

## Original Research Article

# Elastography evaluation of normal thyroid gland and its comparison with diffuse non nodular enlarged thyroid gland using strain ultrasound elastography

Sanjay Kumar, Vishal Kumar Jain\*, Ashutosh Gupta,  
Satya Bhuvan Singh Netam, Nilesh Gupta

Department of Radiodiagnosis, Pt. JNM Medical College, Raipur, Chhattisgarh, India

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**\*Correspondence:**

Dr. Vishal Kumar Jain,

E-mail: [vishpal33@gmail.com](mailto:vishpal33@gmail.com)

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### ABSTRACT

**Background:** The thyroid gland is located in the anterior part of neck, spanning between C5 and T1 vertebra and is located anterior to the thyroid and cricoids cartilage of larynx and first three tracheal rings. Ultrasonography has been widely used for diagnosis of thyroid disease it is highly regarded for its ease of use, real-time capability, portability and low cost.

**Methods:** The current observational study was conducted in Department of Radiology, Dr. BRAM Hospital, Pt. JNM Medical College, Raipur, India. Consecutive sampling method was used for the study. All the cases coming to radiology department during the study period were taken as study subjects.

**Results:** Of the normal subjects, author found 107 normal thyroid subjects and 53 patients were categorized into cases with diffuse non-nodular thyroid swelling groups. Of the diffuse thyroid swelling group about 85% of the study population is between 20-50 years of age group, 13.2% were <20 years of age and one patient is >50 years of age. Females to male ratio for diffuse thyroid disease is 3.4:1.

**Conclusions:** Ultrasound elastography (USE) is a newly developed non-invasive method to evaluate and compare the elasticity of the thyroid gland and other organs like liver, prostate, parotid, breast pathologies. Its use is based on the principle that pathological changes in a tissue also changes its elasticity.

**Keywords:** Elasticity contrast index, Strain ultrasound elastography, Thyroid gland, Ultrasound elastography

### INTRODUCTION

The thyroid gland is located in the anterior part of neck, spanning between C5 and T1 vertebra and is located anterior to the thyroid and cricoids cartilage of larynx and first three tracheal rings. It is an endocrine gland, divided into two lobes connected by an isthmus. It is a butterfly or 'H' shaped organ each with superior and inferior pole.

A swelling in neck due to enlarged thyroid gland is called a goiter.

Ultrasonography has been widely used for diagnosis of thyroid disease since, it was first introduced in clinical practice in the 1970's. Used in clinical practice for more than 40 years, it is highly regarded for its ease of use, real-time capability, portability and low cost.

Since then, new ultrasound modalities have been developed, such as doppler imaging, which provides new information for diagnosis. Elastography was developed in the 1990's to map tissue stiffness and reproduces/replaces the palpation performed by clinicians. Elastography, whose development started about 20 years ago, aims at imaging tissue stiffness, which provides an additional and clinically relevant information.<sup>1</sup>

Elastography is analogous to palpation, therefore wherever palpation has clinical value, elastography is relevant tool for diagnosis. Although palpation is limited to superficial organs, many elastography techniques can be applied to deeper organs opening new possibilities for diagnosis.

Ultrasound elastography is a non-invasive modern imaging technique which represents tissues and organs with evaluation of their elasticity, "stiffness". It is based on the fact that pathological changes in tissues generally affect their stiffness. Strain elastography using internal physiologic force (pulsations from the adjacent carotid artery) to induce the displacement in thyroid tissue necessary to assess tissue elasticity. It is a semi-quantitative method that measures elasticity contrast index (ECI) that represents the stiffness of thyroid tissue. Ultrasonographic elastography is a new, developing method that shows increase in clinical practice.

Thyroid gland disorders include benign and malignant thyroid nodules and diffuse thyroid disorders. Studies had been done to differentiate between benign and malignant thyroid nodules using elastography showing significant difference in elasticity score.<sup>2</sup>

Studies had also been done with significant use in differentiating benign and malignant Breast neoplasm, prostate, some groups of lymph nodes and liver pathologies.<sup>3</sup> Less have been known about the pattern of changes in elastography in diffuse non-nodular thyroid swelling.

Author wished to conduct this study to get a reference value for normal thyroid tissue in the study population and compare the elasticity contrast index (ECI) in the subjects with diffuse non-nodular thyroid swelling using ultrasound strain elastography technique.

