

PRE- AND POSTTREATMENT ULTRASONOGRAPHY OF THE THYROID GLAND IN HYPERTHYROID CATS

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Ultrasonography is useful for assessing the morphology of the thyroid gland in hyperthyroid cats. Our aim was to describe the ultrasonographic changes of the thyroid gland in hyperthyroid cats after ^{131}I therapy. Ultrasonography was performed in 15 hyperthyroid cats at initial presentation and 6 months after ^{131}I using a multifrequency linear transducer set at 12 MHz. The following criteria were evaluated: length, width, height, volume, shape, homogeneity, and vascularity, using Power Doppler. Pretreatment, 10 cats had bilaterally abnormal thyroid lobes, four cats one abnormal lobe with the contralateral lobe being normal or reduced in size, and one cat with one normal lobe and one lobe not visible. Six months after ^{131}I therapy, there was a reduction in median volume from 819 to 210 mm^3 , reduced rounding, reduced heterogeneity, and decreased vascularity. In conclusion, ultrasonography may be used to monitor thyroid changes in order to assess ^{131}I treatment response. Further studies are necessary to determine whether ultrasonography could contribute to the detection of a relapsing course of hyperthyroidism. © 2010 *Veterinary Radiology & Ultrasound*

Key words: feline, hyperthyroidism, radioiodine treatment, thyroid gland, ultrasonography.

Introduction

HYPERTHYROIDISM IS THE most common endocrine disorder in cats, typically being associated with functional thyroid adenomatous hyperplasia or hyperfunctioning adenoma(s). Feline hyperthyroidism is bilateral in 70% of the patients.¹ The diagnosis of feline hyperthyroidism is based on clinical and physical signs, serum thyroid hormone levels, and thyroid scintigraphy.^{1,2} In hyperthyroidism, scintigraphy is characterized by increased radiopharmaceutical uptake in the area of the gland, and allows assessment of bilateral vs. unilateral disease, thyroid size or functional activity estimate, identification of ectopic thyroid tissue, and potential detection of metastatic disease.³⁻⁵ However, thyroid scintigraphy only provides limited morphologic information.

In humans, ultrasonography is used extensively for evaluation of thyroid glands in patients with thyroid nodule(s) or functional hyperthyroidism.⁶⁻⁸ It is the reference method, before ^{131}I therapy, for determining the thyroid

volume being used for radiopharmaceutical dose calculation.⁹⁻¹¹ It has been suggested that thyroid echogenicity can be used to predict the outcome of radioiodine therapy in patients with Grave's disease.¹² In veterinary medicine, ultrasonography is used to evaluate thyroid glands in normal and hypothyroid dogs.¹³⁻¹⁹ Ultrasonography of thyroid glands has been compared with $^{99\text{m}}\text{TcO}_4^-$ scintigraphy in hyperthyroid cats, with an 85.7% agreement of scintigraphy vs. ultrasonography in differentiating normal from abnormal thyroid lobes; thyroid glands in hyperthyroid cats appeared larger and less echogenic than in control cats.²⁰ Significant correlation between palpation score and ultrasonographic thyroid lobe length has also been found in normal and hyperthyroid cats.²¹

The primary objective of the present study was to describe the ultrasonographic features of the thyroid gland in hyperthyroid cats, before and after ^{131}I radioactive iodine therapy. It is hypothesized that these features could be used to predict response to ^{131}I treatment.

Materials and Methods

Data were collected prospectively from May 2005 to August 2006. Fifteen client-owned hyperthyroid cats were studied. Their mean age was 12.4 years (range: 8–16 years). Hyperthyroidism was diagnosed based on clinical findings and results from biochemical blood analysis. Positive biochemical test consisted of elevated serum total thyroxine (TT4) (>25–30 nmol/l). At first presentation, the mean serum TT4 level was 125.9 nmol/l, with a range of 52.6–193.5 nmol/l (normal range: 10–50 nmol/l). Two cats

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had been treated previously with methimazole and four cats with carbimazole. The serum TT4 level of those six cats was similar to that in untreated cats (mean: 137.2 nmol/l, range: 58.1–193.5).

