

Evaluation of the effectiveness of real-time elastography in the differential diagnosis of benign and malignant thyroid nodules

Tiroid nodüllerinin benign ve malign ayırıcı tanısında gerçek zamanlı elastografinin etkinliğinin araştırılması

Lale Tuna¹  Gülğün Kavukçu¹  İlhan Hekimsoy¹  Özer Makay² 
Yeşim Ertan³  Sadık Tamsel¹ 

¹ Ege University Faculty of Medicine, Department of Radiology, Izmir, Türkiye

² Ege University Faculty of Medicine, Department of General Surgery, Division of Endocrine Surgery, Izmir, Türkiye

³ Ege University Faculty of Medicine, Department of Medical Pathology, Izmir, Türkiye

ABSTRACT

Aim: The aim of this study was to evaluate the efficiency of real-time elastography (RTE) in the differential diagnosis of thyroid nodules.

Materials and Methods: Fifty-two patients with 60 thyroid nodules were included in this study. Real-time elastography examinations were performed on the axial and longitudinal planes. Elastography images were classified between score 1 (whole nodule is soft) and score 5 (hardness in whole nodule and surrounding tissues). Nodules with scores of 1, 2 and 3 were considered benign, and nodules with scores of 4 and 5 were considered malignant. Nodule-to-sternocleidomastoid and thyroid tissue-to-nodule strain ratios (SR) were calculated. The nodules were evaluated by means of size, echogenicity, border, presence of halo and micro calcifications. Elasticity scores and mean strain ratios of all nodules were compared with the cytological or histopathological diagnosis.

Results: Forty-three of all cases were benign, and seventeen were malignant. Hypoechoogenicity, micro calcifications and absence of halo were statistically related but irregular margins, and a high elasticity score were not statistically related to malignancy. The diagnostic performance of strain ratio was found insignificant. Nodule echogenicity had the highest accuracy among all nodule characteristics.

Conclusion: Diagnostic performance of real-time elastography in the differentiation of benign and malignant thyroid nodules is suboptimal. Real-time elastography is not an alternative to gray scale ultrasound.

Keywords: Ultrasonography, elastography, thyroid, nodule, thyroid cancer.

ÖZ

Amaç: Çalışmamızın amacı tiroid nodüllerinin benign-malign ayırıcı tanısında gerçek zamanlı elastografinin (GZE) etkinliğinin araştırılmasıdır.

Gereç ve Yöntem: Araştırmaya 52 olgudaki 60 tiroid nodülü dahil edildi. Nodüller boyut, ekojenite, kontur özellikleri, halo ve mikrokalsifikasyon varlığı açısından değerlendirildi. Aksiyel ve longitudinal planlarda gerçek zamanlı elastografi incelemeleri gerçekleştirildi. Elastografi görüntüleri skor 1 (nodülün tamamı yumuşak) ile skor 5 arasında (nodülün tamamı ve çevre dokularda sertlik) sınıflandırıldı. Skor 1, 2 ve 3 nodüller benign, skor 4 ve 5 olan nodüller malign olarak kabul edildi. Nodül/sternokleidomastoid kası ve tiroid dokusu/nodül gerinim oranları hesaplandı. Tüm nodüllerin elastografi skorları ve ortalama gerinim oranları sitolojik ve histopatolojik tanı ile karşılaştırıldı.

Corresponding author: Lale Tuna
Ege University Faculty of Medicine, Department of Radiology,
Izmir, Türkiye
E-mail: tuna.lale@yahoo.com
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Bulgular: Tüm olguların 43'ü benign, 17'si maligndi. Malignite tanısında nodül ekojenitesi doğruluğu en yüksek olan özellikti. Hipoekojenite, mikrokalsifikasyon ve halo yokluğu ile malignite arasında istatistiksel olarak anlamlı ilişki saptandı. Yüksek elastisite skoru ile malignite arasında istatistiksel anlamlı ilişki saptanmadı. Gerinim oranının diagnostik ROC eğrisi analizi önemsiz bulundu.

Sonuç: Tiroid nodüllerinin benign-malign ayırımında gerçek zamanlı elastografinin tanısıl performansı suboptimaldir. Gerçek zamanlı elastografi gri skala ultrasona alternatif olabilecek bir yöntem değildir.

Anahtar Sözcükler: Ultrasonografi, elastografi, tiroid, nodül, tiroid kanseri.

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INTRODUCTION

Thyroid nodules are common lesions that are clinically difficult to diagnose (1). While nodules are detected in 19-67% of the population by ultrasonography, only 5-15% of these nodules are malignant (2). While ultrasonography is a highly sensitive examination in detecting thyroid nodules, its sensitivity and specificity are not sufficient in distinguishing benign from malignant nodules. Fine needle aspiration biopsy (FNAB) used for this purpose is an invasive procedure and causes additional cost and patient stress. There is a need for a diagnostic method that will reduce these invasive procedures.

