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Sonographic Elastography of the Thyroid Gland

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Summary

Thyroid gland disorders include benign and malignant thyroid nodules and diffuse thyroid disorders. The incidence of malignant thyroid nodules is low and the prognosis is good. The diagnosis of thyroid cancer and diffuse parenchymal disorders is generally based on clinical manifestations and histopathological evaluation. Ultrasonography has its place in the diagnostics and follow-up of thyroid disorders. Ultrasonographic elastography is a new, developing method that shows increase in clinical practice. In this study, we aimed to review the data on thyroid ultrasound elastography.

MeSH Keywords: Elasticity Imaging Techniques • Hashimoto Disease • Ultrasonography, Doppler, Color

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Background

The thyroid gland develops in a primitive foregut by originating from the foramen caecum in the tongue root in the 3rd gestational week. During the embryologic development process, it gets located in the neck, coming down from the structures that make up the hyoid bone and the larynx [1]. It is a gland that weights 20 grams on average. It comprises two lobes and one isthmus that unites them. Moreover, the pyramidal lobe, which goes up from the isthmus and which is a remnant of the thyroglossal duct, is present in 50–80% [2]. While each lobe is 4–5 cm high, 2–3 cm wide, and 2–4 cm thick, the lobes are generally located between the 1st and 4th tracheal ring. Left and right lobes partially encircle the trachea from the front. On its lateral side there is the carotid sheath and sternocleiodomastoid muscle [3].

Thyroid follicular cells are responsible for thyroid hormone synthesis and parafollicular cells are responsible for calcitonin secretion. Thyroid hormone secretion is under the control of the hypothalamic-hypophyseal-thyroid axis. T3 and T4 are the hormones that regulate basal metabolism. They regulate protein synthesis by connecting nucleus receptors, which are inside the cell. Also, they increase oxidation in the mitochondria. They also have such functions as controlling the activity of enzymes in the cell membrane structure. That is why the thyroid hormone is necessary for a normal life [4].

As such an important tissue plays many roles in metabolic activity, there are many thyroid pathologies in the society. These are congenital anomalies, diffuse parenchymal diseases, benign and malignant thyroid nodules and carcinomas [5]. Generally, thyroid diseases are common and they are formed in the course of different mechanisms. Among these diffuse parenchymal diseases, diffuse hyperplasia, which follows from iodine deficiency, is the most common cause of Graves' hyperthyroid disease and it is also autoimmune, as Hashimoto's thyroiditis. In Graves' disease, immunoglobulins, which stimulate the thyroid gland as long-acting thyroid stimulators, cause hyperthyroidism by stimulating the TSH receptor. Diffuse enlargement in the thyroid gland is followed by hyperthyroidism and infiltrative ophtalmopathy and dermatopathy [6]. Hashimoto's thyroid is believed to develop because of autoantibodies that form against thyroid proteins (especially TG) [7]. It is believed that viral infections play a role in subacute granulomatous thyroiditis. Painful thyroid gland enlargement, which is usually accompanied by high fever, constitutes the classic clinical chart. Subacute lymphocytic thyroiditis, which is also autoimmune, is accompanied by postpartum hyperthyroid and hypothyroid. It is formed by acute suppurative (infectious) thyroiditis bacteria. Riedel thyroiditis is followed by fibrosis. It is rare [8,9].

Thyroid has also diseases with malignant and benign nodules. Most of the solitary thyroid nodules are follicular

adenomas or such benign lesions as localized, non-neoplastic nodular hyperplasia (hyperplastic nodule), simple cyst, and thyroiditis hypocenter. In contrast, thyroid carcinomas are not frequent and make up less than 1% of solitary thyroid nodules. Nodule prevalence is in a direct proportion to age and it can be roughly calculated with the "patient's age – 10" formula. Although the prevalence is high, only 2–4% of nodules are malignant [10]. It has been reported that thyroid nodules are found in 50% of autopsies [11]. This shows the right way to accurate diagnosis and treatment. In thyroid gland diseases, swelling in the neck, dysphagia and hoarseness are generally present. Also, there are different symptoms in diseases that will cause thyroid hormone deficiency and excess.

