Variation in thyroid volumes due to differences in the measured length or area of the cross-sectional plane: A validation study of the ellipsoid approximation method using CT images.

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Title

Variation in thyroid volumes due to differences in the measured length or area of the cross-sectional plane: A validation study of the ellipsoid approximation method using CT images.

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Abstract

Background

This study examined the variation in the thyroid volume determined by the ellipsoid approximation method due to differences in the measured length or area of the cross-sectional plane of CT images.

Methods

Forty-five patients with Graves' disease were included in this retrospective study. We designated the three-dimensional thyroid volumes extracted manually (V_{CT}) as the reference data and calculated five approximate volumes for comparison: (1) the mean volume of 8100 different thyroid volumes depending on the diameter of the cross-sectional plane at the midpoint of the major axis, ($V_{\mathrm{ellipsoid,mean}}$); (2) the volume using the maximum diameter and its orthogonal diameter, ($V_{\mathrm{ellipsoid,maxlength}}$); (3) the maximum ($V_{\mathrm{ellipsoid,maxvolume}}$) and (4) minimum ($V_{\mathrm{ellipsoid,minvolume}}$) of the 8100 thyroid volumes; and (5) the volume determined with an equivalent circle diameter, ($V_{\mathrm{ellipsoid,Heywood}}$).

Results

Thyroid volumes obtained via the ellipsoid approximation method varied depending on the diameter of the cross-sectional plane and included a mean error of approximately 20%, while the concordance correlation coefficient (CCC) differed for each approximate volume. Among these volumes, $V_{\mathrm{ellipsoid,mean}}$ and $V_{\mathrm{ellipsoid,Heywood}}$ were in good agreement with V_{CT}, according to single regression analyses and the resultant CCC values, with mean errors of 7.0% and 2.5%, respectively.

Conclusion

While $V_{\mathrm{ellipsoid,Heywood}}$ approximated thyroid volumes with vastly reduced errors, we recommend utilizing three-dimensional thyroid volumetry if measurement accuracy is required.

Keywords

CT, Ellipsoid approximation, Graves' disease, Internal radioiodine therapy, Thyroid, Volumetry

Background

Internal radioiodine therapy (iodine-131) is a treatment for Graves' disease [1]. In radioiodine therapy for Graves' disease, the administered radioactivity is often determined based on the patient's thyroid volume [2–4]. Specifically, patients with Graves' disease who have large thyroid volumes will require a higher dose to ensure a therapeutic effect [3–4]. Therefore, accurate thyroid volumetry before radioiodine therapy leads to the accurate determination of the administered radioactivity, thereby ensuring the therapeutic effect. Thyroid volumetry involves analyses of images obtained from: (1) scintigraphy [5–6], (2) ultrasonography [7], and (3) computed tomography (CT) [8–10]. Utilizing these images, the thyroid is approximated as a complex of ellipsoids, known as the ellipsoid approximation method, and it has been in popular use owing to its inherent simplicity. In the ellipsoid approximation method, it is customary to use the maximum diameter of the cross-sectional plane (transverse plane of the body), although there is no clear rule in either past papers or guidelines. Schlögl et al. compared the accuracy of the thyroid volume determined by the ellipsoid approximation method and the three-dimensional segmentation of ultrasound images [11]. In their study, the ellipsoid volumes were determined by measuring the maximum transversal, horizontal, and longitudinal diameters. They reported that the approximate volume was 11% larger than the actual volume with a standard deviation of 26%. However, they did not report on the reason for using the maximum diameter, the method used to measure each diameter, and its variation. We believe the differences in the measured length or area of the cross-sectional plane particularly affect the ellipsoid and thus the approximated thyroid volume. Furthermore, the accuracy of the measurements depends on the subjectivity and skill of the measurers (i.e., physicians, radiological technologists, etc.). The results of three-dimensional thyroid volumetry from CT images were reported to be in good agreement with the actual thyroid volume by Lee et al. [10]. They targeted patients who underwent contrast-enhanced CT examination, and the thyroid regions were extracted from the CT images using a three-dimensional visualization software. However, contrast-enhanced CT scans will delay radioiodine therapy for weeks or months because the contrast media contains iodine [3–4]. Therefore, direct application of their approach is difficult for patients with Graves' disease before radioiodine therapy.

Regardless of the modality employed, it is significant to validate an accurate and simple method for measuring the thyroid volume. We need to investigate how the thyroid volume changes with various diameter combinations, including the combination of the maximum and orthogonal diameter of the cross-sectional plane. This study aimed to calculate the variation in the thyroid volume determined by the ellipsoid approximation method due to differences in the measured length or area of the cross-sectional plane of CT images. To the best of our knowledge, similar studies have not been reported.

Methods

Patients

Forty-five patients (7 males, 38 females, average patient age of 50.8 ± 16 years) with Graves' disease who underwent radioiodine therapy as outpatients from December 2014 to April 2018 were included in this retrospective study, approved by the Ethical Review Committee of Nagoya University Hospital (authorization no. 2018-0179). Because five of this cohort underwent radioiodine therapy twice during this period, our analysis eventually included 50 cases. In our hospital, we determined the administered radioactivity of radioiodine for Graves' disease according to Marinelli's formula [2]. Using Marinelli's formula (Eq. 1), the administered radioactivity, *A*, was calculated using the thyroid volume, amongst other parameters. For this reason, patients underwent non-enhanced neck CT examinations (Aquilion 64 or Aquilion PRIME SP; Canon Medical Systems, Otawara, Japan) for the determination of thyroid volumes. In this study, we performed retrospective analyses using these neck CT images.

The Nuclear Medicine physician determines the administered radioactivity by adjusting the absorbed dose in Equation 1 according to the clinical symptoms of each patient.

$$A\ [\mathrm{MBq}] = C \times \frac{D \times V}{U \times T_{\mathrm{eff}}} \tag{1}$$

where *A* is the administered radioactivity (MBq), *D* is the thyroid absorbed dose (Gy), *V* is the thyroid volume (mL), *U* is the radioiodine uptake fraction at 24 hours after administration, T_{eff} is the effective iodine-131 half-life (d), and *C* is the unit conversion coefficient (MBq d Gy^{-1} g^{-1}). In our hospital, we substitute 0.185 for *C*. Hereafter, the density of the thyroid is assumed to be 1 g/mL.

Three-dimensional thyroid volumetry using CT images

According to Shu et al. [9] and Lee et al. [10], the results of three-dimensional thyroid volumetry using CT images were in good agreement with the actual thyroid volume. Schlögl et al. [11] also reported similar results using ultrasound images. Therefore, we designated the three-dimensional thyroid volumes extracted manually as the reference data (V_{CT}) in this study. First, the thyroid region of interest (ROI) in the CT images were manually extracted from the CT images with a slice thickness of 5 mm. The thyroid region was extracted while excluding the surrounding blood vessels or muscles. Then, the sum of the voxels in each slice was calculated as the thyroid volume.

