Semi-automated 3D CT thyroid volumetry: Prospective comparative study of the thyroid volumes measured by specimen, 2D CT and US

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Aims and objectives

Introduction

The accurate determination of thyroid volume is required for the diagnosis, treatment, and follow-up of many thyroid diseases, such as endemic and sporadic goiter, nodules, thyroiditis, and Graves’ disease [1-4]. A precise thyroid volume measurement is also required for the dosimetry of radioiodine therapies [1, 5-6] and the evaluation of therapeutic effect [1, 7]. In surgical management, thyroid size has become an essential requisite in the selection of patients for minimally invasive surgery [4, 8-11]. In fact, many surgeons agree that a thyroid volume > 25 ml, echographically determined by two-dimensional ultrasonography (US), is a major exclusion criterion in determining eligibility for minimally invasive surgery [4, 8].

Ultrasound estimation of thyroid volume has become the accepted method for the assessment of the thyroid gland, and the World Health Organization and the International Council for the Control of Iodine Deficiency Disorders consider US as the diagnostic method for goiter assessment [1,12]. However, conventional sonography is not sufficiently accurate for thyroid volumetry [1,13-15], as a thyroid with irregular geometry is assumed to be an ellipsoid [1,15]. Deviations of the thyroid shape from the ellipsoidal model may result in errors of up to 30% for the volumetry of the thyroid [1,15].

In previous reports, thyroid volumes measured by computated tomography (CT) scans have been known to be highly accurate [1,16-17]. Shu et al. [1] and Hermans et al. [16] acquired the three-dimensional (3D) CT volume of the thyroid gland by manual segmentation. In a comparison with specimen volume, Hermans et al. [16] did not measure the real volume of the thyroid gland, of which 1 cm³ was considered to weigh 1 g. In a comparative study of thyroid volume measured by US and CT reported by Nygaard et al. [17], the authors calculated the thyroid volume based on recordings of cross-sectional areas through the gland using an ellipsoid volume formula (Vellipsoid = \#/6 × height × width × length). To our knowledge, there are no previous reports of 3D CT volumetry by semi-automated segmentation of the thyroid gland or of comparison among US volume, CT volume, and surgical specimen volume.

The purpose of this prospective study is to measure thyroid volumes by semiautomated 3D CT thyroid volumetry, to compare the thyroid specimen volumes with the estimated thyroid volumes using two-dimensional (2D) US, 2D CT and 3D CT imaging, and to determine the adequate thyroid volumetry in the preoperative assessment of patients with thyroid diseases.
Methods and materials

A total of 47 patients (40 females and 7 males; mean age, 46.3 years; age range, 19-90 years) who underwent total thyroidectomy for papillary thyroid cancer between October 2011 and January 2012, were included in this prospective study. In all patients, neck CT scans and thyroid US scans were performed for the preoperative evaluation of primary tumors and regional lymph node metastasis. The thyroid volumes were measured by 2D US, 2D CT, and 3D CT. The volume of the thyroid specimens was obtained using the excised gland after surgery. Patients with large thyroid volume such as substernal goiter were excluded in this study because the volume measurement was not available due to the coverage of the US scan depth.

Measurement of thyroid volume on 2D US (2D USV)

On the preoperative US (iU22, Philips Healthcare, Bothell, WA, USA), the thyroid volumes were calculated by the ellipsoid volume formula:

\[2D \text{ US Volume} = \frac{1}{6} \times (a \times b \times c)\]

where \(a\) and \(b\) represent the maximum length of the horizontal (a) and vertical (b) axes determined from the transverse scans, and \(c\) represents that of the vertical axis determined from the longitudinal scans. Total thyroid volume is obtained by summing the volumes of both lobes. The isthmus is not taken into account in the volume calculation.

Measurement of thyroid volume on 2D CT (2D CTV)

For the preoperative assessment of regional lymph node metastasis, contrast-enhanced neck CT scans were performed using a 64-slice spiral CT scanner with a reconstructive thickness of 1 mm (Brilliance 64, Philips Healthcare, Best, Netherlands). The thyroid volumes on 2D CT were calculated using the ellipsoid volume formula:

\[2D \text{ CT Volume} = \frac{1}{6} \times (a \times b \times c)\]

where \(a\) and \(b\) represent the maximum length of the horizontal (a) and vertical (b) axes determined from the axial CT images, and \(c\) represents that of the vertical axis determined from the coronal or sagittal CT images. Total thyroid volume is obtained by summing the volumes of both lobes. The isthmus is not taken into account in the volume calculation.

