RESEARCH PAPER | Medical Science | Volume : 6 | Issue : 5 | May 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

Acoustic Radiation Force Impulse (ARFI) Imaging in Differentiating Between Benign And Malignant Thyroid Nodules

KEYWORDS

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ABSTRACT *Background: Acoustic Radiation Force Impulse (ARFI)-Imaging is an ultrasound-based elastography method enabling quantitative measurement of tissue stiffness. The aim of the present study was to evaluate sensitivity and specificity of ARFI imaging between benign and malignant thyroid nodules & measures to overcome the pitfalls Methods: In our study, 48 thyroid nodules were evaluated by both ultrasonography and ARFI aged between 15-60 yrs . Specific history was taken from the subjects regarding family history of malignancy, history of radiation exposure. Detailed ultrasonography and ARFI examinations were performed.Results: In our study, 48 thyroid nodules were evaluated by both ultrasonography and ARFI. Specific history was taken from the subjects regarding family history of malignancy, history of radiation exposure. Our study showed the mean ARFI value of papillary carcinoma at 3.4 m/s. However, we were unable to compare our results with their results ,as the value of "X.XX m/s" is excluded from our study and were not followed with histopathology or cytology.Conclusions: ARFI, when used in conjunction with ultrasonography , increases the specificity of differentiating benign and malignant thyroid nodules.*

INTRODUCTION
Thyroid nodules are a common finding in regions with inadequate iodine supply and are reported in 33% of adults between the age of 18–65 years . On physical examination, a hard or firm nature is suspicious for thyroid malignancy. However, palpation is very subjective and limited in patients with multinodular goiter or small deep-seated nodules [1,2,3]

Ultrasound is an accurate method for the detection of thyroid nodules,but it hasa low accuracy for the differentiation between benign and malignant thyroid nodules . There are several suspicious grey scale US features that predict thyroid malignancy, such as marked hypo echogenicity, a micro lobulated or spiculated margin, micro-calcifications, and a taller-than-wide shape Although conventional US can provide meaningful information in thyroid nodule diagnosis, there has been considerable variation in characterization of thyroid nodules. [4,5]

Therefore, in patients with normal thyroid stimulating hormone , fine-needle-aspiration-biopsy (FNAB) is presently recommended as a supplementary diagnostic method in the evaluation of thyroid nodules with a size of ≥10 mm. In addition, FNAB is advised in nodules smaller than 10 mm with positive history or suspicious ultrasound findings. FNAB is known to have a high specificity (60–98%) but varying sensitivity (54–90%) for the diagnosis of malignant thyroid nodules. Therefore a relevant number of patients with harbouring benign thyroid nodules undergo invasive procedures. [6,7,8]

So the present study was performed to investigate acoustic radiation force impulse (ARFI) imaging in differentiating between benign and malignant thyroid nodules & measures to overcome the pitfalls

Materials & Methods:
This prospective study was performed in accordance with the guidelines of the ethical committee a hospital. Patients presenting to the endocrinology department for work-up of thyroid nodules were evaluated for inclusion in this study .The study was carried out in sonography department on 48 patients (15 males and 33 females) presenting with thyroid nodules between 2013 to 2014.The age range of the patients was 15-60 yrs. All included patients received either cytology using FNAB and/or histology from thyroid surgery to verify the diagnosis.

Patient with Cystic lesions of completely fluid nature or with a solid component <5mm. Background diffuse thyroiditis. Patients who did not undergo tissue sampling / resection& Indeterminate FNAB without repeat procedure were excluded from the study. Informed written consent was obtained from all patients prior to the ARFI examination and any invasive procedure.

Detailed ultrasonography and ARFI examinations were performed and data was entered in the master sheet as per annexure. Each patient was given a unique number. All the details including age of the patient, symptoms,history of malignancy /radiation exposure, size of the lesion, echogenicity,margins of the lesion,presence or absence of micro calcification , color Doppler findings, grey scaleultrasound diagnosis, mean ARFI values and final cytology/histopathology diagnosis were entered in a tabular format.