Elastography is a technique that aims to reveal the elasticity of tissues by using sound waves with a computer software and appropriate hardware. The basic principle in sonoelastography technique is that soft tissues are easier to deform with compression than harder ones. The amount of displacement in different tissues is determined by the displacement of the ultrasound signals reflected from the tissues before and after compression. Accordingly, the strain degree of the tissue is determined in relation to the amount of displacement (3). With the method used in superficial tissues where sound waves can reach, solid pathologies that tend to be less elastic and rigid compared to normal tissues can be shown, and differential diagnosis can be made, especially between benign and malignant ones. Like other US methods, it is inexpensive, easily accessible, real-time, does not contain ionizing radiation, and is noninvasive. The aim of this study was to investigate the effectiveness of real-time elastography technique in revealing malign or benign etiology in nodular growths of the thyroid.

MATERIALS and METHODS

This study was approved by the Ege University Faculty of Medicine Ethical Committee with the protocol number 13-1.1/6. Written informed

consent was obtained from the volunteers. The study was conducted according to the latest form of the Declaration of Helsinki.

A total of 83 thyroid nodules in 70 patients who were admitted to the Ege University Hospital "Endocrine surgery" outpatient clinic and were scheduled for thyroidectomy or referred to the Department of Radiology for fine needle aspiration biopsy of thyroid nodules were prospectively evaluated. The cases were selected according to the criteria specified in Table-1. Thirteen nodules whose cytology or histopathology results could not be reached, and 10 nodules with biopsy results reported as suspicious for malignancy or non-diagnostic and did not undergo thyroidectomy were excluded from the study. The data of 60 nodules in 52 cases were evaluated.

Table-1. Inclusion and exclusion criteria for thyroid nodules.

Recruitment criteria:	Exclusion criteria:
Being between the ages of 19-80	Cases that cannot stand still
At least one solid nodule in the thyroid gland	Cases under the age of 19
Volunteer acceptance to participate in the study	Solid nodules larger than 4 cm in diameter
	Cystic or hemorrhagic nodules
	Nodules containing "eggshell" calcification
	Cases treated with radiotherapy to the neck region
	Cases who had previously undergone thyroid surgery
	Those with severe cardiovascular or lung diseases

Cases with histopathology results or cases with negative or positive results for malignancy after FNAB were included in the study. Nodules with a benign cytology that had no histopathology results were included in the study only if they had no increase in size in the US follow-up for at least six months.

All cases were evaluated in the supine position using an ultrasonography device with real-time strain elastography software (Acuson S2000, Siemens, Erlangen, Germany) and a 4-9 MHz high resolution linear probe. All thyroid nodules were evaluated for size, echogenicity, contours, presence of halo and micro calcifications by real-time B-mode. US images were recorded digitally. Then, real-time elastography images were obtained with the same probe by switching to elastography mode.

Real-time elastography

Elastography examinations were performed by a radiology resident (LT) with four- years of experience in thyroid ultrasonography, in both axial and longitudinal planes with the head slightly extended and in a neutral position. During the examination, light and constant pressure was applied with the probe perpendicular to the thyroid. During real-time examination, the B-mode US and elastogram images of the area evaluated could be viewed side by side in two separate windows on the screen. Images displayed on the screen with a quality factor of 60 and above, indicating that the press is sufficient, were deemed eligible for evaluation. Three elastogram images in axial and longitudinal planes were then digitally recorded to evaluate the elastography score. After the elastograms were obtained, the strain values of the nodule and adjacent normal thyroid tissue were measured numerically with the help of the ROI on the static elastography image in the longitudinal plane and were automatically proportioned by the device. The strain ratio (strain ratio, strain index, SR, SI) obtained by dividing the strain of normal thyroid tissue by the strain of the nodule was measured and recorded three times for each nodule. The sizes of the region of interest (ROI) for nodule and normal tissue were adjusted to be similar. Care was taken to ensure that both measurements were of approximately equal depth (Figure-1). In the axial examination, the strain values of the nodule and the ipsilateral sternocleidomastoid (SCM) muscle were measured numerically with the help of ROI and

were automatically proportioned by the device. The ratio obtained by dividing the strain value of the nodule by the SCM muscle strain was measured and recorded three times for each nodule. The demographic information of the cases was recorded, as well as images.