<u>Thyroid volumetry using ellipsoid approximation</u>

The ellipsoid approximation method for thyroid volumetry was described by Malago et al. [7], Lee et al. [10], and Schlögl et al. [11]. The thyroid volume of each lobe was approximated by an ellipsoid using Equation 2; then, the sum of each lobe was taken as the thyroid volume ($V_{\mathrm{ellipsoid}}$).

$$V_{\mathrm{ellipsoid}}\ [\mathrm{cm}^3] = \left(\frac{\pi}{6} \times a_L \times b_L \times c_L\right)_{\mathrm{Leftlobe}} + \left(\frac{\pi}{6} \times a_R \times b_R \times c_R\right)_{\mathrm{Rightlobe}} \qquad (2)$$

where *a* (cm) is an arbitrary diameter and *b* (cm) is its orthogonal diameter. Each line passes through the centroid of the thyroid ROI on the cross-sectional plane when the thyroid is approximated by an ellipsoid. *c* (cm) corresponds to the length of the major axis of the ellipsoid. The subscripts *L* and *R* indicate left and right, respectively. In this study, the isthmus was not considered in the volume calculation.

The calculation flow is summarized in Figure 1a. First, the calculation for the major axis, *c*, will be described. We set the thyroid ROI at the top and bottom of each thyroid lobe on the CT image manually and calculated the centroid coordinates of each ROI: (x_{upper}, y_{upper}, z_{upper}) and (x_{lower}, y_{lower}, z_{lower}). *c* was calculated from these coordinates according to Equation 3. In addition, we obtained the angles, φ (formed by *c* and the coronal plane) and ρ (formed by *c* and the sagittal plane), as shown in Figure 1b, and Equations 4 and 5.

$$\boldsymbol{c}\ [\mathbf{cm}] = \sqrt{(x_{\mathrm{upper}} - x_{\mathrm{lower}})^2 + (y_{\mathrm{upper}} - y_{\mathrm{lower}})^2 + (z_{\mathrm{upper}} - z_{\mathrm{lower}})^2} \qquad \mathbf{(3)}$$

$$\boldsymbol{\varphi}\ [\mathbf{deg.}] = \mathbf{arctan}\left(\frac{y_{\mathbf{upper}} - y_{\mathbf{lower}}}{z_{\mathbf{upper}} - z_{\mathbf{lower}}}\right) \quad (\mathbf{4})$$

$$\boldsymbol{\rho}\ [\mathbf{deg.}] = \mathbf{arctan}\left(\frac{x_{\mathbf{upper}} - x_{\mathbf{lower}}}{z_{\mathbf{upper}} - z_{\mathbf{lower}}}\right) \quad (\mathbf{5})$$

Subsequently, to calculate *a* and *b*, we created the cross-sectional plane at the midpoint of the major axis, *c*. Further, according to the definition of the ellipsoid, the cross-sectional plane is perpendicular to the two planes (containing *c*). In this study, we limited the plane for defining *a* and *b* to *the cross-sectional plane at the midpoint of the major axis*. Hereinafter, the *cross-sectional plane* refers to *the cross-sectional plane at the midpoint of the major axis*. The thyroid ROI of the thyroid region was set manually for this cross-sectional plane (Fig. 1–3). As shown in Figure 2, the centroid of the thyroid ROI in the cross-sectional plane was determined for each thyroid lobe. Furthermore, the combination of the diameter, a_θ, and its orthogonal diameter, b_θ, at angle θ were set to pass through the centroid of the thyroid ROI. The diameter of the thyroid in the cross-sectional plane can be obtained innumerable, regardless of whether it passes through the centroid of thyroid ROI. However, in this study, we restricted the diameter to those that pass through the centroid to define a strict ellipsoid. If θ is rotated from 0° to 90°, a combination of diameters (a_θ, b_θ) can be obtained. Thus, a combination of diameters was automatically obtained every 1° in each thyroid lobe (i.e. 90 combinations). Finally, a total of 8100 thyroid volumes per patient were acquired using 90 combinations of each thyroid lobe as shown in Equation 6.

$$\boldsymbol{V}_{\mathbf{ellipsoid}}(\boldsymbol{\theta}_L, \boldsymbol{\theta}_R)\ [\mathbf{cm}^3] = \left(\frac{\boldsymbol{\pi}}{\mathbf{6}} \times \boldsymbol{a}_{\boldsymbol{\theta}_L} \times \boldsymbol{b}_{\boldsymbol{\theta}_L} \times \boldsymbol{c}_L\right)_{\mathbf{Leftlobe}} + \left(\frac{\boldsymbol{\pi}}{\mathbf{6}} \times \boldsymbol{a}_{\boldsymbol{\theta}_R} \times \boldsymbol{b}_{\boldsymbol{\theta}_R} \times \boldsymbol{c}_R\right)_{\mathbf{Rightlobe}} \quad (\mathbf{6})$$

As a different concept from the one above, Heywood [12] reported that the ellipsoid approximation method can be satisfactorily performed using an equivalent circle diameter (Heywood diameter) as the diameter of the cross-sectional plane. In this study, we also verified the accuracy of the approximate volume derived from the equivalent circle diameter (Fig. 3). Assuming that the area of the thyroid ROI in the cross-sectional plane is S (cm^2), the equivalent circle diameter, R (cm), can be expressed as follows using S:

$$\boldsymbol{R}[\mathbf{cm}] = 2\sqrt{\frac{\boldsymbol{S}}{\boldsymbol{\pi}}} \quad (7)$$

Equations 8 and 9 is obtained by substituting R into a and b in Equation 6.

$$\boldsymbol{V}_{\mathbf{ellipsoid,Heywood}}\,[\mathbf{cm}^3] = \left(\frac{\boldsymbol{\pi}}{\mathbf{6}} \times \boldsymbol{R_L} \times \boldsymbol{R_L} \times \boldsymbol{c_L}\right)_{\mathbf{Leftlobe}} + \left(\frac{\boldsymbol{\pi}}{\mathbf{6}} \times \boldsymbol{R_R} \times \boldsymbol{R_R} \times \boldsymbol{c_R}\right)_{\mathbf{Rightlobe}} \quad (8)$$

$$\boldsymbol{V}_{\mathbf{ellipsoid,Heywood}}[\mathbf{cm}^3] = \left(\frac{\mathbf{2}}{\mathbf{3}} \times \boldsymbol{S_L} \times \boldsymbol{c_L}\right)_{\mathbf{Leftlobe}} + \left(\frac{\mathbf{2}}{\mathbf{3}} \times \boldsymbol{S_R} \times \boldsymbol{c_R}\right)_{\mathbf{Rightlobe}} \quad (9)$$

Among the thyroid volumes, $V_{\mathrm{ellipsoid}}(\theta_{\mathrm{L}},\theta_{\mathrm{R}})$, obtainable by the methods described in Figures 2–3 and Equations 6–9, five approximate volumes were compared with those determined three-dimensionally from CT images. These volumes are as follows: (1) the mean volume of the 8100 thyroid volumes, ($V_{\mathrm{ellipsoid,mean}}$), (2) the volume using the maximum diameter (either a_θ or b_θ) combined with its orthogonal diameter, ($V_{\mathrm{ellipsoid,maxlength}}$), (3) the maximum volume among the 8100 thyroid volumes, ($V_{\mathrm{ellipsoid,maxvolume}}$), (4) the minimum volume among the 8100 thyroid volumes, ($V_{\mathrm{ellipsoid,minvolume}}$), and (5) the thyroid volume determined with equivalent circle diameter (Heywood diameter), ($V_{\mathrm{ellipsoid,Heywood}}$). From these relationships, the accuracy and validity of the ellipsoid approximation method were examined, and the optimal method was identified.