Among the diagnostic methods, ultrasonography (USG) is the most fundamental one. With the application of high-resolution USG devices, the assessment, with high-frequency linear probes, has become very important in thyroid gland diseases. Ultrasonic waves, which penetrate easily into the thyroid gland, can easily monitor the modifications in the gland. The fact that USG is cheap, common and easy to use makes it very important in characterization of nodules and diagnostics in case of thyroid diseases [5,11]. Moreover, ultrasonography does not have high specificity or sensitivity for including or excluding malignant nodules [10–12]. Fine needle aspiration biopsy is the next accepted step. Generally, fine needle aspiration biopsy is defined as: non-diagnostic, non-neoplastic, atypical/follicular lesions, or malignancy. Almost 20% of biopsy aspirations are non-diagnostic and the procedure requires to be repeated. That is why fine needle aspiration biopsy is not the gold standard and there are limitations in malignancy exclusion [11,13].

Lately, ultrasonographic elastography (UE) technique has become very important for radiologists who apply USG. It is done with the related software and probes to ultrasonography. UE is a method to monitor the response, elasticity and stiffness of tissue. It is cheap, easy to apply, takes short time and has no adverse effect. That is why, researchers have made hundreds of publications lately and a part of them are related to thyroid tissue [11,14–16].

In this article, our aim was to evaluate the application of UE in thyroid tissue, its limitations and correlation with pathology.

Material and Methods

A systematic literature search was conducted using PubMed and Google Scholar for "Ulatrasonographic Elastography" and "Thyroid Elastography". A total of 49 studies concerning the thyroid, thyroid disorders and thyroid elastography were included for review.

Elastography

The oldest method to assess the stiffness of tissues is examination with palpation. It has been used in medicine since ancient Egypt. Palpation is still used today in examination of the breast, thyroid, prostate and liver. Evaluating the stiffness and elasticity of organs with palpation is subjective and it is not always adequate to detect lesions in tissues and organs [14,15].

UE, which is done by sonography lately, does a qualitative or quantitative evaluation depending on the stiffness of the tissue [17,18]. The fact that elastography gives information about the stiffness of tissue provides a new dimension to sonographic diagnostics. Amongst UE methods, strain elastography is the most commonly used one [19]. Evaluating only the superficial tissue stiffness in the first few years, elastography is now used to assess almost all tissues and organs thanks to new methods [20]. of the applied UE methods vary depending on tissue effects and received data. Strain elastography, based on a compression technique, uses shear waves, which move towards the lateral aspect of tissue after its stimulation with an acoustic radiation force. Moreover, the acoustic radiation force stimulates tissues with an impulse, and Acoustic Radiation Force Impulse Imaging (ARFI) measures the speed of shear waves. Transient elastography is also used to measure the speed of shear waves [18,20].

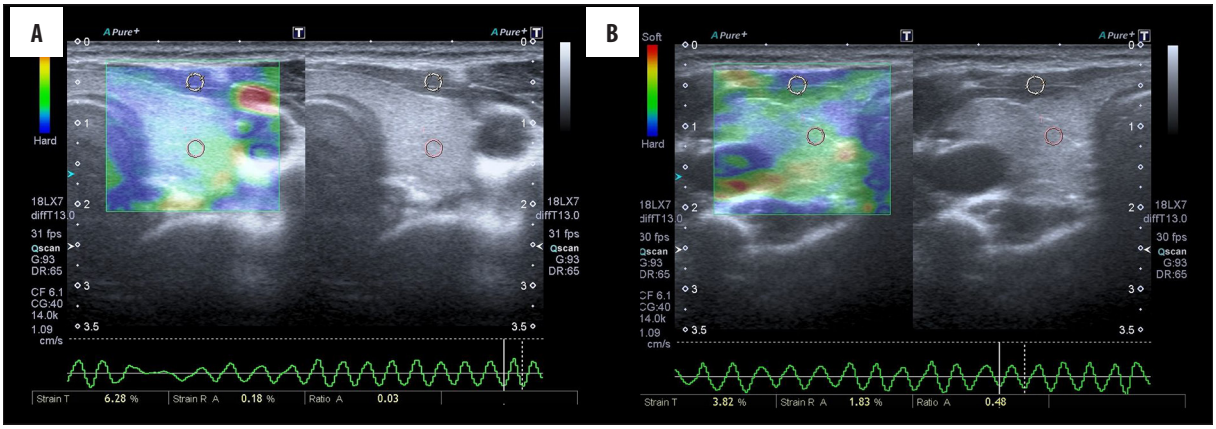
Two methods are used in thyroid tissue: strain and shear wave elastography.

