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RESEARCH ARTICLE

Usefulness of 99mTc-pertechnetate SPECT-CT in Thyroid Tissue Volumetry: Phantom Studies and a Clinical Case Series

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Abstract: ***Background*:** An accurate measurement of the target volume is of primary importance in theragnostics of hyperthyroidism.

***Objective*:** Our purpose was to evaluate the accuracy of a threshold-based isocontour extraction procedure for thyroid tissue volumetry from SPECT-CT.

***Methods*:** Cylindrical vials with a fixed volume of 99mTcO4 at different activities were inserted into a neck phantom in two different thickness settings. Images were acquired by orienting the phantom in different positions, *i.e.*, 40 planar images and 40 SPECT-CT. The fixed values of the isocontouring threshold for SPECT and SPECT-CT were calculated by means of linear and spline regression models. Mean, Median, Standard Deviation, Standard Error, Mean Absolute Percentage Error and Root Mean-Square Error were computed. Any difference between the planar method, SPECT and SPECT-CT and the effective volume was evaluated by means of ANOVA and posthoc tests. Moreover, planar and SPECT-CT acquisitions were performed in 8 patients with hyperthyroidism, considering relevant percentage differences greater than > 20% from the CT gold standard.

***Results*:** Concerning phantom studies, the planar method shows higher values of each parameter than the other two methods. SPECT-CT shows lower variability. However, no significant differences were observed between SPECT and SPECT-CT measurements. In patients, relevant differences were found in 7 out of 9 lesions with the planar method, in 6 lesions with SPECT, but in only one with SPECT-CT.

***Conclusion*:** Our study confirms the superiority of SPECT in volume measurement if compared with the planar method. A more accurate measurement can be obtained from SPECT-CT.

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Keywords: Thyroid, hyperthyroidism, thyroid tissue volumetry, SPECT, SPECT-CT, theragnostics.

1. INTRODUCTION

High accuracy in the measurement of the target volume plays an important role in the successful outcome in radioiodine treatment of hyperthyroidism. High-resolution Ultrasound (US) is considered the best imaging technique for evaluating the thyroid gland but is limited by intraobserver and interobserver variability in the measurements [1, 2]. However, greater accuracy in volume estimation has been demonstrated when the three-dimensional US is available, with low intraobserver variability and high repeatability [3]. US has, in any case, well-known limit in accessibility to the retrosternal portion of a goiter [4]. Other methods are Computed Tomography (CT) and Magnetic Resonance (MR), although poorly used for this purpose for their high costs and scarce availability. Moreover, the volume measured with all these techniques does not always reflect the target volume of radioiodine therapy, that is only the hyperfunctioning one.

Based on the correlation between the cross-sectional gland area in the frontal scintigraphic image and the volume, different methods have been developed for estimating the

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thyroid mass [5]. These methods are based on a certain geometric assumption regarding the configuration of the thyroid. Therefore, they present an intrinsic bias given by the assumption of the equivalence between the measured axes and those of a rotation ellipsoid, resulting in possible underestimation or overestimation of the mass [5, 6]. Sometimes the hyperfunctioning tissue cannot be a priori assimilated to a rotation ellipsoid, for example, in the presence of a group of contiguous hot nodules or in case of drastically enlarged or abnormally shaped basedowified goiters. We described a large hyperfunctioning residue of the thyroglossal duct not attributable to a regular geometric shape at Single Photon Emission Computed Tomography - Computed Tomography (SPECT-CT) images [7].

Since the 90s, Single Photon Emission Computed Tomography (SPECT) has proven to be more accurate in the estimation of the thyroid volume than planar scintigraphy, even without attenuation and scatter correction [5, 8, 9]. Scientific data, obtained from the application of SPECT-CT in benign thyroid pathology, are instead limited, especially in a modern approach to radioiodine treatment of hyperthyroidism, through the combined use of diagnostics and therapy, currently known as "theranostics" or, better, "theragnostics" [10]. To our knowledge, no fixed threshold-based volumetry method from 99mTc-pertechnetate SPECT-CT in benign thyroid disorders has been reported so far. Therefore, the aim of this study was to evaluate the accuracy of a threshold-based isocontour extraction procedure for thyroid tissue volumetry from hybrid SPECT-CT technology. For this purpose, we evaluated through phantom studies three different methods, obtained from planar scintigraphy, SPECT and SPECT-CT, respectively. Furthermore, the measurements obtained with the three methods in patients affected by hot nodules, Graves' disease and a hyperfunctioning ectopic tissue are reported here, considering CT as a gold standard. Both in phantom studies and a clinical case series, we investigated the measurement accuracy with particular regard to the depth of the radioactive volume.

