Scintigraphic thyroid volume calculation in hyperthyroid cats

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Abstract

A successful, euthyroid outcome after radioiodine therapy in hyperthyroid cats ranges from 83% to 95%. Thyroid volume has been reported as one of the factors influencing radioiodine therapy outcome in man and cats. The goal of this study was to describe the most reliable and practically applicable formula to determine thyroid volume using scintigraphy. The volume of each thyroid lobe of 32 hyperthyroid cats was determined by ultrasound and scintigraphy. The ultrasonographically determined volume (ellipsoid formula) for each thyroid lobe was compared with the scintigraphic volume that was calculated using eight different formulas: F1 $[(\pi/6) \times L \times H \times W]$, F2 $[(\pi/2) \times L \times W^2]$, F3 $[0.33 \times (\text{area cm}^2)^{3/2}]$, F4 $[1.08 \times (\pi/6) \times L \times W^2]$, F5 (area × H), F6 (0.27 × area × L), F7 $(\pi \times L \times W^2)$ and F8 $[\pi \times (4/3) \times W^3]$. F1, F3, F4 and F6 did not differ statistically from the volumes measured on ultrasound, while F2, F5, F7 and F8 did. Subjective shape assessment of the thyroid lobes, assigned as cylindrical or spherical, and the use of corresponding formulas, did not appear to be useful.

Introduction

Treatment of hyperthyroidism in cats with radioactive iodine is the therapy of choice whenever this technique is available and the patient is a suitable candidate. Medicinal and surgical treatment have considerable disadvantages, eg, adverse side effects, daily pilling, and the risk of anaesthesia in older cats and postsurgical complications.[1,2] A disadvantage of radioactive iodine treatment is that it requires hospitalisation and specialised infrastructure. Whether a fixed dose, a scoring system or individual dose calculations using kinetic studies are applied seems to have no effect on the outcome. In most cases therapy success or failure is determined based on the combination of total T_4 (TT_4) blood concentration and the presence of clinical signs. Some patients show a TT_4 value just outside the normal limit, but without any clinical signs of hypo- or hyperthyroidism. A euthyroid outcome varies in literature between 83% and 95%.[3–10] The exact causes for therapy failure, either resulting in hypothyroidism or persistent hyperthyroidism, remain unclear to this day. In human medicine a large thyroid volume has been suggested to be one of the predisposing factors for persistent hyperthyroidism,[11–14] although no consensus exists.[15] Extrapolation of data from human medicine has to be considered with care as the aetiology of hyperthyroidism in humans is different from that in cats. Furthermore, hypothyroidism is often

accepted as a successful outcome in human medicine.[11,13,15] The influence of thyroid volume on a hypothyroid outcome specifically has also been described in humans[16] and argued.[17,18] An autoimmune cause has been proposed in the latter case.[17] Follow-up ultrasound volume estimation after radioiodine therapy has also been reported to be a reliable prognostic factor of therapy outcome in human medical literature.[12] In veterinary medicine, one study reported the possible influence of a large thyroid volume on persistent hyperthyroidism following radioiodine treatment in cats.[8] Determination of predisposing factors for therapy failure (persistent hyperthyroidism or hypothyroidism necessitating hormone replacement) may lead to new protocols and individual dose calculations to improve radioiodine therapy outcome. If thyroid volume influences therapy results, this may be a parameter to take into account. Calculation of thyroid volume on a planar scintigram could be

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incorporated easily in the existing diagnostic procedure prior to radioiodine therapy, requiring no additional handling of the patient. The aim of this study was to describe different formulas for scintigraphic thyroid volume measurement, based on the planar scintigraphic acquisition used for diagnosis of hyperthyroidism in cats and to determine the most applicable formula for thyroid volume. Because of its accessibility and non-invasiveness, ultrasound was chosen as the reference method.[19,20]

