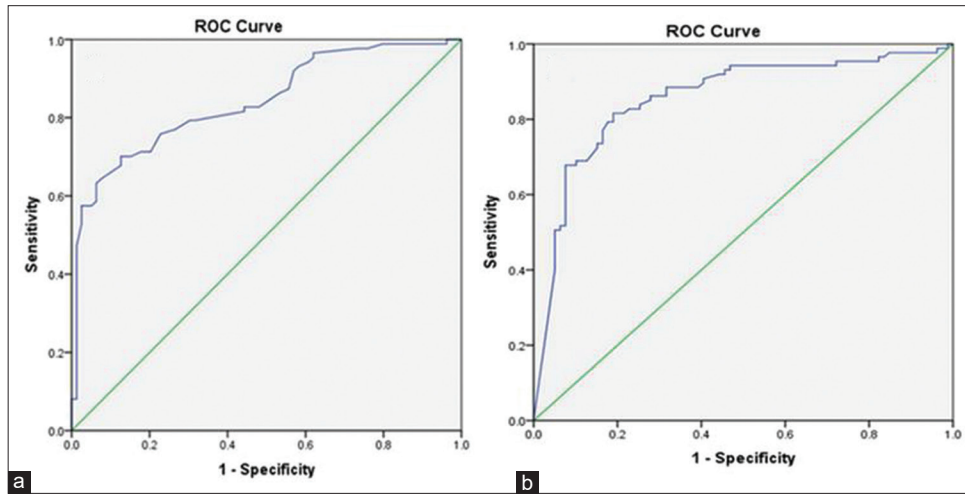


Figure 2: (a) Receiver operator characteristic curves-median area ratio (area under the curve – 0.842) (b) receiver operator characteristic curves-median shear wave velocity (area under the curve – 0.856)

Figure 3 depicts the VTI elastogram and AR derived using gray scale and elastogram in benign cervical LNs.

Shear wave velocity

The median SWV of malignant node (6.7 [2.87–9.1] m/s) was significantly higher than that of the benign node (1.9 [1.56–2.55] m/s); $P < 0.001$ [Table 3]. The cutoff point of SWV for cervical LN was calculated to be 2.68 m/s using the ROC curve [Figure 2b]. On correlating the SWV with the common causes of cervical node enlargement, lymphomatous nodes were found to have a significantly lower median SWV (2.5 [2.11–4.14] m/s) compared to the median SWV of other malignant cervical nodes (6.7 [2.87–9.1] m/s); $P < 0.01$ [Table 3]. Figures 4 and 5 show tubercular and malignant LNs assessed by the SWV, respectively.

False negatives

With predominantly bright nodes considered as benign using VTI elastogram, 12 false-negative cases were identified, which included six nodes due to lymphoma and two due to chronic lymphoid leukemia. The remaining four false-negative cases were one each due to metastatic adenocarcinoma, thyroid carcinoma, squamous cell carcinoma, and undifferentiated metastatic carcinoma. Using AR, 25 false-negative nodes were identified, out of which ten were lymphomatous, six were from metastatic squamous cell carcinomas, five from metastatic adenocarcinomas, two from metastatic thyroid carcinomas, and

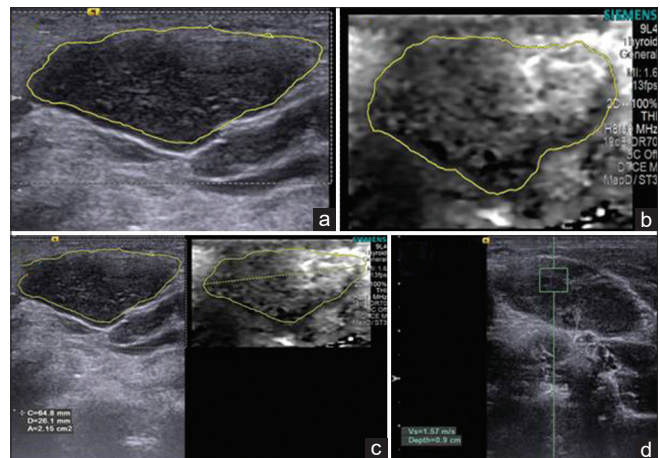


Figure 3: A 22-year-old woman with a reactive cervical lymph node (a) Grayscale ultrasound image (b) Predominantly bright elastogram on Virtual Touch imaging (c) Area ratio – 0.90 (d) Shear wave velocity – 1.57 m/s (obtained from another cervical lymph node from the same patient)