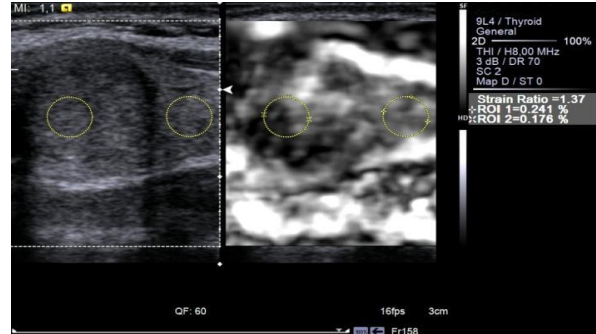


Figure-1. Calculation of strain ratio on static elastography image in the longitudinal plane.

To evaluate the elasticity of thyroid nodules, elasticity scores were determined by using current literature information on the subject (4-12). Table-2. Elasticity scoring

Table-2. Elasticity scoring.

Elastography Score	Definition
1	There is no dark"red" coded area in the drawn area
2	There is a small amount of dark"red" coded areas in the drawn area
3	The ratio of the dark"red" coded area to the whole nodule area in the drawn area is between 30% - 70%
4	Area with code "red" in the drawn area > 70%
5	Dark"red" coding across the entire drawn area + overflow to surrounding soft tissues

The elastography images in the axial and longitudinal planes were evaluated by two physicians (GK and LT), who were unaware of each other and did not know the histopathological diagnoses, in order to determine the consistency between the observers ("inter-observer") in an unbiased and blind way. Scoring was done for the images in both planes. The highest score was recorded among three elastography images of each nodule. The cases graded differently by the two observers were re-evaluated together and a

consensus was reached. Subsequently, the cases were classified as malignant or benign according to their elastography score. Elastography score 1, 2, and 3 nodules were classified as benign, and elastography score 4, and 5 nodules as malignant. These diagnoses were compared with the final histopathological diagnoses in 35 nodules, and cytological diagnoses in 25 nodules, and statistical analysis of the elastography ratings in the axial and longitudinal planes and their performances in characterization were performed.

Statistical analysis

Statistical analysis was performed by an expert faculty member of Ege University, Department of Biostatistics and Medical Informatics, using the SPSS 20.0 for Windows® program. In order to examine the diagnostic performance of each examination method; ROC curve analysis was performed and sensitivity, specificity, positive and negative predictive and accuracy values were calculated. Inter-observer agreement was evaluated using the "Weighted Kappa" test. The inter-observer statistical significance level was accepted as 0.05.

RESULTS

Of the 52 cases included in the study, 12 (23.1%) were male and 40 (76.9%) were female, with a mean age of 46.4. The largest sizes of the nodules varied between 7-40 mm (average 20 mm).

Forty-three (71.7%) of 60 nodules were benign and 17 (28.3%) were malignant.

Twenty-five (58.1%) of benign nodules were diagnosed by FNAB and US follow-up for at least six months, and 18 by histopathological examination. Of the 18 nodules diagnosed histopathologically, 15 (34.8%) were reported as hyperplastic (colloid) nodules, and 3 (6.9%) were reported as nodules developing on the basis of thyroiditis.

All malignant nodules were diagnosed by histopathological examination. Of the 17 malignant nodules, 14 (82.3%) were papillary cancers (seven classic type, three follicular variant, three papillary micro carcinoma and one oncocytic variant), two (11.7%) were medullary carcinomas and one (5.8%) nodule was follicular carcinoma.

B-mode ultrasonography findings

Benign thyroid nodules ranged in size between 0.9-4.0 cm (mean 2.0 cm). The size of malignant

thyroid nodules varied between 0.7-3.7 cm (mean 1.8 cm).

Thirty-seven of the nodules were isoechoic, 20 were hypoechoic, and three were hyperechoic. While 13.5% of isoechoic nodules were malignant, 60% of hypoechoic nodules were malignant. All of the hyperechoic nodules were benign. When the nodules were divided into two groups as hypoechoic and iso-hyperechoic in terms of their echogenicity, there was a significant difference between the two groups in terms of malignancy risk ($p < 0.001$). Sensitivity, specificity, positive and negative predictive value, and accuracy of hypo-echogenicity for malignancy were calculated as 70.6%, 81.4%, 60%, 87.5%, and 78.3%, respectively.

Forty-four nodules had a prominent and smooth contour. The borders of 16 nodules were irregular. Twenty-five percent of those with smooth contours and 37.5% of those with irregular contours were malignant. No statistically significant correlation was found between the irregular contour finding and malignancy ($p=0.35$). When nodules were divided into two groups as smooth and irregular contours according to their contour features; the sensitivity, specificity, positive and negative predictive value and accuracy of the irregular contour for malignancy were 35.3%, 76.7%, 37.5%, 75%, and 65% respectively.

