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# Thyroidal radioisotope uptake in euthyroid cats: a comparison between $^{131}I$ and $^{99M}TcO_4^-$

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**ABSTRACT**

Two thyroidal evaluation systems in euthyroid cats ($n$ = 12) were compared. A single, confirmed hyperthyroid cat was included for interest. Firstly, thyroidal uptake of an intravenous bolus of approximately 111 MBq (3 mCi) $^{99M}TcO_4^-$ was estimated by using a scintillation camera and calculating the ratio of thyroid to salivary activities at 20 min and 4 h. Thyroid to salivary activity ratios were 1:1 at 20 min and 2:1 at 4 h. Two discrete areas of salivary uptake were identified, namely a parotid/mandibular complex and a more rostral buccal/sublingual complex. These results were compared to radioiodine uptake of an oral dose of approximately 0.925 MBq (25 µCi) $^{131}I$ using a standard thyroid uptake system, measured at 1, 2, 4, 6, 8, 10, 12, 24 and 48 h after administration. Mean radioiodine thyroidal uptake started at 33 % at 1 h, stabilised at 21 % between 4 and 24 h, and dropped to 18 % at 48 h. There was a significant correlation between the early thyroid:salivary ratio of the parotid/mandibular complex and the radioiodine uptake at 12 h.

**Key words**: cat, thyroid, thyroid uptake system, $^{131}I$, $^{99M}TcO_4^-$.

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## INTRODUCTION

The use of radionuclides for evaluating thyroid conditions in cats is well documented[9,10,13,16,19]. Hyperthyroidism is the most common indication[9,10]. A feature of hyperthyroidism is an increased uptake of radionuclide[9,13]. The radionuclides most frequently used for thyroidal imaging are $^{123}I$, $^{131}I$, and the pertechnetate ion of technetium ($^{99m}TcO_4^-$)[10]. The radioisotopes of iodine are exclusively taken up by the thyroid gland. $^{99m}TcO_4^-$, in addition to being concentrated in the thyroid gland, is also concentrated in the salivary and sweat glands, choroid plexus and gastric mucosa[4]. $^{123}I$ is used least frequently in veterinary medicine owing to its high cost and limited availability[16].

The purpose of this study was to compare 2 thyroidal uptake evaluation systems in euthyroid cats. Radioiodine uptake measurement (RAIU) using $^{131}I$ in combination with a standard thyroid uptake system (TUS) was compared to an uptake estimated from the ratio of thyroid to salivary activities (T/S) of $^{99m}TcO_4^-$ using a scintillation camera. A single, confirmed hyperthyroid cat was included to add interest to the study.

## MATERIALS AND METHODS

Healthy, adult, sterilised domestic short-haired cats ($n$ = 12; 7 females and 5 males), ranging in age from 2.5 to 4 years (exact ages unknown) were used in this study. Eleven animals originated from the same institution where they were communally housed and fed a balanced commercial ration. The remaining animal was a house pet from a different area, also fed a commercial ration. An individual case of hyperthyroidism was included in the study. This was a 13-year-old, neutered female Siamese with clinical history of hyperthyroidism, including marked polyphagia, chronic weight loss, hyperactivity and a dull hair coat that easily epilated. This case came from a different geographical area, but was fed a similar ration.

All animals were individually housed for the duration of the trial and fed a balanced, commercial ration once daily. Litter trays were provided and regularly cleaned to facilitate disposal of contaminated urine and faeces and to prevent unnecessary surface contamination of the cats.

On admission, all the cats were identified, clinically examined, their body masses determined, peripheral blood smears made and blood drawn for complete blood counts and serum total thyroxine (T4) determinations.

