

Sonoelastography in the diagnosis of thyroid focal lesions

Elastografia w diagnostyce ultrasonograficznej zmian ogniskowych tarczycy

Maciej Ratajczak^{*1, 2}, Małgorzata Gietka-Czernel^{1, 2}

¹ Department of Endocrinology, Centre of Postgraduate Medical Education, Bielański Hospital, Warsaw, Poland

² I Department of Internal Medicine with the Diabetology and Metabolic Disorders Unit and the Endocrine Diagnostics Unit, Bielański Hospital, Warsaw, Poland

KEYWORDS:

- thyroid sonoelastography
- thyroid focal lesions

ABSTRACT

The occurrence of focal lesions in the thyroid gland affects up to 65% of the general population, and an important element of diagnostics is the most precise possible distinction between benign and malignant lesions. Despite advanced knowledge and developed algorithms, in some cases the decision to proceed further may cause problems even for an experienced clinician. A promising tool in estimating oncological risk is sonoelastography. This article aims to approximate and organize knowledge in this field in relation to focal lesions of the thyroid gland and to encourage the implementation of the method in everyday practice.

SŁOWA KLUCZOWE:

- sonoelastografia tarczycy
- zmiany ogniskowe tarczycy

STRESZCZENIE

Występowanie zmian ogniskowych w tarczycy dotyczy do 65% ogólnej populacji, a ważnym elementem diagnostyki jest możliwie najprecyzyjniejsze odróżnienie zmian łagodnych od złośliwych. Pomimo zaawansowanej wiedzy i wypracowanych algorytmów w niektórych przypadkach decyzyja o dalszym postępowaniu może sprawić kłopot nawet doświadczonemu klinicyście. Obiecującym narzędziem w szacowaniu ryzyka onkologicznego jest sonoelastografia. Niniejszy artykuł ma na celu przybliżenie i uporządkowanie wiedzy w tej dziedzinie w odniesieniu do zmian ogniskowych gruczołu tarczowego oraz zachęcenie do implementacji metody do codziennej praktyki.

Introduction

Thyroid gland diseases are one of the most common diseases occurring in patients under the care of endocrinologic clinics. It is assumed that the problem of thyroid focal lesions may affect about 65% of the general population (1). It is estimated that about 5-7% of focal lesions are thyroid cancers (2, 3). The diagnostic procedure first identifies lesions with a high risk of malignancy. For this purpose, a number of clinical and ultrasound features are evaluated (Table 1).

In the case of suspicious nodules, the next diagnostic step involves performing a fine needle aspiration biopsy (FNAB), and further treatment depends on the result of the cytological examination assessed according to the TBSRTC system (The Bethesda System for Reporting Thyroid Cytopathology) (4). Due to the high frequency and multitude of focal lesions in the thyroid gland, which are benign in 85-90% of cases, it is important to correctly type them for BACC. Therefore, based on many years of observations, algorithms and thyroid cancer risk stratification systems are created. However, they do not achieve fully

satisfactory sensitivity and specificity (from 75-95% and 17.8-56.2%, respectively) (5). Therefore, other methods are being developed to support the decision-making process. One of them is sonoelastography, based on the differentiation of malignant and benign lesions based on their hardness.

Palpation – first-line examination

Palpation has been a basic element of diagnostics since the time of ancient medicine. The limitation of palpation, which is a subjective examination, is the experience of the examiner and the availability of the examined tissue. The thyroid gland, due to its superficial location, is relatively easy to palpate. Despite this, nodular lesions are found in palpation in only 5% of the adult population (6). Small and deeply located lesions (near the posterior capsule of the gland) are difficult to palpate. The absence of nodules during palpation of the thyroid gland does not exclude the occurrence of focal lesions within the gland.

Address for correspondence: *Maciej Ratajczak, Department of Endocrinology, Center of Postgraduate Medical Education, Bielański Hospital, Ceglowska 80 Street, 01-809 Warsaw, Poland, e-mail: maciej.ratajczak@cmkp.edu.pl.