Semi-automated 3D thyroid CT volumetry (3D CTV)
The CT data acquired from the contrast-enhanced neck CT scans were transferred to a 3D visualization workstation (Aquarius iNtuition, TeraRecon, Inc., Foster City, CA). The main window display contained one 3D image and three 2D images, which showed bony structures and vascular structures as well as thyroid glands. First, to remove the vascular structures, the region grow mode was used by clicking and holding the mouse on the vessel in order to mask the vessel as much as possible. The Exclude tool was selected to show everything except the masked vessel. By repeating this mask operation, most vascular structures were removed around the thyroid glands. Second, in order to select the thyroid glands, the region grow mode was applied to mask the thyroid glands as much as possible and the Select tool was used to show only the masked thyroid glands (Fig. 1).

Fig. 1: Semi-automated segmentation of the thyroid glands for 3D thyroid CT volumetry.

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Third, the Overlay tool was used to complete the segmentation of the thyroid glands using the green overlay on three 2D images, which showed the masked area that had been removed (Fig. 2). Using the FreeROI (region of interest) tool and hand drawing, the segmentation of the thyroid glands was manually corrected by including or excluding the ROI within the overlay image. Finally, the thyroid volume was automatically calculated in cubic centimeters, and was displayed on the 3D image (Fig. 2).
Fig. 2: Automatic calculation of the thyroid volume using the 3D thyroid CT volumetry and selective manual correction of the segmented thyroid glands.

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Measurement of specimen thyroid volume (STV)

In all patients with papillary thyroid carcinomas, total thyroidectomy was performed by one thyroid surgeon. After surgery, the volume of the excised thyroid specimen was measured by the water displacement method; that is, saline was added in a graduated cylinder in which the removed thyroid gland was placed. The amount of displaced saline (ml) was recorded as the specimen thyroid volume. The volume measurement of the thyroid glands was performed in a blinded fashion.

Statistical Analysis

In all patients, the 2D USV, the 2D CTV, and the 3D CTV were compared with the reference volume, STV. The accuracy of each method (X) was determined as proposed by Bland and Altman [18]. Standardized volume differences (Dx) of the method to be
tested to the reference method (R) were calculated according to the following formula [18]:

\[ D_x [\%] = \frac{(X [ml] - R [ml])}{R [ml]} \times 100 \]

These standardized differences were plotted against the reference volume. The average of these differences should be zero if there are no systematical errors. The standard deviation of the differences is a test of the accuracy of the examined method. Difference between and correlation of 2D USV, 2D CTV, 3D CTV and STV were statistically analyzed using one-way ANOVA with Tukey post-hoc test, Pearson correlation (R), and linear regression with a coefficient of determination (R²). Time intervals between US and CT, US and surgery, and CT and surgery were measured and the processing time of semi-automated 3D thyroid CT volumetry was also evaluated. The relationship between the processing order or the 3D CTV and the processing time was statistically analyzed using a linear regression with a coefficient of determination (R²) and a Pearson correlation (R). Statistical analyses were performed using MedCalc for Windows, version 12.6 (MedCalc Software, Ostend, Belgium) and PASW version 18 (SPSS Inc., Chicago, IL, USA). P < 0.05 was considered statistically significant.
**Fig. 1:** Semi-automated segmentation of the thyroid glands for 3D thyroid CT volumetry.

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Fig. 2: Automatic calculation of the thyroid volume using the 3D thyroid CT volumetry and selective manual correction of the segmented thyroid glands.