Materials and methods

Patients

Data from 32 cats presented to our clinic between October 2010 and October 2011 for a diagnostic [99mTc]-pertechnetate (TcO$_4^-$) scan and radioiodine treatment were collected [mean age 12.2 years (range 8.9–17.6); 18 female/14 male]. The cats were diagnosed with hyperthyroidism by referring veterinarians based on clinical signs and serum TT$_4$. Inclusion criteria were unilateral or bilateral disease where one lobe was obviously larger than the other one, and overlap of lobes on both ventral and lateral planar scan was not an issue. In this latter case, only the measurements of the largest lobe were used in the study, as the smaller focus could not be recognised on the lateral scan. Overlapping lobes were excluded as this could interfere with correct measurements, as well as ectopic intrathoracic thyroid tissue that was not reachable with ultrasound. Cats that received anti-thyroid medication were off this medication for a minimum of 3 days prior to radioiodine treatment. All cats were kept fasted for at least 12 h to avoid complications with anaesthesia.

Scintigraphy

A catheter was placed in a cephalic vein and each cat was injected intravenously with TcO$_4^-$ (mean activity 97.68 ± 28.49 MBq). Approximately 40 mins after injection the diagnostic scans were performed on the gamma camera (GCA 7200 A; Toshiba) equipped with a low energy high resolution (LEHR) collimator. For this procedure patients were anaesthetised with propofol intravenously (IV) (4–8 mg/kg to effect, Propovet; Ecuphar, 10 mg/ml). Two planar static images were made, one in ventral recumbency and one in right or left lateral recumbency, depending on the side of the affected thyroid lobe (eg, left-sided unilateral affected animals would be positioned in left lateral recumbency). The acquisition parameters were 200 kcounts, 256 × 256 matrix size and 0.1 cm pixel size yielding a 25.6 × 25.6 cm field-of-view. All images were processed using multimodality software (Hermes V5.0; Nuclear Diagnostics AB). Regions of interest (ROI) were drawn over the affected thyroid lobes using a 30% threshold ROI tool. This threshold value was established previously using [99mTc]-labelled phantoms with a known volume and known dimensions (mimicking an enlarged
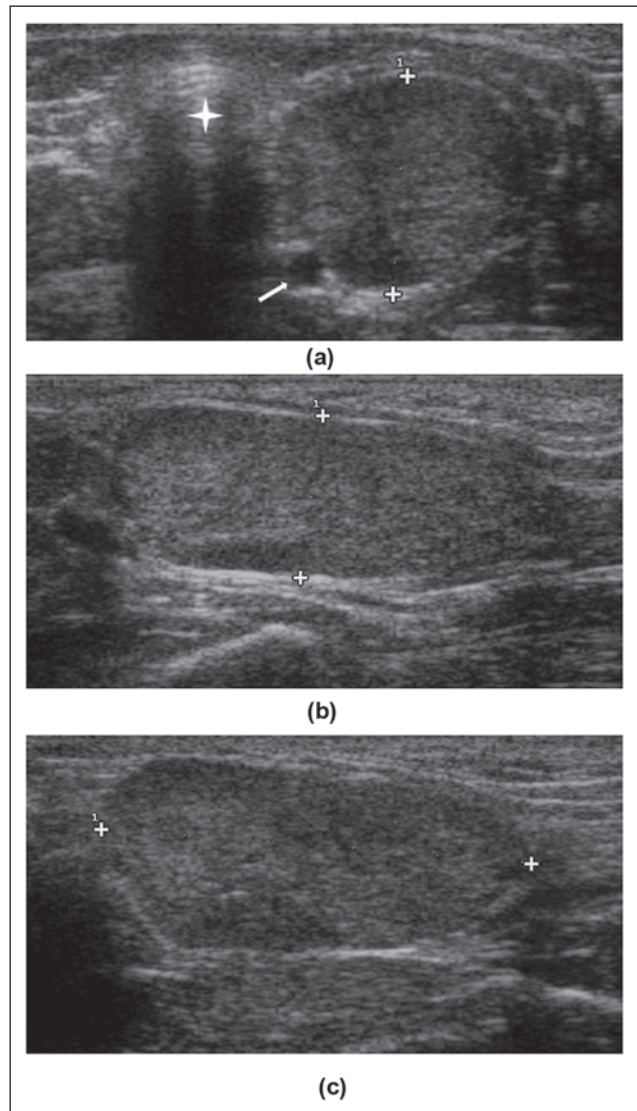