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Table 1. Clinical and ultrasound features of the increased risk of malignancy of the thyroid nodule.

| Clinical features | |
|---------------------|--|
| | appearance of a thyroid nodule before age of 20 or after 60 |
| | family history of thyroid cancer (applies to medullary and differentiated thyroid cancer) |
| | thyroid exposure to ionizing radiation before the age of 20, especially in childhood (radiotherapy, radioactive contamination) |
| | rapid growth of the nodule |
| | the hardness of the nodule and perithyroidal infiltration |
| | nodule diameter >4 cm |
| | perithyroidal or distant metastases |
| | hoarseness associated with paralysis of the vocal cord on the nodule side |
| Ultrasound features | |
| | pathological lymph nodes in the neck indicating the possibility of metastasis |
| | infiltration on the thyroid capsule and/or surrounding organs |
| | microcalcifications in the nodule |
| | solid character and hypoechogenicity of the nodule |
| | taller-than-wide shape (AP to transverse dimension >1) |
| | irregular margin |
| | central, increased, chaotic vascular flow in the nodule |

Source: compiled by the author on the basis of: Endokrynol Pol 2018; 69(1):34-74.

Thyroid ultrasonography

Ultrasound examination is a considerable support in the diagnosis of focal lesions. Since the introduction of the first ultrasound devices in the late 1960s and early 1970s, it has been constantly developed and improved. Performing an ultrasound examination allows the quantitative and qualitative assessment of the thyroid parenchyma. Due to the high sensitivity of focal lesions detection and very good quality imaging, ultrasound has become the basic imaging examination of the thyroid gland, but its possibilities of differentiating benign and malignant foci are still not satisfactory. Therefore, the high sensitivity of ultrasound does not go hand in hand with satisfactory specificity. That is why the methods of "electronic palpation" were developed already in the 1980s. Initially, m-mode and Doppler imaging were used to indirectly assess tissue coherence. Ultrasound elastography (USE) or sonoelastography in a form that allows obtaining data on tissue stiffness was first used in 1991 (7), and the first thyroid elastograms were described in 2005 (8).

Sonoelastography

Sonoelastography is a method based on tissue stiffness/hardness assessment. The essence of the test is to show differences in the cohesiveness of diseased (inflammatory or cancer) tissues in relation to healthy tissues. The division of elastographic techniques results from the applied method of obtaining tissue deformation and the way of presenting its stiffness (Fig. 1) (9).

The first division includes strain elastography (SE) and shear-wave elastography (SWE).

Strain Elastography

Strain elastography to obtain tissue deformation uses physical force: mechanical or acoustic radiation force impulse (ARFI). Mechanical force can come from the outside (free-hand compression applied by a transducer on the neck), or from inside the body (pulsation of the carotid arteries). The strength of acoustic radiation, on the other hand, uses a focused beam of ultrasound. To assess the relationship between the pressure exerted on the tissue (stress – σ) and the degree of its linear deformation (ϵ), a longitudinal elasticity coefficient (Young's modulus – E) is used, which is the quotient of these two values expressed by the formula (10):

$$E = \frac{\sigma}{\epsilon}$$

Further SE division takes into account differences in tissue stiffness presentation. The first, qualitative method, consists in assigning the selected colour (on a scale from blue, through green, yellow to red) to a certain degree of tissue strain in the target region of interest (ROI). For example, soft areas are marked in red, intermediate areas in green, and hard areas in blue (Fig. 2) although some machines may apply the color scale inversely.

The second, semi-quantitative method of assessment is based on a comparison of the examined tissue with another, considered as reference. This relationship is expressed by the strain ratio (SR). In order to measure SR for the examined ROI, a standard ROI is also established, which is the area of healthy thyroid parenchyma (parenchyma-to-nodule SR – PNSR). If it is impossible