Thyroid ultrasonographic and scintigraphic examinations were performed on each cat at first presentation (T0). Therapy with radioactive iodine ^{131}I was then given to each cat. A second ultrasonographic examination of the thyroid gland was performed after 6 months (T6).

Ultrasonographic examinations were performed by two board-certified radiologists (J.S. and O.T.), using previously described techniques.^{13–15,20} Hair was clipped on the ventral aspect of the neck. Cats were in dorsal recumbency with the neck extended and restrained manually, without tranquilization or anesthesia. Minimal transducer pressure was applied to the skin. Both thyroid lobes were imaged with a GE Logic 7 machine* connected to a multifrequency (7–14 MHz) linear matrix transducer with the frequency set at 12 MHz. The image presets were identical for all patients. The overall gain and the time gain compensation were adjusted for each patient. Compound imaging was used in all patients. No standoff pad was used. Each lobe was first evaluated in a longitudinal plane. The maximum length of each lobe was measured on longitudinal images by use of electronic callipers having a precision of 0.1 mm. Following this, a transverse image of each lobe was obtained either by slowly rotating the probe 90° or by using a transverse image of the common carotid artery and the trachea as landmarks. Finally, scanning began on the midline, just caudal to the larynx, followed by a slow gliding motion of the probe caudally. The maximum height and width of each separate lobe were obtained from this plane.

The homogeneity and shape of the gland were assessed on both transverse and longitudinal images. A visual interpretation of an equal echogenicity throughout the parenchyma of the lobes was recorded as a homogeneous parenchyma. Any difference in echogenicity throughout the parenchyma was recorded as a heterogeneous lobe. The presence of hypoechoic to anechoic cyst-like areas was recorded. The shape of the lobes was assessed on transverse and longitudinal images. A lobe was recorded as abnormally shaped if it had a round instead of triangular shape in short axis, or ovoid instead of fusiform shape in long axis. A four-point grading scale was used to grade the change in shape subjectively: normal, mildly, moderately, or severely rounded. The vascularization of the lobes was evaluated with Power Doppler and recorded as absent, mild, moderate, or strong.

The maximum width, height, and length of each lobe were used to calculate its volume according to a formula of a rotation ellipse [volume (mm^3) = length (mm) \times width (mm) \times height (mm) $\times \pi/6$]. Some lobe measurements

were lacking in two lobes pretreatment and seven lobes posttreatment, preventing volume calculation. These cats were excluded from further analysis of thyroid volume, but were included in the calculation of median linear measurements, when available. Total thyroid volume for each cat was estimated by summing the volume of right and left thyroid lobes.

Thyroid scintigraphy was performed on all hyperthyroid cats shortly after the initial ultrasonographic examination by injecting 1.4–3.5 mCi (51.8–129.5 MBq) of pertechnetate ($^{99\text{m}}\text{TcO}_4^-$) intravenously. Ventral images (250,000 counts) of the head, neck, and thorax were obtained approximately 20 min postinjection using a gamma camera fitted with a low-energy high-resolution parallel hole collimator. The presence of unilateral or bilateral lobe involvement and presence of ectopic tissue was determined by visual inspection. The extent of hyperfunctioning of the affected lobe(s) was estimated by calculating the thyroid-to-salivary gland ratio.

The mean injected dose of radioactive iodine was 3.1 mCi (range: 2.4–5 mCi) or 114.7 MBq (range: 88.8–185 MBq), depending on the TT4 levels and the results of the pertechnetate study.

Statistical analysis was performed to compare the different ultrasonographic parameters of the thyroid lobes before and after radioiodine treatment using the stratified Wilcoxon rank sum test with lobe as stratification variable. All analyses were performed at a significance level of 5%.