Statistical analysis

We performed a simple regression analysis between the five approximate volumes and the three-dimensionally extracted thyroid volume, i.e., V_{CT}, in the statistics software package, R (version 3.5.1 for Windows). The error rate between the five approximate volumes ($V_{\text{ellipsoid}}$) and V_{CT} was obtained using Equation 10.

$$\boldsymbol{E}_{\textbf{ellipsoid}}[\%] = \mathbf{100} \times \frac{\boldsymbol{V}_{\textbf{ellipsoid}} - \boldsymbol{V}_{\textbf{CT}}}{\boldsymbol{V}_{\textbf{CT}}} \qquad (\mathbf{10})$$

Furthermore, we calculated a Lin's concordance correlation coefficient (CCC) according to Equation 11 to examine the consistency between V_{CT} and $V_{\text{ellipsoid}}$ in each patient [13].

$$\textbf{CCC} = \frac{\mathbf{2} \cdot \textbf{COV}\left(\boldsymbol{V}_{\textbf{CT}}, \boldsymbol{V}_{\textbf{ellipsoid}}\right)}{\boldsymbol{\sigma}^{\mathbf{2}}_{\boldsymbol{V}_{\textbf{CT}}} + \boldsymbol{\sigma}^{\mathbf{2}}_{\boldsymbol{V}_{\textbf{ellipsoid}}} + \left(\boldsymbol{\mu}_{\boldsymbol{V}_{\textbf{CT}}} - \boldsymbol{\mu}_{\boldsymbol{V}_{\textbf{ellipsoid}}}\right)^{\mathbf{2}}} \qquad (\mathbf{11})$$

where COV(V_{CT}, $V_{\text{ellipsoid}}$) is the covariance between V_{CT} and $V_{\text{ellipsoid}}$, $\sigma^2_{V_{\text{CT}}}$ and $\sigma^2_{V_{\text{ellipsoid}}}$ are the variances of V_{CT} and $V_{\text{ellipsoid}}$, respectively, and $\mu_{V_{\text{CT}}}$ and $\mu_{V_{\text{ellipsoid}}}$ are the mean of V_{CT} and $V_{\text{ellipsoid}}$, respectively.

McBride [14] suggested the following scale to describe the correlation based on values of CCC; < 0.90: Poor, 0.90–0.95: Moderate, 0.95–0.99: Substantial, > 0.99: Almost perfect. Similar to the study of Lee et al. [10], we compared the CCC values for the five approximate volumes with McBride's scale.

Results

Table 1 shows the length of the major axis, *c*, and the angles, φ and ρ, in each thyroid lobe. The value of *c* on both thyroid lobes is approximately 6 cm for all 50 cases. The angle, φ, is 8.30 ± 3.28° in the left lobe and −7.65 ± 3.14° in the right lobe. Similarly, the angle, ρ, is 0.19 ± 4.95° in the left lobe and 1.02 ± 5.41° in the right lobe. Figure 4 shows the relationship between V_{CT} and the 8100 thyroid volumes per patient obtained by systematically combining *a* and *b* of each thyroid lobe [$V_{\mathrm{ellipsoid}}(\theta_{\mathrm{L}},\theta_{\mathrm{R}})$]. The upper end of the error bar represents the maximum thyroid volume ($V_{\mathrm{ellipsoid,maxvolume}}$), and the lower end represents the minimum thyroid volume ($V_{\mathrm{ellipsoid,minvolume}}$). Thyroid volumes obtained by the ellipsoid approximation method varied by changing the combination of *a* and *b*. In particular, the variation in the approximated volume tended to increase as the thyroid volume increased (shaded area in Figure 4).

Table 2 shows the thyroid volumes obtained by three-dimensional volumetry (V_{CT}) and the ellipsoid approximation method ($V_{\mathrm{ellipsoid,mean}}$, $V_{\mathrm{ellipsoid,maxlength}}$, $V_{\mathrm{ellipsoid,maxvolume}}$, $V_{\mathrm{ellipsoid,minvolume}}$, and $V_{\mathrm{ellipsoid,Heywood}}$). Each relationship is shown in Figures 5a to 5e, and the error rates from V_{CT} and the ellipsoid approximation method ($E_{\mathrm{ellipsoid,mean}}$, $E_{\mathrm{ellipsoid,maxlength}}$, $E_{\mathrm{ellipsoid,maxvolume}}$, $E_{\mathrm{ellipsoid,minvolume}}$, and $E_{\mathrm{ellipsoid,Heywood}}$) are shown in Figures 6a to 6e. V_{CT} as the reference volume was widely distributed between 12.0 to 77.4 cm^3. Table 3 lists the values of the correlation coefficient, CCC, and McBride's scale for the thyroid volumes calculated by the ellipsoid approximation method when compared to V_{CT}. All correlations are strong with correlation coefficients of 0.900 or higher. The mean error rate was the highest between $V_{\mathrm{ellipsoid,minvolume}}$ and V_{CT} (–23.5%), and the lowest between $V_{\mathrm{ellipsoid,Heywood}}$ and V_{CT} (2.5%). CCC was used to assess the consistency of each relationship; the highest was for $V_{\mathrm{ellipsoid,Heywood}}$ (0.947; moderate) and the lowest was for $V_{\mathrm{ellipsoid,minvolume}}$ (0.672; poor).