The 1st phase of the study involved the examination of the thyroids with $^{99m}TcO_4^-$. The cats were fasted overnight. Nine euthyroid cats and the hyperthyroid case were sedated with an intravenous bolus of 200 µg of medetomidine hydrochloride (Domitor, Farmos, Finland). An intravenous cephalic catheter was inserted and each cat placed in dorsal recumbency with head and neck extended. The detector head of the gamma camera (Sopha model DSX rectangular, Sopha Medical, France) with a general purpose collimator was lowered against the animal's body. Acquisition was initiated simultaneously with the injection of an intravenous bolus of approximately 111 MBq (3 mCi) of $^{99m}TcO_4^-$ (Amersham, France). A flow image was acquired. All images were captured using an energy 20 % window centred over 140 keV, a matrix size of 64 × 64 pixels, a sample of 250 000 counts, 60 frames of 1 sec and a pool image of 1 min. Twenty min after isotope injection, an early static image was acquired. Sedation was reversed after intravenous administration of 1 mg of atipamezole hydrochloride (Antisedan, Farmos, Finland). Three cats were not sedated, a similar bolus of $^{99m}TcO_4^-$ was given but no flow study was performed. Only a 20 min single static image was obtained with the cats manually restrained against the camera head. In all 13 cats an additional delayed static image was acquired 3–4 h after isotope administration. For this purpose all the animals were sedated and positioned against the camera as described above. Relative thyroid versus

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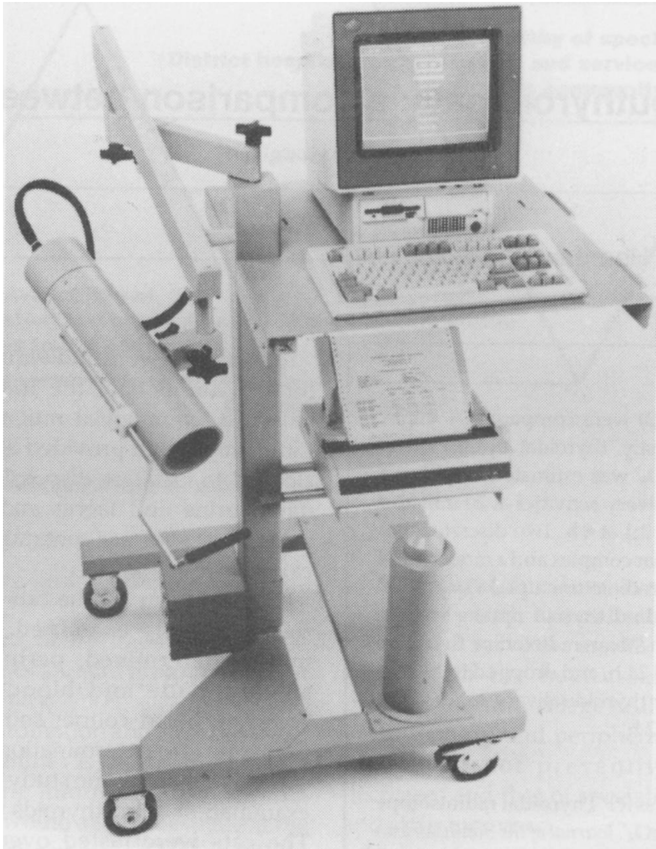

Fig. 1: **Photograph of a standard thyroid uptake system**.

salivary counts were measured on both early and delayed statics, using a profile method.

The 2nd phase of the trial was performed 2 days later. The animals were again fasted overnight. At time $t_0$, the animals were orally dosed, in capsule form, with $^{131}I$ with an activity of approximately 0.925 MBq (25 μCi) (Atomic Energy Corporation, South Africa). An accurate activity count ($C_0$) of each capsule was measured immediately before dosing. The cats were manually restrained in a ventrally recumbent, extended-neck position, 25 cm above the probe of a standard TUS (Model number ND62TR, Nuclear Data Instruments, Illinois, USA) (Fig. 1).

An energy window of 250–440 keV was used with a 5 min collection time. Counts were performed on all animals at 1, 2, 4, 6, 8, 10, 12, 24 and 48 h after isotope administration. Room background activity (BG) was recorded between performing counts on the cats. A phantom was constructed to simulate the amount of scattered radiation expected in the cats' necks. This consisted of a plastic container of roughly the same diameter as a cat's neck filled with rice surrounding a capsule of $^{131}I$ of approximately the same activity as dosed. A scatter correction factor (F) was calculated as follows:

$$F = \frac{\text{capsule count}}{\text{capsule count with phantom}}$$

This factor was calculated to be 1.08.

RAIU was calculated using the following equation:

$$\text{RAIU} = \frac{T - BG}{C} \times F \times 100$$

where $C = C_0e^{-\lambda\Delta t}$, $\Delta t$ = time of cat count (t) - $t_0$, $\lambda$ = decay constant, T = thyroid count at time t.