## **METHODS**

The current observational study was conducted in Department of Radiology, Dr. BRAM Hospital, Pt. JNM Medical College Raipur, India during period August 2017-September 2018. Consecutive sampling method was used for the study.

Samsung RS-80 Ultrasound Machine with Linear Array Transducer (LA4-18B), Color Doppler and Strain Elastography Software used for the study purpose. As this is a clinical setting-based time bound study, all the

cases coming to radiology department and qualifying inclusion and exclusion criteria, during the study period will be taken as study subjects.

### ***Inclusion criteria***

- Patients between the age groups 20-50 years came for ultrasound abdomen with no significant abnormality detected on routine ultrasound neck for normal thyroid subjects,
- Patients with non-nodular diffuse thyroid swelling with or without symptoms of hypothyroidism or hyperthyroidism.

### ***Exclusion criteria***

- Patient with focal thyroid nodules, cystic lesion diagnosed on ultrasound,
- Patient with previous history of thyroid surgery,
- Patient who received radiation therapy,
- Pregnant women,
- Unwilling patients.

### ***Protocol for thyroid elastography***

Colour doppler diagnostic ultrasound instrument with linear probe having frequency 4-18 MHz and strain elastography software is used. Patient took supine position with neck in slight hyperextension for adequate exposure of thyroid. The probe was kept perpendicular to the skin over thyroid in transverse plane to routinely scan both the lobes and isthmus of thyroid to judge the type of thyroid gland.

Thyroid dimensions are recorded to categorize the patient into normal thyroid or diffuse thyroid swelling group. It is of importance to choose the shortest path for the exploratory US beam to the ROI, thus avoiding strain decay with distance. It is also important to exclude vessels (carotid), eso-tracheal structures, bones and muscles from ROI.<sup>4</sup>

Elastoscan mode is selected and the probe is hold still perpendicular to the thyroid lobe. No external compression with the transducer was needed as Elastoscan uses the pulsations of the carotid artery (in vivo compression) for the elastography response.<sup>5</sup> Patient is instructed to hold breath and swallowing for 10-15 seconds during scan.<sup>6</sup> The image is paused after all the colour bar turned green.

Elastogram was considered optimal when the screen quality indicator turned to green (multiple boxes that change color from red, to yellow or green). ROI is selected. The operator performed the examination in transverse plane and then drew the region of interest (ROI) of approximately 5 mm.

A ROI as described above was manually placed by the operator. On the elastograms (placed on the left side of

the screen, side by side with the B-mode image) the thyroid were color coded depending on their stiffness with a colorimetric scale on the screen indicating the corresponding hard and soft areas, color coded red and blue respectively.<sup>5</sup> Within the ROI the software assessed the elasticity contrast index (ECI), a semiquantitative stiffness evaluation.

The elasticity contrast index (ECI), which quantifies local strain contrast within a ROI, was computed and displayed on the screen.<sup>5</sup> Total of 6 readings were obtained i.e. two readings of ECI was obtained from each right and left lobe and from the isthmus. Average of the two was noted. ECI of each was obtained and interpreted separately. In few cases where isthmus was <2.5 mm, only readings from right and left lobes were obtained.

**Elasticity Contrast Index (ECI)**

Ultrasound elasticity contrast index (ECI) is the difference of tissue strain determined by elasticity imaging and can reflect the uniformity of strain in tissue. ECI is an ultrasonic quantitative index developed on the basis of ultrasonic elastography, avoids the limitation of the traditional triggered elastography, and can determine the tissue hardness as well as the difference and homogeneity of all pixel strain in the ROI at the same time.<sup>4,5,7-10</sup>

**Statistical evaluation**

Data was collected and analyzed with the help of excel and graph-pad in stat software for statistical analysis. Proportion as number and percentage was determined for categorical variable like gender.

**RESULTS**

Of the normal subjects, author found 107 normal thyroid subjects and 53 patients were categorized into cases with

diffuse non-nodular thyroid swelling groups. Of the normal subjects only the age group between 21-50 years were included to get ECI value of adult population. Of the diffuse thyroid swelling group about 85% of the study population is between 20-50 years of age group, 13.2% were <20 yrs of age and one patient is >50 years of age (Table 1).