Figure 1 Transverse (a), sagittal (b) and dorsal (c) images of the left thyroid lobe of a unilaterally affected hyperthyroid cat. The caliper indicates the height of the lobe in (a) and (b), and the length in (c). Common carotid artery (white arrow), trachea (star)

thyroid gland), scanned identically to the cats. A 30% threshold ROI was found to give measurements most comparable with the phantom's real dimensions. Length, height and width of each thyroid lobe were measured manually using this ROI delineation. The area (cm²) of each lobe was calculated automatically by the thyroid volume function of the Hermes software.

For volume estimation, eight formulas that were described previously in human and veterinary literature or incorporated in the Hermes software were tested using these four parameters.[8,21–25] The following formulas were tested. Formula 1 to calculate the volume of an ellipsoid [F1 = $(\pi/6) \times L \times H \times W$], formula 2 [F2 = $(\pi/2) \times L \times W^2$], formula 3 [F3 = $0.33 \times (\text{area cm}^2)^{3/2}$], formula 5 (F5 = area × H) and formula 6 (F6 = $0.27 \times$ area × L).

Table 1 Mean length, height and width (mm), range and standard deviation, measured on ultrasound and scintigraphy

	Length	Height	Width
Ultrasound	26.7 (13.3–46; ± 6.6)	10.5 (5.4–25.4; ± 4.2)	13.3 (5.1–35.1; ± 5.6)
Scintigraphy	20.7 (8–35; ± 6.3)	13.2 (6–21.9; ± 3.8)	13.1 (6–25.8; ± 3.7)

Table 2 Mean volume (mm³), range and standard deviation for the different formulas by measurements made on the scintigraphic acquisitions

Ultrasound	F1	F2	F3	F4	F5	F6	F7	F8
$(\pi/6) \times L \times H \times W$	$(\pi/6) \times L \times H \times W$	$(\pi/2) \times L \times W^2$	$0.33 \times (\text{area } cm^2)^{3/2}$	$1.08 \times 0.523 \times L \times W^2$	Area $\times$ H	$0.27 \times$ area $\times$ L	$\pi \times L \times W^2$	$\pi \times (4/3) \times W^3$
2012 (191.8–10550; ± 2116.6)	2223 (188–8250; ± 1753)	6680 (565–29157; ± 5707)	1472 (157–4705; ± 1059)	2403 (203–10490; ± 2053)	3771 (366–12877; ± 2794)	1622 (160–4429; ± 1171)	3340 (283–14579; ± 2854)	1482 (113–8987; ± 1615)

L = length, H = height, W = width

Formula 4 is incorporated in the Hermes software [F4 = $1.08 \times (\pi/6) \times L \times W^2$]. Formula 7 is the formula of the volume of a cylinder (F7 = $\pi \times L \times W^2$) and formula 8 is the formula of the volume of a sphere [F8 = $\pi \times (4/3) \times W^3$]. Additional to the application of both formulas to all thyroids, formulas 7 and 8 were also tested on the respective shapes (F7 to cylindrical-shaped thyroid lobes and F8 to spherical-shaped lobes) to examine a potential influence of the shape on the usefulness of these formulas. All measurements and shape evaluation were performed by the same clinician (VV).

Ultrasound

Ultrasound was performed immediately following scintigraphy, while the patients were still sedated. The cats were placed in dorsal recumbency in a cushion with the head extended. B-mode ultrasound was performed using a 10–15 MHz, multi-frequency linear array probe (CnTI Mylab 30; Esaote). The highest frequency (15 MHz) was used for all patients; gain and position of the focal spot were optimised for each patient individually.