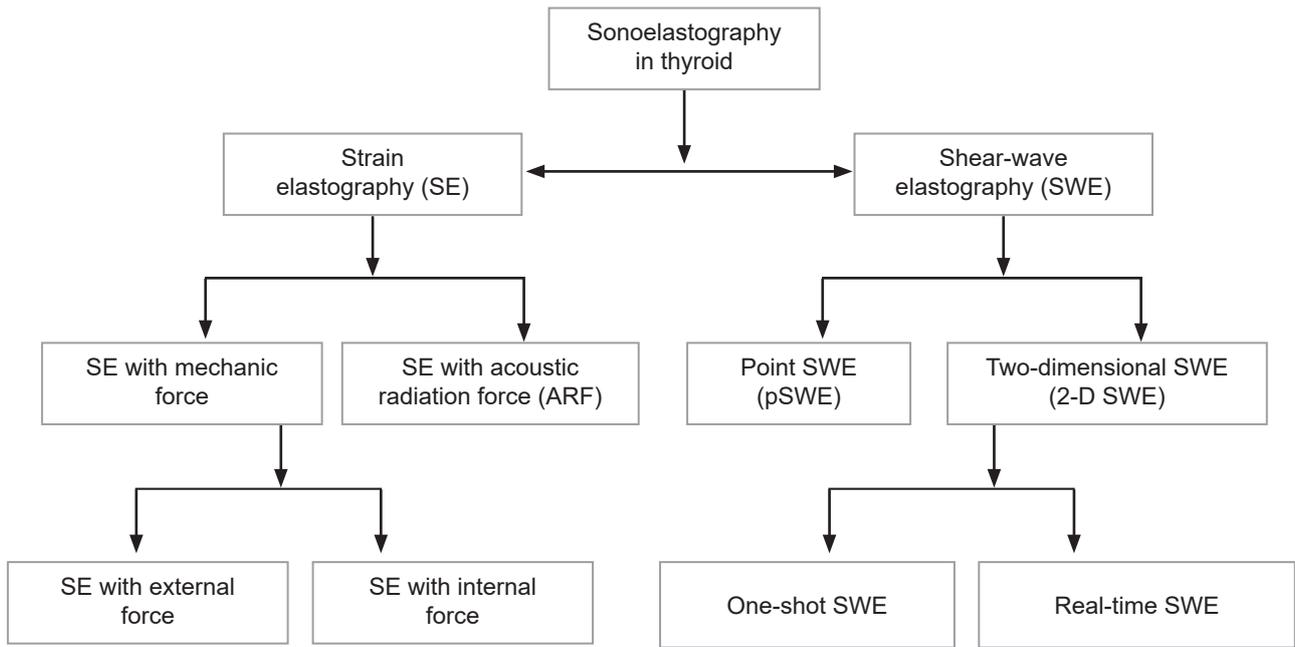


Fig. 1 Classification of thyroid elastographic techniques.

Source: Ultrasonography 2019; 38(2):106-124.