The lesions were characterized as Benign , Probably Benign , Suspicious for malignancy , Highly suspicious for malignancy .

Acoustic Radiation Force Impulse (ARFI)Imaging involves targeting of an anatomic region to be interrogated for elastic properties with a Region-of-Interest(ROI) cursor while performing realtime B-mode-imaging. [9,10 ,11] Tissue at the ROI is mechanically excited using acoustic pulses to generate localized tissue displacements. The maximum displacement is estimated for the ultrasound tracking beams and the shear wave speed of the tissue can be reconstructed.

This technique was performed by two radiologists with 25-35 years of experience .On a B-mode US image ,using

Volume : 6 | Issue : 5 | May 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

the 9L4-linear ultrasound-probe,the lesion was identified and interrogated for elastic properties by utilizing a Region of Interest (ROI) with fixed dimension of 1 cm × 0.5 cm. Short, high intensity focused ultrasound beam is introduced for target tissue displacement. The shear waves produced propagate perpendicular to the acoustic pulse away from the target ROI. The ROI is placed such that it is entirely included into the lesion. In larger lesions, the ROI was located in different portions of the lesions, in order to evaluate the entire massand mean value of ARFI is calculated. Two Experienced senior pathologists at Pathology department conducted the diagnostic examination on the FNAB or resected specimen. Data was analyzed using SPSS Ver. 15 and Epiinfo(3.5) data software & appropriate statistical tests.

Observation & Results

Table 1: Diagnosis by USG and Cytology/Histopathology and ARFI Values.

	Diagnosis on USG	Mean ARFI value of the lesion	Diagnosis on Cytology/Histopathology
1	Benign	2.03	Adenoma
2	Suspicious for malignancy	2.11	Colloid nodule
3	Suspicious for malignancy	3.44	Papillary carcinoma
4	Benign	2.44	Adenoma
5	Highly suspicious for malignancy	4.33	Papillary carcinoma
6	Probably benign	1.86	Colloid nodule
7	Benign	2.87	Colloid nodule
8	Probably benign	1.79	Colloid nodule
9	Suspicious for malignancy	1.91	Adenoma
10	Probably benign	1.84	Colloid nodule
11	Benign	2.11	Adenoma
12	Benign	1.78	Colloid nodule
13	Probably Benign	1.89	Adenoma
14	Benign	2.33	Colloid nodule
15	Highly suspicious for malignancy	3.11	Papillary carcinoma
16	Probably benign	1.62	Colloid nodule
17	Benign	1.77	Adenoma
18	Suspicious for malignancy	1.68	Adenoma
19	Benign	1.74	Adenoma
20	Suspicious for malignancy	2.11	Adenoma
21	Highly suspicious for malignancy	3.17	Medullary carcinoma
22	Probably benign	1.99	Colloid nodule
23	Benign	2.06	Adenoma
24	Benign	1.99	Adenoma
25	Suspicious for malignancy	4.89	Follicular carcinoma
26	Probably benign	2.33	Colloid nodule
27	Highly suspicious for malignancy	4.45	Papillary carcinoma
28	Benign	2.29	Adenoma
29	Suspicious for malignancy	2.33	Adenoma
30	Benign	2.11	Adenoma
31	Probably benign	1.44	Colloid nodule
32	Highly suspicious for malignancy	2.86	Papillary carcinoma
33	Benign	1.77	Adenoma
34	Benign	2.09	Adenoma
35	Probably benign	1.33	Colloid nodule
36	Suspicious for malignancy	3.97	Lymphoma
37	Suspicious for malignancy	1.77	Colloid nodule
38	Benign	3.43	Medullary carcinoma
39	Benign	1.84	Adenoma
40	Benign	1.97	Adenoma
41	Benign	2.08	Colloid nodule
42	Probably Benign	1.43	Adenoma
43	Suspicious for malignancy	2.68	Papillary carcinoma
44	Benign	2.13	Adenoma
45	Probably Benign	1.96	Colloid nodule
46	Highly suspicious for malignancy	2.99	Papillary carcinoma
47	Benign	2.66	Adenoma
48	Probably Benign	2.33	Adenoma

