

Comparison of three volumetric techniques for estimating thyroid gland volume

Ümit Erkan VURDEM¹, Niyazi ACER², Tolga ERTEKİN², Ahmet SAVRANLAR¹, Ömer TOPUZ³,
Mustafa KEÇELİ³

Aim: The aims of this study were to estimate the preoperative thyroid volume in patients with a multinodular goiter by the use of ultrasonography (USG) and magnetic resonance imaging (MRI), and then to compare these approaches with the postsurgical total volume measured by Archimedes' principle.

Materials and methods: In this study, we compared 3 methods for the determination of thyroid volume: thyroid volume measured with ellipsoid formula via 2-dimensional ultrasonography (2D USG); the stereological (point-counting) method using MRI; and the postsurgical total volume determined by the fluid displacement technique as a gold standard.

Results: Thyroid volumes were calculated in a total of 20 patients (15 women and 5 men) who underwent total thyroidectomy. The mean \pm SD thyroid volumes of the fluid displacement, point-counting, and ellipsoid methods were 82.75 ± 48.87 , 80.45 ± 48.96 , and 75.50 ± 46.59 cm³, respectively. No significant difference was found among the methods of calculating thyroid volume ($P > 0.05$). The mean coefficient of error for the thyroid gland estimates derived from the technique of point-counting with MRI was under 4%. The 2D USG volume is a 10.62% underestimation of the thyroid gland volume compared with the actual volume.

Conclusion: It can be concluded that there was no statistically significant difference between the 2 methods, but the 2D USG volume was underestimated; therefore, we think that the stereological method is a more efficient and reliable method than USG for thyroid gland volume estimation.

Key words: Thyroid volume, actual volume, ultrasound, stereology

Introduction

The thyroid gland, which is located in the anterior cervical region, belongs to the endocrine system. It consists of right and left lobes connected by an isthmus that extends across the trachea (1,2). Several factors influence the size of the thyroid gland.

There is no information available about some of these factors or the complex ways in which they affect the thyroid gland (3). The thyroid volume is higher in males than in females (4,5), and there is a correlation between lean body mass, body mass index, and thyroid

volume (6–8). Presumably, in females, thyroid size may be affected by sex hormones during pregnancy and menstruation (4,9). The thyroid gland controls the secretion of thyroid hormone. Too much or too little thyroid hormone causes pathological changes. Therefore, clinicians usually diagnose disorders of the thyroid gland by assessing its volume.

The precise estimation of the size of the thyroid gland is a very useful tool for the evaluation and management of thyroid pathologies (2). Changes in goiter size are important for the prognosis of

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¹ Department of Radiology, Kayseri Training and Research Hospital, Kayseri - TURKEY

² Department of Anatomy, Faculty of Medicine, Erciyes University, Kayseri - TURKEY

³ Department of General Surgery, Kayseri Training and Research Hospital, Kayseri - TURKEY

Correspondence: Ümit Erkan VURDEM, Department of Radiology, Kayseri Training and Research Hospital, TR-38010 Kayseri - TURKEY

E-mail: uervurdem@hotmail.com

Graves' disease. The accuracy of radioiodine dosage calculations is proportional to the accuracy of thyroid volume measurements. The validation of these measurements is therefore important (10,11). There are many studies that estimate the accuracy of thyroid volume using 2-dimensional ultrasonography (2D USG), planar scintigraphy, 3-dimensional (3D) USG, computed tomography (CT), single-photon emission computer tomography (SPECT), and magnetic resonance imaging (MRI) (1,11–14).

There are different methods for the assessment of the thyroid gland volume (15). The Archimedean principle as the criterion method is the most accurate in vitro technique for the measurement of thyroid gland volume. The Archimedean principle is that an object displaces its own volume. This method has been used to measure volumes of large organs such as the liver and lungs. The Archimedean principle is highly accurate for determination of volume, but it is not applied in routine practice (16).

The point-counting method is based on the Cavalieri principle using CT images and MRI. The point-counting method consists of overlaying each selected section with a regular grid of test points, which is randomly positioned. After each superimposition, the number of test points hitting the structure of interest on the sections is counted, and the volume of the structure is estimated by multiplying section thickness, total number of points, and the representing area per point in the grid (17).

The aims of this study were to estimate the preoperative thyroid volume in patients undergoing total thyroidectomy by the use of an ellipsoid formula and a stereological (point-counting) method, and to compare these approaches with the postsurgical total volume measured by Archimedes' principle.