The presence of any cystic lesions that could interfere with therapy efficacy was evaluated, as well as the thyroid parenchyma, and measurements were made for volume determination. For this purpose the thyroid lobes were scanned in three planes (transverse, sagittal and dorsal) (Figure 1). Maximal dimensions in each plane were searched for before freezing the image and making measurements with the electronic caliper. The sagittal view provided length and height, the transverse view provided height and width, and the dorsal view provided length and width parameters. Of these six measurements the maximal length (L), height (H) and

width (W) values were chosen and thyroid volume was calculated by the ellipsoid formula (volume = $\pi/6 \times$ length $\times$ height $\times$ width).[19,20] Ultrasounds were performed by two of the authors (AC, VV).

Statistics

A paired *t*-test was used to compare the volume measured on ultrasound with the volume obtained by scintigraphy for each thyroid lobe using the different formulas. Thyroid shapes on planar scintigraphy were divided into two groups: cylinder- and sphere-shaped. Both groups were tested separately for applicability of the cylinder and sphere formula using a paired *t*-test.
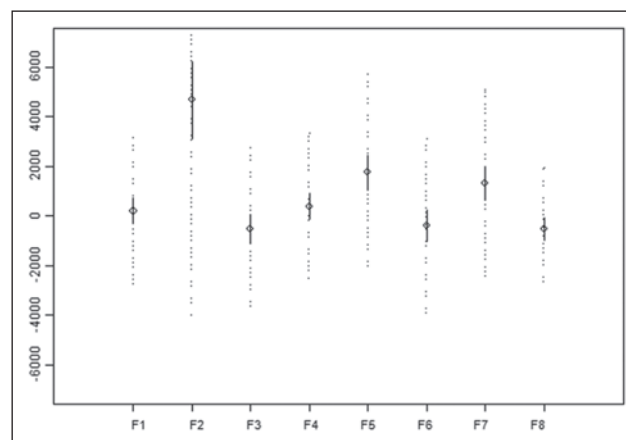

Figure 2 Mean difference between volumes measured on ultrasound (y-axis) and on scintigraphy (x-axis) for each of the eight formulas. Full line = 95% confidence interval, dotted line = 95% reference interval
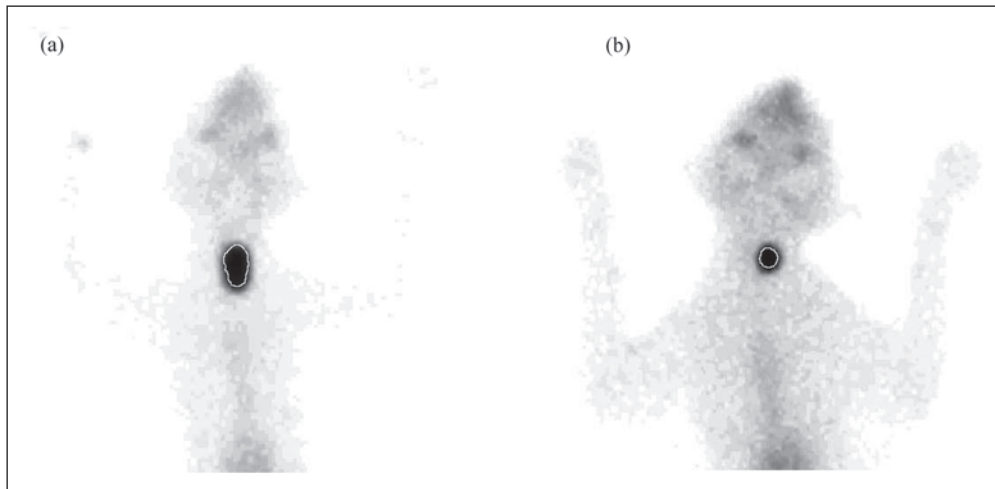
Figure 3 A cylinder-shaped (a) and sphere-shaped (b) thyroid lobe with a 30% threshold ROI in two unilaterally affected hyperthyroid cats