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2. MATERIALS AND METHODS

2.1. Phantom studies

Five cylindrical vials were obtained for planar images at activities of 2.9 MBq, 6.2 MBq, 8.7 MBq, 11.86 MBq, 14.74 MBq and five ones were also obtained for SPECT-CT at activities of 2.98 MBq, 6 MBq, 8.61 MBq, 11.92 MBq, 14.82 MBq, each in a volume of 15 ml of $^{99m}TcO_4^-$ solution. Each vial was inserted into a neck phantom of poly(methyl methacrylate) (PMMA) (Biodex Medical System) in two different anterior thickness settings: "p" (minimum thickness) and "g" (maximum thickness), obtained by rotating the carrier inside the phantom's cylinder (Fig. **1**). Planar and SPECT-CT images were acquired by orienting the neck phantom in different positions: 00.00 in which the phantom is in a horizontal position along the axis of the bed; 00.25 in which it is inclined by 25° on the sagittal plane, 25.00 in which the phantom, in a horizontal position, is inclined by 25° laterally; 25.25 in which it is oriented by 25° both with respect to both coronal and sagittal plane (Fig. **2**). In all cases, we took 8 planar and 8 SPECT-CT acquisitions (p 00.00, g 00.00, p 00.25, g 00.25, p 25.00, g 25.00, p 25.25, g 25.25) for each vial of different activity, *i.e.* 40 planar images and 40 SPECT-CT. These different acquisition modalities for each vial reflect the possibility of having patients with both thin and fat necks and patients who, for various reasons, cannot be acquired with an ideal neck orientation. Moreover, all acquisitions can be divided into two groups, A and B, according to the shape taken by the radioactive liquid inside each vial with respect to the orientation of the neck phantom. Acquisitions p 00.00, g 00.00, p 25.00, g 25.00 were included in group A and acquisitions p 00.25, g 00.25, p 25.25, g 25.25 were included in group B (Fig. **3**).

Planar scans and SPECT-CT were performed using a dual-head γ-camera with an integrated 16 slices CT for a combined transmission and emission tomography (GE Discovery 670 Pro), equipped with low energy high-resolution collimators set in H-mode. The study protocol consisted of 5 minutes of acquisition, in a 128 x 128 matrix, at a distance of 10 cm in anterior view for planar images, and in 60 projections in a 128 x 128 matrix, at 15 s for view, a zoom factor of 1.0, automated body contour detection for SPECT; CT acquisitions were performed at 120 keV, 60 mA and a slice thickness of 2.5 mm.

Therefore, three measurement systems called planar method, SPECT method and SPECT-CT method were carried out:

2.2. Planar method

A 9-point smoothing filter was applied to the planar image of the mediastinum without electronic magnification. According to the protocol in use in our Department, an iso-contouring ROI with a threshold of 40% was drawn and, subsequently, an elliptical ROI drawn manually was superimposed. The short and long axes were measured for each ellipse, and the target volume was then estimated according to the following formula of the rotation ellipsoid: $V = \pi / 6 \ a \ b^2$, where V is the volume, a and b are the major and the minor axes [11].

2.3. SPECT and SPECT-CT method

Each SPECT-CT acquisition has been processed on GE Xeleris Workstation (version 3.1) using Volumetrix Evolution software. Two iterative reconstructions (OSEM, 2 iterations, 10 subsets) were obtained, differing in the use of the attenuation correction by means of CT and an algorithm of resolution recovery (Volumetrix Evolution) in each other. No scatter correction has been applied. They are respectively named IRACRR (iterative reconstruction CT-based attenuation correction resolution recovery) and IRNC (iterative reconstruction no attenuation correction). In each axial series, the three thresholds of isocontour ROIs, which best allowed to estimate the volume from the sum of all slices, were found. The fixed values of the threshold for both methods (SPECT: 50%, SPECT-CT: 41%) were then calculated by means of linear and spline regression models for the dependency of the volume estimation error on the chosen threshold [12]. The optimal values were found minimizing the error by identifying the intersection of the fitted error with the horizontal axes in the linear model and the flattening point in the spline model (Fig. **4**). The linear and spline regression methods gave very similar results, and the fixed threshold values were used to recalculate the volumes (Fig. **5**).

