Elastography of the Thyroid Nodule, cut-off points between benign and malignant lesions for Strain, 2D Shear Wave Real Time and Point Shear Wave. A correlation with pathology, ACR TIRADS and Alpha Score.

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Elastography of the Thyroid Nodule, cut-off points between benign and malignant lesions for Strain, 2D Shear Wave Real Time and Point Shear Wave. A correlation with pathology, ACR TIRADS and Alpha Score.

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Cross-sectional prospective study of 170 thyroid nodules studied with elastography and fine needle aspiration (FNA) at Alpha Imagen, Quito, Ecuador, from January 2020 to December 2021. Materials and methods: Nodules classified with ACR TIRADS (ACRT), Alpha Score (AS) and Bethesda; malignant nodes had post-surgical histopathological evaluation. All nodes were studied with 2D Shear Wave Real Time Elastography (RT-SWE), point Shear Wave (pSWE) and Strain Elastography (SE) in a Mindray ultrasound equipment, Resona 7 and analyzed by two radiology experts and a technologist trained in image and data processing. Data analysis included ROC curves, quantitative and nominal variable analysis with absolute and relative frequencies, Shapiro-Wilk test, T test, Chi-squared test and ANOVA. Means, medians, modes, standard deviations, skewness, mean, deviation error, ranges, significance, and risk are all reported. **Results:** Cut-off points between benign and malignant nodules (C/O) were: RTSWE Emax 115kPa and 6.5 m/s, Emean 47.5 kPa and 4.1 m/s, pSWE (average) 52.4 kpa and 4.15 m/s, Sensitivity 81.2%; Specificity 57.6%; PPV 72.4% and NPV 70.4%. The SE Value A (elastic deformation of the nodule) had a C/O of 0.20%, Sen 84%, Spe 57%, PPV: 72,4% and NPP: 73.6%; and Strain Ratio (SR) nodule/tissue of 2.69, Sem 84%, Spe 57%, PPV 72.3%, NPV 73.5%. The RLBIndex quality control must be equal to or greater than 92%. Regarding the pSWE, the recommended mean interquartile ratio (MIQR) is less than or equal to 15.7% for kPa and 8.1% for m/s, the recommended depth is between 1.2 and 1.5 cm and the most commonly used ROI boxes were 3x3 and 5x5mm. Conclusions: RT SWE and pSWE with Emax and Emean values presented C/O with good diagnostic tests both in kPa and in m/s; with SE the C/O was 0.20 % and SR nodule/tissue was 2.69. The recommended MIQR is less than 15% with kPa and 8% with m/s. We recommend adding any of the elastographies that obtained good diagnostic tests in this study to ACRT and AS predictors to optimize the diagnosis of thyroid nodules.

KEY WORDS: Thyroid Elastography, Thyroid nodule, 2D SWE, RT SWE, pSWE, Strain Elastography, TIRADS, Alpha Score.

Introduction

Every day, thyroid elastography (TE) is used more as a diagnostic method to differentiate benign from malignant lesions such as thyroid nodules (TN); additionally, when including it in diffuse type lesions (Filho et al., 2020), there is greater confidence due to its good correlation with predictors of malignancy such as TIRADS, ACRT (Tessler et al., 2017), or others like the American Thyroid Association (ATA) (Haugen et al., 2016), or EU TIRADS (Russ et al., 2017); in South America some countries also use Alpha Score (AS) (Mena et al., 2018) and Alpha Score 2.0 (Mena et al., 2021). TE also performs well as a standalone tool and correlates well with the latest Bethesda (Cibas & Ali, 2017).

Multiple studies focusing on TE have been published throughout the years, for instance studies used to employ Strain Elastography (SE) using different color maps, such as the Asteria classification (Asteria et al., 2008) and RAGO (Rago et al., 2007), methods that have been progressively discontinued because quantitative TE has shown better results. Specific values of the elastic deformation of the TN, known as Value A, are also being used (Zhou et al., 2014), an example is the result obtained by Zhang et al, with a value of 0.21% as the C/O to differentiate benign from malignant lesions (Zhang et al., 2018); here the C/O was also reported at 15.8 kilopascals (kPa) using the shear wave modulus (G) of elasticity, which in theory represents a third of the value of Young's modulus of elasticity (E) which is the one that is used more frequently (Taljanović et al., 2017).

The Strain Ratio (SR), widely used in various studies, is usually the ratio of Value A to a value obtained in a sector of normal thyroid tissue, known as Value B, (Görgülü, 2019) this measurement is known as SR nodule/tissue (SR N/T); several studies have been published related to this measurement, for example one reports a value of 2.32 with a sensitivity of 95.2% and specificity of 86.5% (Di et al., 2019). On the other hand, when we compare Value with the sternocleidomastoid muscle it is known as SR nodule/muscle (SR N/M), of which reported results show a C/O of 3.59 with sensitivity of 100% and specificity of 86.4% (Görgülü, 2019). The Elastographic Contrast Index (EI) has also been analyzed in studies that reported that the values for malignant TN were significantly higher than benign TN (3.67 vs. 1.80), the best C/O was of 2.16, with a sensitivity of 90.3%, specificity of 82.9%, Positive Predictive Value (PPV) of 83.7% and Negative Predictive Value (NPV) of 91.2% (Di et al., 2019).

In quantitative TE, C/Os are very diverse, for example, Liao et al. published results of ROC curves with Shear Wave (SWE), reporting a mean value of ET waveform (Emean) of 32 kPa with sensitivity, specificity, PPV, and NPV of 81%, 65%, 23%, and 96%, respectively (Liao et al., 2019). Additionally, studies have also employed new TE measurements such as the 2D Shear Wave (2D-SWE), with the best reported C/O at 34.5 kPa for Emean (Sensitivity 83.7%, Specificity 77.4%, VPP 63.3% and NPV 89.7%) (Swan et al., 2021) and the results of Farghadani that found an optimal value at 39.6 kPa (Farghadani et al., 2019); however, other studies report higher C/O values with good results, as reported by Park et al. which presents a value of 94 Kpa with TE of maximum value (Emax) with a sensitivity of 46% and specificity of 86% (Park et al., 2015). Using SWE in units of meters/second (m/s), the best C/O reported by Aghaghazvini L et al. was 3.63 m/s for Emax (Sen 90%, Spe 77.6%) and 3.44 m/s for Emean (Sen 90%, Spe 76.4%)(Aghazvini et al., 2020). The TE type ¨Acoustic Radiation Force Impulse¨ (ARFI), also known as point Shearwave (pSWE), showed optimal C/O for best performance at 2.87 m/s (Sen 75%, Spe 95) (Goel et al., 2020), another author reported similar values, with 2.57 m/s as the best C/O (Sen 57%, Spe 85%)(Bojunga et al., 2012).

The World Federation for Ultrasound in Medicine and Biology (WFUMB) published in 2017 a "White Paper" with recommendations to try to standardize the values of the different TE; its most significant results were for SR with a C/O of 3.79, with sensitivity of 97.8% and specificity of 85.7%; they also report SR values of 1.5 and up to 5 in their investigations. In the same consensus, the lack of homogeneity in terms of the values and C/O for 2D Shear Wave Real Time (RT-SWE) and pSWE was noted (Cosgrove et al., 2017), these technologies will be addressed later in this study.