Discussion

Elastography has emerged as a valuable tool in the evaluation of thyroid lesions. The high reproducibility, less inter observer variation, operator non- dependence has made ARFI more favourable tool in thyroid imaging. In our study, 48 thyroid nodules were evaluated by both ultrasonography and ARFI. Specific history was taken from the subjects regarding family history of malignancy, history of radiation exposure.

Ryuhei Okada et al[12] aimed to evaluate the diagnostic value of shear wave velocities (Vs) of thyroid nodules in diagnosis of the thyroid carcinoma.They measured the Vs of thyroid nodules in 39 nodules from 34 patients.However, 16 nodules showed "X.XX m/s". These 16 nodules showed either "black" or "honeycomb" patterns of elasticity in VTTI. This value suggested that the Vs of these nodules were too fast or heterogenous to measure by this device. In their study, nodules from five out of 21 papillary carcinomas showed average Vs of 4.00 ± 2.37 m/s. In the nodules of 16 papillary carcinomas, Vs were measured as "X.XX m/s" and this value was only observed in nodules of papillary carcinoma. These data reflected high and/or heterogenous elasticity of papillary carcinoma, in other words, the tissue of papillary carcinoma was hard and/or heterogenous. It was notable that the Vs value of "X.XX m/s" strongly suggested papillary carcinoma. [12]

Our study showed the mean ARFI value of papillary carcinoma at 3.4 m/s. However, we were unable to compare our results with their results ,as the value of "X.XX m/s" is excluded from our study and were not followed with histopathology or cytology.

Pitfalls in the interpretation of ARFI and measures taken to minimize them: Non-valid measurements like X.XXm/swereusually found in very hard lesion. Our study showed inconsistent results with X.XXm/s and hence were excluded. The necrotic or cystic portion of a nodule, vessels or fibrotic scarwithin the ROI showed variable ARFI measurements. Hence, we measured the velocity in solid components of the nodule.Patient motion or deglutition during the measurement and nodules close to the carotid vessels reveal erroneous measurements. We excluded these non-valid measurements from our study. In large nodules, we measured multiple ARFI values in multiple regions of the nodule and calculated the mean of these multiple values. In multiple nodules, we measured the ARFI value of thenodule which was most suspicious for malignancy on USG. In case of no suspicious nodules, we measured the largest nodule. We did not assess deep nodules by ARFI, as these values are inconsistent and not reproducible. We assessed the role of ARFI in 48 nodules in 48 patients. Larger study may be required for further validation of our results. The present study seems to

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confirm the potential application of ARFI technology for characterizing focal solid thyroid nodules and differentiating benign from malignant nodules. According to the results, significant differences between the mean wave velocity values for benign and malignant nodules have been achieved. In the clinical setting, ARFI technique seems to be a useful tool in thyroid imaging, more so as an adjunct to grey scale ultrasonography and color Doppler imaging.

ARFI Elastography provides new set of information that is not based on the anatomical features but on the relative elasticity of the lesion and hence becomes complementary to the ultrasound features. It is more sensitive and specific than Ultrasound in differentiating benign and malignant thyroid nodules , but cannot be used in isolation for diagnosis of thyroid nodules. Histotype and size of the nodules have an influence on the degree of elasticity. A larger malignant tumor can have intranodular vascularity, necrotic or hemorrhagic components, which can affect the ARFI velocity. ARFI values are also affected by the depth of the nodule and by any movement during acquisition.

Hence, our study shows that ARFI, when used in conjunction with ultrasound increases the specificity of differentiating benign and malignant thyroid nodules.

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