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Results

<table>
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<tr>
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<th>2D CT</th>
<th>3D CT</th>
<th>Specimen</th>
</tr>
</thead>
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<td>7.7 – 32.8</td>
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<td>Median (ml)</td>
<td>17.8</td>
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</table>

Table 1: Summary Statistics of Thyroid Volumes Measured by 2D US, 2D CT, 3D CT and Specimen in 47 Patients

References: Department of Radiology, Chung-Ang University College of Medicine, Chung-Ang University Medical Center - Seoul/KR

Table 1 summarizes the thyroid volumes measured by 2D US, 2D CT, and 3D CT, and the STV. The mean 2D USV, 2D CTV, 3D CTV, and STV were 19.34 ml, 22.58 ml, 18.71 ml, and 18.55 ml, respectively. Using 2D USV, 38% (18/47) of the volumes were underestimated and 60% (28/47) were overestimated. Using 2D CTV, 13% (6/47) of the volumes were underestimated and 87% (41/47) were overestimated. Of 3D CTV, 47% (22/47) were underestimated and 47% (22/47) were overestimated (Fig. 3). The mean volume difference was 0.78 ± 3.10 ml between STV and 2D USV, 4.03 ± 4.66 ml between STV and 2D CTV, and 0.16 ± 2.52 ml between STV and 3D CTV. Bland-Altman plots of volume measurements taken with 2D US, 2D CT, and 3D CT versus specimen are shown in Fig. 4. The mean differences of 2D USV, 2D CTV, and 3D CTV were situated above the zero horizontal axes (line of equality, difference = 0). Despite this, the limits of agreement (-5.1 and 13.2) were relatively large in 2D CT, compared to 2D US (-5.3 and 6.9) and 3D CT (-4.8 and 5.1).
Fig. 3: A box plot of thyroid volumes measured by 2D US, 2D CT, 3D CT and specimen.

References: Department of Radiology, Chung-Ang University College of Medicine, Chung-Ang University Medical Center - Seoul/KR

Fig. 4: Bland-Altman plots of volume measurements taken with 2D US (A), 2D CT(B) and 3D CT(C) versus specimen.

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There was a statistically significant difference in the mean volume between 2D USV, 2D CTV, 3D CTV, and STV groups as determined by one-way ANOVA (p = 0.009). There was no statistically significant difference between 2D USV and STV (p = 0.937), or between 3D CTV and STV (p = 0.999). However, there was a statistically significant difference between 2D CTV and STV (p = 0.016), as well as between 2D CTV and 3D CTV (p = 0.023) (Table 2). A Tukey post-hoc test revealed that the 2D CTV was statistically significantly higher than both 3D CTV and STV. Compared to the 2D USV, there was no statistically significant difference in the 2D CTV group (p = 0.077) or in the 3D CTV group (p = 0.967). The coefficients of correlation (R) of STV and 2D USV, STV and 2D CTV, and STV and 3D CTV were 0.885, 0.725 and 0.929, respectively (Table 3). Linear regression analyses applied to the thyroid volumes between 2D US, 2D CT, 3D CT, and specimen are shown in Fig. 5. The correlation between 2D CTV and STV (R² = 0.526) was poor, whereas the correlation between 2D USV and STV and between 3D CTV and STV was reasonable (R² = 0.783 and R² = 0.863).

<table>
<thead>
<tr>
<th>Method</th>
<th>Mean Difference</th>
<th>Std. Error</th>
<th>Sig.</th>
<th>95% Confidence Interval</th>
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<td>Specimen</td>
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<td>1.3413</td>
<td>.967</td>
<td>-2.854</td>
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<tr>
<td>2D CT</td>
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<td>1.3413</td>
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<td>.389</td>
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<td>Specimen</td>
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<td>.016</td>
<td>.549</td>
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</tr>
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* The mean difference is significant at the 0.05 level.

Table 2: One-way ANOVA Analyses with Tukey Post-Hoc Test for Volume Measurement by Using 2D US, 2D CT, 3D CT and Specimen

References: Department of Radiology, Chung-Ang University College of Medicine, Chung-Ang University Medical Center - Seoul/KR
Table 3: Pearson correlation matrix for volume measurement of 2D US, 2D CT, 3D CT and specimen.

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<tr>
<td>2D CT</td>
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Correlation is significant at the 0.01 level.

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The time intervals were as follows: 11.2 ± 16.1 days between US and CT, 16.5 ± 16.2 days between US and surgery, and 10.4 ± 10.4 days between CT and surgery. The mean processing time of semi-automated 3D thyroid CT volumetry was 7.0 ± 4.1 minutes (range, 2-21 minutes). Linear regression analysis showed a weak negative correlation between the image processing time and image processing order (R² = 0.295 and R = 0.543) and no correlation between the image processing time and the 3D CTV (p = 0.078).
Table 1: Summary Statistics of Thyroid Volumes Measured by 2D US, 2D CT, 3D CT and Specimen in 47 Patients

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* The mean difference is significant at the 0.05 level.