Until now, it has not been possible to establish a consensus guided by important institutions such as RSNA, European Radiology, Asiatic Radiology or endocrinological societies such as ATA, ETA (European Thyroid Association), bringing together the top researchers in TE in order to standardize the values to be applied in all TE; an example of such consensus is the one published by the RSNA in relation to Liver Elastography, where regulations, conditions, cut-off levels and values are presented and standardized measurement units between the different brands of equipment of ultrasound are established (Barr et al., 2020).

Here, we present our results using three types of TE using the Mindray Resona 7 model, a pioneering equipment in "Ultra-Wide Beam Tracking Imaging" technology that provides real-time processing of all signals in a target area from 0.2mm to 40mm. (Li Shuangshuang (Mindray Bio-Medical Electronics Co. Ltd), 2015); two of these TEs are quantitative and use SWE technology, the first is “Sound Touch Elastography” (STE) based on real-time SWE; the second “Sound Touch Quantification” (STQ) based on focused point SWE and the third elastography, the deformation Strain Elastography technology, known in this equipment as Natural Touch Elastography (NTE). In addition, we present important results with STQ on the values of the mean interquartile ratio (MIQR) for TN, for both kPa and m/s, the recommended depth ranges for sample acquisition in centimeters (cm), the size of the boxes recommended for the Region of Interest (ROI), and the quality control values for STE known as “Reliability Index & Map” (RLB-Index & RLB-Map),

To better understand the technologies used in this study, we present a technical summary of them:

STE (Sound Touch Elastography) / RT-SWE:

STE is the RT-SWE elastography technology that shows us the stiffness information of the tissue located in a ROI using various modulus and maps of elasticity in real time, among them is the Young's modulus of elasticity (E) expressed in kPa , shear wave modulus (G) expressed in kPa, and shear wave velocity modulus (Cs) expressed in m/s. (Figures 2-7). (Li Shuangshuang (Mindray Bio-Medical Electronics Co. Ltd), 2015).

STQ (Sound Touch Quantification) / pSWE:

STQ is the pSWE elastography technology, which is based on an ARFI impulse focused on a specific area of the tissue to be evaluated. A ROI is used (modifiable both in size and depth) and an average of up to 8 samples can be evaluated. When using the STQ tool, specific elasticity values are shown such as Emean, Emax, minimum elasticity value (Emin) and MIQR (Figures 4-7) (Li Shuangshuang (Mindray Bio-Medical Electronics Co. Ltd), 2015)

NTE (Natural Touch Elastography) / SE:

SE elastography is performed by superficially placing the transducer on the patient and applying the "Natural Touch" technology that detects changes in deformation of the nodule, with an elasticity histogram that indicates whether a region is soft or hard. We also use a ratio between lesion and thyroid tissue through ROI A/B. With these semi-quantitative values we can identify how hard the lesion is in comparison with the surrounding thyroid tissue (Figures 2, 3, 6, 7) (Zhou et al., 2014).

The following measurement modules were used:

Young's modulus

is used based on the equation $E = \sigma / \varepsilon$ where E is the modulus of elasticity expressed in kPa, σ is the stress, and ε the strain (Sigrist et al., 2017).

Shear Modulus

based on the equation G = pcs2 where G is the shear modulus expressed in kPa, p is the tissue density expressed in kg/m3 and Cs is the shear wave velocity expressed in m/s (Sigrist et al., 2017).

Young's modulus and Shear modulus relationship

is equal to , where the Young's modulus of elasticity E is three times the shear wave modulus G. (Sigrist et al., 2017).

In all TE studies, control and reliability tools are used, which in our case were:

Elasticity bar:

There is an elasticity bar which indicates, with a green color, if the obtaining of the sample is acceptable (Figure 1).

Motion Stability Index / M-STB Index:

TE can be affected by breathing or movement of the transducer, so a motion stability analysis tool is available at the time the measurements are made. It is formed by a scale of 5 stars, from 1 to 3 stars there is movement and the TE measurement should not be carried out since the values obtained will be erroneous; in contrast, from 4 to 5 stars it indicates that the measurement must be carried out since the external movement is null (Figures 2-7).

Reliability Index & Map / RLB-Index & RLB-Map:

The indicator and reliability map indicate the homogeneity of the sample box; in this case the value must be greater than 90% (92% in our study) and the green map indicates that we have a sample without artifacts (Figures 3 and 4).

In our study, all benign and malignant TNs were analyzed with the three types of TE, classified with ACRT and AS, and correlated with Bethesda cytopathological results and histopathological results in malignant cases. These comparisons will result in high reliability of the results, which will contribute to the growing scientific evidence to obtain, in the future, proper validation of the technique and consensus in the measurements used and the C/O to be applied.

MATERIALS AND METHODS.

At the Institute of Radiology and Interventionism, Alpha Imagen, Quito, Ecuador, from January 2020 to December 2021, 196 TNs were analyzed, all of them had fine needle aspiration (FNA) by different specialists; all TNs were classified by ultrasound using two types of malignancy predictors (AS and ACRT). Of those, 170 TNs with benign (Bethesda II) or malignant results (Bethesda V and VI verified with post-surgical histopathological results) were selected. TNs with Bethesda I results were eliminated due to insufficient number of samples; similarly, Bethesda III and IV nodules without a definitive histopathological result were also eliminated.

A Mindray® brand ultrasound equipment, model RESONA 7®, was used, equipped with a multifrequency linear transducer model L 11-3U with a frequency range of 3 to 11 MHz and a central frequency of 7 MHz; equipped with TE software type SE, RT-SWE and pSWE, named in the used equipment as NTE, STE and STQ respectively. The same soft tissue protocol was used for optimal evaluation of the thyroid gland. The interpretation was performed by 2 radiologists with more than 5 years of experience in thyroid ultrasound diagnosis and training to perform FNA, use of ACRT and AS. Data collection, and imaging acquisition was performed by a medical technologist in radiology trained for the processing of both scores, as well as for the processing of images, and data analysis. The entire process was analyzed, corrected and verified by an experienced statistician from our imaging institute and by a biomedical engineer who is an expert in the brand's applications and technologies.

FNAs were always obtained hands-free with an MD TECH ® brand vacuum cytoaspirator and a 20 ml syringe with a 23 g 1 ¼ inch needle. The samples were prepared in dry slides for Giemsa studies and others were fixed in absolute ethanol for Papanicolaou, a part of the sample was sent in base cytology carrier liquid for its cytopathological process and/or as a cell block (histopathological); the malignant cases (n= 46), all managed surgically, had a confirmation of the malignant lineage through histopathological studies of the surgical sample.

The complete measurement of the entire contour of the nodule was performed with TE STE (RT-SWE), following its internal border, without exceeding its external contour, including all the content, whether solid or mixed; the tracing was made manually by the operator, to determine the measurements of Young's modulus with values of Emax, Emean and Emin, both in kPa and m/s units and the values of the colorimetric scale used in kPa were also selected (Figures 2-7). Measurements with TE STQ (pSWE) were made inside the nodule with a modifiable rectangular or square ROI, whose limits should not exceed any of its edges. All of the different textures of the TN were included inside the ROI, either solid or mixed; the largest possible ROI that could fit inside the nodule was used. The automatic values of the multiple pSWE pulse sequences (up to 8) provided multiple measurements and the best average values (Average) and the value of the median, both in kPa and in m/s, provided by the machine itself were used (figures 4 to 7). Additionally, depth values in cm, the size of the ROI in mm x mm, the value of the MIQR for kPa and for m/s, and the values of the kPa and m/s scales when using STQ, were also collected.