Results

On scintigraphic examination, seven cats (40%) had bilateral uptake and eight cats (53%) had unilateral uptake (three left-sided, five right-sided). In one cat, only ectopic tissue appeared hyperfunctioning. Ectopic thyroid tissue was detected in six cats (one with bilateral and four with unilateral involvement). The mean thyroid-to-salivary ratio of abnormal lobes was 5.85:1 (range: 1.4–11.3:1) for the left lobe and 4.65:1 (range: 1.2–12:1) for the right lobe. Six months following ^{131}I treatment, the mean serum TT4 level was 17.0 nmol/l (range: 6.5–28.4 nmol/l).

Ultrasonographically, one thyroid lobe could not be detected at the initial evaluation, and three lobes could not be seen 6 months following ^{131}I treatment. There was a statistically significant reduction in median thyroid volume (from 819 to 210 mm^3 , corresponding to 75% of volume reduction) measured with ultrasonography before and after treatment with radioiodine (Table 1) ($P < 0.0001$). The volume of all the individual lobes decreased after treatment, including lobes that had a normal pretreatment volume ($< 200 \text{mm}^3$).

Based on abnormal size, shape, echogenicity, and/or vascularization, thyroid lobes were abnormal bilaterally on ultrasonography in 10 of 15 cats before ^{131}I treatment.

*GE Logic 7, General Electrics Medical Systems, Milwaukee, WI.

TABLE 1. Median (Interquartile Range) of Linear Measurements (mm) and Volume (mm³) for Left and Right Thyroid Lobes of Hyperthyroid Cats Pre- and Posttreatment with Radioactive Iodine

	Pretreatment		Posttreatment	
	Left lobe	Right lobe	Left lobe	Right lobe
Length	20.3 (9.5)	20.8 (8.2)	14 (7.7)	14.1 (5.7)
Height	6 (3.9)	5.9 (4.9)	3 (2.4)	3.1 (3.1)
Width	7.3 (4.6)	5.2 (5.2)	3.9 (2.2)	4.5 (3.2)
Volume	429 (742)	390 (916)	84 (131)	126 (123)
Total volume	819		210	

Four cats had unilateral lobe involvement. One cat had one normal thyroid lobe and one lobe not visible. Of the 10 cats with bilaterally abnormal glands on ultrasonography, six had bilateral thyroid involvement scintigraphically and three had unilateral scintigraphic abnormalities, with the scintigraphically affected side also being more severely affected ultrasonographically. The remaining cat with bilateral ultrasonographic changes had only hyperfunctioning ectopic tissue on scintigraphy. Of the four cats with unilaterally abnormal glands on ultrasonography, all had unilateral scintigraphic abnormality of the same lobe. The final cat had a normal ultrasonographic examination with one lobe appearing normal and one lobe not visible, but scintigraphically both lobes were abnormal.

At the initial ultrasonographic examination, only one right thyroid lobe could not be seen. The thyroid glands were classified as heterogeneous in 10/15 left lobes and 11/14 right lobes. Hypoechoic to anechoic areas were found in 7/15 left lobes and 8/14 right lobes. Some foci of mineralization were detected in only one lobe. The shape of the left lobe was normal in 3/15 lobes, mildly round in 3/15 lobes, moderately round in 5/15 lobes, and severely round in 4/15 lobes. The shape of the right lobe was normal in 4/14 lobes, being mildly round in 2/14 lobes, moderately round in 3/14 lobes, and severely round in 5/14 lobes. With

Power Doppler, the vascularity of the left lobe was recorded as absent (4/15), mild (3/15), moderate (2/15), or strong (6/15). The vascularity of the right lobe was recorded as absent (3/14), mild (3/14), moderate (6/14), or strong (2/14). The six cats that received medical antithyroid treatment before their first ultrasonographic examination did not have different morphologic features than the cats that had not received any treatment.