Peripheral halo was observed in 45 of the nodules. While 18% of nodules with halo were malignant, 60% of nodules without halo were malignant. A statistically significant difference was found between nodules with and without halos in terms of malignancy ($p=0.003$). When nodules were divided into two groups according to the absence of halo, the sensitivity, specificity, positive and negative predictive value, and accuracy of absence of halo for malignancy were calculated as 52.9%, 86%, 60%, 82.2%, and 76.7%, respectively.

Micro calcification was observed in 17 nodules. While nine of these (53%) were malignant, eight (19%) of 43 nodules without micro calcification were malignant. A statistically significant relationship was found between the presence of micro calcification and malignancy ($p=0.012$). When nodules were divided into two groups according to the presence of micro calcification, the sensitivity, specificity, positive and negative predictive value and accuracy of micro calcification for malignancy were calculated as

52.9%, 81.3%, 52.9%, 81.3%, and 73.3% respectively.

Real-time elastography findings

Since the highest score was recorded among three elastography images taken from each nodule, no nodule was scored as 1 in both transverse, and longitudinal images.

Elastograms of appropriate quality (QF≥60) in the transverse plane could not be obtained in four cases. The distribution of scores in 56 nodules evaluated in the transverse plane is shown in Table-3.

The distribution of thyroid nodules according to elastography scores in the longitudinal plane is presented in Table-4.

In determining the elastography scores, the "inter-observer" agreement strength between the observers was "moderate" for transverse images ($\kappa = 0.597$), and "very good" ($k = 0.867$) for longitudinal evaluation, and was calculated as 84% and 93%, respectively.

Nodules with elastography score 1, 2, and 3 were accepted as benign, and score 4, and 5 as malignant.

A statistically significant difference was investigated for malignancy between score 1-3, and score 4-5. There was no statistically

significant correlation between US elastography scores obtained in transverse and longitudinal planes and malignancy ($p=0.75$, $p=0.083$). The sensitivity, specificity, positive and negative predictive value, and accuracy value in distinguishing benign and malignant thyroid nodules of scoring in transverse images on US elastography were calculated as 75%, 32.5%, 30.8%, 76.5%, 44.6% respectively. Sensitivity, specificity, positive and negative predictive value, and accuracy of scoring in longitudinal images in distinguishing benign and malignant thyroid nodules were calculated as 64.7%, 62.8%, 40.7%, 81.8%, 63.3% respectively.

The diagnostic value of the Nodule / SCM strain ratio values in distinguishing malignant nodules from benign nodules was found to be insignificant by ROC curve analysis ($p=0.517$). Similarly, for thyroid / nodule strain ratio, ROC curve analysis of both the mean ($p=0.293$) and the maximum ($p=0.201$) value of three measurements were found to be insignificant. The strain indices of benign and malignant nodules overlapped, and a threshold value for differentiation could not be determined (Table-5).

Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy value according to all parameters studied are presented in Table-6.

Table-3. Distribution of thyroid nodules according to elastography scores obtained in the transverse plane.

Elastography score	Benign	Malignant	Total
1	0 (0%)	0 (0%)	0 (0%)
2	5 (100%)	0 (0%)	5 (8.9%)
3	8 (66.7%)	4 (33.3%)	12 (21.4%)
4	27 (73%)	10 (27%)	37 (66.1%)
5	0 (0%)	2 (100%)	2 (3.6%)
Total	40 (71.4%)	16 (28.6%)	56 (100%)

Table-4. Distribution of thyroid nodules according to elastography scores obtained in the longitudinal plane.

Elastography score	Benign	Malignant	Total
1	0 (0%)	0 (0%)	0 (0%)
2	12 (92.3%)	1 (7.7%)	13 (21.7%)
3	15 (75%)	5 (25%)	20 (33.3%)
4	15 (65.2%)	8 (34.8%)	23 (38.3%)
5	1 (25%)	3 (75%)	4 (6.7%)
Total	43 (71.7%)	17 (28.3%)	60 (100%)

Table-5. Mean values of strain index in benign and malignant nodules.

Strain Ratio	Benign	Malignant	P value
SR Nodule / SCM Average	1.19±1.30	1.07±1.10	0.517
SR Thyroid / nodule Average	1.69±0.88	2.35±1.57	0.293
SR Thyroid / nodule Maximum	2.23±1.18	3.34±2.63	0.201

SR: Strain Ratio, SCM: sternocleidomastoid muscle

Table-6. Sensitivity, specificity, positive and negative prediction and accuracy values according to the different parameters investigated.