**Table 1: Age wise distribution of normal thyroid and diffuse thyroid swelling subjects.**

Age (years)	Normal thyroid		Diffuse thyroid swelling	
	No.	Percentage	No.	Percentage
Upto 20	NIL	0.00%	7	13.20%
21-30	49	45.80%	23	43.40%
31-40	32	29.90%	15	28.30%
41-50	26	24.30%	7	13.20%
>50	NIL	0.00%	1	1.90%
Total	107	100%	53	100%

Out of 160 patients scanned, 112 patients were females and 48 were males. 63.4% out of total 112 females had normal thyroid dimensions and 36.6% had diffuse thyroid swelling. Out of 48 males studied, 75% were normal thyroid subjects and 25% had diffuse non-nodular thyroid swelling. Thus, in this study female patients had more diffuse thyroid disease (36.6%) compared to the male (25%) counterparts. Thus, females to male ratio for diffuse thyroid disease is 3.4:1 (Table 2).

**Table 2: Gender wise distribution of patients with diffuse thyroid swelling and normal thyroid dimensions.**

Gender	Diffuse thyroid swelling	Normal thyroid dimensions	Total
Male	12 (25%)	36 (75%)	48 (100%)
Female	41 (36.6%)	71 (63.4%)	112 (100%)
Total	53 (33%)	107 (67%)	160 (100%)

**Table 3: Comparison of elasticity contrast index (ECI) value of normal thyroid vs diffuse thyroid swelling.**

Thyroid lobe	USG diagnosis	N	Mean ECI	SD	Std. error mean
Right lobe	Normal thyroid	107	1.05822	0.428	0.041376
	Diffuse thyroid swelling	53	1.23915	0.640562	0.087988
Left lobe	Normal thyroid	107	1.06925	0.454869	0.043974
	Diffuse thyroid swelling	53	1.35783	0.737744	0.101337
Isthmus	Normal thyroid	107	1.14407	0.471209	0.045554
	Diffuse thyroid swelling	53	1.20847	0.623912	0.085701

Author found elasticity contrast index (ECI) value of normal thyroid subjects with normal thyroid dimensions as ECI of right lobe=1.05±0.42 (range=0.63 to 1.47), Left lobe=1.06±0.45 (range=0.61 to 1.51) and Isthmus

1.14±0.47 (range=0.67 to 1.61). Elasticity Contrast Index (ECI) value of diffuse thyroid swelling subjects as ECI of right lobe=1.23±0.64 (range=0.59 to 1.87), left lobe=1.35±0.73 (range=0.62 to 2.08) and Isthmus=1.20±0.62 (range=0.58 to 1.82). On comparison between

groups of normal thyroid group and diffuse thyroid group using independent t-test, p-value of right lobe and left lobe was 0.035 and 0.003 respectively, which is

statistically significant, while p-value of isthmus was found to be 0.467 which is not statistically significant (Table 3, Table 4).

**Table 4: Independent ‘T’ test result.**

Thyroid lobe		T-test for equality of means					95% confidence interval of the difference	
		T	Df	Sig. (2-tailed)	Mean diff.	Std. error difference	Lower	Upper
Right lobe	Equal variances assumed	-2.121	158	0.035*	-0.1809	0.08531	-0.3494	-0.0124
	Equal variances not assumed	-1.861	75.724	0.067	-0.1809	0.09723	-0.3746	0.01274
Left lobe	Equal variances assumed	-3.047	158	0.003*	-0.2886	0.09471	-0.4756	-0.1015
	Equal variances not assumed	-2.612	72.172	0.011	-0.2886	0.11047	-0.5088	-0.0684
Isthmus	Equal variances assumed	-0.728	158	0.467	-0.0644	0.08842	-0.239	0.11022
	Equal variances not assumed	-0.664	82.311	0.509	-0.0644	0.09706	-0.2575	0.12866

\* Significant

The independent T - test result (Table 4 shows that there is a significant difference in mean value of right lobe (p=0.035) and left lobe (p =0.003) of thyroid between the groups at 95% confidence interval. However, the difference in the isthmus was found to be in significant (p- 0.467).