Six months after ¹³¹I treatment, one left lobe and two right lobes were not seen ultrasonographically. The thyroid lobes were usually decreased in size and became more homogeneous and less round (Figs. 1 and 2). The thyroid glands were classified as heterogeneous in echogenicity in 6/14 left lobes and 6/13 right lobes. Hypoechoic to anechoic areas were found in 5/14 left lobes and 4/13 right lobes. The shape of the left lobe was normal in 10/14 lobes, mildly round in 1/14 lobes, moderately round in 2/14 lobes, and severely round in 1/14 lobes. The shape of the right lobe was normal in 8/13 lobes, mildly round in 3/13 lobes, moderately round in 1/13 lobes, and severely round in 1/13 lobes. Thyroid glands generally had decreased or absent vascularity compared with the first examination (Fig. 3). With Power Doppler, vascularity of the left lobe was recorded as absent (9/14) or mild (5/14). Vascularity of the right lobe was recorded as absent (10/13), mild (2/13), or moderate (1/13). There was a statistically significant difference in heterogeneity ($P=0.039$), shape ($P<0.0001$), and vascularity ($P<0.0001$) of thyroid lobes after treatment. No significant difference was detected regarding the presence of hypoechoic/anechoic areas ($P=0.1791$) after treatment (Table 2).

Discussion

Initially, thyroid glands of hyperthyroid cats appeared generally increased in size, more round, heterogeneous, with hypoechoic/anechoic areas, and with an increased

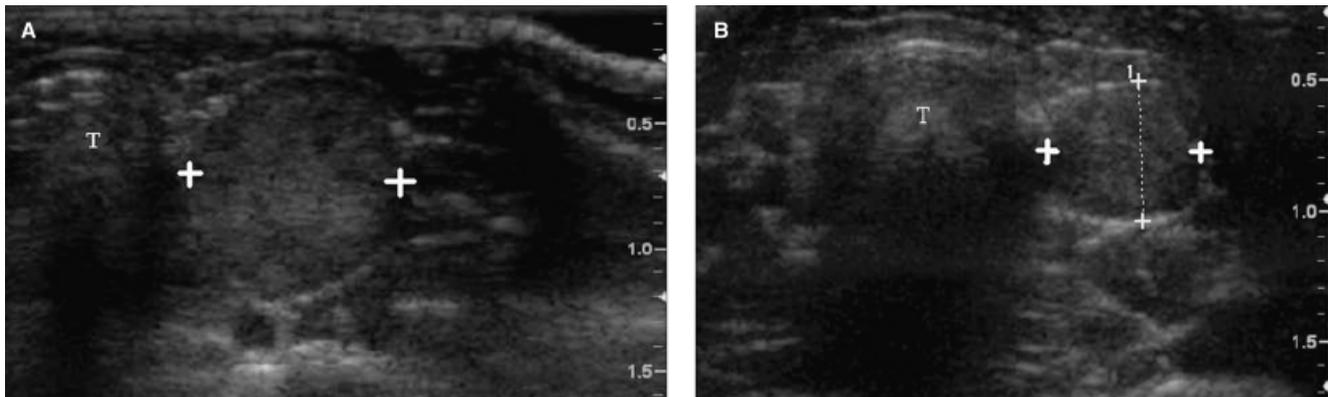


FIG. 1. Transverse ultrasound images of the left thyroid lobe of a hyperthyroid cat pre- (A) and posttreatment (B) with ¹³¹I. Left is to the right side of the image. The linear scale on the right of the image is in centimeters. Pretreatment, the lobe was very round and heterogeneous with small ill-defined hypoechoic areas. Six months posttreatment, the lobe was graded as moderately round. T, trachea.