one each from metastatic sarcoma and metastatic anaplastic carcinoma. Ten out of twenty-five (40%) false negatives were due to lymphomatous nodes. Lymphomatous nodes showed a median SWV of 2.5 (2.11–4.14) m/s which was found to be significantly lesser than the median SWV of other malignant nodes which were 6.7 (2.87–9.1) m/s ($P < 0.01$).

False positives

With predominantly dark nodes considered as malignant, the present study found 22 false-positive cases, out of which 12 were reactive nodes, nine were tuberculous or granulomatous, and one was due to lupus lymphadenitis. Out of the 24 tuberculous/granulomatous nodes, nine nodes (~38%) showed false-positive elastograms. Using the SWV cutoff of 2.68 m/s, 15 false-positive cases were identified. Out of the 15 false-positive cases, 10 (66.66%) were tuberculous/granulomatous nodes [Figure 4].

Predictive accuracy

Among the ARFI parameters, VTI was found to be the most sensitive parameter (86.2%), and AR at a cutoff of 1.155 was found to be the most specific parameter (82.3%). Overall, the most accurate parameter was SWV at a cutoff of 2.68 m/s (81.3%).

DISCUSSION

The present study aimed at assessing the role of ARFI in the evaluation of cervical LNs showed that malignant nodes were significantly darker on VTI elastogram and had higher AR and higher SWV as compared to the benign nodes. VTI was the most sensitive parameter, and AR at a cutoff of 1.155 was the most specific parameter in the present study.

Causes (n)	Median SWV in (m/s) with (IQR)
All benign nodes (79)	1.9 (1.56–2.55)
All malignant nodes (87)	6.7 (2.87–9.1)
TB and granulomatous LN (24)	2.5 (1.89–3.78)
Reactive nodes (53)	1.7 (1.48–2.1)
Lymphomas (17)	2.5 (2.11–4.14)
Metastatic thyroid carcinoma (7)	3.5 (2.6–9.1)
Metastatic adenocarcinoma (17)	9.1 (6.6–9.1)
Metastatic squamous cell carcinoma (35)	9.1 (4.3–9.1)

IQR: Interquartile range, TB: Tuberculosis, LN: Lymph nodes

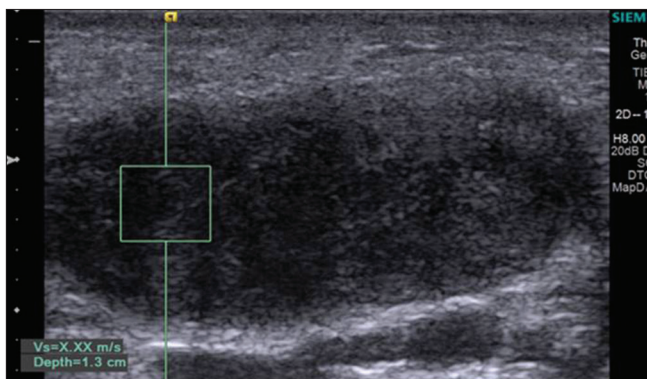


Figure 4: A 49-year-old man with a tuberculous cervical lymph node. This heterogeneous cervical lymph node showed a high shear wave velocity of 4.37 m/s

Overall, SWV at a cutoff of 2.68 m/s was found to be the most accurate parameter.