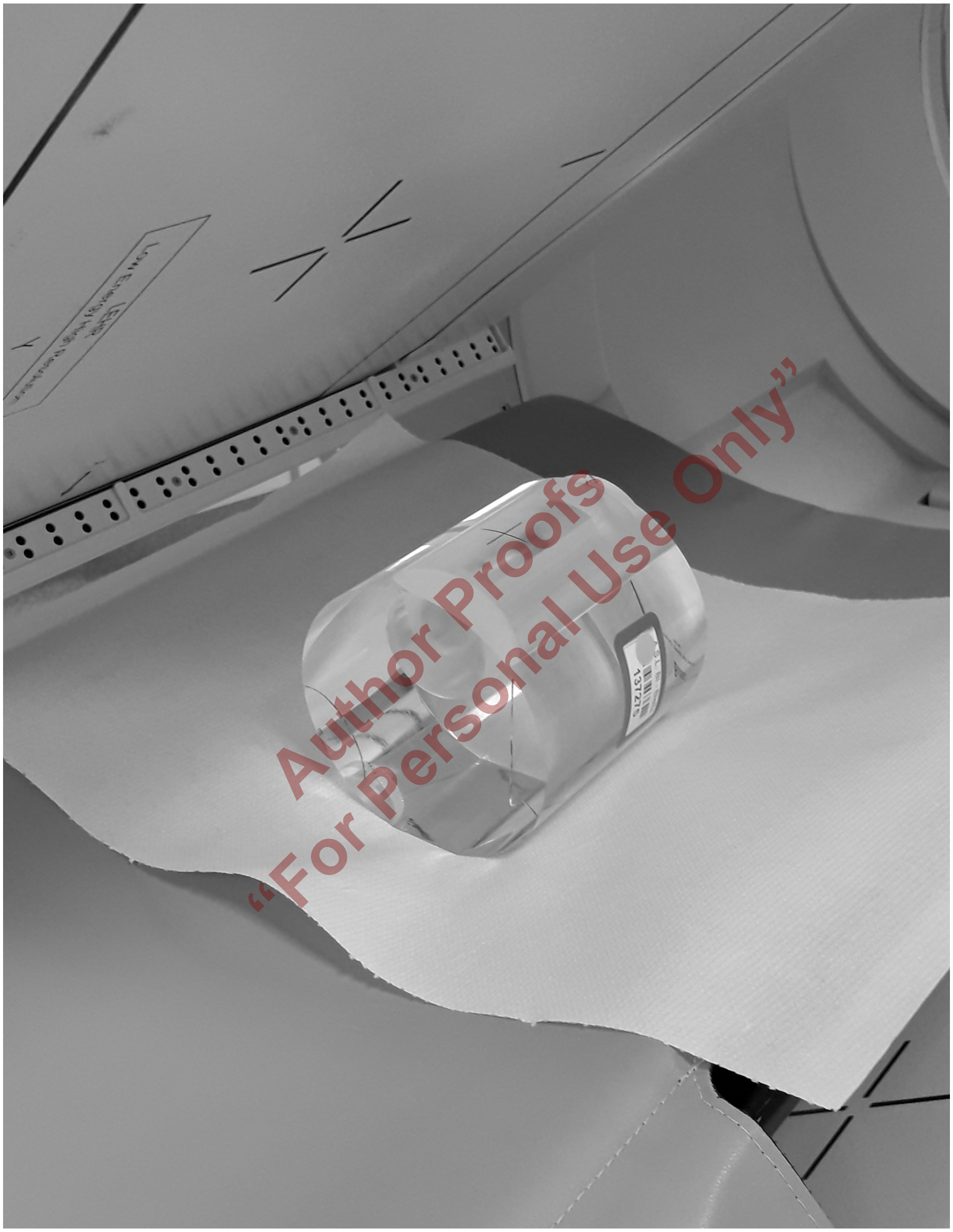

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Fig. (1). A photograph of the neck phantom we used, with a vial inside containing 15 ml of radioactive liquid.