Materials and methods

Patients

The series comprised 20 patients (15 women and 5 men) treated from January 2011 to April 2011 with a mean age of 45.65 ± 9.80 years. All patients, after a preoperative assessment (hormonal evaluation, USG, and fine-needle aspiration cytology), underwent a total thyroidectomy due to a multinodular goiter (all cases). All were given informed consent forms,

and the Kayseri Training and Research Hospital and the Institutional Review Board of Erciyes University approved our study.

We used 3 different techniques for the calculation of the thyroid volume:

1. Actual volume as a reference volume,
2. Ellipsoid formula with USG,
3. Cavalieri principle applied to MRI sections.

Actual volume as a reference volume

The exact thyroid gland volumes were measured using Archimedes' principle, also known as the 'fluid displacement technique', in a measuring cylinder (18). For this purpose, we performed a transverse skin incision of 30–50 mm between the cricoid and jugular notch. This incision was performed in one of the skin creases of the neck. After thyroidectomy, each gland was immersed in a 500-mL graduated cylinder filled with distilled water at room temperature. The displaced water was measured volumetrically using a sensitive ruler attached to the outer surface of the cylinder. Each measurement was performed twice, and the average was calculated as the fluid displacement technique. The mean of all volumes for an individual patient was accepted to be the best estimate of the true thyroid gland volume and was defined as the thyroid gland reference volume.

Ellipsoid formula with USG

A real-time ultrasound scanner (Toshiba Xario, SSA-660A) was used with an 8-MHz linear array transducer and a 3.5-MHz convex transducer. The 2D USG estimation of total volume, calculated by the ellipsoid volume formula of $\text{width} \times \text{depth} \times \text{length} \times 0.524$, has become the accepted method for the assessment of the thyroid gland (11,15). In the USG examination of the thyroid, both lobes are scanned individually in the transverse and longitudinal planes. Transverse planes are perpendicular to the tracheae, whereas longitudinal planes are slightly oblique, following the bisector of the angle made by the tracheae and the sternocleidomastoid muscle. The depth (A, C) and width (B, D) are measured on a transverse section of the lobe: the depth is the maximum anteroposterior distance in the middle third of the lobe, and the width is the distance between the most lateral point of the lobe and the

acoustic shadowing of the trachea (Figure 1a). The length (A, B) is measured on a longitudinal section; it represents the maximum distance from the most cranial to the most caudal part of the lobe (Figure 1b) (2). The isthmus depth (A), width (B), and length (C) were measured on transverse and sagittal sections, respectively (Figure 2). The isthmus and thyroid lobe volumes were added to calculate the total thyroid volume.

Cavalieri principle applied to MRI sections

MRI procedure

In all patients, the thyroid gland was scanned (GE Medical Systems Signa HDi). Standard T2 weighted axial slices with a 5-mm thickness without a gap were obtained in a 1.5T scanner. The acquisition

parameters for T2 were as follows: TR/TE, 4850/201 ms; FOV, 26 cm; 20 transverse slices; and a matrix of 320 × 256 pixels.

Point-counting method

An estimation of the thyroid volume was obtained according to the principle of Cavalieri (19).

Using the Cavalieri method, an estimate of the volume of a structure of arbitrary shape and size may be obtained efficiently and with known precision. The Cavalieri estimator of volume is as follows in Eq. (1) (20,21):

$$V = T \times \sum_{i=1}^n V_i \tag{1}$$

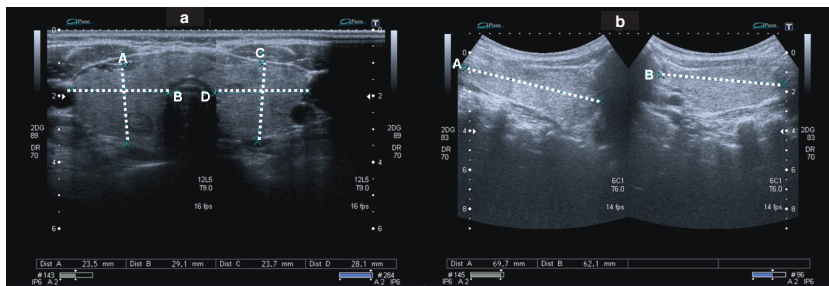


Figure 1. USG images of the cross-section of the thyroid gland. a) Measurement of the width and depth of the thyroid lobes: A, C = maximal depth; B, D = maximal width. b) Measurement of the sagittal length of the thyroid lobes: A, B = maximal sagittal length.

