

# **Role of Ultrasound Elastography in prediction of malignancy in thyroid nodules**

THESIS

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# **Abstract**

Thyroid nodules come to clinical attention when noted by the patient, or as an incidental finding during routine physical examination, or during radiologic procedure, such as carotid ultrasonography or neck CT. Their clinical importance is primarily related to the need to exclude thyroid cancer, which accounts for 4-6% of all thyroid nodules.

Elastography is a newly developed dynamic technique that uses ultrasound (US) to provide an estimation of tissue stiffness by measuring the degree of distortion under the application of an external force. US elastography has been applied to differentiate malignant from benign lesions in the thyroid gland.

**Patients and methods:** 46 nodules were studied in 40 patients, ultrasound, ultrasound elastography and FNAC were done for each of these nodules.

**Results:** 35 of the nodules had score 1 or 2 and all proved to be benign by FNAC, 7 had score 3 one of them was malignant, 3 had score 4 and were all malignant. For the score 4, sensitivity was 75.0 % & specificity was 100 % , for the score 3 and 4 sensitivity was 100% and specificity was 85.37%.

**Conclusion:** US elastography seems to have great potential as a new tool for the diagnosis of thyroid cancer, especially in nodules with indeterminate cytology. Larger prospective studies are needed to establish the diagnostic accuracy of this technique and to evaluate its role in routine work up of cases with thyroid nodules.

**Key words:** ultrasound- elastography- thyroid- nodule- malignancy.

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## **List of abbreviations**

- ACTH: Adrenocorticotrophic hormone.
- AGES: Age, grade, extent, size.
- AJCC: American joint cancer committee.
- AMES: Age, metastasis, extent, size.
- ATP: Adenosine triphosphate.
- AUC: Area under curve.
- cAMP: cyclic adenosine monophosphate.
- CDI: Colour Doppler imaging.
- CEA: Carcinoembryonic antigen.
- CFD: Colour flow Doppler.
- CT: Computed Tomography.
- CUS: Conventional Ultrasound.
- DIT: Di-iodotyrosine.
- DVT: Deep venous thrombosis.
- ECF: Extracellular fluids.
- EORTC: European organization for research on treatment of cancer.
- E-score: Elastography score.
- EUS: Endoscopic ultrasound.
- FDG-PET: Fluorodeoxyglucose positron emission tomography.
- FMTC: Familial medullary thyroid carcinoma.
- FNAC: Fine needle aspiration cytology.
- FT<sub>3</sub>I: Free T<sub>3</sub> index.
- FT<sub>4</sub>I: Free thyroxine index.
- FTC: Follicular thyroid cancer.
- ITC: Insular thyroid cancer.
- IV: Intravascular.
- MACIS: Metastasis, age, completeness of resection, invasion, size.
- MIFC: Minimally invasive follicular carcinoma.
- MIT: Mono-iodotyrosine.
- MRI: Magnetic Resonance Imaging.
- NIS: Sodium- Iodine Symporter.
- NTCTCS: National thyroid cancer treatment corporation study.
- PD: Power Doppler.
- PNS: Proportion of no strain
- RAI: Radioactive iodine.
- ROC: Receiver Operating Characteristic.
- RT<sub>3</sub>: Reverse T<sub>3</sub>.
- SEER: Surveillance, Epidemiology and End Results.

- T<sub>3</sub>: Tri- iodothyronine.
- T<sub>4</sub>: Thyroxine.
- TBG: Thyroxine binding globulin.
- TBPA: Thyroxine binding prealbumin.
- T<sub>g</sub>: Thyroglobulin.
- TNM: Tumour- lymph nodes- metastasis.
- TPO: Thyroid peroxidase.
- TR: thyroid hormone nuclear receptor.
- TSH: thyroid stimulating hormone.
- TSH-R: TSH-receptor.
- UICC: International union against cancer.
- US: Ultrasound.
- WHO: World Health Organization.
- WIFC: Widely invasive follicular carcinoma.

## **Introduction and aim of work**

Thyroid nodules come to clinical attention when noted by the patient, or as an incidental finding during routine physical examination, or during radiologic procedure, such as carotid ultrasonography or neck CT. Their clinical importance is primarily related to the need to exclude thyroid cancer, which accounts for 4-6% of all thyroid nodule (**Hegedus L; et al, 2004**).