Ultrasound elastography methods

Semi-static methods

Strain elastography

It is the most common UE method. In this method, compression is applied with a probe on the area. Tissue deformation and change, being a response to the applied force, are monitored. The applied force causes axial change in tissue and this is calculated by comparing the 'before' and 'after' echoes. Young's elastic module, developed by the Hooke's rule, is the tissue stiffness measurement scale. This is a ratio of the applied pressure to the measured intensity (E=pressure/intensity). Intensity is the change of shape or dimension caused by force. In this method, this is the contraction or expansion of tissue in the direction of the applied force. With real time monitoring, the movement of tissue, pressure (compression) and decompression can be watched as a B-mode on the USG monitor and as a colored elastogram. Moreover, the applied compression and decompression waves can be watched as sinusoidal waves on the ultrasonography monitor. It is preferable to measure the monitored decompression wave while measuring the strain value because in the phase of decompression wave, no external force is applied on tissues. This phase includes the process of tissue getting back to its previous state and it shows the response it gives with its own internal dynamics to the applied force. That is why, it is believed that the measurements done in the decompression phase better reflect the elasticity of tissue than in the compression phase. In this method, differences in pressure applied by hand, depth of tissue and accurate application of the probe cause differences in change rates of tissue. In general, stiff tissues are coded as blue, while soft tissues are red. Tissues with average stiffness are coded as green/yellow. In this method, elasticity measurement is qualitative or semi-quantitative [19–21].



Figures 1. (**A, B**) Elastogaphy calculation of the normal thyroid parenchyma. The left side of the windows is a color-coded elastography image and the right side is a gray-scale image. The circles indicate the ROIs where we measured the stiffness ratios. One is on the starp muscle and one is on the normal thyroid parenchyma. At the bottom of the screen, a normal sinusoidal wave can be seen. It shows that the pressure of the probe is appropriate and regular. The numbers indicates the strain values and '%' indicates the strain ratio.

Qualitative approach – teal time elastography (RTE)

In RTE, compression is applied to the area with a probe, and strain characteristics, which form as a response to the applied force, are coded on gray scale images. In general, stiff tissues are coded as blue, soft tissues are red and tissues with average stiffness are coded as green. In strain elastography, echoes, which come from the examined area during the pre-compression phase, are analyzed. In this phase, radio frequency signals, which make up the image, are stored. The same process is done after compression as well, and signals obtained in two windows are compared to determine the difference. This difference is relocation of the tissue. Then, depending on the distance from the probe, the speed of relocation differences of each point in the image is recorded as digital data. These relocation speed values obtained during the decompression and compression phase, are named as strain values and are shown in elastogram. Later, with the use of a score system, they are given points of 4–5. With the help of mechanical tools or a free-hand method, force can be applied to tissues with probe compression. The data obtained in elastography with a free hand showed no significant difference between observer values [12,20,22,23].

Semi-quantitative approach – strain ratio elastography

During the process, two regions of interest (ROI) are chosen. By putting one ROI on the area and one ROI on the reference tissue, strain ratio values are obtained [24,25]. In images obtained with strain elastography, tissues are coded as color or grey depending on strain characteristics. In general, stiff tissues are coded as red, while soft ones are blue. Tissues with average stiffness are coded as green. Strain index (SI) is the ratio of the strain value around the examined tissue to the strain value of the examined tissue. In the calculation of the strain index, an ROI is placed on the area to be compared. By measuring from the reference tissue, which is on the same alignment, the ratio of the reference ROI to the first ROI is obtained. This obtained data is called SI. Stiff tissues have a high value of SI as, in general, they can be less compressed and deformed compared to surrounding tissues. In comparison of elasticity of different lesions, the SI value is accepted as a criterion. In strain elastography, strain monitoring and measurement can be done in the whole examined area. The parameters that affect image quality are window width, probe compression speed and force (Figure 1A, 1B) [26].