Ultrasound is a sensitive tool for distinguishing benign and malignant LNs, with a sensitivity of 97%.^[1,5] When FNAC is carried out under ultrasound guidance, a specificity as high as 93% could be achieved.^[23,24] Grayscale ultrasound has been used in assessing the morphological properties of the cervical nodes; however, it has certain limitations. It is incapable of measuring the tissue elasticity, which possesses a higher specificity in distinguishing the benign and malignant nodes. ARFI is a useful new technique to assess the elastic properties of tissues and thereby differentiate benign and malignant pathology.^[17]

ARFI assessment is performed with the aid of three parameters-VTI elastogram, AR, and SWV. VTI detects the relative stiffness of tissues in the ROI and displays the grayscale image and the elastogram side by side. The harder a tissue, the darker is the elastogram. The benefits of VTI as compared to SE technique include no manual compression, superior image quality, decreased inter-operator variability, and deep tissue imaging.^[25] In VTQ, the speed of the shear waves generated in the tissues targeted by acoustic pulses is measured as SWV, which gives an indication of tissue stiffness. The speed of the shear waves propagating in tissues is dependent on their density and elasticity. As malignant LNs generally tend to be harder than the benign nodes, SWV is higher in the malignant nodes.^[26] Quantitative elasticity measurements such as SWV (m/s) or elastic moduli of tissues (kPa) which are generated in SWE technique using ARFI cannot be obtained in VTI.^[9] VTI elastogram in the present study showed that the bright elastogram was significantly associated with benign nodes and dark elastogram with the malignant ones. About 72.2% of benign nodes showed a predominantly bright elastogram, while 86.2% of malignant nodes showed a predominantly dark pattern. Results of the present study were consistent with those derived in the study by Meng *et al.*^[27]

AR was found to be the most specific SWV parameter in differentiating malignant cervical nodes in the present study.

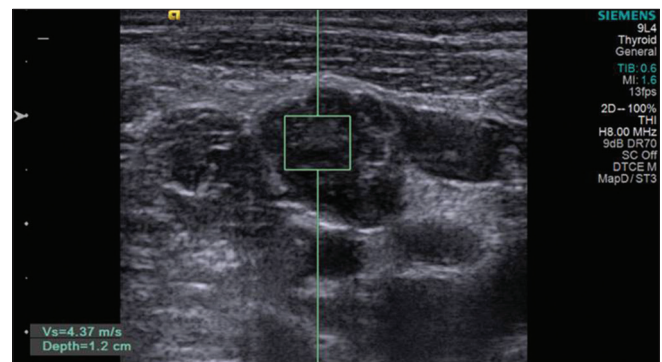


Figure 5: A 57-year-old woman with a metastatic adenocarcinoma of the cervical lymph node from a breast cancer. This ill-defined hypoechoic lymph node showed a shear wave velocity of X.XX. This was considered as 9.1 m/s based on the manufacturer recommendations

On ROC curve analysis, the AUC generated an AR cutoff value of 1.155 at sensitivity and specificity of 71.3% and 82.3%, respectively. A similar study by Che *et al.* found an AR cutoff of 1.16 at sensitivity and specificity of 91.1% and 83.3%, respectively.^[25] Shear elastograms have superior image quality with decreased inter-operator variability with consistent size ratios compared to that of SEs.^[8-10]

SWV cutoff of 2.68 m/s obtained in the present study was comparable to the study by Meng *et al.* (2.595 m/s).^[27] In another similar study by Fujiwara *et al.*, an SWV cutoff of 1.9 m/s was generated, which is lower compared to most other studies.^[11] The lower SWV in their study could be possibly due to the smaller sample size of 42 (22 reactive and 20 malignant/metastatic).^[27]

Table 4 shows the SWV generated in other studies to differentiate benign and malignant cervical nodes. Forty-one nodes in the present study showed an SWV of X.XX m/s. Out of these, 37 were found to be malignant, three due to tuberculous or granulomatous lymphadenitis, and one due to lupus lymphadenitis during the subsequent FNAC/biopsy.

False negatives

In the present study, 10 out of 25 (40%) false negatives were due to lymphomatous nodes. Consistent findings were found in a study by Chen *et al.*, in which the SWV values of lymphomatous nodes were significantly lesser than that of metastatic carcinoma.^[28] Using SWV, 16 false-negative cases were identified, out of which ten were due to lymphomas. A study by Lenghel *et al.* found that the lymphomatous nodes showed predominantly benign elastogram patterns and removing lymphomatous nodes from the data improved the sensitivity of sonoelastography in differentiating benign and malignant nodes.^[29] This is likely due to that the lymphomatous nodes are usually softer than the other malignant nodes and have well-defined borders showing lesser infiltration of the adjacent parenchyma as compared to the other malignant nodes. Though the Lymphomatous nodes are less stiffer than the other malignant nodes, they are more stiffer than the reactive benign LNs.^[28,29] Hence, this histological makeup of lymphomatous nodes might be the reason for their brighter appearance on the elastograms and lower SWV.