Ultrasonography is considered useful in the following situations;

1. To distinguish between solid and cystic thyroid nodules.
2. To stratify a nodule's risk of cancer as low, medium or high.
3. To direct biopsy of nonpalpable nodules, and palpable but small nodules.
4. To detect nonpalpable recurrent tumor in the neck in patients with thyroid carcinoma who have had surgery.

Certain sonographic criteria may increase the incidence of suspicion of malignant nodules such as hypoechoic texture, ill defined edge, absence of a halo, presence of punctate microcalcification, increase central color flow and anteroposterior to transverse diameter (A-P/T) greater than one.

Elastography is a newly developed dynamic technique that used ultrasound (US) to provide an estimation of tissue stiffness by measuring the degree of distortion under the application of an external force.

US elastography has great potential as an adjunctive tool for the diagnosis of thyroid cancer, possibly it will solve the dilemma in writing an accurate diagnosis for the cytologically known as (indeterminate nodules) (**Rago T; et al, 2007**)

The aim of the present work is to evaluate the sensitivity and specificity of ultrasound elastography in diagnosis of thyroid cancer.

## Chapter 1

### Thyroid gland

#### **Anatomy and histology:**

The thyroid is one of the largest of the endocrine organs, weighing approximately 15 to 20 g in North American adults. Moreover, the potential of the thyroid for growth is tremendous. The right lobe is normally more vascular than the left, is often the larger of the two, and tends to enlarge more in disorders associated with a diffuse increase in gland size. Two pairs of vessels constitute the major arterial blood supply, the superior thyroid artery, arising from the external carotid artery, and the inferior thyroid artery, arising from the subclavian artery. Estimates of thyroid blood flow range from 4 to 6 mL/min/g, well in excess of the blood flow to the kidney (3 mL/min/g). In diffuse toxic goiter due to Graves' disease, blood flow may exceed 1 L/min and be associated with an audible bruit or even a palpable thrill (**Larsen P R; et al, 2008**).

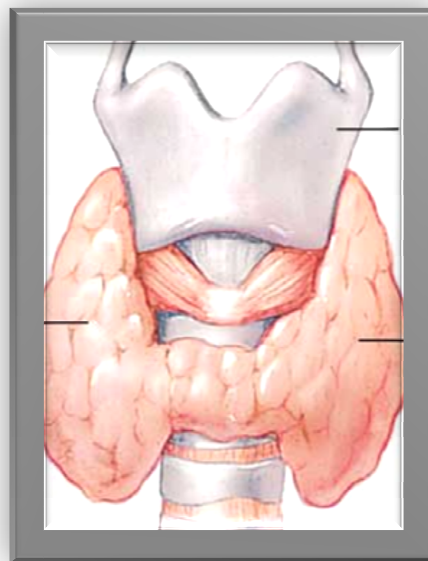


Fig. (1.1)

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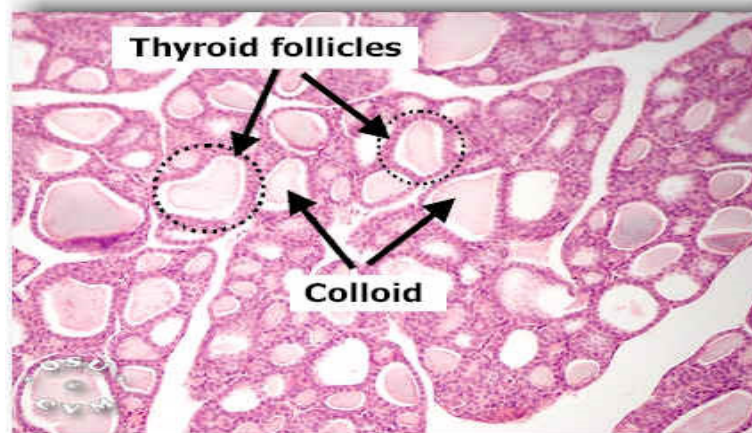
The gland is composed of closely packed spherical units termed *follicles*, which are invested with a rich capillary network. The interior of the follicle is filled with the clear proteinaceous colloid that normally is the major constituent of the total thyroid mass. On cross section, thyroid tissue appears as closely packed ring-shaped structures consisting of a single layer of thyroid cells surrounding a lumen. The diameter of the follicles varies considerably, even within a single gland, but averages about 200  $\mu\text{m}$ . The follicular cells vary in height with the degree of glandular stimulation, becoming columnar when active and cuboidal when inactive. The epithelium rests on a basement membrane that is rich with glycoproteins separating the follicular cells from the surrounding capillaries. From 20 to 40 follicles are demarcated by connective tissue septa to form a lobule supplied by a single artery. The function of a given lobule may differ from that of its neighbors (**Larsen P R; et al, 2008**).