In this method, probe movement must be done in one direction carefully so as to reduce image noise; palpation speed must be chosen carefully and the dimensions of elastography windows must be determined as localized to the examined area. Probe compression must be as equal gap as possible. Slow probe compression provides better image quality than fast compression. Havre et al. obtained the best data with compression rate of 0.5 per second while Doyley et al. 1.3–2 per second. To better assess the elasticity of the tissues in strain elastography, the probe and the target must be <3–4 cm. In the examination of such homogenous organs as liver, there must not be any structures that may absorb compression waves between the probe and the examined area [22, 26, 27].

Shear-wave measurement approach – the shear wave elastography (SWE)

Two- or three-dimension images can be obtained with shear wave elastography. In this method acoustic waves are sent to the tissue on the examined depth. Emission speed that forms on the tissue is measured. The detection of the movement of shear waves is realized by processing ultrasound waves in a fast way (20000 images per second). In this way, data is obtained in a few milliseconds. The shear wave elastography technique is a real-time UE method. The speed of shear waves is shown in m/sec, whereas the elasticity of the tissue is shown in kiloPascal (kPa). The elasticity of the tissue is measured with the $E=pc^2$ formula. In this formula, E is tissue elasticity, p is tissue elasticity (kg/m^3) and c is SW speed (m/sec) [28].

ARFI technique

Acoustic radiation force is related to the emission of acoustic waves [29]. In the ARFI technique, short-term (0.03–0.4 msn) acoustic pulses with high energy formed with the

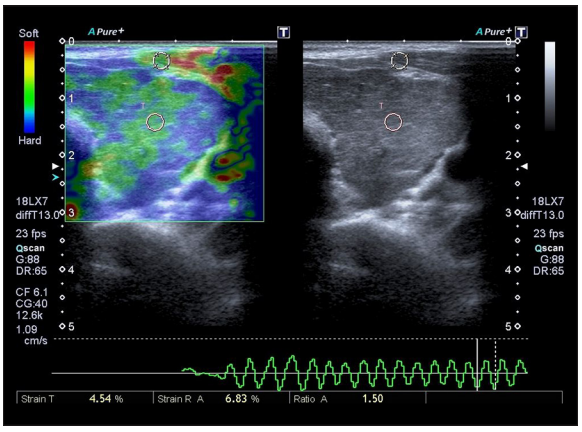


Figure 2. Elastogaphy calculation of thyroid parenchyma with Hashimoto's disease.

USG probe cause localized small relocation (1–20 um) (35). As a result of this relocation, shear waves are formed and these waves are detected with ultrasound correlation by the USG device [29,30]. With the ARFI technique, by measuring relocation in the tissues, qualitative images can be obtained without measuring the speed of shear waves. In ARFI monitoring, soft tissues are in bright colors whereas stiff tissues are darker. In the quantitative assessment, on the other hand, SW speed goes up with tissue stiffness. In the ARFI technique, the measurement of shear waves is performed in a rectangular 1×0.5-cm box. The speed of shear waves is shown in m/sec and is equal to the square root of tissue elasticity [31,32].

Transient elastography

It is also known as vibration elastography and is a kind of shear wave elastography. However, there is a device that applies vibration externally in this technique. In this method, shearing speed in the tissue is measured [19]. To differentiate precursor waves from reflecting waves in the tissue, vibration is applied on a short term. It is more likely to be used in liver examinations [19].

Discussion

Normal thyroid is soft-looking, green and homogenous in elastography. It is interpreted as score 1. Score 2 can generally be green/red/yellow and it can arise from a situation that causes parenchymal hyperplasia or tissue complication [33]. There are few articles about the normal values of thyroid parameters. There are usually normal values in articles written on a pathological basis. In literature, the strain ratio value in normal individuals has been found to be 0.76+0.55 [34]. Normal values, with the ARFI technique, were similar. A general value has been found to be approximately 2+0.40 m/s [21,35,36]. In another ARFI study, the value has been found as 1.98 m/sec [37]. In a study carried out with strain elastography, the normal value was 20.8+10.4 kPa [38].