The procedures described above are based on a previously described technique[10]. All procedures were supervised by medical physicists and conformed to recognised international radiation safety standards.

The correlation between RAIU and T/S was assessed using Pearson's correlation coefficients and associated probability values.

## RESULTS

No clinical abnormalities could be detected in any of the euthyroid cats and all haematological profiles were within the normal range. Appetite and rectal temperatures were within normal range for the duration of the trial. All of these cats had total T4 concentrations within a narrow range except cat 10 which was somewhat higher than the rest (Table 1). Clinical examination of the suspected hyperthyroid cat confirmed the clinical history, as well as revealing a tachycardia and a firm nodule measuring 1 × 1 cm palpable in the mid-cervical area, ventral to the trachea. An electrocardiographic examination confirmed a sinus tachycardia (270 beats per min) with deep Q-waves, prominent R-waves and wide QRS-complexes (Leads I and II). Serum activities of alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase and creatine kinase were elevated. Serum total T4 concentration was markedly elevated.

### Scintillation

Initial flow studies and static studies at 20 min after $^{99m}TcO_4^-$ injection demonstrated very poor uptake in sedated as well as non-sedated euthyroid cats. The delayed static 3–4 h later, however, demonstrated a significantly larger uptake. Cats 11 and 12 revealed slightly

Table 1: **Body mass, sex and serum thyroxine concentrations in euthyroid** (*n* = 12) **cats.**

| Cat no. | Body mass (kg) | Sex[1] | Total T4 (nmol/ℓ)[2] |
|---|---|---|---|
| 1 | 4.29 | NM | 35 |
| 2 | 3.46 | NM | 32 |
| 3 | 4.44 | NM | 31 |
| 4 | 3.70 | NM | 34 |
| 5 | 2.78 | NF | 33 |
| 6 | 2.84 | NF | 32 |
| 7 | 3.68 | NM | 37 |
| 8 | 2.44 | NF | 28 |
| 9 | 2.92 | NF | 29 |
| 10 | 3.50 | NF | 49 |
| 11 | 2.70 | NF | 35 |
| 12 | 3.70 | NF | 37 |

[1]NF = neutered female; NM = neutered male.
[2]Serum thyroxine concentration reference range: 13–41 nmol/ℓ (mean: 27.0 nmol/ℓ).
(Total T4 of hyperthyroid cat: 255 nmol/ℓ).

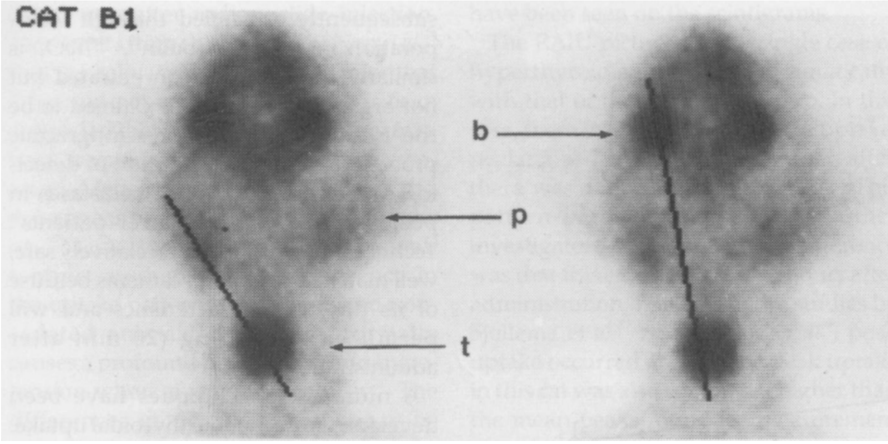


Fig. 2: **Scintigram of a euthyroid cat demonstrating the thyroids** (t) **and the 2 salivary complexes namely parotid/mandibular** (p) **and buccal/sublingual** (b). **The diagonal bars represent sampling for T/S determination.**