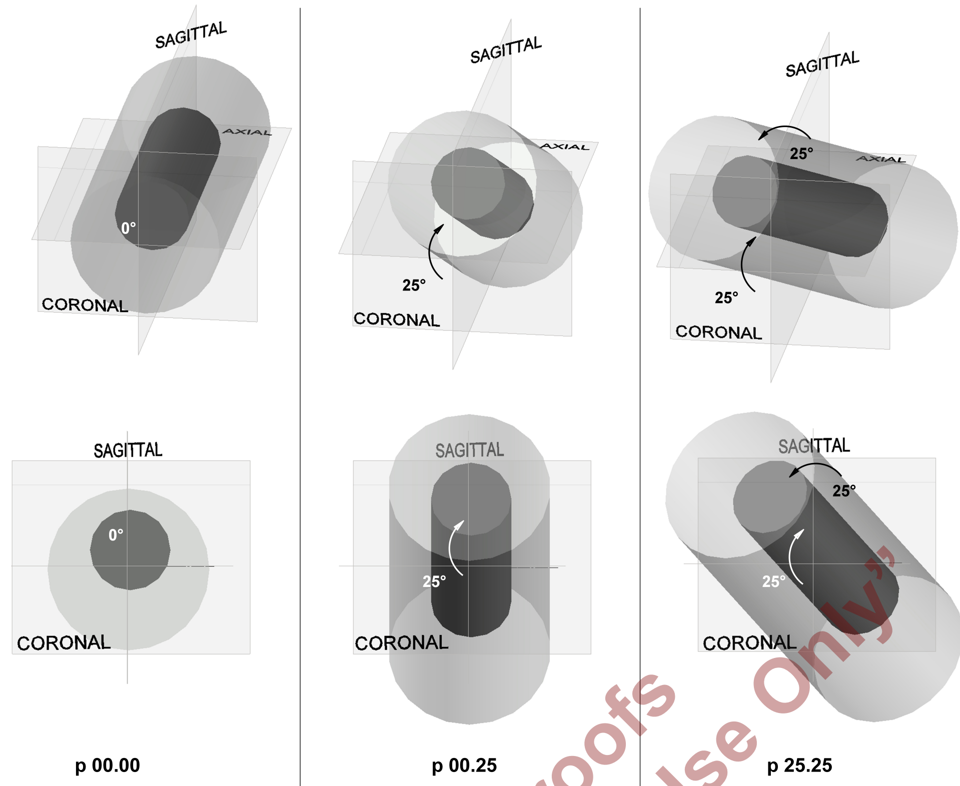

Fig. (2). Examples of different orientations of the neck phantom in the space - p 00.00: the neck phantom, seplified in the figure as a cylinder, is in horizontal position along the axis of the bed; p 00.25: the phantom is tilted upwards by 25°; p 25.25: it is oriented by 25° both with respect to the coronal and sagittal plane.

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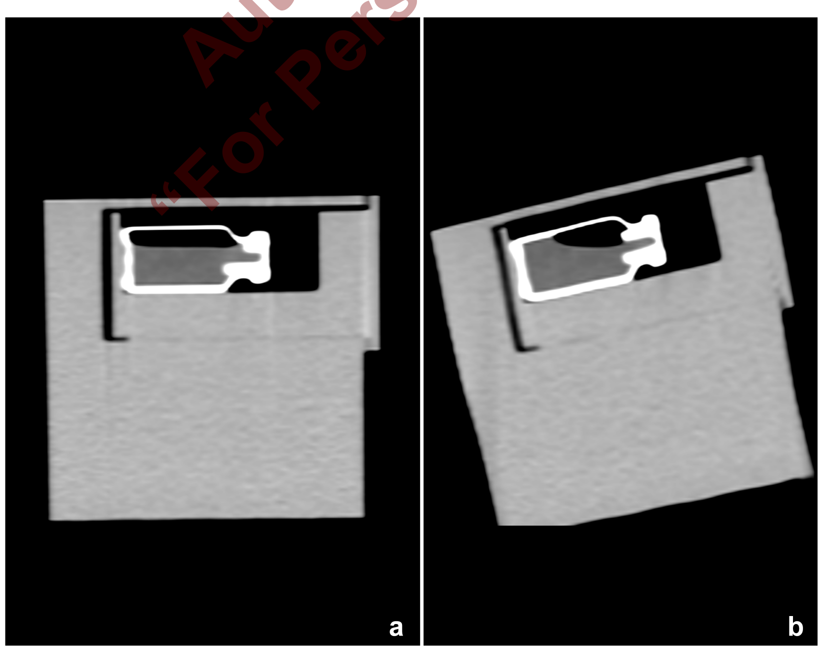

Fig. (3). Two different orientations of the neck phantom in sagittal view, p00.00 and p 00.25, allow the radioactive liquid to obtain two different forms, respectively called A (a) and B (b).