On electron microscopy, the thyroid follicular epithelium has many features in common with other secretory cells and some peculiar to the thyroid. From the apex of the follicular cell, numerous microvilli extend into the colloid. It is at or near this surface of the cell that iodination, exocytosis, and the initial phase of hormone secretion, namely colloid resorption, occur. The nucleus has no distinctive features and the cytoplasm contains an extensive endoplasmic reticulum laden with microsomes.

The endoplasmic reticulum is composed of a network of wide irregular tubules that contain the precursor of Thyroglobulin. The carbohydrate component of Thyroglobulin is added to this precursor in

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the Golgi apparatus which is located apically. Lysosomes and mitochondria are scattered throughout the cytoplasm. Stimulation by TSH results in enlargement of the Golgi apparatus, formation of pseudopodia at the apical surface, and the appearance in the apical portion of the cell of many droplets that contain colloid taken up from the follicular lumen (Larsen P R; et al, 2008).



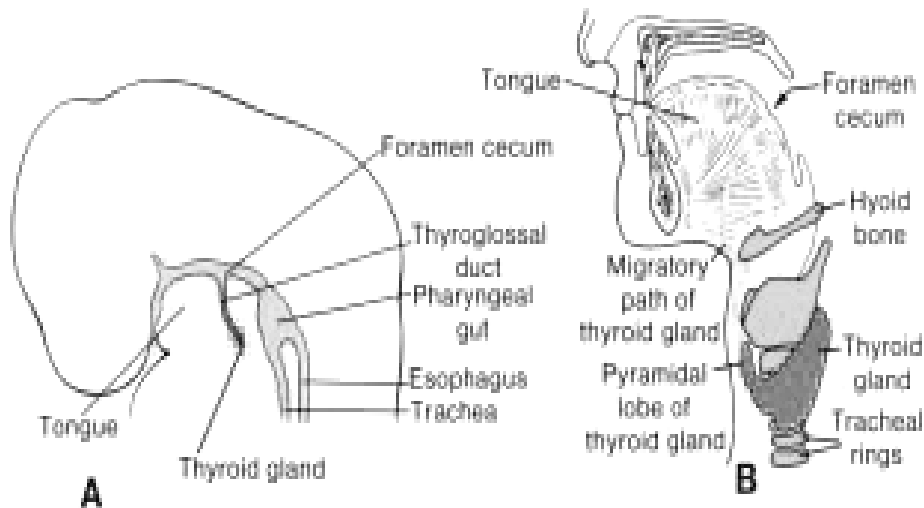
**Fig. (1.2) Thyroid histology.**

### **Embryology:**

The thyroid gland appears as an epithelial proliferation in the floor of the pharynx between the tuberculum impar and the copula at a point later indicated by the **foramen cecum**. Subsequently the thyroid descends in front of the pharyngeal gut as a bilobed diverticulum. During this migration, the thyroid remains connected to the tongue by a narrow canal, the **thyroglossal duct**. This duct later disappears. With further development, the thyroid gland descends in front of the hyoid bone and the laryngeal cartilages. It reaches its final position in front of the trachea

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in the seventh week. By then it has acquired a small median isthmus and two lateral lobes. The thyroid begins to function at approximately the end of the third month, at which time the first follicles containing colloid become visible (Langman's medical embryology, 2005).



**Fig (1.3)** A. The thyroid primordium arises as an epithelial diverticulum in the midline of the pharynx immediately caudal to the tuberculum impar. B. Position of the thyroid gland in the adult.

### Hormonal secretion and mode of action:

Thyroid hormones are critical determinants of brain and somatic development in infants and of metabolic activity in adults; they also affect the function of virtually every organ system. Thyroid hormones must be constantly available to perform these functions. To maintain their availability, there are large stores of thyroid hormone in the circulation and in the thyroid gland. Furthermore, thyroid hormone biosynthesis and secretion are maintained within narrow limits by a regulatory mechanism that is very sensitive to small changes in circulating hormone concentrations. Thyroid hormone, in the form of triiodothyronine (T<sub>3</sub>), acts by modifying gene transcription in virtually all tissues to alter rates of protein synthesis and substrate turnover (Yen, PM; et al, 2006).