Table 2: **Thyroid/salivary uptake ratio** (T/S) **comparing different salivary tissues.**

| Cat No. | Early T/S[1] | Delayed T/S |
|---|---|---|
| 1 | 1.0 (NS) | 2.22 (NS) |
| 2 | 1.15 (NS) | 2.0 (1.48) |
| 3 | 1.14 (1.33) | 2.5 (0.70) |
| 4 | 1.18 (1.43) | 5.7 (1.74) |
| 5 | 1.25 (NS) | 5.7 (1.54) |
| 6 | 1.48 (NS) | 2.22 (0.70) |
| 7 | 1.15 (1.18) | 2.0 (0.83) |
| 8 | 1.10 (NS) | 2.22 (1.0) |
| 9 | NS | 2.22 (0.83) |
| 10 | NS | 6.66 (3.33) |
| 11 | NS | 2.86 (0.95) |
| 12 | 1.4 (NS) | 10.0 (1.6) |
| Mean | 1.205 (1.288) | 3.842 (1.336) |
| Standard error | 0.0499 | 0.743 (0.231) |

[1]NS = not sampled; T/S = thyroid/salivary uptake ratio. First value represents the T/S when using the parotid/mandibular salivary gland complex.The values in parentheses are the ratios using the buccal and sublingual salivary glands. (Early T/S for the hyperthyroid cat using the parotid/mandibular gland complex was 20.0.)

higher levels of activity than the rest.

The T/S in the euthyroid cases also varied considerably with time. The mean T/S determined from the initial static image was 1.2:1. The mean T/S seen with the delayed static image was, however, greater than 3.8:1 when compared to the mandibular and parotid salivary glands.

The hyperthyroid case demonstrated an immediate uptake in both thyroid lobes. This high level of activity seen with the flow study remained constant when compared to the static image 20 min later. The T/S in this case was immediately equal to 20:1.

Two discrete areas of tracer uptake were identified in this study (Fig. 2). The 1st area located at the level of the ear base, we believe, represents the parotid and mandibular glands. The 2nd area corresponds to areas identified by Beck *et al.*[4], and probably represents the more rostrally situated buccal and sublingual glands. The uptake varied between different salivary tissues (Table 2). At the time of the early static image the salivary glands sampled demonstrated approximately equal uptake. Later imaging revealed considerably more activity in the upper cervical area than the more rostral glands.

### Thyroid uptake system

Mean RAIU started at 33 % at 1 h, declined to 20 % between 6 and 12 h, rose slightly to 22 % at 24 h, and finally dropped to 18 % at 48 h. Cats 9, 11 and 12 had conspicuously higher uptakes than the rest of the euthyroid cases (Table 3). Fig. 3 summarises these trends.

The uptake pattern of the hyperthyroid case differs considerably. The initial (1 h) uptake value similarly started at 30 % followed by a rapid increase in uptake, peaking at close to 80 % at 10 h. Subsequent values declined gradually.

### Correlation between RAIU and T/C

Table 4 summarises the correlation between RAIU and T/C. The only correlation that approached significance ($p$ = 0.051) was that between the RAIU at 12 h and the early T/S (20 min) using the parotid/ mandibular salivary gland complex.

Table 3: **Mean percentage uptake of** $^{131}$**I** (RAIU) **over time.**

| Hours | Cat No. | | | | | | | | | | | | Mean | SE[1] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | | |
| 1 | 53.26 | 33.48 | 25.36 | 37.88 | 29.70 | 35.22 | 31.36 | 26.59 | 30.36 | 34.24 | 31.73 | 23.07 | 32.688 | 2.236 |
| 2 | 20.42 | 23.84 | 19.13 | 40.13 | 31.60 | 36.12 | 29.70 | 29.14 | 27.55 | 26.21 | 27.11 | 25.14 | 28.008 | 1.732 |
| 4 | 16.89 | 20.08 | 12.50 | 30.02 | 26.79 | 24.85 | 24.40 | 22.01 | 24.74 | 18.25 | 25.34 | 23.73 | 22.463 | 1.389 |
| 6 | 13.82 | 18.01 | 11.74 | 27.59 | 18.33 | 21.37 | 22.28 | 23.45 | 23.42 | 19.28 | 26.78 | 22.84 | 20.743 | 1.375 |
| 8 | 13.10 | 16.83 | 13.18 | 22.43 | 16.10 | 20.64 | 23.26 | 20.54 | 25.83 | 20.31 | 22.76 | 23.76 | 19.895 | 1.207 |
| 10 | 14.09 | 18.43 | 18.02 | 22.22 | 24.06 | 20.20 | 20.79 | 20.45 | 23.70 | 16.19 | 23.88 | 24.60 | 20.553 | 0.971 |
| 12 | 13.39 | 18.07 | 17.81 | 17.51 | 17.70 | 21.96 | 19.36 | 22.46 | 23.39 | 18.06 | 25.62 | 22.43 | 19.813 | 0.978 |
| 24 | 13.25 | 19.49 | 18.31 | 21.00 | 15.46 | 17.10 | 20.81 | 22.56 | 29.91 | 19.89 | 36.66 | 31.81 | 22.188 | 2.030 |
| 48 | 10.67 | 14.61 | 15.07 | 16.28 | 11.16 | 14.24 | 16.27 | 19.65 | 20.35 | 15.18 | 31.83 | 29.66 | 17.922 | 1.912 |