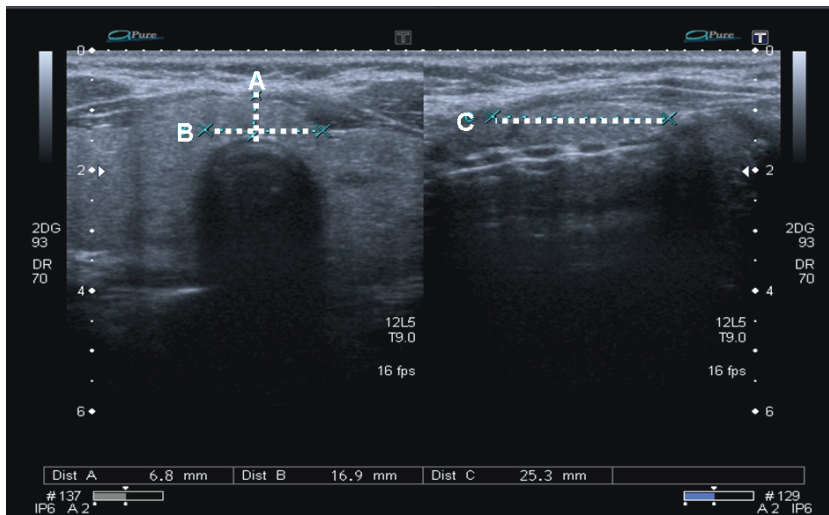


Figure 2. Measurement of the isthmus.

where V_i is the total volume of the tissue slice (which may comprise several slice profiles) in the i th slab. The MRIs of a series of sections that were 5 mm thick were used to estimate thyroid gland volume. The films were saved on a computer and the transparent square grid test system with $d = 0.4$ cm between test points was superimposed, randomly covering the entire image frame. The points touching the thyroid gland's sectioned surface area were counted for each section, and the volume of the thyroid gland was estimated using the modified formula shown below in Eq. (2) for the volume estimations of radiological images (17,21).

$$V(PC) = T \times \left[\frac{SU \times d}{SL} \right]^2 \times \sum P \quad (2)$$

where T is the section thickness, SU is the scale unit of the printed film, d is the distance between the test points of the grid, SL is the measured length of the scale printed on the film, and $\sum P$ is the total number of points hitting the sectioned cut surface areas of the thyroid gland. According to this volumetric technique, a square grid of test points was positioned on each MRI, and all points touching the thyroid gland were counted (Figure 3).