In B-mode USG, most of the benign nodules were found as isoechogenic or hyperechogenic and hypoechogenic halo and there were different color patterns in Doppler [39,40]. As a benign nodule is softer in UE, it deforms easily. A malignant nodule, on the other hand, is harder to deform [25,41–43]. Benign thyroid nodules are 1.7 times harder than the surrounding thyroid tissue. Malignant nodules, on the other hand, are 5 times stiffer [44]. As cystic nodules and nodules with calcification will prevent technically accurate assessment, they are not taken into elastographic assessment [45,46].

In a meta-analysis conducted in 2010, quasi-static elastography recognized thyroid cancer with 92% sensitivity and 90% specificity [47]. In a study with 92 cases conducted in 2007, the sensitivity of UE was found to be 97% whereas the specificity 100%. However, it should be underscored that all cases included in the study were cytologically malignant and that the size of the nodules were big. In a study on 391 nodules, scoring with UE made a significant differentiation between thyroid nodules compared to histopathology results. In this study, the performance of score 5 in detecting malignancy was lower than of score 1 to detect benign lesions. Also, the sensitivity and specificity of UE scoring was 58.4% and 71.0%, respectively [48]. The fact that there are many studies on UE application in thyroid nodules attracts attention despite its high specificity and sensitivity. It has been reported that UE accuracy in detecting malignant thyroid nodules is suboptimal. There are cases where UE application is limited as well. As USG waves do not pass through calcifications, the method can be misleading in strongly calcified nodules. In purely cystic nodules, it is not right to apply UE as nodules neighboring bigger veins and complex nodules with cystic components have more liquid tissue elasticity [48,49]. Technically, it may not be applied on patients with conglomerate-looking multiple nodules. Although UE has more successful results in classic papillas and variant papillary cancer, there is not enough data about its application in follicular, medullary, anaplastic carcinoma, lymphoma and secondary metastasis [41,43,45,48].

There are also studies in literature where UE has been used for diffuse thyroid diseases. These are chronic autoimmune thyroiditis, Basedow-Graves' disease and multi-nodular goiter. In these diseases, it has been observed that stiffness value in elastography rises depending on the histological state of the patient [21]. In a study on Hashimoto's thyroiditis, the strain index value turned out to be 1.39+0.72 (Figure 2). It has been found considerably higher than in the average stiffness group. The value in the control group was 0.76+0.55 [34]. In the ARFI study, autoimmune thyroiditis value and Graves value were found to be 2.07+0.44 m/sec and 2.68+0.50 m/sec, respectively ($p<0.0001$) [21].

Conclusions

UE is a monitoring method that measures shape change in tissue after application of internal or external compression with conventional USG devices. It is a non-invasive method that gives information about all nodules. Like other USG methods, it is cheap, easy to access, performed in real time, non-invasive, easy to apply, it takes short time and does not contain ionising radiation. While different thyroid studies have shown that UE can be beneficial, it is a new technique. Moreover, there are some limitations. It is still far from being used primarily for the thyroid gland. However, new studies can be promising for the future.

References:

1. Güllü D, Utlu Y, Özkan H et al: Incidence of pyramidal lobe on thyroid scintigraphies. Ege Journal of Medicine, 2008; 47(3): 159–62
2. Meller J, Becker W: The continuing importance of thyroid scintigraphy in the era of high-resolution ultrasound. Eur J Nucl Med Mol Imaging, 2002; 29(Suppl.2): S425–38
3. Henry JF, Clark OH, Duh QY: Surgical anatomy and embryology of the thyroid and parathyroid glands and rekürrent and external laryngeal nerves, in Textbook of Endocrine Surgery. WB Saunders, Philadelphia, 1997
4. Kaynaroğlu ZV: Tiroid fizyolojisi ve fonksiyon testleri, in Temel Cerrahi, Sayek İ, Editor. Güneş Kitabevi: Ankara, 1996; 1523–24 [in Turkish]
5. Coşkun ZÜ, Secil M, Karagöz E: Radiologic approach to thyroid gland pathologies. Medical Journal of Okmeydanı, 2012; 28: 56–70
6. Ralls PW, Mayekawa DS, Lee KP et al: Color-flow Doppler sonography in Graves disease: "thyroid inferno". Am J Roentgenol, 1988; 150(4): 781–84
7. Loy M, Cianchetti ME, Cardia F et al: Correlation of computerized gray-scale sonographic findings with thyroid function and thyroid autoimmune activity in patients with Hashimoto's thyroiditis. J Clin Ultrasound, 2004; 32(3): 136–40
8. Cotran RS, Kumar V, Collins T, Robbins SL: Robbins pathologic basis of disease. 5th ed.: W.B Saunders Company, 2012
9. Langer JE, Khan A, Nisenbaum HL et al: Sonographic appearance of focal thyroiditis. Am J Roentgenol, 2001; 176(3): 751–54
10. Frates MC, Benson CB, Charboneau JW et al: Management of thyroid nodules detected at US: Society of Radiologists in Ultrasound consensus conference statement. Ultrasound Q, 2006; 22(4): 231–38; discussion 239–40
11. Dudea SM, Botar-Jid C: Ultrasound elastography in thyroid disease. Med Ultrason, 2015; 17(1): 74–96
12. Shuzhen C: Comparison analysis between conventional ultrasonography and ultrasound elastography of thyroid nodules. Eur J Radiol, 2012; 81(8): 1806–11
13. Mehrotra P, McQueen A, Kolla S et al: Does elastography reduce the need for thyroid FNAs? Clin Endocrinol (Oxf), 2013; 78(6): 942–49
14. Khaled W, Reichling S, Bruhns OT, Ermert H: Ultrasonic strain imaging and reconstructive elastography for biological tissue. Ultrasonics, 2006; 44(Suppl.1): e199–202
15. Luo J, Ying K, Bai J: Elasticity reconstruction for ultrasound elastography using a radial compression: an inverse approach. Ultrasonics, 2006; 44(Suppl.1): e195–98
16. Garra BS: Imaging and estimation of tissue elasticity by ultrasound. Ultrasound Q, 2007; 23(4): 255–68
17. Hall TJ: AAPM/RSNA physics tutorial for residents: topics in US: beyond the basics: elasticity imaging with US. Radiographics, 2003; 23(6): 1657–71
18. Garra BS: Elastography: current status, future prospects, and making it work for you. Ultrasound Q, 2011; 27(3): 177–86
19. Yakut İZ, Turan A, Teber MA: Ultrasound elastography for musculoskeletal applications. Selcuk Medical Journal, 2014; 30(2): 88–92
20. Onur MR, Goya C: Ultrasound elastography: Abdominal applications. Türkiye Klinikleri J Radiol-Special Topics, 2013; 6(3): 59–60
21. Cantisani V, Lodise P, Grazhdani H et al: Ultrasound elastography in the evaluation of thyroid pathology. Current status. Eur J Radiol, 2014; 83(3): 420–28
22. Havre RF, Elde E, Gilja OH et al: Freehand real-time elastography: impact of scanning parameters on image quality and *in vitro* intra- and interobserver validations. Ultrasound Med Biol, 2008; 34(10): 1638–50
23. Rubaltelli L, Corradin S, Dorigo A et al: Differential diagnosis of benign and malignant thyroid nodules at elastosonography. Ultraschall Med, 2009; 30(2): 175–79
24. Cakir B, Aydin C, Korukluoglu B et al: Diagnostic value of elastosonographically determined strain index in the differential diagnosis of benign and malignant thyroid nodules. Endocrine, 2011; 39(1): 89–98
25. Lyshchik A, Higashi T, Asato R et al: Thyroid gland tumor diagnosis at US elastography. Radiology, 2005; 237(1): 202–11
26. Bamber J, Cosgrove D, Dietrich CF et al: EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 1: Basic principles and technology. Ultraschall Med, 2013; 34(2): 169–84