Fujiwara *et al.* found a sensitivity of 95% using SWV; however, in their study only one case of lymphoma was assessed compared to seventeen cases in the present study.^[11] The

specificity using AR in the present study was comparable with that of the study by Che *et al.*; however, the sensitivity in the current study was lower. Similar to Fujiwara *et al.*'s study, the study by Che *et al.* had no lymphomatous nodes in their study population.^[25] This could probably be the reason for a lower sensitivity using SWV and AR in the present study.

False positives

With predominantly dark nodes considered as malignant, 22 false-positive cases were found in the current study. Similar results were obtained in a study by Cheng *et al.*, in which they found high false-positive results among the tuberculous nodes.^[30] Another study by Chen *et al.* also found consistent results where the SWV of the tuberculous nodes was significantly higher as compared to the reactive LNs.^[28] Nodes with large necrotic areas were not included in the present study. Even though visible areas of calcification were excluded from the ROI, higher value of SWV among the tuberculous nodes could be due to the microcalcifications or interstitial fibrosis within the nodes.^[2,31] Reactive cervical LNs are soft in consistency and show lymphocytosis without interstitial fibrosis. Tuberculosis nodes with fibrosis and microcalcifications are relatively stiffer as compared to the reactive nodes. Tuberculous nodes contributing to nearly half of the false-positive cases could be the reason for reduced specificity in the present study. Only 14 out of 24 (~58%) tuberculous nodes were identified as benign by SWV, akin to a mere 50% nodes being correctly identified in the study by Cheng *et al.* Hence, the diagnostic performance of SWV seems weak in tuberculous nodes, as suggested by Cheng *et al.*^[30]

Limitations of the study

The decision to carry out either a cervical LN biopsy or a FNAC was taken by the treating surgeon. Accordingly not all patients underwent LN biopsy for reference diagnosis which is better in terms of higher sensitivity and specificity compared to FNAC. Size of the ROI box was fixed as 5 mm × 5 mm and could not be changed as the presetting manufacturer was not adjustable. This could have produced sampling errors in measuring SWV of small nodes where areas of calcification and necrosis could not be reliably excluded. Nodes which were smaller than 5 mm could not be studied. The real stiffness of the cervical nodes could not be determined in many cases, as SWV value was taken as 9.1 m/s when measurement showed X.XX m/s repeatedly in dark elastograms [Figure 5]. In a few cases, false estimation of the SWV could have occurred due

Table 4: Shear wave velocity cutoffs generated in different studies to differentiate benign and malignant cervical nodes

Study	Mean/median SWV of benign nodes (m/s)	Mean/median SWV of malignant nodes (m/s)	SWV cutoff (m/s)	Sensitivity (%)	Specificity (%)
Present study	1.9 (1.56–2.55)*	6.7 (2.87–9.1)*	2.68*	81.6	81
Meng <i>et al.</i> ^[27]	2.01 ± 0.95†	4.61 ± 2.56†	2.595†	82.9	93.1
Fujiwara <i>et al.</i> ^[11]	1.52 ± 0.48*	2.46 ± 0.75*	1.9*	95	81.8
Cheng <i>et al.</i> ^[30]	2.71 ± 0.85†	4.46 ± 1.46†	3.34†	78.9	74.4
Zhang <i>et al.</i> ^[31]	2.32 ± 0.57†	4.36 ± 1.25†	3.14†	77.1	85.7

*Median with IQR, †Mean ± SD. IQR: Interquartile range, SD: Standard deviation, SWV: Shear wave velocity

to transmission of carotid artery pulsations or due to undue pressure by the superficial nodes. The proportion of dark and bright areas were visually analyzed in the elastogram and hence was subjective. Due to the small sample size in various subgroups of benign and malignant LNs, it was not possible to do a subgroup analysis for each histological type. Further studies with larger sample size are required to explore the potential of ARFI in differentiating the various etiological types of cervical LNs.