Variables	Sensitivity	Specificity	PPV	NPV	Accuracy
Echogenicity	70.6%	81.4%	60%	87.5%	78.3%
Contour feature	35.3%	76.7%	37.5%	75%	65%
Absence of halo	52.9%	86%	60%	82.2%	76.7%
Micro calcification	52.9%	81.3%	52.9%	81.3%	73.3%
Elastography:					
TRANSVERSE	75%	32.5%	30.8%	76.5%	44.6%
LONGITUDINAL	64.7%	62.8%	40.7%	81.8%	63.3%

NPV: Negative predictive value, PPV: Positive predictive value

DISCUSSION

According to the results of this prospective cohort, diagnostic performance of B-mode ultrasonography was superior to qualitative and semi-quantitative real-time elastography in the differentiation of benign-malignant thyroid nodules. The most statistically significant finding among both grey scale findings and elastography findings was found to be 'hypo-echogenicity'. The sensitivity of this finding was consistent with the literature (9, 12-15). The sensitivity of contour irregularity and absence of halo for malignancy was 35.3% and 52.9%, respectively, and were found to be lower than in the literature. This can be explained by the histopathological subtypes of malignant nodules in our study (16-18). Oncocytic and follicular variants of papillary carcinoma and follicular carcinoma, which make up five of 17 malignant nodules in our study, tend to be well-circumscribed and to have a halo (Figure-2, 3, 4). The sensitivity of the presence of micro calcification for malignancy was 52.9%, and it was found to be lower than the literature (13-15, 19-21). This result can be explained by the proportional excess (41%) of follicular carcinoma or papillary carcinoma follicular variant and oncocytic variant subtypes in our malignant cases, in which micro calcification is observed less frequently than papillary carcinoma.

In real-time elastography studies evaluating thyroid nodules, multivariate sensitivity and specificity values are reported in the differentiation of malignant thyroid nodules from benign ones. This may be due to different patient selection criteria and the use of different scoring systems for qualitative assessment. The prevalence of malignant nodules in studies varies according to patient selection criteria. The highest sensitivity and specificity values observed in the literature were reported by Rago et al. (Sensitivity 97% and specificity 100%) (6). In recent studies, sensitivity and specificity values are not reported as high as in previous years. In general, these values decrease as the number of cases increases.

In our study, the sensitivity and specificity of RTE examination in the evaluation of malignancy were found to be lower than the literature in previous years. In our study, three color map images were archived in each case. There were score differences between the elastograms recorded by the same practitioner. When there was a difference in score between the three images, the highest score was accepted. The highest score may not reflect the true elasticity of the nodule. Excessive compression on the nodule can lead to deterioration of the linear relationship between compression and strain and the tissue to be perceived as harder than it is (8).



Figure-2. Fifty seven-years-old female. Ultrasound elastography images A. Transverse plane. B. Longitudinal plane. The nodule was evaluated as score 3 in both planes. Postoperative histopathology result was papillary ca oncocytic variant.

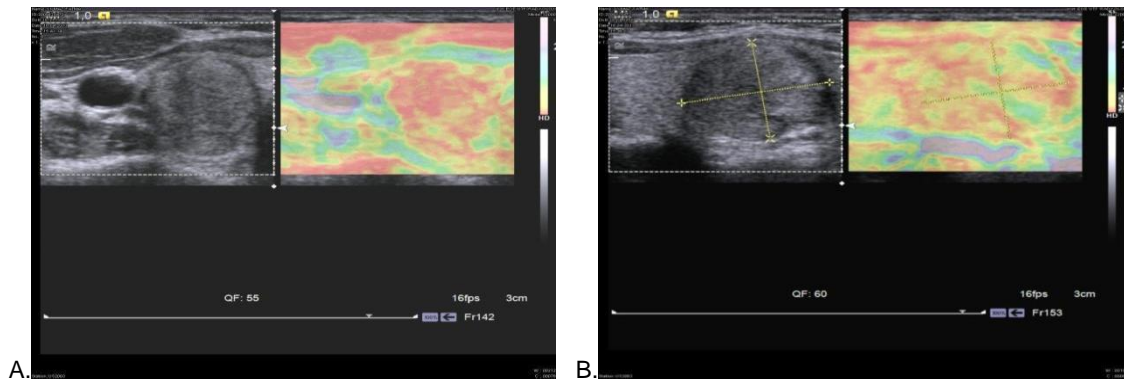


Figure-3. Thirty one-years-old female. Ultrasound elastography images A. Transverse plane B. Longitudinal plane. The nodule was evaluated as score 4 in both planes. Postoperative histopathology result was papillary ca macro follicular variant.