When using the SE technology, with the transducer supported by its own weight, without significant compression of it, and applying NTE, the following measurements were made: with the complete contour of the nodule, traced manually and following its internal edges, the percentage of deformation of the nodule (Value A) was obtained and compared with a circular ROI of fixed size (3 mm) located in the healthy thyroid tissue and oriented by the color map to choose an area with the least hardness (in this equipment it is represented with a light blue color); the value obtained from this comparison is known as Value B (Figures 6 and 7). For a second comparison, value A was obtained in the same way as explained before, but an area in the ipsilateral sternocleidomastoid muscle (SCM) was chosen for value B, which was included within the SE measurement box (a ROI of up to 3 mm was manually traced) (Figures 2 and 3). The B/A ratio in both cases was determined automatically by the equipment and used to determine the SRN/T and SRN/M, respectively.

All measurements were saved in the equipment and in a digital image storage system (PACS) for future reviews and comparisons, all studies were again randomly reviewed by the two expert radiologist and by the medical technologist. This analysis resulted in the creation of a TN database that included all of those cases with an adequately acquired measurement and eliminating those with an incomplete or inadequately acquired measurements.

Inclusion criteria:

Patients sent to perform a FNA by specialists in thyroid pathology, and that have not received radioactive iodine therapy, nor have a history of previous surgery or FNA in the last 3 months. In the case of patients with multinodular pathology, only the TN with the highest score obtained in AS and ACRT was selected.

Exclusion criteria:

Patients who had received radioactive iodine treatment, previous surgery, or any other intranodular treatment such as sclerosis or radiofrequency were excluded, as well as those who underwent FNA in the last 3 months.

Statistical Methodology:

The evaluation of the diagnostic capacity and the efficiency of the software used was carried out through a prospective study based on a pre-established protocol. The final analysis included 170 TNs from 170 patients studied in "Alpha Imagen", whose participation was voluntary and affirmed by the signature of an informed consent. Women represented the 88.8% (n=151) with a mean age of 51.8 years; whereas males represented the 11.2% (n=19) with a mean age of 56.9 years; the mean age for the entire cohort was 52.2 years. Data was collected in units of m/s or kPa, grouped into STE, STQ and SE, which determined the following measurements: STE kPa Emax, STE kPa Emean, STE kPa Emin, STE m/s Emax, STE m/s Emean, STE m/s Emin, median STQ m/s, average STQ m/s, median STQ kPa and average STQ kPa, Value A, SRN/T and SRN/M. The data series were initially used to calculate the graphs of the ROC curves, evaluating the distances with the diagonal and the area under the curve (AUC). To determine the best level of the indicators, various C/O were made using the technique of successive approximations. The calculation of the diagnostic tests used the "MSD Calculator professional version"(Merck and Co., Inc., Kenilworth, NJ, 1899). For the quantitative, nominal and continuous variables, absolute and relative frequencies were used. The assumption of normality for continuous data was validated using the Shapiro-Wilk test. The data was refined by computerized identification of atypical cases; the intergroup differences of men and women was analyzed through the comparison test of means (T test) and (ANOVA). All the analyzes were carried out with the SPSS statistical package, version 25. The required complementary evaluation was examined through the ROI, MIQR and RLBINDEX indicators, for which the point statistics were generated using measurements of central tendency: Means, Medians, Modes, Standard Deviations, Skewness, Mean Deviation Error and Ranges. The statistical results were analyzed by the entire group of authors in different meetings to establish the clinical-radiological and statistical correlations and to be able to obtain the different C/O for benign and malignant TNs.

RESULTS

From a total of 195 TN studied, 170 whose cytopathological results were Bethesda II, V and VI were selected, of which 46 patients were confirmed as malignant after post-surgical histopathological analysis, Bethesda I (3 patients), III (15 patients) and IV (7 patients) were excluded from the statistical analysis in order to work only with benign lesions diagnosed by cytopathology and malignant results confirmed by histopathology.

Table 1 shows the C/O and the diagnostic tests of the different types of quantitative TE used in this study, six with RT SWE and four with pSWE. The average diagnostic tests were: sensitivity 81.2%; specificity 57.6%; PPV 72.4% and NPV 70.4%.

Table 1. Diagnostic tests: sensitivity, specificity, PPV, NPV by Cut-Off Points according to the type of measurements for Real Time Shear Wave and Point Shear Wave.

Elastography Type	Point Statistics				
	Cut-Off Value	Sensitivity %	Specificity %	PPV %	NPV %
RT-SWE kPa E max. (STE)	115	79.57	64.74	73.27	72.46
RT-SWE kPaAverage (STE)	47.5	83.16	59.46	72.48	73.13
RT-SWE kPaand min. (STE)	13.0	75.27	70.13	75.27	70.12
RT-SWE m/s E max. (STE)	6.5	84.62	56.92	73.33	72.55
RT-SWE m/s E mean(STE)	4.0	84.31	55.88	74.14	70.37
RT-SWE m/s E min. (STE)	2.0	64.94	79.5	75.76	69.66
pSWE kPa Median (STQ)	52.6	83.84	57.75	73.45	71.93
pSWE kPa Average (STQ)	52.4	80.2	62.32	75.7	68.28
pSWE m/s Median (STQ)	4.15	81.37	58.57	74.11	68.33
pSWE m/s Average (STQ)	4.1	75.47	64.38	75.47	64.38

Source: Alpha Elastography Image Database 2021 Note: The results of the diagnostic tests obtained for Real Time Shear Wave: STE (RT-SWE) and Point Shear wave: STQ (pSWE) are detailed in units (kPa or m/s) and with its different values in Young's modulus, Emax, Emean, E min for RTE SWE and mean and median value for STQ (pSWE).

Table 2. Strain Elastography, Strain Value (A), Nodule/Muscle Strain Ratio and Strain Ratio Nodule/Tissue

Elastography of Thyroid Nodules	A-value Relationship Nodule/ Muscle	B-value Relationship Nodule/ Muscle	B/A ratio SRN/M	A-value Relationship Nodule/ Tissue	B-value Relationship Nodule/ Tissue	B/A ratio SRN/T
Valid	169	168	167	167	167	167
Lost	1	2	3	3	3	3
Mean	**0.19**	**0.18**	**1.15**	**0.20**	**0.50**	**2.69**
Standard error of the mean	0.006	0.011	0.10	0.0069	0.01679	0.08
Median	0.17	0.15	0.85	0.18	0.46	2.32
Mode	0.15	0.14	0.41	0.15	0.41	1.71
Standard Deviation	0.08	0.15	1.31	0.08	0.21	1.15
Minimum	0.07	0.03	0.17	0.09	0.2	1.04
Maximum	0.51	1	11.8	0.59	1.89	7.57

Note: The mean of the results indicates the C/O found for the main values obtained, the TN Value A, the Strain Ratio SRN/M (nodule/muscle) and the Strain Ratio SRN/T (nodule/tissue). Note how the A values have fairly close results and correspond to measurements made by different observers. The B value does not have a radiological clinical meaning in this study since it's a tissue sample (in the thyroid or in the ECM) to obtain the B/A ratio of the Strain Ratio.