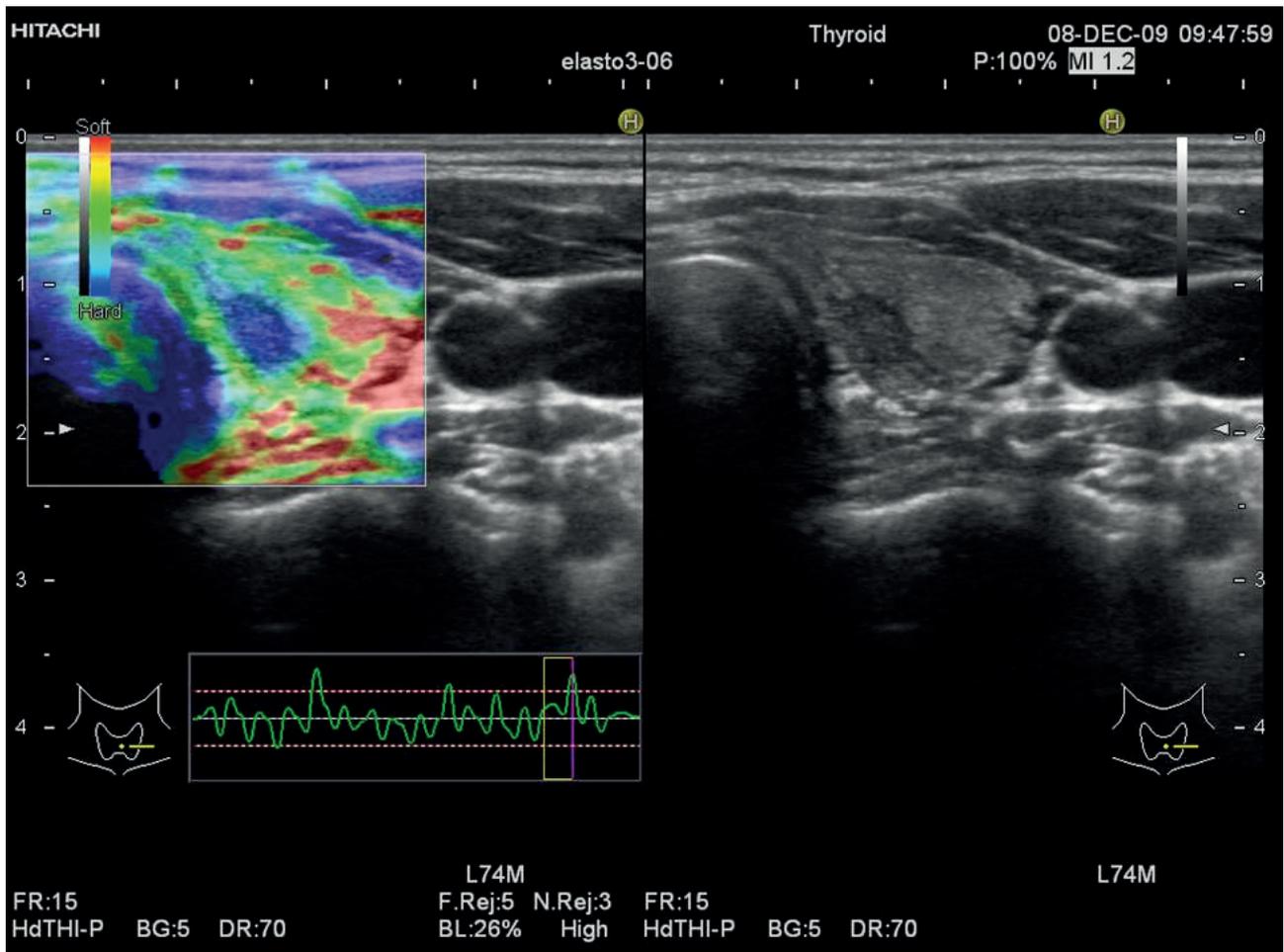


Fig. 2 Strain elastography with qualitative assessment within the ROI.

On the left, colour coding of the high-density area (blue area). Within ROI visible colour scale – red – soft tissue, green intermediate elasticity; blue – hard. Below you can see the test quality control frame – it determines the repeatability of subsequent compressions (pressure force graph over time). On the right, a classic B-mode image. The nodule has suspicious features in conventional US: solid and hypoechoic nature, irregular boundaries, AP dimension > width.

Source: own elaboration.

to compare with healthy tissue (e.g., in multinodular goitre, after radioiodine treatment or after thyroid surgery), the strain coefficient is evaluated in relation to the adjacent muscles (muscle-to-nodule SR – MNSR), most often sternocleidomastoid.

To interpret the obtained elastographic image in SE, scales based on colour patterns are used. To assess the mechanical strain using elastography, the five-stage Rago scale (Fig. 3) (11) and the four-stage Asteria scale (12) are used (Fig. 4).

The increased risk of malignant lesion according to Rago is 4th and 5th grade, according to the Asteria scale 3 and 4. For elastograms obtained using ARFI, a six-grade scale developed by Xu et al. is used (13). (Fig. 5.)

Stress changes are presented in grayscale, where the lighter areas correspond to relatively more elastic (more deformed) tissue, while the darker ones are to harder (or less deformable) tissue – which means that the darker the area, the harder the area. On this scale, grades 4, 5 and 6 correspond to an increased risk of malignant lesion.

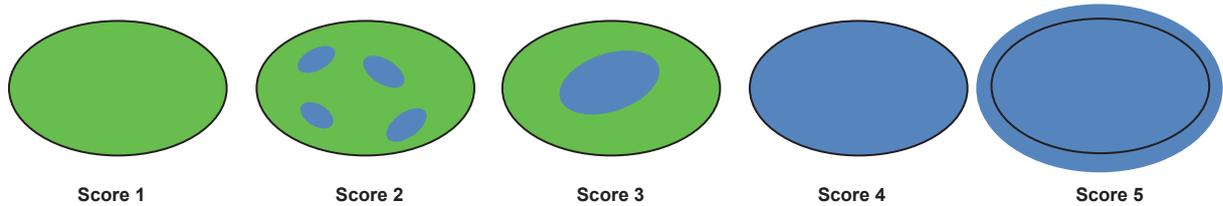


Fig. 3 The five-point Rago's scale for strain elastography of thyroid nodules.