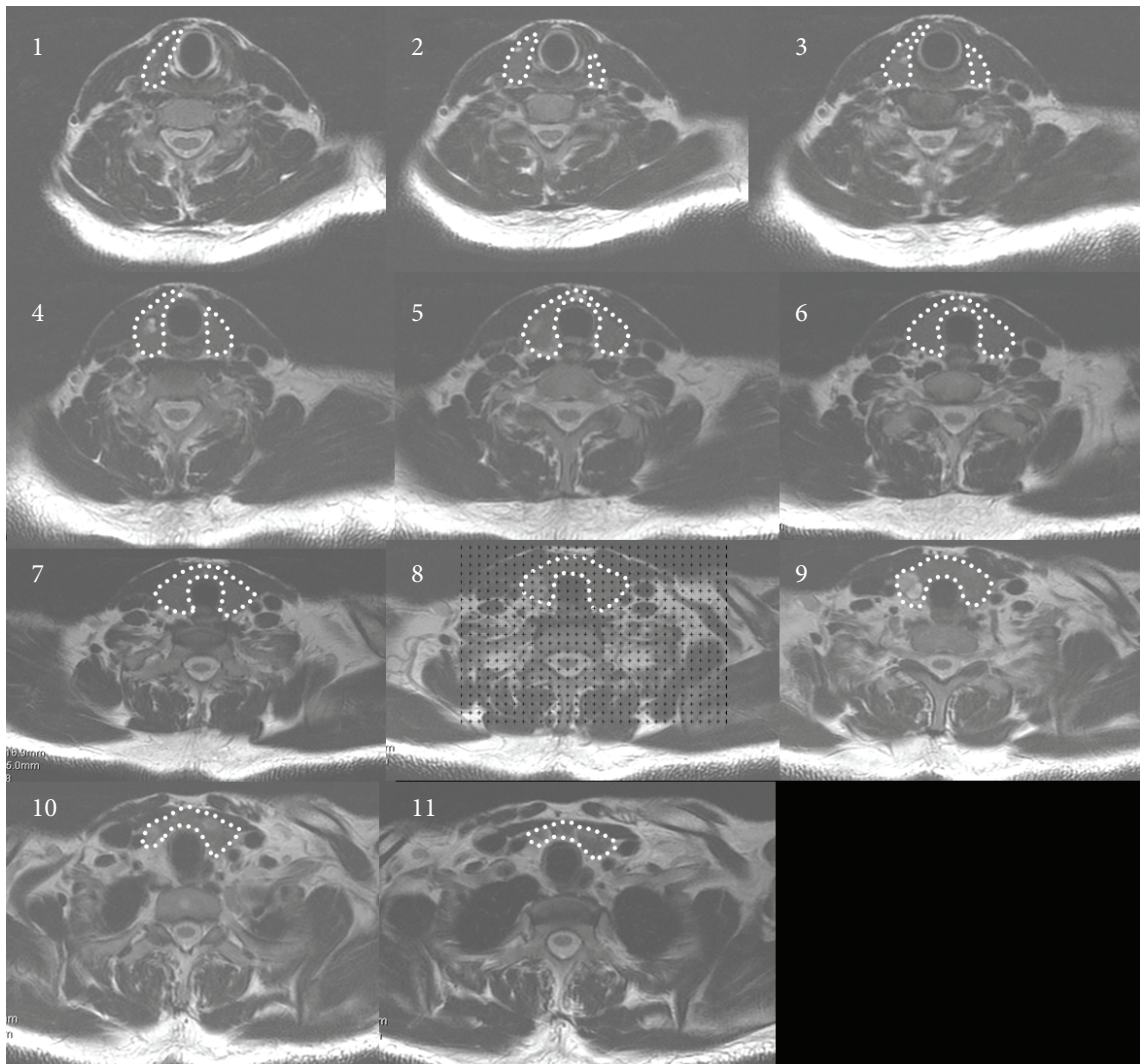


Figure 3. An axial MRI with point-counting for the estimation of the thyroid gland volume from the first to the last section.

Error prediction for point-counting

The variance prediction or the coefficient of error (CE) given in Eq. (3) was calculated according to methods given in recent papers (22,23). The error of the volume is computed as follows:

It can be shown that

$$CE^2(\tilde{V}) = CE^2(\hat{V}) + CE_{PC}^2(\tilde{V})$$

where $CE^2(\tilde{V}) = CE$ of the volume estimate,

$CE_{PC}^2(\tilde{V}) =$ true mean variability due to point-counting within sections,

$CE_{CAV}^2(\hat{V}) =$ true contribution of the variability among sections.

In Eq. (3), $CE^2(\tilde{V})$ is the square CE of the estimator of V when the areas are measured exactly.

Statistical analysis

Data are presented as means and standard deviations (SDs). The differences between the estimated volumes obtained by 3 different approaches – namely, the ellipsoid formula with USG, point-counting with MRI, and Archimedes’ principle or actual volume – were compared using Tukey’s post hoc test to check the methodological differences. A Pearson correlation test was also applied to assess the associations between the results of the 3 different approaches. The accepted significance level was $P < 0.05$.

Results

The mean age of the subjects was 45.65 ± 9.80 years (range: 29–62). The mean thyroid gland depth, width, and length determined by USG measurements were 28.65 ± 0.65 , 31.75 ± 0.79 , and 66.47 ± 1.12 mm, respectively. The mean depth, width, and length of the isthmus were 10.3 ± 0.25 , 18.2 ± 0.39 , and 25.95 ± 0.51 mm, respectively. The mean volume by fluid displacement was 82.75 ± 8.87 cm³. By the Cavalieri principle (point-counting) using MRI, the volume was 80.45 ± 48.96 cm³. The mean thyroid volume by USG was 75.50 ± 46.59 cm³ (Table 1). The 3 methods were correlated with each other (Table 2) and there were no differences between the 3 methods according to ANOVA ($P = 0.888$). We compared USG volume with fluid displacement, which is the gold standard. The upper and lower differences in the thyroid volume between the USG and the fluid displacement measurements are in the range of 5.2%–22.2%. The mean difference is a 10.62% underestimation of the thyroid gland volume by USG. For point-counting by MRI compared with fluid displacement, the volume differences are between –4.65% and 18.52%, and the mean difference is a 3.64% underestimation (Table 3). The agreements between methods were subjected to Bland–Altman plots using volume differences of 95. This showed that the volumes estimated by point-counting and actual volume

Table 1. Mean \pm SD values for 3 methods (cm³).