Table 3. Diagnostic tests obtained with Strain Elastography analysis according to Strain measurements in tissue, muscle and the ratios with tissue and muscle

STRAIN ELASTOGRAPHY	SENSITIVITY	SPECIFICITY	PPV	NPV
STRAIN A (nodule/muscle) 0.19	0.81	0.61	0.7	0.74
STRAIN B (nodule/muscle) 0.18	0.79	0.59	0.765	0.755
STRAIN RATIO B/A (nodule/muscle) 1.15	0.82	0.65	0.824	0.64
STRAIN A (Nodule/ Tissue) 0.20	0.84	0.57	0.724	0.736
STRAIN B(Nodule/ Tissue) 0.50	0.85	0.65	0.786	0.736
STRAIN RATIO B/A (Nodule/ Tissue) 2.69	0.84	0.57	0.7238	0.735

Source: Alpha Database Image Elastography 2021
Note: Consider of greater importance the tests obtained in the results of the value A (Strain A) that correspond to the TN, as well as to ratios, the Strain B value is just the comparative tissue value. It is worth noting that the TN elasticity strain value is quite similar to the ECM strain value, which explains its close SR at 1.0, but not so with the strain value in the thyroid tissue, which reaches higher values and therefore its SR increases, which is why SRN/T is considered the best option.

Table 4. Measurements of central tendency by region of interest (ROI) size and sample acquisition depth using pSWE.

ELASTO pSWE (STQ) in cm		GLOBAL Benign and Malignant	ROI 3x3 and 5x5mm	ROI 3x3mm	ROI 5x5mm	Malignant TN
N	Valid	170	116	38	78	46
	Lost	0	0	0	0	0
Mean(cm)		**1.37**	**1.36**	**1.53**	**1.28**	**1.47**
Standard Error of the Mean		0.03	0.03	0.06	0.03	0.06
Median		1.32	1.34	1.45	1.29	1.40
Mode		1, 2	1.29	1.00	1.5	1.24
Standard Deviation		0.42	0.37	0.039	0.33	0.41
Minimum		0.38	0.55	0.79	0.55	0.88
Maximum		2.87	2.26	2.64	2.222	2.51

Source: Alpha Database Image Elastography 2021
Note: ROI: region of interest, TN: thyroid nodule. Cross analysis of the depth in cm of the acquisition of the samples with pSWE and the different sizes of the ROI boxes. The mean should be considered as the best test statistic in this table.

Table 5. Central tendency measurements of the Reliability Index (RLB INDEX) by Total, Benign, and Malignant TN according to type of measurement

Statistics	Total	Benign	Malignant
N	170	124	46
Mean%	**92.59**	**92.81**	**92.02**
Standard Error of the Mean	0.78	0.95	1.33
Median %	96	97	94
Mode %	100	100	100
Minimum %	51	51	63
Maximum %	100	100	100

Source: Alpha Database Image Elastography 2022
Note: It has been found that the RLB INDEX quality control must have a minimum mean value of 92%, note that for benign or malignant TN the values are similar for the mode, but not for the standard error where in malignant it was higher (1,3) for which the largest possible value of RLB INDEX is needed. For practical purposes, a value lower than 92 is not recommended, thus ensuring an optimal measurement.

TABLE 6. Mean Interquartile Index (MIQR) by type of central tendency measurement, according to scales (kpa/ m/s) for benign and malignant TN

MIQR in m/s	Mean	Mean Standard Error	Median
TOTAL (170)	**8.16**	0.48	6.7
BENIGN (124)	7.75	0.4	6.65
MALIGNANT (46)	9.23	1.2	7.45
MIQR in kPa			
TOTAL (170)	**15.7**	0.88	13.15
BENIGN (124)	14.89	0.82	13.2
MALIGNANT (46)	18.2	2.39	12.2

Source: Alpha Database Image Elastography 2021
Note: We present the recommended values of MIQR both in m/s and in kPa, so far values less than 30% using kPa and less than 15% using m/s are standardized for Liver TE. Roughly, we found that for TN the values are about half, 15.7% for kPa and 8.1% for m/s.

Transforming the Bethesda, ACRT and AS scales into dichotomous variables and relating them to each other, the following results were observed:

Table 7. Diagnostic tests of Real Time Shear Wave Elastography (STE) and Point Shear Wave (STQ) vs. Bethesda, ACR TIRADS and Alpha Score

SCALES	Bethesda				ALPHA SCORE				ACR TIRADS			
Elastography Type	Sen	Spe	PPV	NPV	Sen	Spe	PPV	NPV	Sen	Spe	PPV	NPV
RT SWE (STE) kPa E max.	79.6	64.9	73.3	72.4	74.1	68.9	82.1	57.9	75.8	64.0	79.2	59.4
RT SWE (STE) kPa Average	83.1	59.4	72.4	73.1	79.9	60.0	76.1	65.0	79.8	67.2	83.4	61.6
RT SWE (STE) kPaE min.	75.2	70.1	75.2	70.1	76.5	67.8	70.9	74.0	76.5	75.0	80.6	70.1
RT SWE (STE) m/s Emax.	84.6	56.9	73.3	72.5	79.4	59.2	80.1	58.1	80.5	66.7	85.6	58.1
RT SWE (STE) m/s Emean	84.3	55.8	74.1	70.3	81.0	55.7	76.7	62.9	82.0	52.4	76.1	61.4
RT SWE (STE) m/s Emin.	64.9	79.5	75.7	69.6	60.2	77.4	71.2	73.0	67.9	83.1	80.3	71.9
pSWE (STQ) kPa Median	83.6	57.7	73.4	76.9	81.1	57.8	76.1	64.9	81.5	64.3	82.3	63.1
pSWE (STQ) kPa Average	80.2	58.5	74.1	68.3	804	58.7	76.7	63.8	78.1	65.4	83.1	58.0
pSWE (STQ) m/s Median	75.4	64.4	75.4	64.3	77.7	62.9	78.5	61.9	77.4	71.7	85.8	59.3
pSWE (STQ) m/s Average	75.5	64.4	75.5	64.4	77.8	62.9	78.5	61.9	77.8	71.7	85.9	59.4
Strain A Muscle	72.4	77.8	68.8	80.7	71.4	72.8	68.8	75.3	76.0	75.5	71.3	79.8
Strain A Fabric	74.4	70.9	76.1	72.3	73.6	69.6	76.1	77.5	77.5	75.0	69.2	81.8
Strain Ratio B/A Nodule/ Tissue	78.2	63.1	79	62.0	80.2	62.1	76.4	67.2	82.3	66.1	79.2	70.4

Source: Alpha Database Image Elastography 2022.
Note: Sen: sensitivity, Spe: specificity. PPV: positive predictive value, NPV: negative predictive value. RT SWE(Real Time Shear Wave) STE , pSWE (Point Shear wave) STQ, A: elastic deformation of the TN.