The green area corresponds to the tissue with retained elasticity (deformable), and the blue tissue to the less degree of strain (harder).
Score: 1 – elasticity uniformly preserved throughout the entire focal length; 2 – flexibility preserved within a significant part of the lesion; 3 – flexibility preserved in the marginal part of the lesion; 4 – lack of flexibility within the lesion; 5 – lack of flexibility within the lesion and surrounding tissues.
 Source: Clin Endocrinol Metab 2007; 92:2917-2922.

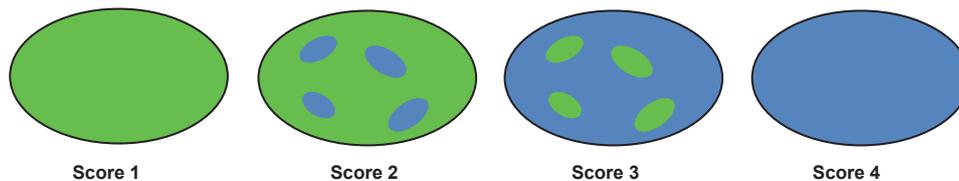


Fig. 4 The four-point Asteria's scale for strain elastography of thyroid nodules.

The green area corresponds to the tissue with retained elasticity (deformable), and the blue tissue to the less degree of strain (harder).
Score: 1 – elasticity uniformly preserved throughout the entire focal length being studied; 2 – flexibility preserved within a significant part of the lesion; 3 – lack of flexibility within a significant part of the lesion; 4 – lack of flexibility within the lesion.
 Source: Thyroid 2008; 18:523-531.

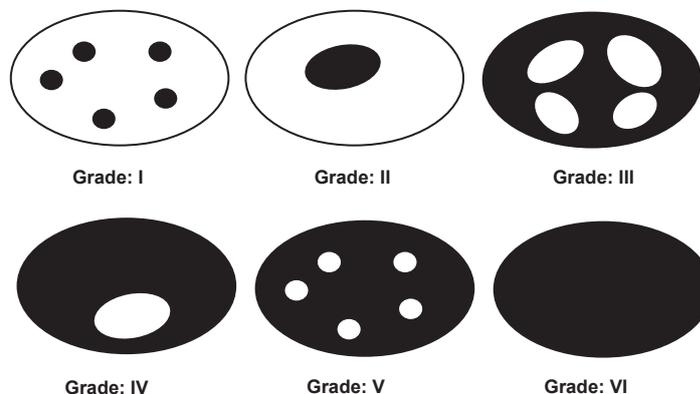


Fig. 5 The six-point scale used in the assessment of strain elastography using the force of acoustic radiation.

The white areas correspond to the tissue with retained elasticity (deformable), and the black areas to the non-deformable tissue (harder).
Grade: I – elasticity preserved in most of the lesion with individual small hard areas; II – elasticity preserved in the most part of the lesion with a small central hard area; III – tissue area with preserved elasticity and hard comparable; IV – lack of tissue elasticity within almost the entire lesion with a small area of tissue with preserved elasticity; V – lack of tissue elasticity within almost the entire lesion with individual small areas with preserved elasticity; VI – lack of elasticity within the lesion.
 Source: Radiology 2014; 272:577-586.

Shear-wave elastography

In the technique of shear-wave elastography (SWE) to generate transverse waves, the aforementioned method of acoustic force – ARFI – is used. Acoustic pulses sent perpendicularly by the transducer (the acoustic wave moves at a speed of 1450-2660 m/s) are absorbed by tissues, and the resulting movement of particles generates relatively slowly (1-10 m/s) moving transverse waves which speed is then recorded. This value is closely related to the Young's modulus value and tissue deflection can be calculated. The results are presented as a coloured scale (as in SE) or quantitatively: in kilopascals (KPa) or meters per second (m/s). A higher value indicates greater cohesion of the examined tissue. The technique using shear-waves is divided into point (pSWE) and two-dimensional (2-D SWE).