27. Doyley MM, Bamber JC, Fuechsel F, Bush NL: A freehand elastographic imaging approach for clinical breast imaging: system development and performance evaluation. Ultrasound Med Biol, 2001; 27(10): 1347–57
28. Ferraioli G, Tinelli C, Zicchetti M et al: Reproducibility of real-time shear wave elastography in the evaluation of liver elasticity. Eur J Radiol, 2012; 81(11): 3102–6
29. Fahey BJ, Nelson RC, Bradway DP et al: *In vivo* visualization of abdominal malignancies with acoustic radiation force elastography. Phys Med Biol, 2008; 53(1): 279–93
30. Yu H, Wilson SR: Differentiation of benign from malignant liver masses with Acoustic Radiation Force Impulse technique. Ultrasound Q, 2011; 27(4): 217–23
31. Davies G, Koenen M: Acoustic radiation force impulse elastography in distinguishing hepatic haemangiomata from metastases: preliminary observations. Br J Radiol, 2011; 84(1006): 939–43
32. Nightingale K, McAleavey S, Trahey G: Shear-wave generation using acoustic radiation force: *In vivo* and *ex vivo* results. Ultrasound Med Biol, 2003; 29(12): 1715–23
33. Melmed S, Polonski KS, Larsen PR, Kronenberg HM: Williams texbook of endocrinology. 12th ed. Philadelphia: Sanders, 2011
34. Menzilcioglu MS, Duymus M, Gungor G et al: The value of real-time ultrasound elastography in chronic autoimmune thyroiditis. Br J Radiol, 2014; 87(1044): 20140604
35. Sporea I, Vlad M, Bota S et al: Thyroid stiffness assessment by acoustic radiation force impulse elastography (ARFI). Ultraschall Med, 2011; 32(3): 281–85
36. Sporea I, Sirli R, Bota S et al: ARFI elastography for the evaluation of diffuse thyroid gland pathology: Preliminary results. World J Radiol, 2012; 4(4): 174–78
37. Friedrich-Rust M, Romenski O, Meyer G et al: Acoustic Radiation Force Impulse-Imaging for the evaluation of the thyroid gland: A limited patient feasibility study. Ultrasonics, 2012; 52(1): 69–74
38. Veyrieres JB, Albarel F, Lombard JV et al: A threshold value in Shear Wave elastography to rule out malignant thyroid nodules: A reality? Eur J Radiol, 2012; 81(12): 3965–72
39. Reiners C, Wegscheider K, Schicha H et al: Prevalence of thyroid disorders in the working population of Germany: Ultrasonography screening in 96,278 unselected employees. Thyroid, 2004. 14(11): 926–32
40. Gharib H, Papini E, Paschke R et al: Medical guidelines for clinical practice for the diagnosis and management of thyroid nodules. Endocr Pract, 2006; 12(1): 63–102
41. Rago T, Vitti P, Chiovato L et al: Role of conventional ultrasonography and color flow-doppler sonography in predicting malignancy in 'cold' thyroid nodules. Eur J Endocrinol, 1998; 138(1): 41–46
42. Soto GD, Halperin I, Squarcia M et al: Update in thyroid imaging. The expanding world of thyroid imaging and its translation to clinical practice. Hormones (Athens), 2010; 9(4): 287–98
43. Rago T, Santini F, Scutari M et al: Elastography: New developments in ultrasound for predicting malignancy in thyroid nodules. J Clin Endocrinol Metab, 2007; 92(8): 2917–22
44. Luo S, Kim EH, Dighe M, Kim Y: Thyroid nodule classification using ultrasound elastography via linear discriminant analysis. Ultrasonics, 2011; 51(4): 425–31
45. Hong Y, Liu X, Li Z et al: Real-time ultrasound elastography in the differential diagnosis of benign and malignant thyroid nodules. J Ultrasound Med, 2009; 28(7): 861–67
46. Rago T, Vitti P: Potential value of elastosonography in the diagnosis of malignancy in thyroid nodules. Q J Nucl Med Mol Imaging, 2009; 53(5): 455–64
47. Bojunga J, Herrmann E, Meyer G et al: Real-time elastography for the differentiation of benign and malignant thyroid nodules: A meta-analysis. Thyroid, 2010; 20(10): 1145–50
48. Bender Ö, Kılıç Y, Hot S et al: Diagnostic accuracy and reliability of ultrasoundelastography in the evaluation of thyroid nodules. Okmeydanı Medical Journal, 2012; 28(3): 151–56
49. Vorlander C, Wolff J, Saalabian S et al: Real-time ultrasound elastography – a noninvasive diagnostic procedure for evaluating dominant thyroid nodules. Langenbecks Arch Surg, 2010; 395(7): 865–71