Results

Table 1 summarises the mean L, H and W as measured on scintigram, as well as the same measurements on ultrasound. The mean area on the scintigram was 2.56 cm² (SD = 1.26; range 0.61–4.92 cm²). The mean thyroid volumes calculated on ultrasound and scintigraphy are summarised in Table 2. Thirteen cats (40.6%) had cystic lesions of variable size in the affected thyroid lobe. This ranged from small diffuse lesions to cystic lesions that occupied nearly the entire lobe in two cats. In another cat both thyroid lobes had an abnormal ultrasonographic appearance, although on the scintigram only one lobe showed TcO_4^- uptake.

F1 ($P = 0.426$), F3 ($P = 0.072$), F4 ($P = 0.142$) and F6 ($P = 0.220$) showed no significant difference with the volume calculated from ultrasound measurements. On the contrary, F2 ($P < 0.00001$), F5 ($P = 0.00002$), F7 ($P = 0.0004$) and F8 ($P = 0.021$) did show a significant difference. F4, F6 and F1, in particular, showed best agreement with ultrasonographically-determined volumes (Figure 2).

Twenty-three of 32 thyroid lobes (72%) were defined as being cylinder-shaped and 9/32 lobes (28%) were defined as sphere-shaped (Figure 3). Small variations in shape, such as bean-shaped or bi-lobated, were recognized. Overall, the differences between the volume measured on ultrasound and scintigraphy were smaller for both shapes when F8 was used, making this formula more applicable than F7. F8 performed significantly ($P = 0.003$) better to calculate the volume of a cylinder-shaped lobe, ie it differed less from the ultrasound volume.

Discussion

Although little is known about the influence of thyroid volume on radioiodine therapy outcome in veterinary medicine or about the most suitable method to determine this volume, it is one of the parameters that has been implicated in therapy failure both in humans and in cats.[8,11–14] In this study threshold-dependent automatic ROI drawing (exclusion of pixels containing activity below a preset threshold) on planar thyroid scintigrams was used to minimise operator-dependent inaccuracies. The threshold has inevitable influence on the size of the ROI and, consequently, on the determined volumes. The ROI threshold for thyroid volume calculation in humans varies from 5% to 30%.[24–26] This is comparable to the 30% threshold value we found most suitable for quantitative scan processing.

Forrest et al calculated thyroid volume with the sphere and cylinder formula (applied according to the visual evaluation of the lobes) in 80 cats and found a mean thyroid volume of 10400 mm³ (range 2100–28400 mm³).[8] This volume is more than five times the mean volume determined by the formulas with best agreement with ultrasound in this study. However, in this latter study, measurements of multiple thyroid foci were added up to calculate total active thyroid volume for dosimetric purposes. This does not allow a direct comparison with our results as volumes were calculated for well-delineated single lobes. Moreover, they did not compare the volume with the real volume or a volume measured with other imaging modalities; also no ROI threshold was mentioned.

Inevitably, differences in shape will have a considerable influence on the volume calculations and the formula to be used for these. For this reason the volumetric formulas of a sphere and a cylinder were tested in this study for the respective shapes. Surprisingly, agreement between volume measurements with ultrasound and F8 for cylinder-shaped thyroid lobes was higher than for sphere-shaped lobes, while for sphere-shaped thyroids F8 was not superior to F7. The reason for this is unclear.