Discussion

Thyroid volumes obtained by the ellipsoid approximation method varied by changing the combination of *a* and *b* as shown in Figure 4. In particular, the variation in the approximated volumes tended to increase as the thyroid volume increased. Generally, when performing thyroid volumetry on an ultrasound image, the length of the cross-sectional plane is subjectively determined by the operator. Thyroid volumetry using the ellipsoid approximation method that requires the lengths, *a* and *b*, is prone to error. According to Figures 5 and 6, and Table 3, although there was a correlation between V_{CT} and the ellipsoid approximation volumes, CCC differed depending on the approximate volume (0.672–0.947). $V_{\mathrm{ellipsoid,maxlength}}$ and $V_{\mathrm{ellipsoid,maxvolume}}$ were overestimated by 12.9% and 20.0%, respectively, and $V_{\mathrm{ellipsoid,mean}}$ and $V_{\mathrm{ellipsoid,minvolume}}$ were underestimated by 7.0% and 23.5%, respectively. Schlögl et al. reported that the approximate volume was 11% larger than the actual volume. Our study supported their findings because they used the maximum diameter to approximate the ellipsoid. In radioiodine therapy for Graves' disease, any error in the measurement of the thyroid volume directly affects the absorbed dose by the thyroid, and thereby the therapeutic effect, as shown in Equation 1. The success rate of internal radioiodine therapy in Graves' disease has been reported by Peters et al. [15] to depend on the thyroid absorbed dose and thyroid weight. By applying these errors to Marinelli's formula (Eq. 1) and calculating backwards with the administered radioactivity, *A*, as a constant, the thyroid absorbed doses, *D*, are reduced by 11.4% and 16.6% when $V_{\mathrm{ellipsoid,maxlength}}$ and $V_{\mathrm{ellipsoid,maxvolume}}$ are used as thyroid volumes, respectively. Similarly, when $V_{\mathrm{ellipsoid,mean}}$ and $V_{\mathrm{ellipsoid,minvolume}}$ are used, the thyroid absorbed doses are 7.6% and 30.8% in excess of the reference.

$V_{\mathrm{ellipsoid,mean}}$ can be obtained by automatically measuring the volume of the thyroid using a combination of *a* and *b* and then averaging these multiple volumes (8100 volumes per patient in this study); thus, the mean error with V_{CT} could be reduced to 7.0% because of error cancellation due to averaging. In contrast, $V_{\mathrm{ellipsoid,Heywood}}$ was in good agreement with V_{CT} according to the results of single regression analyses and the resultant CCC values; the mean error with V_{CT} was 2.5%. There are no reports of past studies in which the thyroid volumes were calculated by the ellipsoid approximation method using the equivalent circle diameter. Therefore, this result represents a new finding. For $V_{\text{ellipsoid,Heywood}}$, it is not necessary to consider the variation due to *a* and *b* because this approximated thyroid volume is calculated from the equivalent circle diameter derived from the thyroid ROI on the cross-sectional plane. Therefore, if the ROI can be set accurately in the thyroid region, the accuracy and robustness of the ellipsoid approximation method should be higher than that for the conventional ellipsoid diameters.

We also considered the length of the major axis, *c*. The angle between *c* and the coronal plane was approximately 8°, and the angle between *c* and the sagittal plane was approximately 1°, for all cases. At these angles, the error between the projected length of *c* on the coronal or sagittal plane and the actual length of *c* was approximately 1%. Lee et. al. measured the length of the major axis on the coronal or sagittal planes and calculated the thyroid volume by the ellipsoid approximation method [10]. Our study supported the validity of measuring the axial length from the coronal or sagittal planes described in their method. The length of the major axis could be measured accurately and easily if we use CT images. An arbitrary cross-sectional image can be obtained using ultrasonography, although this route is prone to subjectivity in measurement. In recent years, it has become possible to acquire volume images with less distortion using three-dimensional ultrasound images. If the knowledge of this study is applied to ultrasound images, thyroid volumetry could be acquired more easily and accurately in the future.

For each volume determined in this study, the error due to the ellipsoid approximation method was in the range, 0–50%, and in some cases the error exceeded 50%. Although it is possible to easily obtain an approximate thyroid volume by the ellipsoid approximation method, the limitation is the approximation itself. Even $V_{\text{ellipsoid,mean}}$ and $V_{\text{ellipsoid,Heywood}}$ contains non-negligible errors due to the approximation. Therefore, we conclude that thyroid volumetry using the ellipsoid approximation cannot be a viable alternative to three-dimensional thyroid volumetry in radioiodine therapy; it is necessary to perform three-dimensional thyroid volumetry using CT or ultrasound images for therapeutic efficacy.

In this study, we set *the cross-sectional plane at the midpoint of the major axis* according to the definition of the ellipsoid, and obtained the cross-sectional diameters, *a* and *b*, on this plane. In clinical practice, the cross-sectional diameter of the thyroid is often obtained from the *trans-axial plane of the body* (*cranial to caudal axis*) using CT or ultrasonography. That is, *the cross-sectional plane at the midpoint of the major axis* in the ellipsoid is inclined with *the trans-axial plane of a body* (Table 1). In the 50 cases of this study, even if *the trans-axial plane of a body at the midpoint of the major axis* was used in place of *the cross-sectional plane at the midpoint of the major axis*, the difference between the cross-sectional areas of the two planes was 1% or less. Therefore, the inclination of the cross-sectional plane cannot be a large variation factor. However, it can be concluded that the cross-sectional diameters (*a*, *b*) or area (*S*) are the main parameters affecting the ellipsoid volume.

Patients with Graves' disease tend to have low CT values in the thyroid. There were some cases where it was difficult to extract thyroid regions in this study. If the CT value of the thyroid is low, the accuracy of the extraction becomes a problem. Although Shu et al. and Lee et al. reported good agreement for the results of three-dimensional thyroid volumetry using contrast-enhanced CT images with the actual thyroid volume [9–10], one of the limitations of our study is that the measurement accuracy of three-dimensional volumetry was not examined. Contrast-enhanced CT scans will improve thyroid visibility and segmentation, but they will delay radioiodine therapy for weeks or months because the contrast media contains iodine [3–4]. In addition, we need to consider the inter- and intra-operator error of the manually extracted-thyroid ROI. In contrast, visibility of the thyroid is improved in ultrasound images. Therefore, it would be easier to extract the region, although determining the cross-sectional plane of the thyroid lobe could be difficult. In our hospital, we measure thyroid volumes using CT images. Therefore, ultrasound images were not available as part of a retrospective study. Further studies are needed to verify the accuracy of our five ellipsoid-approximation-method volumes using ultrasound images to extract reference volume data.

Conclusion

We determined the variation in the approximated thyroid volumes determined by the ellipsoid approximation method using CT images; thyroid volumes varied depending on the diameter or area of the cross-sectional plane. Furthermore, we found that the ellipsoid approximation method using the equivalent circle diameter can determine thyroid volumes in good agreement with those extracted manually by three-dimensional volumetry. However, thyroid volumetry by the ellipsoid approximation method included an error in the range 0–50% and in some cases the error exceeded 50%. Consequently, we recommend three-dimensional thyroid volumetry if measurement accuracy is required.

Abbreviations

ROI: Region of interest, CCC: Concordance correlation coefficient

Declarations

Ethics approval and consent to participate:

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Ethical Review Committee of Nagoya University Hospital and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by the Ethical Review Committee of Nagoya University Hospital (authorization no. 2018-0179). Since this study analysed clinical data retrospectively, we did not obtain informed consent directly from each patient. Instead of direct informed consent, we published the research contents on the university web page and provided an opt-out opportunity.

Consent for publication

Not applicable.

Availability of data and material:

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions:

KK is the guarantor of integrity of the entire study. NF and KK contributed to the study concepts and design. NF and KK contributed to the literature research. NF, KK, SA, and SN contributed to the clinical studies. NF and KK contributed to the experimental studies/data analysis. NF contributed to the statistical analysis. KK and NF contributed to the manuscript preparation. KK contributed to the manuscript editing. All authors read and approved the final manuscript.