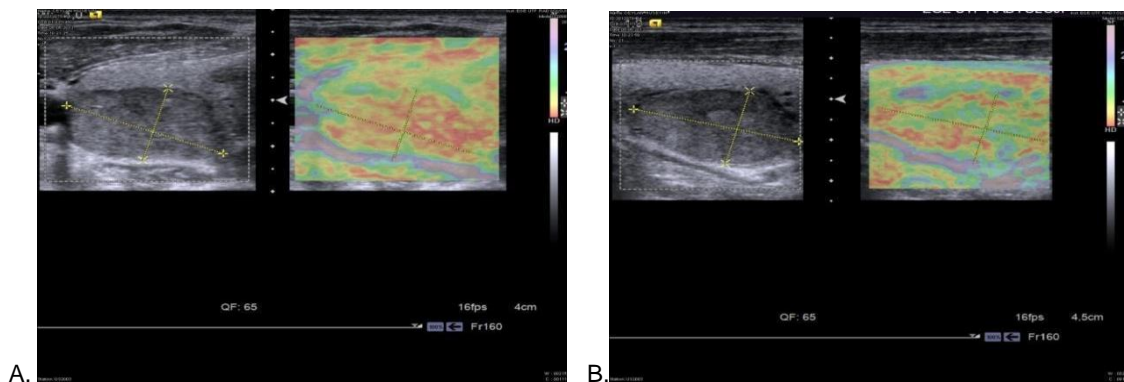


Figure-4. Fifty three-years-old male. Ultrasound elastography images A. Transverse plane B. Longitudinal plane. The nodule was evaluated as score 4 in the transverse plane and score 3 in the longitudinal plane. Postoperative histopathology result was follicular carcinoma of the thyroid.

Inclusion of only solid nodules and exclusion of nodules containing large cystic areas might have affected the results. In solid nodules, especially in long-term follow-up, areas of fibrosis that develop within the nodule increase the elastography score

and reduce the difference between benign and malignant nodules (22, 23).

Histopathological subtypes of malignant nodules in our study might have affected the results.

Medullary thyroid cancers and follicular neoplasms have a cellular pattern and are softer than papillary cancers (22). There is no significant difference between the cellular pattern and gross anatomy of follicular adenomas and carcinomas (24). In our cases, the proportional excess of follicular carcinoma or papillary carcinoma follicular variant subtypes among malignant nodules might have affected the sensitivity and sensitivity results of grey scale findings as well as elastography results and strain ratio values.

It has been reported that calcifications observed in benign nodules affect elastography results and SR values (22). Nodules with eggshell calcification were not included in our study. However, since coarse calcifications were not excluded from the study, this factor might have decreased the diagnostic value of the examination.

Nine of 16 nodules, whose elastography findings were compatible with malignancy and pathology results were reported as benign, were evaluated with FNAB. Since there was no histopathological examination in these cases, malignancy could not be completely ruled out. The small number of cases included in the study might have affected the results.

Studies in recent years have reported lower sensitivity and specificity values for qualitative evaluation compared to previous years. Scoring made on the color map is subjective, and despite different scoring systems, inter-observer agreement is not sufficient. In their meta-analysis study, Dobruch-Sobczak et al. stated that there are inconsistencies between the results obtained by different examiners (inter-observer variability) and by the same examiner (intra-observer variability) in performing sonoelastographic techniques such as relative strain sonoelastography and shear wave sonoelastography (25).

In our study, real-time examinations were performed by a single radiologist (LT). The recorded elastography images were evaluated and scored by two physicians. Inter-observer agreement was not achieved in 14 (28.5%) of 49 nodules in the transverse plane with a score of 3 and 4, and in 10 (23.2%) of 43 nodules in the longitudinal plane, with a score of 3 and 4. Agreement between different operators who use different amounts of compression is likely to be lower.

It has been suggested that semi-quantitative methods such as the strain ratio in RTE or quantitative assessment methods such as elasticity index measurement in shear wave elastography can increase the diagnostic performance by eliminating the operator dependence of the RTE method. Different strain ratio and elasticity index threshold values have been reported in the literature for the distinction between benign and malignant thyroid nodules (26, 27). Hu et al, in their meta-analysis studies investigating the contribution of RTE and SWE in the differentiation of benign and malignant thyroid nodules, concluded that both methods have diagnostic potential and similar sensitivities, while the specificity of RTE is higher (28). There is no consensus and further research is needed.

In our study, the diagnostic value of Nodule / SCM strain ratio in distinguishing malignant nodules from benign nodules was found to be insignificant with the ROC curve analysis ($p=0.517$). Similarly, for thyroid parenchyma / nodule strain index, the diagnostic value of both the average value of three measurements ($p = 0.293$) and the maximum of the three measurements in distinguishing malignant nodules from benign nodules were found to be insignificant by ROC curve analysis ($p=0.201$). The strain indices of benign and malignant nodules overlapped, and a threshold value for differentiation could not be determined.