**DISCUSSION**

Ultrasound elastography is a newer non-invasive modern imaging technique which measures the stiffness of the tissue examined. It is based on the fact that pathological changes in tissue also alters its stiffness. Diffuse thyroid swelling is caused by various diffuse thyroid diseases like Hahimoto`s disease, Graves`s disease, chronic autoimmune thyroiditis, de Quervain`s disease, Riedel`s struma, painless thyroiditis, acute suppurative thyroiditis, etc.<sup>11,7,12-14</sup> In previously published papers, thyroid elastography has been used to evaluate thyroid nodule stiffness in order to differentiate malignant from benign ones. Sebag FJ et al, used shear wave elastography (SWE) for differential diagnosis of benign and malignant thyroid nodules and compared SWE with ultrasound (US) and found that Elasticity Index (EI) was significantly higher in malignant nodules (150±95 (30-356 kPa) than in benign nodules (36±30 (0-200 kPa) and normal thyroid glands. T Rago et al, found promising results using strain elastography in differentiating nodules, which were of indeterminate significance in gray scale ultrasound.<sup>15,16,19</sup> Choi WJ et al, did a study on 102 patients with indeterminate thyroid nodules using ultrasound elastography with carotid pulsation as the compression

source and found that, ECI values for malignant nodules (3.07±2.01) were significantly higher than those for benign nodules (1.44±0.47). The specificity of ECI (97.8%) was higher than that of the gray-scale ultrasound score (72.2%).<sup>2</sup>

Author have used similar technique to measure elasticity (ECI) using carotid artery pulsation, in 107 subjects (36 male and 71 females) with normal thyroid dimensions in this study to find a normal reference range of ECI in adult population (age 20-50 years) and calculated Elasticity Contrast Index (ECI) value. In this study, normal thyroid subjects with normal thyroid dimensions ECI of right lobe=1.05±0.42 (Range=0.63 to 1.47), left lobe=1.06±0.45 (Range=0.61 to 1.51) and Isthmus 1.14±0.47 (Range=0.67 to 1.61). Author compared the mean of ECI score with the diffuse thyroid subjects. Author examined 53 patients (12 males, 41 females ) with diffuse thyroid swelling having AP diameter >2 cm. Author found that Elasticity Contrast Index (ECI) value in diffuse thyroid swelling subjects are as ECI of right lobe=1.23±0.64 (range=0.59 to 1.87), left lobe=1.35±0.73 (range=0.62 to 2.08) and Isthmus=1.20±0.62 (range=0.58 to 1.82). On comparison between groups of normal thyroid group and diffuse thyroid group using independent t-test, author found that the p-value of right lobe and left lobe was 0.035 and 0.003 respectively, which is statistically significant, while p-value of isthmus was found to be 0.467 which is not statistically significant. Similar study was done by Fukuhara T et al, they used shear wave elastography (SWE) using acoustic radiation force impulse (ARFI) for diagnosing chronic

autoimmune thyroiditis (CAT) and to verify the effect of fibrotic thyroid tissue on shear wave velocity (SWV).<sup>17</sup>

They scanned 229 patient's normal thyroid lobes (controls) and 150 chronic autoimmune thyroiditis (CAT) lobes. They found that the mean SWV for CAT was  $2.47 \pm 0.57$  m/s, which was significantly higher than the mean shear wave velocity for normal controls ( $1.59 \pm 0.41$  m/s) ( $P < 0.001$ ).

Another study done by Sporea I et al, on diffuse thyroid gland pathology using ARFI to assess whether acoustic radiation force impulse (ARFI) elastography can differentiate normal from pathological thyroid parenchyma.<sup>18</sup> They evaluated 136 subjects (106 women and 30 men), 44 (32.3%) without thyroid pathology, 48 (35.3%) with Graves' disease (GD), 37 (27.2%) with chronic autoimmune thyroiditis (CAT), 4 (2.9%) with diffuse thyroid goiter and 3 (2.2%) cases with thyroid pathology induced by amiodarone. They found that thyroid stiffness (TS) assessed by means of ARFI in healthy subjects ( $2 \pm 0.40$  m/s) was significantly lower than in GD ( $2.67 \pm 0.53$  m/s) ( $P < 0.0001$ ) and CAT patients ( $2.43 \pm 0.58$  m/s) ( $P = 0.0002$ ), but the differences were not significant between GD vs CAT patients ( $P = 0.053$ ). They concluded that ARFI seems to be a useful method for the assessment of diffuse thyroid gland pathology.

## CONCLUSION

Ultrasound elastography (USE) is a newly developed non-invasive method to evaluate and compare the elasticity of the thyroid gland and other organs like liver, prostate, parotid, breast pathologies. Its use is based on the principle that pathological changes in a tissue also changes its elasticity.

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