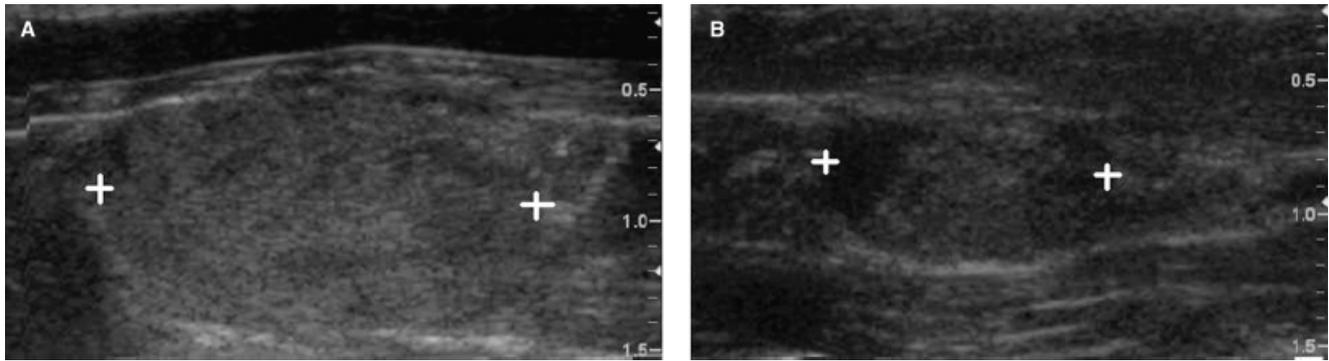


FIG. 2. Longitudinal ultrasound images of the left thyroid lobe of a hyperthyroid cat pre- (A) and posttreatment (B) with ^{131}I . Left is to the right side of the image. The linear scale on the right of the image is in centimeters. Pretreatment, the lobe was very round and heterogeneous with small ill-defined hypochoic areas. Six months posttreatment, the lobe was graded as moderately round but still heterogeneous.

vascularity. Six months after ^{131}I treatment, thyroid glands decreased in size by approximately 75% and became less round and less heterogeneous with decreased vascularity in 14 of the 15 cats.

It has been stated that, in cats with unilateral disease, the contralateral lobe is often atrophic and difficult to visualize ultrasonographically.²⁰ Also, in normal cats, thyroid lobes were more often difficult to evaluate in cross-section than in longitudinal section, which hampered width measurement.²⁰ Neither of those difficulties was encountered in this study, as only one lobe was not detected at the first examination and three lobes after ^{131}I treatment. After ^{131}I treatment, width measurements could be obtained even though thyroid lobes were smaller. This difference may be related to the different resolution of the ultrasound equipment.

Our length measurements were similar to those described previously.²⁰ The mean length of the left lobe in our study was 21.4 mm (median 20.3 mm) vs. the published value of 20.2 mm, and for the right lobe in our study mean length was 19.7 mm (median 20.8 mm) vs. the published

value of 21.9 mm.²⁰ It was also noted previously that thyroid length was comparable in control and hyperthyroid cats, even though thyroid volume was increased in the hyperthyroid cats. The increased volume was therefore related to increased height and width of the lobes. In our study, length measurements decreased by 25% after radioactive iodine treatment. A decrease in height of 50% and a decrease in width of 30% were equally responsible for the decreased volume of thyroid glands posttreatment.

The lobar volume and total volume of thyroid lobes in our hyperthyroid cats were also comparable to published results.²⁰ The mean volume of the left lobe was 572 mm³ in hyperthyroid cats at first examination (median 429 mm³) vs. 382 ± 312 mm³ in the previous study. The mean volume of the right lobe was 552 mm³ here (median 390 mm³) vs. 782 ± 449 mm³ in the previous study. The mean total thyroid volume was 1124 mm³ here (median 810 mm³) vs. 889 ± 540 mm³ in the previous study.

It is important to obtain accurate thyroid volume measurements as volume can be used as the basis of calculating