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Tables and Figures

Table 1. Length of the major axis, *c*, and the angles, φ and ρ, in each patient's thyroid lobe.

Table 2. Thyroid volumes calculated by three-dimensional volumetry (V_{CT}) and the ellipsoid approximation method ($V_{\mathrm{ellipsoid,mean}}$, $V_{\mathrm{ellipsoid,maxlength}}$, $V_{\mathrm{ellipsoid,maxvolume}}$, $V_{\mathrm{ellipsoid,minvolume}}$, and $V_{\mathrm{ellipsoid,Heywood}}$).

Table 3. Correlation coefficient, CCC, and McBride's scale between V_{CT} and each approximate volume. CCC for assessing the consistency of each relationship was above 0.900 for $V_{\mathrm{ellipsoid,mean}}$ and $V_{\mathrm{ellipsoid,Heywood}}$.

Fig. 1. a) Calculation method for thyroid volumes by the ellipsoid approximation method. b) Calculation method for the length of the major axis, *c*, and the angles, φ, and ρ, in each patient's thyroid lobe.

Fig. 2. Measurement of arbitrary diameters and their corresponding orthogonal diameters (*a* and *b*) on the cross-sectional plane at the midpoint of the major axis. Four approximate volumes ($V_{\mathrm{ellipsoid,mean}}$, $V_{\mathrm{ellipsoid,maxlength}}$, $V_{\mathrm{ellipsoid,maxvolume}}$, and $V_{\mathrm{ellipsoid,minvolume}}$) were obtained from *a* and *b*.

Fig. 3. Ellipsoid approximation method for thyroid volumes using the equivalent circle diameter (Heywood diameter).

Fig. 4. Relationship between V_{CT} and the 8100 thyroid volumes obtained by combining *a* and *b* of each thyroid lobe [$V_{\mathrm{ellipsoid}}(\theta_{\mathrm{L}},\theta_{\mathrm{R}})$]. The upper and lower end of the error bar represents the maximum and the minimum thyroid volume, respectively. The shaded area indicates an area surrounded by the regression lines of $V_{\mathrm{ellipsoid,maxvolume}}$ and $V_{\mathrm{ellipsoid,minvolume}}$ (Corresponding to Fig. 5c and 5d, respectively). The variation in the approximate volumes tended to increase as the thyroid volume increased.

Fig. 5. Relationship between V_{CT} and the five approximate volumes ($V_{\mathrm{ellipsoid,mean}}$, $V_{\mathrm{ellipsoid,maxlength}}$, $V_{\mathrm{ellipsoid,maxvolume}}$, $V_{\mathrm{ellipsoid,minvolume}}$, and $V_{\mathrm{ellipsoid,Heywood}}$). Although there was a strong correlation between V_{CT} and these approximate volumes, the slopes of the regression equation were different for each relationship (0.79–1.20). For this reason, CCC differed for each approximate volume (0.672–0.947).

Fig. 6. Error rate between V_{CT} and the five approximate volumes ($E_{ellipsoid,mean}$, $E_{ellipsoid,maxlength}$, $E_{ellipsoid,maxvolume}$, $E_{ellipsoid,minvolume}$, and $E_{ellipsoid,Heywood}$). The mean error rate was the highest between $V_{ellipsoid,minvolume}$ and V_{CT} (–23.5%), and the lowest between $V_{ellipsoid,Heywood}$ and V_{CT} (2.5%).

Figures

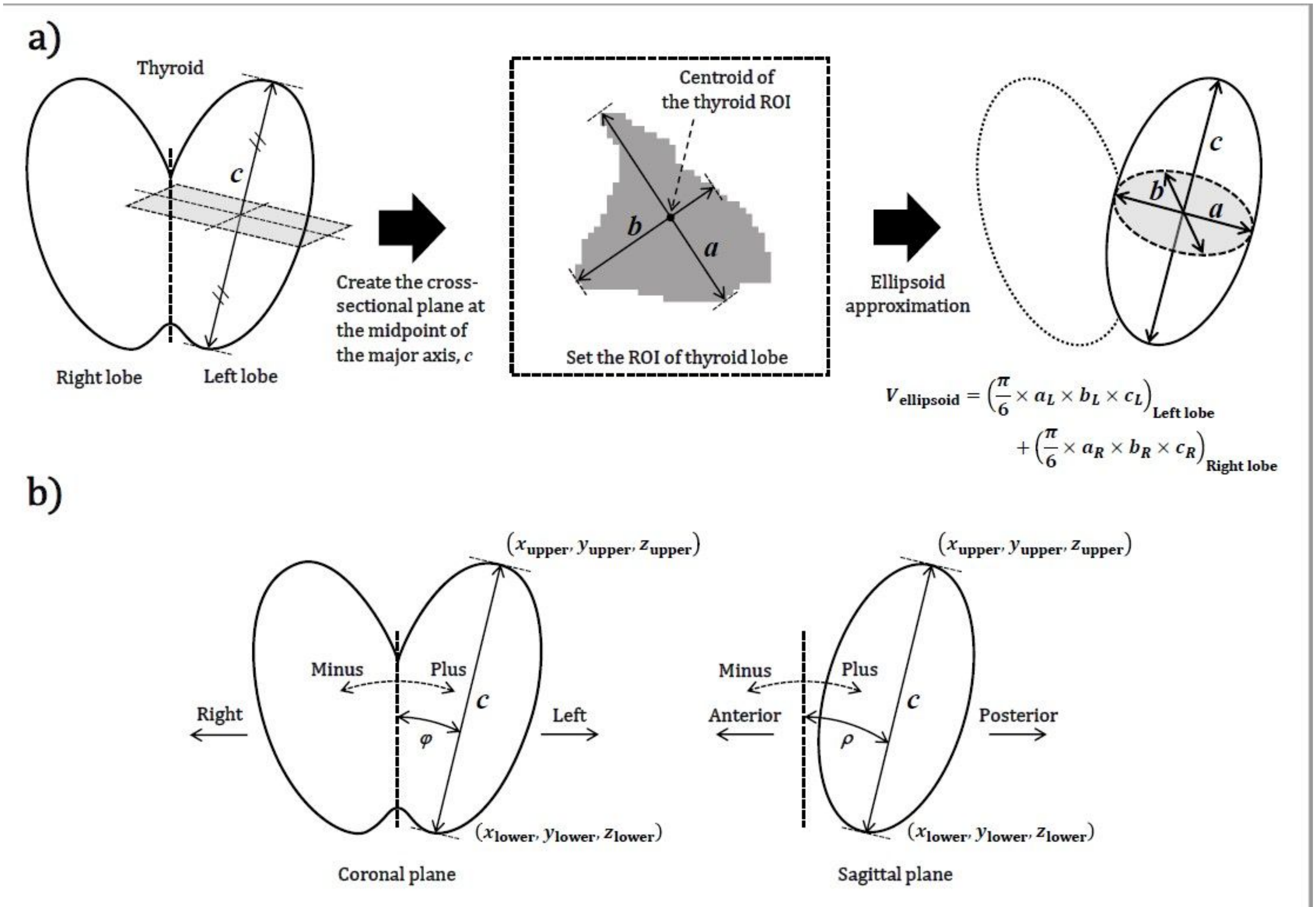


Figure 1

a) Calculation method for thyroid volumes by the ellipsoid approximation method. b) Calculation method for the length of the major axis, c, and the angles, φ, and ρ, in each patient's thyroid lobe.