In the pSWE method, a shear-wave is generated in a single location, tissue elasticity is expressed in meters/second, without creating a color-coded image.

In the 2-D SWE method, the SW speed is measured inside the ROI. This method is divided into SWE single measurement (one-shot SWE) and real-time SWE (real-time SWE).

In one-shot SWE, as a result of a single "shot", a color-coded image of the change is created, in which the transverse wave velocity at all points is marked with the appropriate color. Inside such ROI it is possible to assess the SW speed at specific points (Fig. 6).

Each time after the measurement the probe requires time to cool down before the next measurement is possible. In addition, it is possible to obtain a quality map of the measurement that allows you to assess the reliability of the test.

Real-time SWE allows the testing person to observe the density of examined tissues on an ongoing basis. The measurement result is presented in the form coded with the map color and the average and maximum tissue density inside ROI are given. It can be presented both in meters per second and in kilopascals.

Limitations of sonoelastography

Due to the techniques used, SE and SWE differ in methodological limitations. For both techniques, the common factor is the experience and skills of the testing person (too much force or unevenly distributed pressure of the probe may be the reason for errors). Therefore, there are tools used to control pressure and repeatability of subsequent compressions of the head. An additional frame visible on the screen of the camera informs the testing person about the quality of the test (SE) or it is possible to obtain a quality map of shear wave propagation (SWE). SE is more operator dependent than SWE – depends on the angle, strength, and duration of compression.

Limitation for the elastography implementation are costs. To perform SWE there is need to get a special probe that allows to generate acoustic pulses.

For both methods the quality of the image is excellent, but for SE only if it is properly performed. In SWE maximum depth of imaging is limited (typically 6 cm), while in SE it is unlimited, depends on force (kind and/or strength) and displacement applied.

In the case of SE, the assessment of tissue stiffness as a deflection factor is limited, especially in the case of multinodular goitre or coexistence of chronic lymphocytic thyroiditis. In addition, SE is unreliable in the case of follicular cancers and lesions having the following characteristics: large size, predominantly fluid component, presence of macrocalcifications, localization within the isthmus. SE is better in assessment for focal lesions than diffuse disease, while SWE is better for diffuse lesions than focal ones.

SWE is less dependent on the operator than SE, it is reproducible and allows for quantitative and qualitative assessment of thyroid gland tissue.

The role of SWE in prediction of malignancy among lesions of indeterminate cytology in FNAB (categories 3-5 in TBSRTC) is uncertain. The incidence, risk of malignancy, and clinical significance differs among each category and there is need for further studies to evaluate the value of US