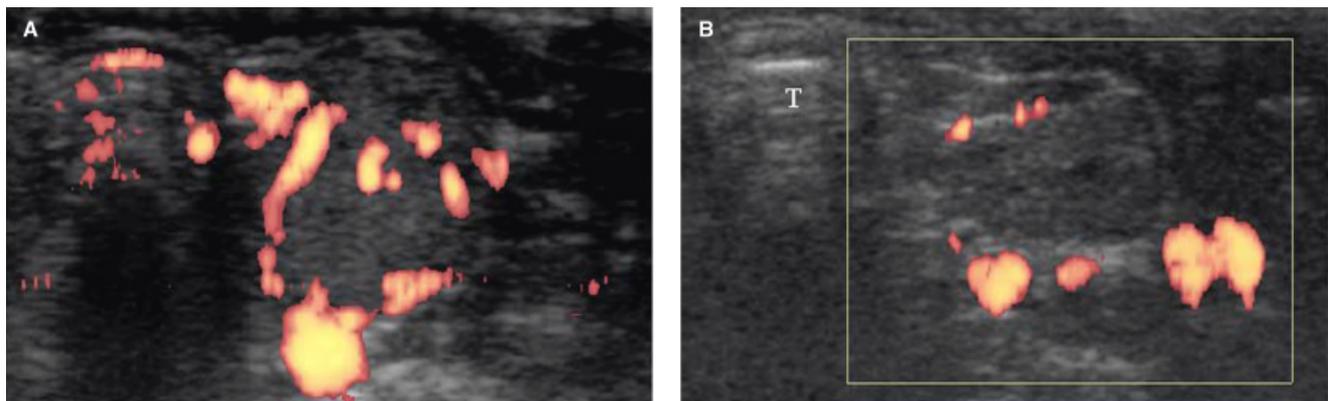


FIG. 3. Transverse Power Doppler ultrasound images of the left thyroid lobe of a hyperthyroid cat pre- (A) and posttreatment (B) with ^{131}I . Left is to the right side of the image. The linear scale on the right of the image is in centimeters. On initial examination, this lobe was graded as strongly vascularized. Six months posttreatment, the vascularity was considered mild. T, trachea.

TABLE 2. Aspect and Vascularity for Both Thyroid Lobes of Hyperthyroid Cats Pre- and Posttreatment with Radioactive Iodine

	Pretreatment (n = 29)	Posttreatment (n = 27)
Heterogeneity	22	12
Hypoechoic areas	15	9
Shape		
Normal	7	18
Mildly round	5	4
Moderately round	8	3
Severely round	9	2
Vascularity		
Absent	7	19
Mild	6	7
Moderate	8	1
Strong	8	0

the ^{131}I dose to be administered. In cats, as in humans, the correlation between thyroid gland palpation scores and ultrasonographic measurements is poor.^{22,23} Palpation can be used to detect an enlarged thyroid gland in cats, but is not sufficient to estimate thyroid volume.²¹ In humans, ultrasonography is the reference method for determining thyroid volume, as ultrasonographic thyroid volume is significantly correlated with MRI measurements and gives a better precision than scintigraphic thyroid volume estimation.⁹⁻¹⁰ Estimating volume from thyroid scintigrams provides an estimate of functional thyroid volume, whereas ultrasonographic measurements lead to a morphologic thyroid volume. In humans, thyroid volume can be assessed accurately using scintigraphy in patients with diffuse goiter, but differences are observed in the size of nodular goiters measured using scintigraphy vs. ultrasonography. In multinodular goiter, the heterogeneous uptake of $^{131}\text{I}/^{99\text{m}}\text{Tc}$ and the irregular shape of nodules hinder accurate assessment of thyroid volume. Also, because of limited resolution, partial volume artefact and/or radiation-scatter, which are particularly problematic on ^{131}I scintigrams, a larger region of interest is often drawn on scintigrams leading to an overestimation of the morphologic thyroid volume.⁹

Ultrasonography also has limitations when used for thyroid volume calculation, as with disseminated or multifocal autonomous thyroid disease. Further, ultrasonography does not allow differentiation between adenomas and regressive changes, which can be a problem as regressive or hypofunctioning thyroid volume should be subtracted from total volume estimates.²⁴

There are numerous methods for determining the dose of ^{131}I to use to treat hyperthyroid cats. Often, a fixed or empiric dose is used, but this carries the risk of delivering excessive ^{131}I .^{25,26} Individualized methods take some patient specific variables, such as volume of adenomatous tissue or degree of thyrotoxicosis, into consideration.²⁶ A modified fixed method of dose determination, based on the

volume of hyperfunctioning thyroid tissue estimated from pertechnetate scans, could be inadequate for patients with extremely elevated serum thyroxine levels or large thyroid glands.²⁷ In humans, the same limitations apply to ultrasonographic measurement of thyroid volume.²⁸ It is uncertain whether ultrasonographic volume measurements are reliable for calculation of the dose of ^{131}I . However, scintigraphy is invaluable to detect ectopic thyroid tissue, which would be overlooked in ultrasonographic volume calculations. Perhaps a combination of scintigraphy and ultrasonography will be more reliable for determining radioiodine dose.