The causes affecting the elastography results such as operator's experience and pressure applied to tissue may also affect the strain ratio values. In addition, the strain ratio varies if the parenchymal tissue surrounding the nodule is normal, thyroiditis, or multinodular goiter (22, 29). Especially in cases with MNG, small foci of papillary cancer may not be detected by elastogram and strain ratio values. The large size of MNG nodules may affect the results. In this case, there is not enough normal thyroid tissue to be used as a reference. In our study, 8 out of 25 nodules evaluated by FNAB had findings compatible with MNG, and one with thyroiditis on B-mode ultrasonography. Histopathologic evaluation revealed MNG in 15 of 35 patients and thyroiditis in seven of them.

Nodules of 4 cm and smaller were included in the study. During the evaluation of the strain ratio in large nodules, a small normal thyroid area remains as a reference. Comparison with normal thyroid parenchyma cannot be made ideally.

Therefore, if strain ratio measurement is to be made, it may be more accurate to determine a smaller upper limit for the nodule size.

Among the gray scale and elastography findings in our study, the variables with the highest sensitivity were RTE in the transverse plane (75.0%), echogenicity (70.6%), RTE in the longitudinal plane (64.7%), absence of halo (52.9%), presence of micro calcification (52.9%) and contour feature (35.3%). The variables with the highest specificity are the absence of halo (86.0%), echogenicity (81.4%), presence of micro calcification (81.3%), contour feature (76.7%), RTE in the longitudinal plane (62.8%) and RTE performed in the transverse plane (32.5%). The variable with the highest overall accuracy was echogenicity (78.3%). The accuracy of RTE performed in the longitudinal plane was higher

than the RTE performed in the transverse plane, but lower than B-mode ultrasonography findings such as echogenicity, contour feature, absence of halo, and micro calcification.

In this study it was shown that elastographic findings of benign and malignant nodules overlapped and the diagnostic performance of real-time elastography is suboptimal. The specificity, PPV and accuracy of RTE performed in both the transverse and longitudinal planes were lower than the gray scale US features. RTE is not an alternate method to gray scale US. Multi-Center studies involving large numbers of patients are needed to search RTE efficiency and to add this method to the diagnostic algorithm of thyroid nodules.

Conflict of interest: The authors declare that they have no conflict of interest.

References

1. Bender Ö, Kılıç Y, Hot S, Ertürk A, Coşkun Z.Ü, Akan A. Tiroid Nodüllerinin Değerlendirilmesinde Ultrason elastografinin Tanısal Doğruluğu ve Güvenilirliği. Okmeydanı Eğitim ve Araştırma Hastanesi Genel Cerrahi Kliniği, Radyoloji Kliniği, İstanbul Okmeydanı Tıp Dergisi 2012; 28 (3):151-6.
2. Cooper DS, Doherty GM, Haugen BR, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2009;19:1167–214.
3. Merritt CRB. Physics of ultrasound. In: Rumack MC, Wilson RS, Charboneau JW, editors. *Diagnostic Ultrasound*. 3rd ed. Missouri: Mosby, 2005; 3–35.
4. Itoh A, Ueno E, Tohno E, et al. Breast Disease: Clinical Application of US Elastography for Diagnosis. *RSNA, Radiology*. 2006 May;239(2):341-50.
5. Moon HJ, Kim EK, Yoon JH, Kwak JY. Clinical implication of elastography as a prognostic factor of papillary thyroid microcarcinoma. *Ann Surg Oncol*. 2012 Jul;19(7):2279-87.
6. Rago T, Santini F, Scutari M, Pinchera A, Vitti P. Elastography: New developments in ultrasound for predicting malignancy in thyroid nodules. *J Clin Endocrinol Metab*. 2007 Aug;92(8):2917-22.
7. Hong Y, Liu X, Li Z, Zhang X, Chen M, Luo Z. Real-time ultrasound elastography in the differential diagnosis of benign and malignant thyroid nodules. *J Ultrasound Med*. 2009 Jul;28(7):861-7.
8. Asteria C, Giovanardi A, Pizzocaro A, et al. US-elastography in the differential diagnosis of benign and malignant thyroid nodules. *Thyroid*. 2008 May;18(5):523-31.
9. Trimboli P, Guglielmi R, Monti S, et al. Ultrasound sensitivity for thyroid malignancy is increased by real-time elastography: a prospective multicenter study. *J Clin Endocrinol Metab*. 2012 Dec;97(12):4524-30.
10. Rago T, Scutari M, Santini F, et al. Real-time elastosonography: useful tool for refining the presurgical diagnosis in thyroid nodules with indeterminate or nondiagnostic cytology. *J Clin Endocrinol Metab*. 2010 Dec;95(12):5274-80.
11. Chong Y, Shin JH, Ko ES, Han BK. Ultrasonographic elastography of thyroid nodules: is adding strain ratio to colour mapping better? *Clin Radiol*. 2013 Dec;68(12):1241-6.
12. Xing P, Wu L, Zhang C, Li S, Liu C, Wu C. Differentiation of Benign From Malignant Thyroid Lesions Calculation of the Strain Ratio on Thyroid Sonoelastography. 2011 by the American Institute of Ultrasound in Medicine | *J Ultrasound Med* 2011;30:663–9.
13. Unlutürk U, Erdoğan MF, Demir O, Güllü S, Başkal N. Ultrasound elastography is not superior to grayscale ultrasound in predicting malignancy in thyroid nodules. *Thyroid*. 2012 Oct;22(10):1031-8.
14. Mansor M, Okasha H, Esmat S, Hashem AM, Attia KA, El-din Hussein H. Role of ultrasound elastography in prediction of malignancy in thyroid nodules. *Endocr Res*. 2012;37(2):67-77.