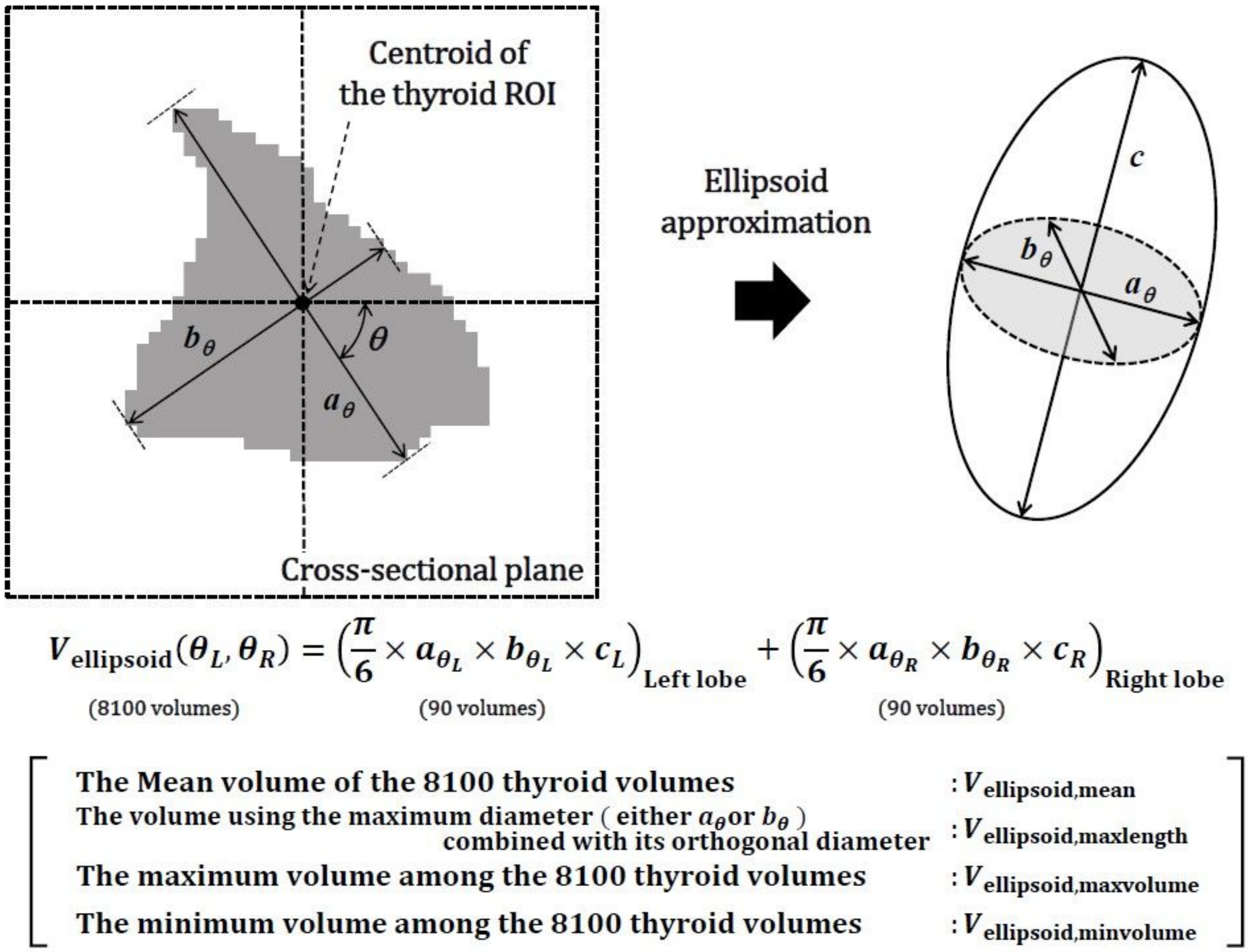
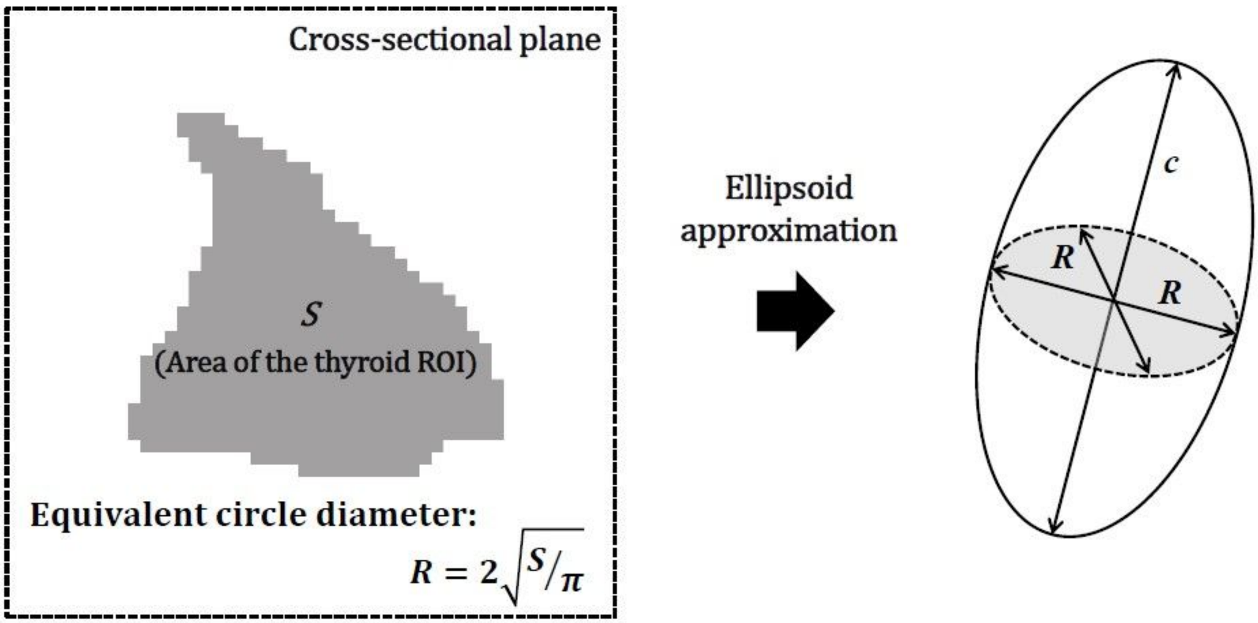


Figure 2

Measurement of arbitrary diameters and their corresponding orthogonal diameters (a and b) on the cross-sectional plane at the midpoint of the major axis. Four approximate volumes (Vellipsoid,mean, Vellipsoid,maxlength, Vellipsoid,maxvolume, and Vellipsoid,minvolume) were obtained from a and b.



$$V_{\text{ellipsoid,Heywood}} = \left(\frac{\pi}{6} \times R_L \times R_L \times c_L\right)_{\text{Left lobe}} + \left(\frac{\pi}{6} \times R_R \times R_R \times c_R\right)_{\text{Right lobe}}$$

$$= \left(\frac{2}{3} \times S_L \times c_L\right)_{\text{Left lobe}} + \left(\frac{2}{3} \times S_R \times c_R\right)_{\text{Right lobe}}$$

Figure 3

Ellipsoid approximation method for thyroid volumes using the equivalent circle diameter (Heywood diameter).