Our mean total posttreatment thyroid volume was 398 mm^3 (median 210 mm^3), which is larger than the mean normal total thyroid volume reported in a former study ($169 \pm 28 \text{ mm}^3$).²⁰ This is likely due to inaccurate width measurements in the prior study. In fact, the authors used an arbitrary reference width of 2.5 mm for volume calculations. In our study, the mean posttreatment width of thyroid lobes was 4.2–4.5 mm, which is larger. Thus, it is misleading to compare the thyroid volume of those control cats with our results.

Normal feline thyroid volume has also been estimated using computed tomography (CT) and was found to be 215.3 mm^3 determined by the sum of areas method vs. a volume of 231.2 mm^3 determined by the maximum prolate ellipse method.²⁹ These volumes are larger than when determined using the ultrasonographic prolate ellipse method.²⁰ However, the volume determined using CT is less than that determined in this study at 6 months following ^{131}I treatment, likely due to the fact that thyroid glands did not return to a completely normal size 6 months after therapy.

In the present study, 22 out of 29 thyroid lobes were heterogeneous and/or contained hypoechoic to anechoic cyst-like areas. Such a change was detected in only 3/28 lobes in the former study of thyroid ultrasonography of hyperthyroid cats.²⁰ Again, this is likely related to lower transducer frequency used in the former study.

In our study, 16 out of 29 thyroid lobes had moderate to severe vascularity at the initial examination while at the posttreatment examination, only one lobe had moderate vascularity and no lobe severe vascularity. In humans, thyroid glands exhibited hypervascularity in Grave's disease when examined before treatment.³⁰⁻³⁵ Also, there was a direct correlation between pretreatment thyroid vascularity in the periphery of autonomous nodules and laboratory parameters of hyperthyroidism.³³ Diffuse thyroid hypervascularity was also found in the thyroid gland in 23 hyperthyroid patients. Twelve of these patients had moderate thyroid vascularity and seven marked thyroid vascularity.³⁴ This corresponds to our results, as moderate to severe hypervascularity was observed in >50% of cats pretreatment. In humans, the intensity of the Power Doppler flow pattern was not related to the severity of the disease.³⁴

During or after treatment with antithyroid drugs, Doppler ultrasonography may contribute to the detection of a relapsing course of hyperthyroidism as significantly increased blood flow parameters were observed in euthyroid patients who relapsed shortly after withdrawal of antithyroid drug treatment.^{31,32} Whether Doppler ultrasonography can be used to predict the outcome of hyperthyroid cats after treatment is unknown but worthy of study.

Six cats in our study received antithyroid medication before radioiodine therapy. The thyroid gland in these cats did not have different ultrasonographic features compared with the cats that did not receive antithyroid medication. Antithyroid drugs, such as methimazole and carbimazole, block organification of thyroid hormones and have no effect on the underlying pathologic lesion. Thus, over months to years of treatment, thyroid nodules can continue to grow.¹ This may explain the absence of differences in the ultrasonographic appearance of the thyroid glands in hyperthy-

roid cats receiving antithyroid medication compared with hyperthyroid cats that did not receive medication.

Some discrepancies between ultrasonographic and scintigraphic results were found in four cats where there was bilateral ultrasonographic involvement of the thyroid gland but unilateral scintigraphic involvement, or ectopic thyroid uptake only. This could be due to the limited resolution of planar imaging. Another explanation is that the scintigraphically suppressed lobe appears abnormal ultrasonographically because of regressive/degenerative changes.

In conclusion, at first ultrasonographic examination, thyroid glands in hyperthyroid cats appeared to be generally increased in size, round, heterogeneous, and hypervascular. Ultrasonographic changes were observed in thyroid lobes in the majority of hyperthyroid cats 6 months after ¹³¹I radioactive iodine therapy and were characterized by size reduction, a less round shape, a more homogeneous structure, and decreased vascularity.

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