CONCLUSION

Malignant nodes had significantly darker VTI elastogram and higher AR and SWV compared to the benign nodes. Among the ARFI parameters, VTI was found to be the most sensitive parameter, and AR at a cutoff of 1.155 was the most specific parameter. Overall, the most accurate parameter was SWV at a cutoff of 2.68 m/s. ARFI is a noninvasive technique that can complement grayscale ultrasound in the differentiation of benign and malignant cervical LNs. In its current form, though ARFI cannot replace FNAC or biopsies, it can be effectively used in selecting the suspicious cervical LNs for cytological examination or biopsy for higher histopathological yield. ARFI can potentially reduce unwarranted biopsies and aid in the proper therapy selection and prognosis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Ahuja AT, Ying M. Sonographic evaluation of cervical lymph nodes. *AJR Am J Roentgenol* 2005;184:1691-9.
- Teng DK, Wang H, Lin YQ, Sui GQ, Guo F, Sun LN. Value of ultrasound elastography in assessment of enlarged cervical lymph nodes. *Asian Pac J Cancer Prev* 2012;13:2081-5.
- Lyshchik A, Higashi T, Asato R, Tanaka S, Ito J, Hiraoka M, *et al.* Cervical lymph node metastases: Diagnosis at sonoelastography – Initial experience 1. *Radiology* 2007;243:258-67.
- Shozushima M, Suzuki M, Nakasima T, Yanagisawa Y, Sakamaki K, Takeda Y. Ultrasound diagnosis of lymph node metastasis in head and neck cancer. *Dentomaxillofac Radiol* 1990;19:165-70.
- Ahuja AT, Ying M, Ho SY, Antonio G, Lee YP, King AD, *et al.* Ultrasound of malignant cervical lymph nodes. *Cancer Imaging* 2008;8:48-56.
- Ophir J, Céspedes I, Ponnekanti H, Yazdi Y, Li X. Elastography: A quantitative method for imaging the elasticity of biological tissues. *Ultrason Imaging* 1991;13:111-34.
- Bhatia KS, Lee YY, Yuen EH, Ahuja AT. Ultrasound elastography in the head and neck. Part I. Basic principles and practical aspects. *Cancer Imaging* 2013;13:253-9.
- Dietrich C, Barr R, Farrokhi A, Dighe M, Hocke M, Jenssen C, *et al.* Strain elastography – How to do it? *Ultrasound Int Open* 2017;03:E137-49.
- Yoon JH, Song MK, Kim EK. Semi-quantitative strain ratio determined using different measurement methods: Comparison of strain ratio values and diagnostic performance using one- versus two-region-of-interest measurement. *Ultrasound Med Biol* 2017;43:911-7.
- Menezes R, Sardessai S, Furtado R, Sardessai M. Correlation of strain elastography with conventional sonography and FNAC/Biopsy. *J Clin Diagn Res* 2016;10:C05-10.
- Fujiwara T, Tomokuni J, Iwanaga K, Ooba S, Haji T. Acoustic radiation force impulse imaging for reactive and malignant/metastatic cervical lymph nodes. *Ultrasound Med Biol* 2013;39:1178-83.
- Lo WC, Hsu WL, Wang CT, Cheng PW, Liao LJ. Incorporation of shear wave elastography into a prediction model in the assessment of cervical lymph nodes. *PLoS One* 2019;14:e0221062.
- Chae SY, Jung HN, Ryoo I, Suh S. Differentiating cervical metastatic lymphadenopathy and lymphoma by shear wave elastography. *Sci Rep* 2019;9:12396.
- Heřman J, Sedláčková Z, Fürst T, Vachutka J, Salzman R, Vomáčka J, *et al.* The role of ultrasound and shear-wave elastography in evaluation of cervical lymph nodes. *Biomed Res Int* 2019;2019:4318251.
- Sasaki Y, Ogura I. Shear wave elastography in differentiating between benign and malignant cervical lymph nodes in patients with oral carcinoma. *Dentomaxillofac Radiol* 2019;48:20180454.