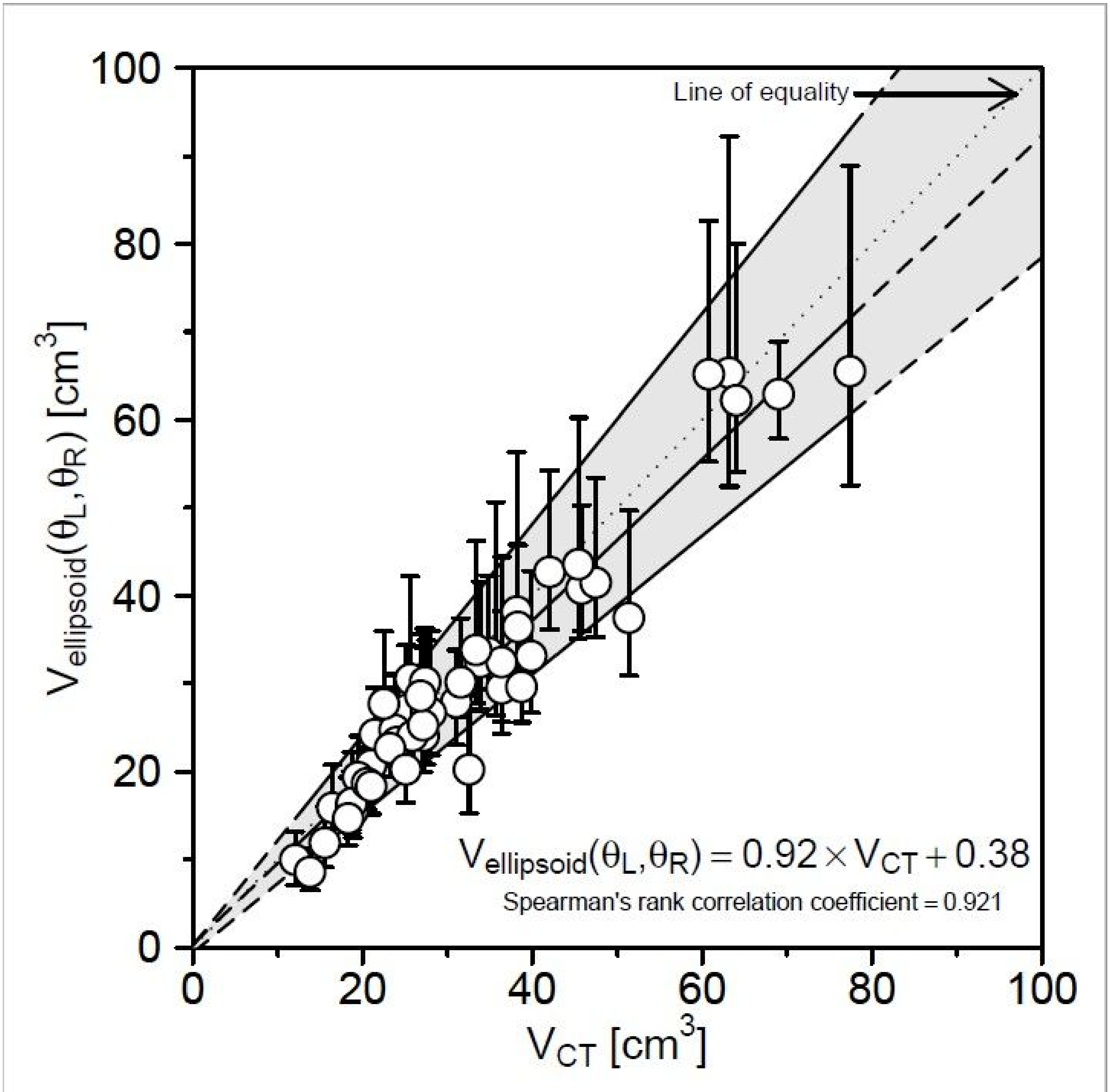


Figure 4

Relationship between VCT and the 8100 thyroid volumes obtained by combining a and b of each thyroid lobe [Vellipsoid(θL,θR)]. The upper and lower end of the error bar represents the maximum and the minimum thyroid volume, respectively. The shaded area indicates an area surrounded by the regression lines of Vellipsoid,maxvolume and Vellipsoid,minvolume (Corresponding to Fig. 5c and 5d, respectively). The variation in the approximate volumes tended to increase as the thyroid volume increased.