Table 7 shows the diagnostic tests when the best types of elastography, according to our analysis, are crossed with Bethesda, ACRT and AS. As shown, they are similar with some variants that are defined in the same table.

Scales:

In the RESONA 7®equipment,the scales that can be seen on the left side of each image (Figures 2-7), represent the interval between the minimum and maximum values that can be used in that measurement; the minimum values that can be used are 10 kPa and 1.8 m/s and for the maximum 400 kPa and 11.5 m/s. The color scale available for the TE STE allows establishing an interval with the possible values to be found during the exams and can be manually modified in the equipment. In our study, scales with maximum values from 75 kPa to 400 kPa were used, finding that the most frequent were the maximum scale of 180 kPa with 48.5% and that of 140 kPa with 34.1%. Considering that the average values found by us range from 13 kPa (Emin) to 115 kPa (Emax), these scales perfectly cover the biometric requirements of the nodules. It is worth remembering that when the colorimetric scale is used as an orientation to see the areas of greater hardness of the TN, the scale can be modified until the desired balance is found, this does not affect the TE measurement values, they only help to visually differentiate areas with different elasticity. We measured the complete integrity of the TN, its entire circumference without considering the areas of lesser or greater hardness, that would be represented by the machine with different shades of color. When the scale is changed to units in m/s, the most used maximum scales were 6.5 m/s with 42.4% and 7.7 m/s with 41.8%; we recommended to use the latter, which would cover all the average values found between 2.0 m/s (Emin) and 6.5 m/s. (Emax). Regarding the kPa scale, it is shown that the majority of benign TN (Bethesda II) are located in maximum scales of up to 140 kPa, while Bethesda V are located in the range of 140 to 160 kPa, and VI are generally located in scales greater than 160 kPa. Comparing the Bethesda scale with the speed in m/s, it is noted that nodules with a speed of up to 6.4 m/s would qualify as benign (Bethesda II), between 6.5 and 7 m/s would be Bethesda V, and 7 m/s or higher, Bethesda VI. No significant differences were found between the results obtained for the TE values regardless of the scale used (Figures 2-7).

Region of Interest (ROI):

The size of the ROI box is modifiable when using STQ, it determines the TN sector where the pSWE elastography samples will be acquired, it can vary from small sizes such as 1x 1 mm to 30 x 25 mm; the results of the analysis of the median, mode and means determined that the interval between 3x3 mm to 5x5 mm will be the ROI used in this study. This is directly proportional to the most frequently found nodule size in our study, which were between 1 and 9 mm. In our study, the smallest ROI was 1 x 1 mm and the largest was 20 x 20 mm with an average of 5x 5mm. No significant differences were found between the results obtained from the TE values regardless of the ROI size used. (Figures 4-7)

Figure 1

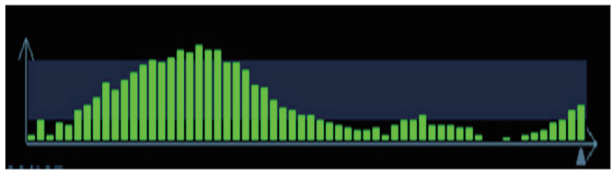

Figure 1. Strain Elastography quality control bar, shows variations with green values that indicate lower or higher security percentage for the measurement prior to the final acquisition, the higher and constant the bars are, the greater the reliability in the sample obtained.

Figure 2

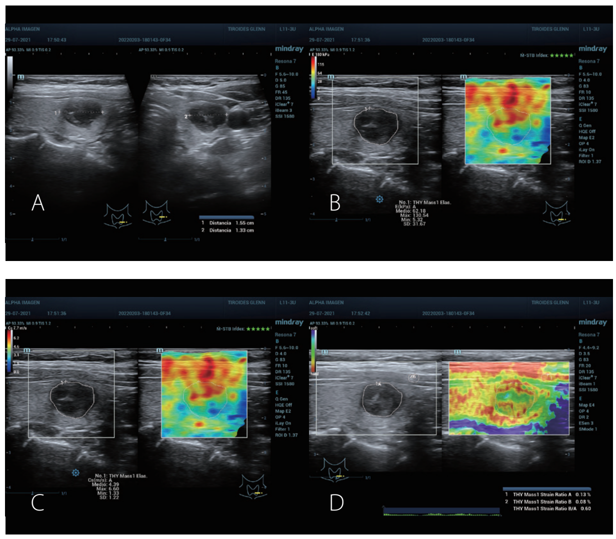

Fig 2.A: Nodule in the lower left third. ACRT 4, AS highly suspected, diameter greater than 1.55 cm. **B and C:** TE RT SWE Emean and Emax above the C/O both in kPa and m/s, **D:** Strain (SE) A value of 0.13% suspicious for malignancy, and nodule/muscle SR of 0.6, lower than expected, not useful. Cytopathology: Bethesda VI. Post-surgical result: Papillary Thyroid Carcinoma.

Figure 3

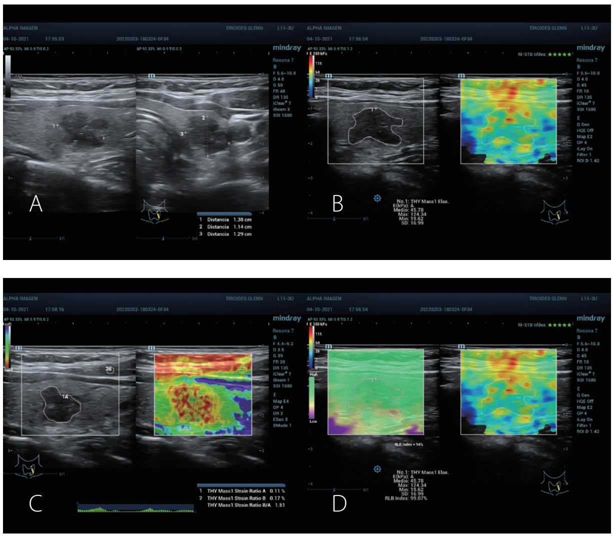

Fig 3.A: Nodule in the left middle third, 1.38 cm in its largest diameter, ACRT 4, AS high suspicion. **B, C, and D:** TE RT SWE Emean, Emax above the C/O, A value 0.11% suspicious for malignancy, SR nodule/muscle slightly elevated. **D:** quality maps, homogeneous green hue (optimum), M-STB Index with 5 stars and RLB index with 94%, values considered optimal. Bethesda VI result, post-surgical histopathology: Papillary Thyroid Carcinoma.