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Correlation is significant at the 0.01 level.

Fig. 3: A box plot of thyroid volumes measured by 2D US, 2D CT, 3D CT and specimen.
Fig. 4: Bland-Altman plots of volume measurements taken with 2D US (A), 2D CT(B) and 3D CT(C) versus specimen.

Fig. 5: Linear regression analyses applied to thyroid volumes between 2D US (A), 2D CT (B) or 3D CT (C) and specimen. These are the scatter diagrams with the regression line (solid line) and identity line (dotted line). R is the Pearson correlation coefficient.
Conclusion

In a comparative study of thyroid volume measured by US and CT by Nygaard et al. [17], the authors measured the 2D CT volume by computerized calculation of the volume of the cross-section, which was a reproducible method and could be also used in goiters with substernal extension. The US volumetry, however, was calculated by the ellipsoid formula, which measured the height, width, and length of the thyroid, and was less reproducible, especially in large, multinodular goiters in which the thyroid size was underestimated. In 3D CT volumetry, Jian et al. [1] and Hermans et al. [16] applied the manual segmentation of the thyroid gland. For 3D CT volumetry by manual segmentation, Jian et al. [1] reported that the intraobserver and interobserver differences were not significant, and the intraobserver and interobserver correlations were very high. In a phantom study, there was excellent correlation between the true and CT calculated volumes [1]. Additionally, in a specimen study, Hermans et al. [16] reported that there was no significant difference between the real thyroid volume and the 3D CT volume, in which 1 cm$^3$ of the thyroid tissue was considered to weigh 1 g.

In the present study, in contrast to previous studies, the 2D USV was automatically calculated using the ellipsoid volume formula, $V_{\text{ellipsoid}} = \pi/6 \times \text{height} \times \text{width} \times \text{length}$, which was measured using a real-time US scanner. The 2D CTV was manually calculated using the aforementioned ellipsoid volume formula, but the height, width, and length were manually measured on multiplanar CT images obtained by using CT scans with 1-mm reconstructive thickness. For 3D CT volumetry, an iterative, semi-automated segmentation was first applied to acquire the 3D volume rendering image of the thyroid gland, of which the volume was automatically calculated on a workstation. The true thyroid volume could be measured by the water displacement method from the excised specimen. However, the present study showed no significant difference between STV and 2D USV, or between STV and 3D CTV.

In the present study, there was a weak negative correlation between the image processing time and the imaging processing order; whereas there was no correlation between the image processing time and the 3D CTV. To our knowledge, there has been no comparative study of thyroid volumes and image processing procedures on 3D thyroid CT volumetry. Concerning CT liver volumetry, however, Suzuki et al. reported that the average user time for automated volumetry was 0.57 minutes per case, whereas those for interactive and manual volumetry were 27.3 and 39.4 minutes per case [19]. In our study, the mean processing time of semi-automated 3D thyroid CT volumetry was 7.0 minutes even though we included the manual correction time.

There were a few limitations to this study. First, the volume of the surgical specimen may not exactly represent the true thyroid volume because of incomplete dissection, dissection of adjacent connective tissue, or dryness and bleeding of the gland tissue after dissection, although we could measure the real volume of the thyroid gland after surgery.
Second, large thyroids such as substernal goiter were excluded in this study because the volume measurement was not available due to the coverage of the US scan depth. Third, there was a difference in the scanning axis of thyroid glands between US and CT scans. Fourth, we did not evaluate intraobserver and interobserver variability of thyroid volume measurements because the purpose of our study was to validate the semi-automated 3D thyroid CT volumetry in the present study. Further research about intraobserver and interobserver variability of the semi-automated 3D thyroid CT volumetry is anticipated.

In the present study, there was no volume difference between 2D US volume or semi-automated 3D CT volume and the specimen volume. Ultrasonography can provide a reliable preoperative estimate of thyroid volume. Semi-automated 3D CT thyroid volumetry provides a more reliable thyroid volume, which may contribute to a more appropriate surgical management of thyroid disease. In the near future, accuracy and convenience of planar CT volumetry will be improved by invention of 3D automated CT volumetry.
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