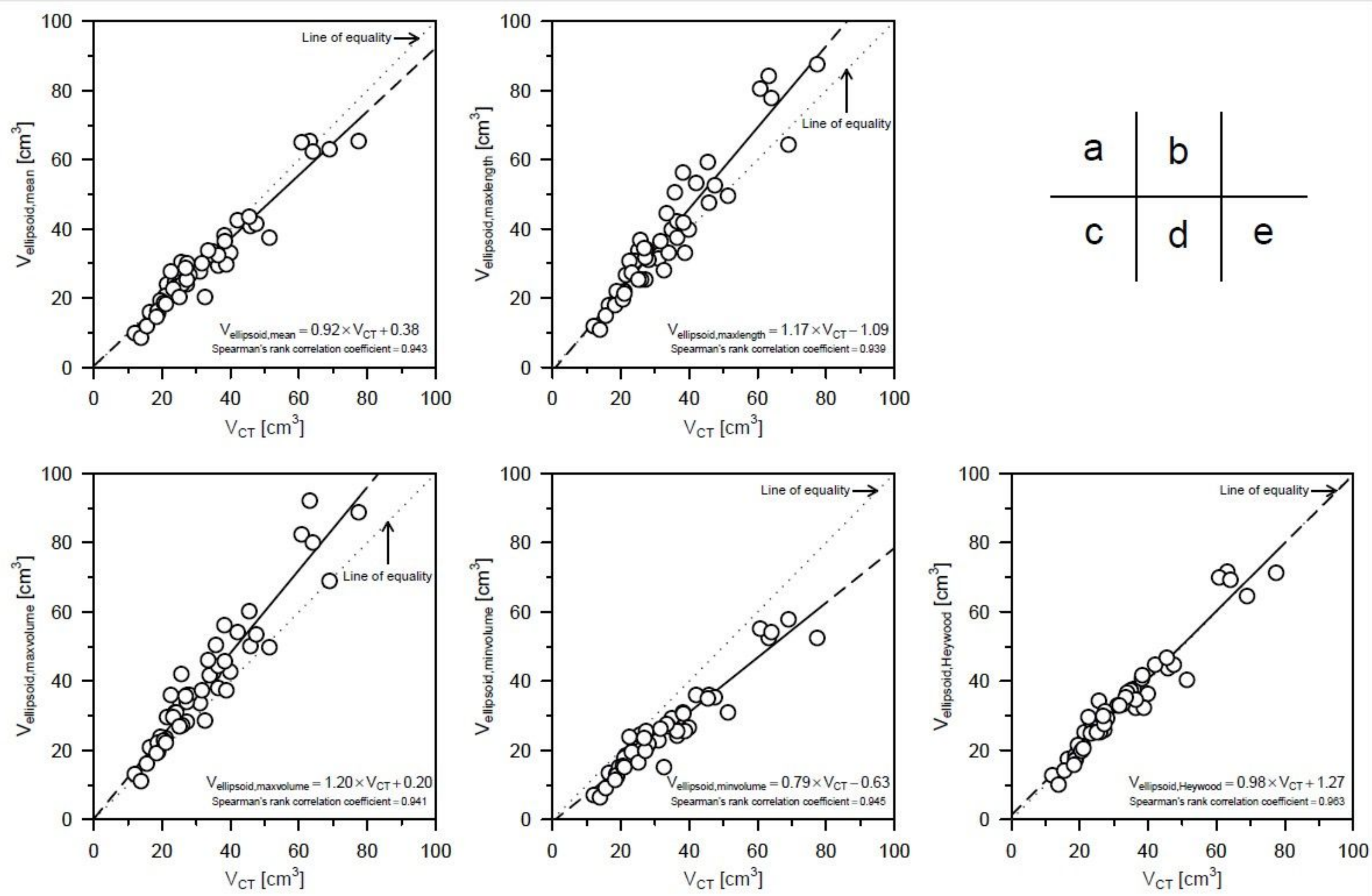


Figure 5

Relationship between VCT and the five approximate volumes (Vellipsoid,mean, Vellipsoid,maxlength, Vellipsoid,maxvolume, Vellipsoid,minvolume, and Vellipsoid,Heywood). Although there was a strong correlation between VCT and these approximate volumes, the slopes of the regression equation were different for each relationship (0.79–1.20). For this reason, CCC differed for each approximate volume (0.672–0.947).

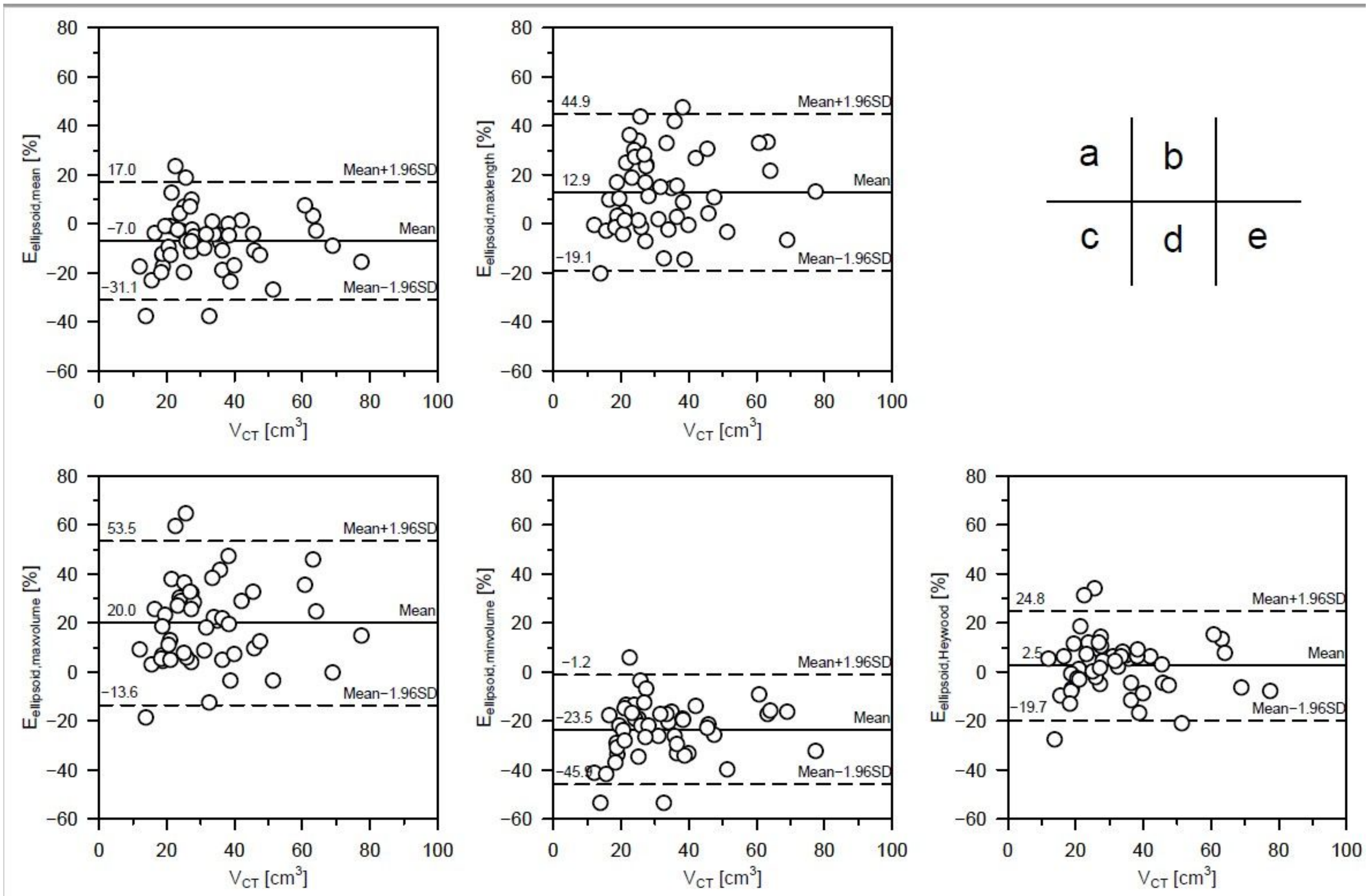


Figure 6

Error rate between VCT and the five approximate volumes (Eellipsoid,mean, Eellipsoid,maxlength, Eellipsoid,maxvolume, Eellipsoid,minvolume, and Eellipsoid,Heywood). The mean error rate was the highest between Vellipsoid,minvolume and VCT (−23.5%), and the lowest between Vellipsoid,Heywood and VCT (2.5%).