Figure 4

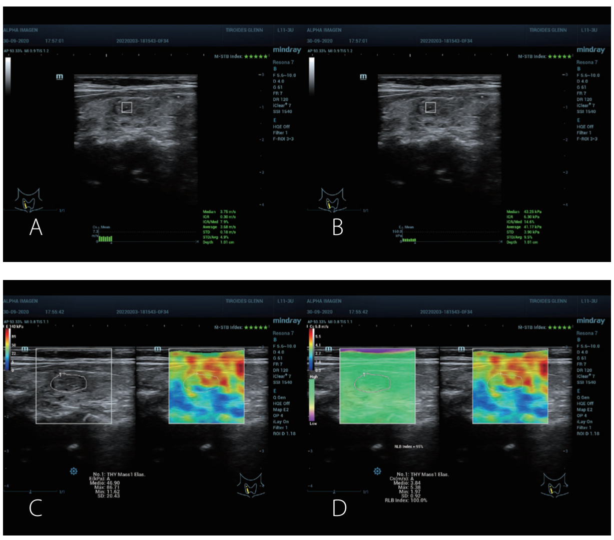

Fig4: Nodule in the right middle third ACRT 3, AS low suspicion. **A and B:** pSWE with values below C/O, observe the optimal MIQR values for both kPa and m/s, 3x3 mm ROI box, 1.0 cm depth. **C and D:** Emean in kPA, maximum scale 140 kPa, the C/O is slightly elevated, but not the values: E max kPa , E max m/s and E mean m/s that are below the C/O. **D:** The maximum scale in m/s of 6.8 has been used, the quality maps M-STB Index with 5 stars and RLB index with 95% with optimal values for obtaining the samples. Cytopathological result: Bethesda II, benign.

Figure 5

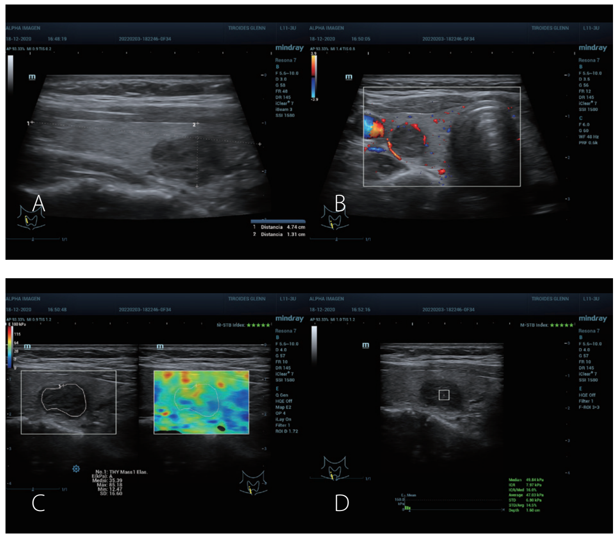

Fig 5.A: Nodule in the lower right third, maximum diameter 2.0 cm, ACRT 4. **B:** Peripheral Doppler vascularization, AS moderate suspicion. **C:** Maximum scale of 180kPa, TE RT SWE Emean and Emax with kPa below C/O. **D:** pSWE kPa below C/O, MIQR 16%, ROI box 3 x 3 mm, depth 1.6 cm. Result: cytopathological Bethesda: II, benign.

Figure 6

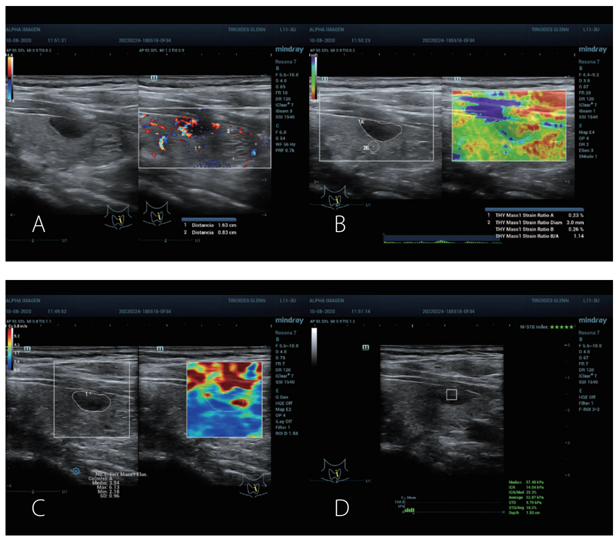

Figure 6. A: Nodule in the left middle third, diameter greater than 1.6 cm, peripheral vascularization, ACRT 4, AS moderate suspicion. **B:** SE with ROI B of 3 mm, Nodule/Tissue SR of 1.14 under the C/O and Value A of 0.23% not suspicious. **C:** RT SWE, full scale 5.8 m/s, Emean 3.5 and Emax 6.1 cm/s below C/O. **D:** pSWE slightly above C/O, 52.8 kPa average, 57.4 kPa median, unreliable values by the MIQR of 25% above the recommended value (15% for kPa), depth also at the maximum limit 1.53 cm. Cytopathological result: Bethesda II, benign.

Figure 7

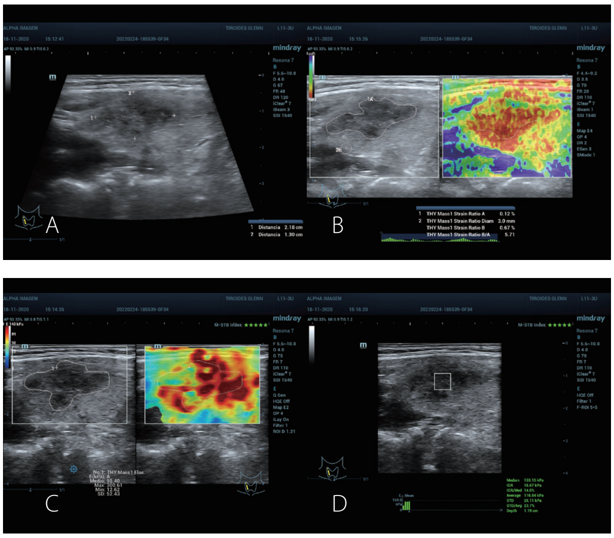

Fig 7. A: Right upper third and middle nodule, diameter 2.1 cm. ACRT 5 and AS high suspicion. **B:** SE with Nodule/Tissue SR of 5.7 above the C/O and A value of 0.12%, suspicious of malignancy. **C:** RT SWE Emean 95.4 and Emax 300 Kpa, above C/O. **D:** pSWE with 118 kPa (average) and 113 kPa (median), above the C/O, with a good MIQR of 14% and a good depth of 1.19 cm. Result: cytopathological Bethesda V, post-surgical result Papillary Thyroid Carcinoma.

DISCUSSION

One of the first reports on the use of TE reported an exceptionally high AUC of 0.94 (Park et al., 2015), but later studies did not managed to reproduce it; we believe that one reason lies with the fact that there is a lot of diversity in the different measurements and parameters that can be obtained in TE such as the definition of ROI, the type of SR, the C/O and its values with Emax, or Emean, the elasticity scale settings, and the scan planes used. This results in a lack of consensus regarding the appropriate values and parameters to be applied, regardless of the brand of sonography equipment being used.

When looking at SE, elasticity assessments around the stiffest area of the nodule are the most commonly reported IE or SR results; we have considered that the analysis of the entire content of the nodule can provide more useful information by allowing other observers and researchers to obtain similar results by establishing the complete measurement of the TN circumference as a fundamental parameter. According to our experience, measuring only the solid area has many inter-observer errors, it is not always uniform, it discards thick areas, it requires more expertise on the technique, and is time consuming; all this makes the overall SE results less reliable.