A limitation of this study is that most formulas that were tested are derived from human medical publications; therefore, the correction factors may not be applicable to cats. Even in human medicine, there is a discrepancy between different publications concerning the formulas for volumetric calculations. Human medicine also faces the additional difficulty that thyroid pathology is more diverse compared with feline hyperthyroidism, with an inevitable influence on shape and volume calculations. F1 has been reported to be applicable for volume calculation of diffuse goitres in humans.[24] F3 was found to be an acceptable formula to estimate thyroid gland volume in patients with non-specified thyrotoxicosis, especially in combination with ultrasound and the use of the correction factor 0.419 instead of 0.33.[22] Other authors reported F3 and a formula similar to F3 ($0.326 \times area^{3/2}$) not to be useful in multinodular goiters or Graves' disease.[23–25] A formula very similar to F6 ($0.323 \times area \times length$) showed a reasonable correlation to ultrasound in patients with Graves' disease.[26]

In this study scintigraphic volume measurements were compared with ultrasound. However, in human medicine it was reported that the volume, as measured ultrasonographically prior to thyroidectomy, was underestimated in comparison with the real volume (after thyroid excision) for all pathologies.[27] Despite this the standard technique in human and veterinary medicine to determine thyroid volume is the use of ultrasound and the ellipsoid formula.[8,19,20,22,26,28] To our knowledge no other formulas than the ellipsoid model have been used for routine ultrasonographic thyroid volume determination.

Ideally, computed tomography (CT) or magnetic resonance imaging (MRI) should be performed for volume calculations. Measurements and volumes calculated on CT data have already been reported for clinically healthy cats, but not in hyperthyroid cats.[29] The need for prolonged anaesthesia in a geriatric population often suffering from concurrent cardiac and/or renal disease and the additional cost hamper the use of these modalities in clinical settings. Moreover, studies in human medicine comparing MRI and ultrasound volume determination proposed ultrasound as a reliable alternative technique, provided that a correction factor is used.[25,30]

The mean volume of 2012 mm³ per hyperthyroid lobe was remarkably larger than the volume reported in previous publications. Some thyroid lobes were ill-defined on ultrasound, which possibly impeded reliable measurements. Barberet et al[20] described a mean volume of 572 mm³ for the left lobe and 552 mm³ for the right lobe, while Wisner et al[19] described a mean lobe volume of 578 mm³. When we have a closer look at the separate parameters we can conclude that the mean length of 26.7 mm is rather comparable with the mean length of Barberet et al[20] and Wisner et al[19] with 21.4 mm for the left lobe and 19.7 mm for the right lobe, and 20.2 ± 3.6 mm for the

left lobe and 21.9 ± 4.4 mm for the right lobe, respectively. However, the mean height (10.5 mm) and width (13.3 mm) in this study are approximately double those measured by Wisner et al,[19] who determined the mean height for the left lobe to be 5.5 ± 2.4 mm and the mean height for the right lobe to be 8.1 ± 3.0 mm. The mean width was 5.7 ± 2.1 mm for the left lobe and 7.7 ± 2.4 mm for the right lobe. Mean values for height and width were not mentioned in the study of Barberet et al.[20] The reason for this difference is unclear. Most likely, the discrepancy between this study and the two others[19,20] is owing to simple coincidence, as the degree of clinical hyperthyroidism in cats is also very variable. Furthermore, the group of cats in this study was approximately twice as large as in the other two studies.

Our aim was to define the most reliable formula to determine thyroid volume on scintigraphy. Given that thyroid volume is suggested to be a factor influencing therapy outcome, the determination of volume on planar scintigrams may provide an easy method in clinical surroundings where a scintigram is often used as a diagnostic tool prior to radioiodine therapy. Statistical analysis showed three formulas to be promising. F1, showing the best agreement with ultrasound, has the disadvantage that two scans, one in ventral and one in lateral recumbency, are necessary to obtain all parameters needed. On the contrary, F4 only requires one image. F6 requires determination of the thyroid area, which is a function specific to the Hermes software and may not be available in all systems. Applying specific formulas based on subjective assessment of thyroid shape on the planar scintigram does not seem to be of any use as the shape of the thyroid and its corresponding formula do not appear to improve volume calculations. The advantage of volume measurements on the scintigram is that only one examination has to be performed for information on thyroid activity and volume. Additional studies are needed to determine whether a correction factor, more applicable to cats, has to be introduced.

Conflict of interest The authors do not have any potential conflicts of interest to declare.

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