	Minimum–maximum	Mean \pm SD
Actual volume	27.0–173.0	82.75 \pm 48.87
Ellipsoid with USG	21.0–164.0	75.50 \pm 46.59
Point-counting with MRI	22.0–176.0	80.45 \pm 48.86

Table 2. Correlation values among the 3 methods.

Methods	Pearson correlation test	
	Correlation	Significance
Actual volume – ellipsoid with USG	0.999	$P < 0.001$
Actual volume – point-counting with MRI	0.998	$P < 0.001$
Ellipsoid with USG – point-counting with MRI	0.999	$P < 0.001$

Table 3. Differences between actual thyroid volume and that obtained by other methods.

Methods	Minimum–maximum	Mean ± SD
Actual volume – ellipsoid with USG	5.20–22.22	10.62 ± 4.69
Actual volume – point-counting with MRI	(–4.65)–18.52	3.64 ± 5.70

(fluid displacement) differed by between -3.8 and 8.4 cm^3 ($P > 0.001$) (Figure 4), and the actual volume and ellipsoid methods varied by between 1.9 and 12.6 cm^3 ($P > 0.001$) (Figure 5); there were no significant differences between the 2 methods. Bland–Altman analysis showed that the volumes estimated by the point-counting and ellipsoid methods differed by -1.6 and 11.50 cm^3 ($P > 0.001$) (Figure 6). The mean CEs for the thyroid gland estimates derived from the technique of point-counting with MRI were 2% and 4%.

Discussion

Enlargement of the thyroid gland occurs for several reasons, such as hormonal or immunological stimulation and inflammatory, proliferative, infiltrative, or metabolic disorders (24). Estimation of the size of a thyroid gland using palpation has low sensitivity and specificity for the management and diagnosis of thyroid gland disorders. Recently,

interest in accurate estimation of thyroid volume has increased because the accurate determination of thyroid volume is needed in the selection of patients for surgery and for radioiodine therapy dosage calculations (11,25). There are several different methods for estimating thyroid volume, including USG (1,2,15), scintigraphy, (11) SPECT (26), and MRI (27). USG has become the accepted method for the estimation of thyroid volume. It is inexpensive and easy to use, and it is noninvasive and does not require ionizing radiation. However, 2D USG thyroid volume may result in inaccurate measurements of in vivo volume for many reasons, including an irregular profile of the gland (28,29). Nygaard et al. (12) compared thyroid volumes estimated by USG and CT, and they did not find differences between the 2 techniques, except in cases with a substernal goiter. Rago et al. (13) compared thyroid volumes measured by 3D USG and 2D USG. They determined that there was very good agreement between 2D USG and 3D USG, but in 94/208 lobes with nodular lesions,

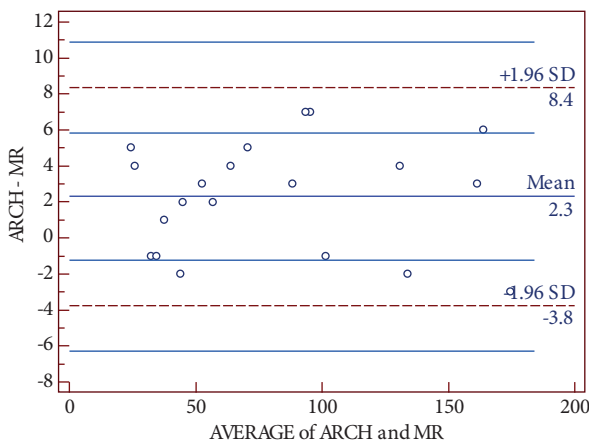


Figure 4. A Bland–Altman plot analysis of the thyroid gland volume as measured by actual volume versus point-counting with MRI.