- Zhang P, Zhang L, Zheng S, Yu C, Xie M, Lv Q. Acoustic radiation force impulse imaging for the differentiation of benign and malignant lymph nodes: A systematic review and meta-analysis. *PLoS One* 2016;11:e0166716.
- Alam F, Naito K, Horiguchi J, Fukuda H, Tachikake T, Ito K. Accuracy of sonographic elastography in the differential diagnosis of enlarged cervical lymph nodes: Comparison with conventional B-mode sonography. *AJR Am J Roentgenol* 2008;191:604-10.
- Arda K, Ciledag N, Gumusdag P. Differential diagnosis of malignant cervical lymph nodes at real-time ultrasonographic elastography and Doppler ultrasonography. *Hung Radiol Online* 2010;1:10-3.
- Kurt A, Gunes Tatar I, Ipek A, Hekimoglu B. B-mode and elastosonographic evaluation to determine the reference elastosonography values for cervical lymph nodes. *ISRN Radiol* 2013;2013:895287.
- Zhang F, Zhao X, Ji X, Han R, Li P, Du M. Diagnostic value of acoustic radiation force impulse imaging for assessing superficial lymph nodes: A diagnostic accuracy study. *Medicine (Baltimore)* 2017;96:e8125.
- Bai M, Zhang HP, Xing JF, Shi QS, Gu JY, Li F, *et al.* Acoustic radiation force impulse technology in the differential diagnosis of solid breast masses with different sizes: Which features are most efficient? *Biomed Res Int* 2015;2015:410560.
- Wojcinski S, Brandhorst K, Sadigh G, Hillemanns P, Degenhardt F. Acoustic radiation force impulse imaging with Virtual Touch™ tissue quantification: Mean shear wave velocity of malignant and benign breast masses. *Int J Womens Health* 2013;5:619-27.
- Ying M, Bhatia KS, Lee YP, Yuen HY, Ahuja AT. Review of ultrasonography of malignant neck nodes: Greyscale, Doppler, contrast enhancement and elastography. *Cancer Imaging* 2014;13:658-69.
- Baatenburg de Jong RJ, Rongen RJ, Laméris JS, Harthoorn M, Verwoerd CD, Kneeg P. Metastatic neck disease. Palpation vs ultrasound examination. *Arch Otolaryngol Head Neck Surg* 1989;115:689-90.
- Che D, Zhou X, Sun ML, Wang X, Jiang Z, Wu CJ. Differentiation of metastatic cervical lymph nodes with ultrasound elastography by virtual touch tissue imaging: Preliminary study. *J Ultrasound Med* 2015;34:37-42.
- Rubaltelli L, Stramare R, Tregnaghi A, Scagliori E, Cecchelerio E, Mannucci M, *et al.* The role of sonoelastography in the differential diagnosis of neck nodules. *J Ultrasound* 2009;12:93-100.
- Meng W, Xing P, Chen Q, Wu C. Initial experience of acoustic radiation force impulse ultrasound imaging of cervical lymph nodes. *Eur J Radiol* 2013;82:1788-92.
- Chen S, Lin X, Chen X, Zheng B. Noninvasive evaluation of benign and malignant superficial lymph nodes by virtual touch tissue quantification: A pilot study. *J Ultrasound Med* 2016;35:571-5.
- Lenghel LM, Bolboaca SD, Botar-Jid C, Baciut G, Dudea SM. The value of a new score for sonoelastographic differentiation between benign and malignant cervical lymph nodes. *Med Ultrason* 2012;14:271-7.
- Cheng KL, Choi YJ, Shim WH, Lee JH, Baek JH. Virtual touch tissue imaging quantification shear wave elastography: Prospective assessment of cervical lymph nodes. *Ultrasound Med Biol* 2016;42:378-86.
- Zhang Y, Lv Q, Yin Y, Xie M, Xiang F, Lu C, *et al.* The value of ultrasound elastography in differential diagnosis of superficial lymph nodes. *Front Med China* 2009;3:368-74.