The AUC for SE and IE ranges from 0.61 to 0.94 and 89% of studies show an AUC within the range of 0.70 to 0.90, however the specificity and sensitivity were 48% to 97% and 42% to 95%, respectively. Therefore, although several studies provide cut-off levels of IE that can be easy to use on a group basis, the diagnostic value in the individual patient is suboptimal, which is explained by the large overlap of results between benign and malignant TNs (Swan et al., 2021). Regarding the value provided by our analysis of SE, which in theory is also an IE, we found significant findings with a C/O of value A at 0.20% with sensitivity of 84%, specificity of 57%, PPV of 72% and NPV of 73% (Tables 2 and 3). A previous study using the same make and model as ours reported a value of 0.215% with sensitivity, specificity, positive likelihood ratio (LR+) and negative likelihood ratio (LR–) of 71%, 73%, 2.58 and 0.40 , respectively, quite close to ours. (Park et al., 2015)

When SR is used, cut-off values > 2.32 have been reported with a sensitivity of 95.2% and specificity of 86.5% (Goel et al., 2020), using the relationship of the SR between the inner edges of the lesion as value A and taking the value B to be an area of healthy thyroid tissue, that is, similar to our SRN/T; we propose a C/O of 2.69 (Sensitivity 84%, Specificity 57%, PPV 72%, NPV 73%), tables 2 and 3. In another study, a longitudinal and axial measurement was performed in the TN, as well as the A value inside the nodule versus muscle and normal thyroid tissue, finding better values in the axial measurement and when value B was used to thyroid tissue, the optimal C/O was 0.17% for value A and 2.66 for SR (Sensitivity:58% and Specificity:78%) (Friedrich-Rust et al., 2016); results also similar to our study.

To compare the difference of using SRN/T and SR Node/M, we repeated the measurement process in all nodes; this time we chose value B in the tissue closest to the SCM muscle and used a circumferential manual ROI of 2 to 3 mm in a sector free of pathology. Our results were that the A value was very close to that obtained when we used SR nodule/T (0.20%), this time it was 0.19% (Sensitivity 81%, Specificity 61%, PPV 70% and NPV 74%), something that confirms the degree of interobserver reproducibility in the circumferential measurement of the TN since it was performed by all the experts in this study randomly; the SRN/M obtained was 1.15 (Sensitivity 82%, Specificity 65%, PPV 82% and NPV 64%), Table 3. We do not consider this SR the most appropriate, since it has a standard error of the mean of 0 .10 and a SD of 1.31, Table 2. Other authors have found different and higher values of SRN/M with C/O of 3.59 (Sensitivity, Specificity, and AUC were 100%, 86.4%, and 0.969, respectively) (Görgülü, 2019). Possibly the value B chosen by them was different or certainly softer than the TN so that the ratio is very high. Görgülü et al also compared SRN/T vs. SRN/M and found that the values were significantly successful in differentiating benign from malignant histopathological types ($p < 0.001$ for both) and reported an SRN/M with a C/O of 5.75, Sensitivity: 100%; Specificity: 96.3%; and the AUC was 0.996, one of the highest reported in the literature. When AUC was compared for both methods, the difference was 0.0265 and was statistically significant (p= 0.046). The diagnostic accuracy of the SRN/M was superior to that of the SRN/T (Görgülü, 2019), this differs from our results. We consider that the variability of the B value chosen as a sample in the ECM muscle and the similarity of some areas of the muscle tissue with the TN of our sample are responsible for finding a lower SR than that published. Additionally, imaging acquisition in longitudinal slices and the limited space in the ECM that is included within the SE measurement box, might also be responsible for our results. Another factor to consider is that there is no consensus regarding the area to select and how the B value is chosen in the ECM or any other nearby muscle. We recommend using the A value of the TN and the SRN/T for all of the above.

Regarding quantitative TEs, a meta-analysis of 15 SWE studies, including 1,867 TNs, showed that the sensitivity and specificity of SWE was 84.3% and 88.4%, respectively. (Zhao & Xu, 2019). Several meta-analyses of the diagnostic accuracy of thyroid SWE have been performed with divergent results (Swan et al., 2021), thus the pooled sensitivity and specificity found in some studies seems encouraging, but the clinical usefulness of these analyzes is questionable since several technologies were pooled (SWE, pSWE, ARFI), the patient cohorts were very heterogeneous and there were several different C/Os applied. For this reason, we analyzed each test separately and present the results of each of the Elastographies with different units of measurement, C/O and individualized diagnostic tests (Table 1). We managed to obtain good statistical results with both RT SWE as well as with pSWE, using values in kPa, m/s, Emax, Emean, mean and median; the differences were not significant and the values for sensitivity were between 64.3% and 84.6%, for specificity between 55.7 and 77.6%, for the PPV between 70.1% and 73.5% and for the NPV between 64.4% and 73.2%, The reported values are within the ranges published by other authors using different equipment brands, especially one of the most used, such as the RT SWE Emean had a C/O of 47.5 (Sensitivity 82.9%, Specificity 56.8%, PPV 70.1%, and NPV 73.2%), Table 1. The study published by Szczepanek-Parulska found values very similar to those of our study, with an average value of kPa with a cut-off point of 49 kPa (Sensitivity: 86%, Specificity: 81%) (Szczepanek-Parulska et al., 2013).

With RT SWE E max we find a C/O of 115 kPa (S: 79.5%, E: 61.6%, PPV: 72.1, NPV: 70.4%), table 1, some studies report values of 94 kPa (S : 46%, E: 86%)(Park et al., 2015), results close to our values, however in an updated meta-analysis(Swan et al., 2021)multiple cut-off values are reported without finding a consensus again; It is noteworthy in said meta-analysis that most studies report lower cut-off points for RT SWE Emax, so the tendency will be to use Emean values that have closer reports.

In relation to the published values focusing on m/s, we found an Emean value of 4.0 m/s using RT SWE, Sensitivity: 84%, Specificity 55.8%, PPV 74.1% and NPV 70% and with average pSWE 4.15 m/s, Sensitivity 81.3%, Specificity 58.7%, PPV 74.1%, NPV 68.3% (Table 1); publications such as Kyriakidou et al., report a lower C/O of 2.65 m/s (Emean) with sensitivity 73%, specificity 67% and NPV: 94% (Kyriakidou et al., 2018). Another investigation identified a C/O with Emax of 3.54, the sensitivity and specificity were 79.2% and 71.5%, respectively, with a PPV of 26.7% and NPV of 96.3% (Azizi et al., 2015).

Our study reveals that the RT SWE Emax has a C/O of 6.5 m/s with sensitivity of 84.6%, specificity of 56.9%, PPV 73.3% and NPV 72.5%, one of the factors that can explain these differences is that we measured the complete contour of the TN and other authors only use the most solid regions of the nodule or the isolated solid regions in a mixed TN. We have not found significant use for the value of Emin with RT SWE, its diagnostic tests are not as good as those of Emean or Emax, nor are there important references in the literature, however, its values are recorded in Table 1 for future comparison; additionally, we didn't find statistically significant differences in the SD values of each of the TE studied.

Zhang et al, using the same make and model of equipment as ours, published C/Os using the shear wave G modulus, thus reported a Gmax, Gmean and GsD of 15.82 kPa (Sensitivity 79%, Specificity 79%), 6.715 kPa (Sensitivity 86%, Specificity 68%) and 2.00 kPa (Sensitivity 78%, Specificity 64%), respectively (Zhang et al., 2018). It's important to note that the value of the G-mode elastography is three times less than the value of the TE Young's modulus (E); there are not many publications using this type of TE, so it's difficult to issue compare our results to those of the literature. In a meta-analysis that included only SWE studies, a suboptimal performance of the method was found, reflected by a sensitivity and specificity of 66% and 78%, respectively (Swan et al., 2021).