15. Dighe M, Luo S, Cuevas C, Kim Y. Efficacy of thyroid ultrasound elastography in differential diagnosis of small thyroid nodules. *Eur J Radiol.* 2013 Jun;82(6):e274-80.
16. Köseoğlu R.D, Filiz NO. The Oncocytic Variant of Papillary Thyroid Carcinoma *Turk J Med Sci* 2006;36(6):387-92.
17. Lloyd RV, Buehler D, Khan Afshar E. Papillary thyroid carcinoma variants. *Head Neck Pathol.* 2011; 5(1):51-6.
18. Hoang JK, Lee WK, Lee M, Johnson D, Farrell S. US Features of thyroid malignancy: pearls and pitfalls. *Radiographics.* 2007 May-Jun;27(3):847-60.
19. Kagoya R, Monobe H, Tojima H. Utility of elastography for differential diagnosis of benign and malignant thyroid nodules. *Otolaryngol Head Neck Surg.* 2010 Aug; 143(2):230-4.
20. Shweel M, Mansour E. Diagnostic performance of combined elastosonography scoring and high-resolution ultrasonography for the differentiation of benign and malignant thyroid nodules. *Eur J Radiol.* 2013 Jun;82(6):995-1001.
21. Cappelli C, Pirola I, Gandossi E, et al. Real-time elastography: a useful tool for predicting malignancy in thyroid nodules with nondiagnostic cytologic findings. *J Ultrasound Med.* 2012 Nov;31(11):1777-82.
22. Shuzhen C. Comparison analysis between conventional ultrasonography and ultrasound elastography of thyroid nodules. *Eur J Radiol.* 2012 Aug;81(8):1806-11.
23. Lippolis PV, Tognini S, Materazzi G, et al. Is elastography actually useful in the presurgical selection of thyroid nodules with indeterminate cytology? *J Clin Endocrinol Metab.* 2011 Nov;96(11):E1826-30.
24. Lyshchik A, Higashi T, Asato R, et al. Thyroid gland tumor diagnosis at US elastography. *Radiology.* 2005 Oct;237(1):202-11.
25. Dobruch-Sobczak K, Adamczewski Z, Dedecjus M, et al. Summary of Meta-analyses of Studies Considering Lesion Size Cut-off Thresholds for The Assessment of Eligibility for FNAB and Sonoelastography and Inter- and Intra-observer Agreement in Estimating the Malignant Potential of Focal Lesions of The Thyroid Gland. *J Ultrason.* 2022 Apr 27;22(89):130-5.
26. Cantisani V, Grazhdani H, Ricci P, et al. Q-elastosonography of solid thyroid nodules: assessment of diagnostic efficacy and interobserver variability in a large patient cohort. *EurRadiol.* 2014 Jan;24(1):143-50.
27. Chong Y, Shin JH, Ko ES, Han BK. Ultrasonographic Elastography of thyroid nodules: is adding strain ratio to colour mapping better? *ClinRadiol.* 2013 Dec;68(12):1241-6.
28. Hu X, Liu Y, Qian L. Diagnostic potential of real-time elastography (RTE) and shear wave elastography (SWE) to differentiate benign and malignant thyroid nodules: A systematic review and meta-analysis. *Medicine (Baltimore).* 2017 Oct;96(43):e8282.
29. Ning CP, Jiang SQ, Zhang T, Sun LT, Liu YJ, Tian JW. The value of strain ratio in differential diagnosis of thyroid solid nodules. *Eur J Radiol.* 2012 Feb;81(2):286-91.