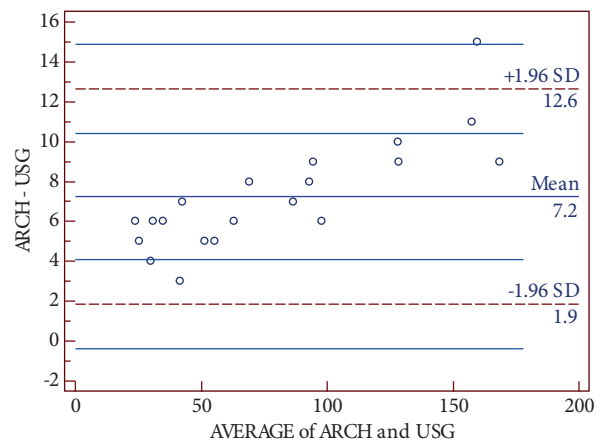


Figure 5. A Bland–Altman plot analysis of the thyroid gland volume as measured by actual volume versus ellipsoid formula with USG.

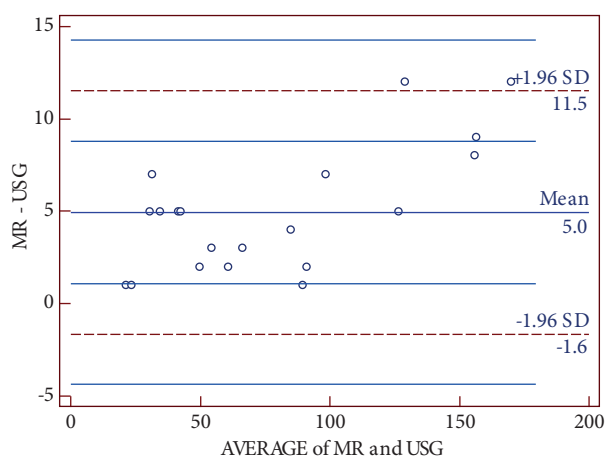


Figure 6. A Bland–Altman plot analysis of the thyroid gland volume as measured by point-counting with MRI versus ellipsoid formula with USG.

2D USG showed a 10% systematic overestimation compared with 3D USG, with the percentage error being higher in lobes with lower volumes. Van Isselt et al. (11) compared planar scintigraphy, SPECT, and USG with MRI. They accepted MRI as the gold standard.

Comparisons with MRI indicate that thyroid volume estimations with planar scintigraphy are inaccurate and that SPECT can offer an acceptable alternative. However, USG is superior for this purpose if a correction is made for bias. In a paper in which USG volume was compared with that measured after surgery in 101 patients undergoing total thyroidectomy, it was shown that USG volume was underestimated in 89 cases, perfectly matched the postsurgery volume in 5, and was overestimated in 7. The mean USG volume was 28.3 mL (range: 7–50) and the mean postsurgery volume was 36.2 mL (range: 7–76); this difference was estimated to be statistically significant (30). We compared USG volume with the actual volume as the gold standard.

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USG resulted in a 10.62% underestimation of thyroid gland volume. For point-counting by MRI compared with the actual volume, the underestimation rate is only 3.64%. Ruggieri et al. (15) estimated the preoperative thyroid volume in 53 patients using an elliptic formula by 2D USG and compared it with the postsurgical total thyroid volume measured by Archimedes' principle. They found that the mean USG volume (14.4 ± 5.9 mL) was significantly lower than the mean postsurgical total thyroid volume (21.7 ± 10.3 mL), and the USG volume was underestimated in 41 cases (77%), with a disagreement of up to 200%. They developed mathematical formulas in order to reduce USG volume underestimation and to predict the real thyroid volume using a linear model.

Additionally, they demonstrated that a predicted thyroid volume under 25 mL was confirmed postsurgery in 94% of cases. There are many studies using the Archimedean principle and stereological methods for volume estimation in different organs. These studies use both the Archimedean principle and MRI or CT images. They found agreement between the 2 methods (17).

There have been some studies about thyroid volume estimation using different methods, but no study in the literature has used stereological methods. In conclusion, we found no differences among the 3 methods. We also found the method of point-counting with MRI to be more precise than the USG volume method. We concluded that MRI sections with a 5-mm section thickness can be used to estimate thyroid volumes with a CE of less than 4%. In addition, the determination of thyroid volume is required for the selection of patients for surgery and the selection of surgical technique, whether performing a minimally invasive thyroidectomy or not. Therefore, surgeons should be aware of a possible USG preoperative underestimation.

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