In reality, there is still a long way to go before standardizing the values between the different brands, but possibly in a future consensus, such values of TE will be used in addition to well-known predictors such as ACR TIRADS , ATA, EUROTIRADS, AS or KTIRADS (Petersen et al., 2022) and not just as an isolated tool. We believe that if TE measurements are combined with prediction tools such as TIRADS, greater statistical weight and confidence will strengthen the prediction value of the tool, even more when correlated with commonly used sonographic signs (solid, hypoechoic, microcalcifications, height greater than width, jagged edges). It's likely that future updates of TIRADS will have quantitative standardized values of TE. Such combinations are shown in the work of Trimboli et al., 2012, who reported that the addition of ultrasound mode B(US) with TE resulted in a sensitivity of 97% and NPV of 97%, which was higher than using SE or sonographic characteristics of the mode B by themselves. Other authors, on the contrary, report that the diagnostic accuracy of the specificity and PPV were inferior to conventional ultrasound by itself (Zhao & Xu, 2019); also, they found that neither TE alone nor the combination of TE and US showed better performance in diagnosing thyroid cancer; this is also shown by Moon et al., 2012. We disagree with these conclusions, our experience and results from other publications (AS) and (AS2.0), showed that individually and together (TE and US) present reliable results verified with Bethesda, histopathology and statistical comparisons with ACRT and AS, as can be seen in table 7, where all the values of sensitivity, specificity, PPV and NPV are significant.

In our study we also managed to stablish some technical parameters that can serve as a guide for the correct use of the TE and for comparison with future research, thus, in relation to the most used scales, it is recommended to use intervals between 140 and 180 kPa as the maximum limit at the top of the colorimetric scale when using RT SWE and 7.7 m/s when using the scale in m/s, this results in optimum color and velocity maps considering that our Emax cut-off value was between 115 kPa and 6.5 m /s. Using a larger scale would not be recommended, it is unnecessary, and it also generates color patterns in the 2D map that are not very useful and speed scalation intervals become very wide, more details are shown in the results section.

When considering the size of the ROI box when using pSWE, the ones we used mostly were the 3x3 mm and 5x5 mm, data that only has informative relevance since, as was mentioned in the methodology section, we always used a ROI that included the TN without exceeding its external borders, therefore the size of the ROI will depend fundamentally on the size of the nodule (Table 4). No statistically significant differences were observed when using smaller or larger ROI boxes than those mentioned and the usefulness of using the aforementioned measurements lies in the speed of sample acquisition (the larger the size, the lower the speed) and in the correct positioning of the ROI that allows up to 8 pSWE samples with automatic calculations of MIQR, kPa and m/s; we have observed that when the ROI is smaller and its edges do not exceed any of the edges, the MIQR tends to be lower, therefore optimal as we will discuss later.

The equipment we used (RESONA 7 of the MINDRAY brand) has quality controls for the optimal measurement of TE; the so-called RLB INDEX has an optimal preset value equal to or greater than 90%, despite the fact that the machine software identifies values lower than what was found and codifies them with a green color when adequate or in red when inappropriate; our recommendation is that this value should be equal to or greater than 92%. The results of our study did not establish significant differences between benign and malignant TN, which informs us about its usefulness exclusively to standardize the measurements to be performed in this equipment (Table 5).

Another aspect that has not been reported in scientific publications is the value of depth in cm. Considering the 3x3 and 5x5 ROIs that constitute the largest proportion, our average acquisition depth of the STQ sample was 1.38 cm and the mean depth was between 1.28 and 1.53 cm; note that in malignant TN the mean was 1.47 cm (Table 6). When comparing the depth with the cohort of benign and malignant TN, the results were homogeneous and the differences were not significant; although the interval of 1.2 to 1.5 cm is recommended, the use of other values does not result in significant differences when comparing benign and malignant TNs. It's important to know the manufacturer's technical recommendation of the equipment being used, although if the equipment's software allows detection of very superficial (0.38 cm) or very deep (2.87 cm) TN, as in our case, the measurement should be accurate; however, we recommend using the intervals shown on Table 6.

The value of MIQR also has a limited amount of publications, however, we consider that our results can be used to recommend an optimal percentage of acquisition for TNs or for the thyroid gland as it's commonly done with liver (which is 15% or less when using m/s and 30% or less when using kPa) (Barr et al., 2020). Our analysis showed that the relationship of the MIQR between kPa and m/s is almost doubled, specifically 1.9 for all 170 TNs, 1.86 for the benign nodules and 2.1 for the malignant ones; therefore, for all TNs (benign and malignant) the recommended value would be 8.1% for m/s and 15.7% for kPa, although for malignant TN these values may be higher with means of 9% for m/s and 19.2% for kPa; we would recommend to use the standard values of 8% for m/s and 15% for kPa (Table 6).

Lastly the statistical analysis between Bethesda, ACRT and AS showed correlation between the three classifications, although Bethesda is considered the gold standard for pathological classification, in Table7 we can observe the values of sensitivity, specificity, PPV and NPV between the three. Our recommendation, which was already widely discussed in our previous publications of AS and AS2.0 (Mena et al., 2018, 2021), is that two classifications should be used. In our experience, when reporting ACRT and AS together, clinicians have commented that the classification of the patient becomes easier; if we add to this report the different TE values that show suspicion of malignancy, physicians can properly select potentially malignant TN that should have FNA, or microcarcinomas that go to active surveillance, or potentially benign TN that should not be punctured and the Bethesda III and IV, which in particular would benefit from active surveillance versus a new FNA in 3 months as currently established by the guidelines (Cibas & Ali, 2017).

Study limitations

Our reported results and C/O need to be confirmed in the future with a larger number of cases that will result in the strengthening of the statistical tests; we are actively collecting new cases for a future update. Also, our results should be reproduced in countries from other continents so that the population studied will be genetically different and have another type of risk, in order to confirm the validity our results. In any case, we believe that especially for Iberoamerica, Latin America, and the Caribbean, the values we found are applicable due to population similarity.

In our study when using the SE we could not establish an SRN/M consistent with what was published; we argue that this may be due to multiple factors such as the type of comparative value of the tissue chosen, the type of acquisition plane, the varying size of the value B in mm, and to the area of the SCM muscle that will always differ and will be impossible to standardize, which is why we do not recommend it. We did not report the ROC curves due to the low precision of the AUC and we give priority to the other results of the diagnostic tests.

Conclusions:

The diagnostic tests carried out for both Shear Wave Real Time, Point Shear Wave, Value A of the Strain Elastography and Nodule/Tissue Strain Ratio had very good results and few significant differences between them; the type of elastography, its measurement mode and the units in kPa or m/s can be used according to the preferences of each researcher, however, we do not recommend to use Emin values with RT SWE. The MIQR recommended is less than 15% (kPa) and 8% (m/s) and the recommended depth for pSWE is 1.2 to 1.5 cm. Statistical tests were promising when comparing the different elastographies with the Bethesda, ACR TIRADS and Alpha Score.

Conflict of interests:

None to declare.

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