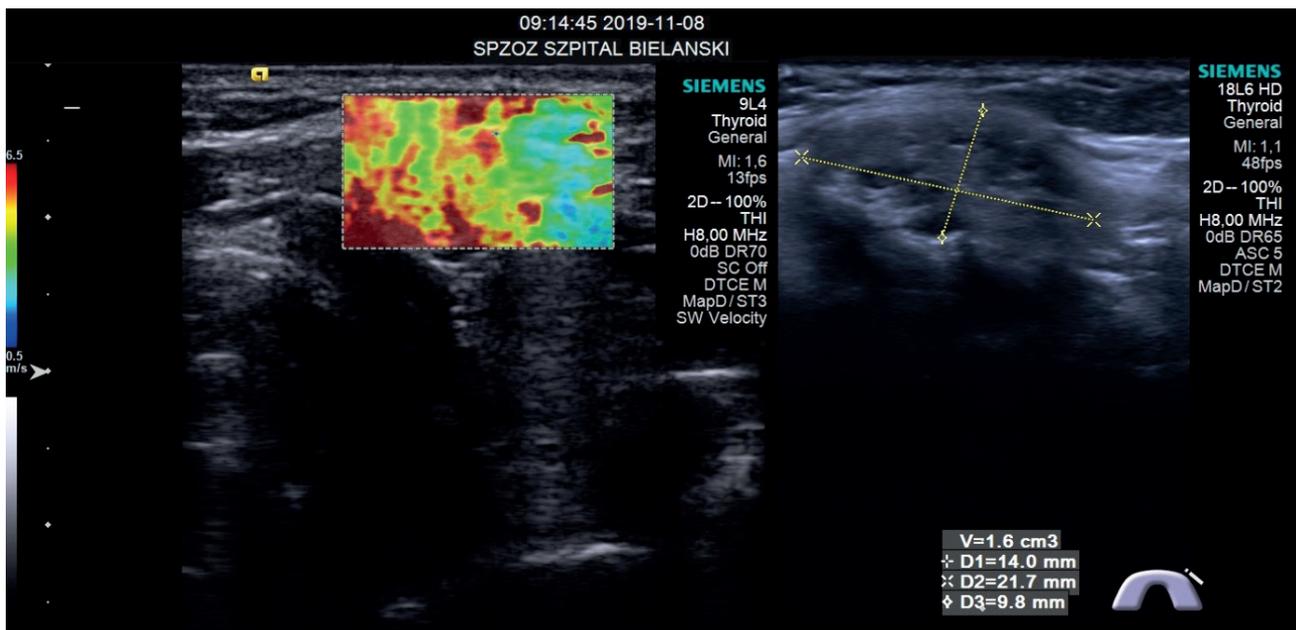


Fig. 6 Shear-wave elastography with quantitative assessment within the ROI.

On the left there is the shear-wave velocity map – tissue with higher velocity is harder (coded as red), tissue with lower velocity is softer (coded as blue). It is possible to measure velocity in specific point within ROI. On the right, a classic B-mode image.

Source: own elaboration.

elastography in each of them. It is important to note there is the lack of a typical "stiff" elastographic image in the case of follicular thyroid cancer. Taking into account the fact that also in 2D examination this type of cancer often does not show typical ultrasound features of malignancy, it is still a big diagnostic problem.

Some recent studies prove, that medullary thyroid carcinomas (MTC) are lesions stiffer than the surrounding tissues and SWE can be helpful to evaluate risk of malignancy even in small lesions, but usefulness of this technique still need to be evaluated.

The use of sonoelastography in the light of current guidelines

One of the first recommendations recognizing sonoelastography as a tool to assist in preoperative thyroid cancer risk assessment was included in the 2015 American Thyroid Association (ATA) guidelines. (14). Published a year later, the guidelines of the American Association of Clinical Endocrinologists (AACE), American College of Endocrinology (ACE) and Associazione Medici Endocrinologi (AME) (15) stated that elastography is complementary to conventional ultrasound, especially in the case of lesions that in cytological tests are indeterminate or suspicious (cytological group III, IV and V according to the Bethesda system). In 2017 The World Federation for Ultrasound in Medicine and Biology (WFSUMB) has developed guidelines for the use of elastographic techniques for the thyroid gland (16). They contain recommendations for the use and limitations of individual techniques with presentation of the level of evidence (LoE) and grade of recommendation (GoR).

In the recommendations of the Polish Scientific Societies regarding the diagnosis and treatment of thyroid cancer in the 2018 update it has been stated that although elastographic assessment is not obligatory when assessing thyroid focal changes, it may support the best possible choice of FNAB performing (17).

Summary

Ultrasound examination is very sensitive for detecting and good for characterizing thyroid nodules, but neither single ultrasound feature nor combination of them can reliably predict malignancy. Ultrasound elastography can be used as an extension of conventional ultrasound but not as an independent test. Ultrasound examination combined with elastography showed higher sensitivity than conventional ultrasound alone.

The assessment of the elasticity of thyroid focal lesions can be relatively easily used as a supplement to conventional ultrasound examination. Although this is associated with a slight extension of the duration of testing, the benefits of the data received, with their skilful interpretation, seem to support its implementation.

Elastography is a painless, safe procedure and does not require additional patient preparation. Awareness of the limitations of the method allows proper interpretation of the test results. Thanks to sensitivity (up to 87.5%) and specificity (up to 95%) it significantly expands the range of tools for differentiating benign and malignant lesions. Its basic value lies in the better typing of focal lesions for FNAB. It provides support in making therapeutic decisions regarding observation or surgery in the case of non-diagnostic or indeterminate results of cytological examination.

Elastography is a constantly improved and developing technique, it requires further validation and standardization. Past experience encourages the implementation of sonoelastography in everyday clinical practice.

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