[1]SE = standard error.

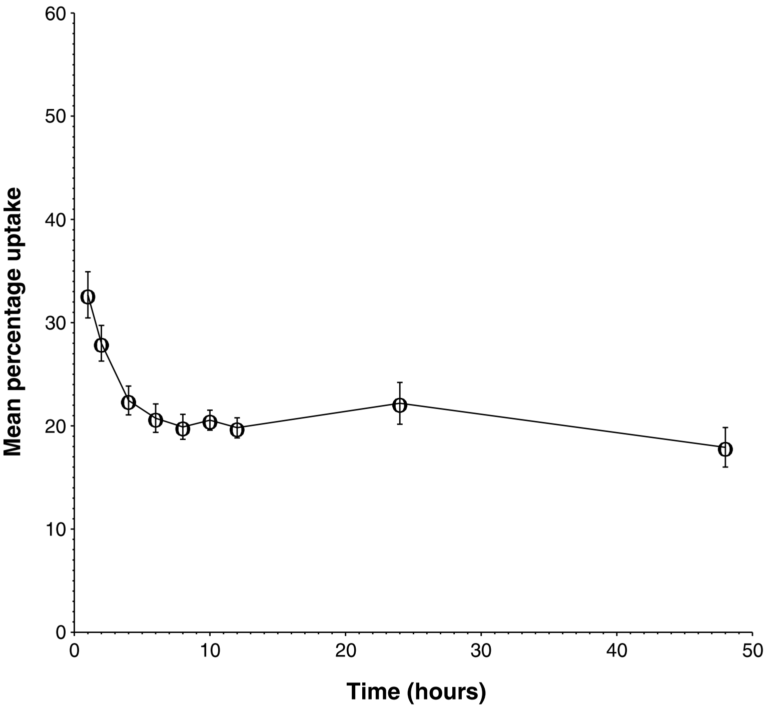


Fig. 3: **Mean percentage uptake of $^{131}$I** (RAIU) **over time in euthyroid cats**. Vertical bars represent 1 standard error (SE) of the mean.

Table 4: **Correlation[1] between RAIU and T/S and associated probability values.**

| RAIU[2] at hour | Early T/S[3] (parotid/mandibular) | Early T/S (buccal/sublingual) | Delayed T/S (parotid/mandibular) | Delayed T/S (buccal/sublingual) |
|---|---|---|---|---|
| 1 | –0.417 ($p$ = 0.26)[4] | 0.191 ($p$ = 0.758) | –0.288 ($p$ = 0.36) | 0.278 ($p$ = 0.408) |
| 2 | 0.439 ($p$ = 0.237) | 0.144 ($p$ = 0.817) | 0.130 ($p$ = 0.688) | 0.012 ($p$ = 0.973) |
| 4 | 0.438 ($p$ = 0.238) | 0.185 ($p$ = 0.766) | 0.233 ($p$ = 0.466) | –0.077 ($p$ = 0.823) |
| 6 | 0.351 ($p$ = 0.355) | 0.046 ($p$ = 0.942) | 0.197 ($p$ = 0.539) | –0.016 ($p$ = 0.964) |
| 8 | 0.496 ($p$ = 0.176) | 0.011 ($p$ = 0.987) | 0.230 ($p$ = 0.473) | –0.020 ($p$ = 0.953) |
| 10 | 0.622 ($p$ = 0.074) | 0.418 ($p$ = 0.484) | 0.337 ($p$ = 0.284) | –0.357 ($p$ = 0.281) |
| 12 | **0.663 ($p$ = 0.051)** | –0.411 ($p$ = 0.492) | 0.006 ($p$ = 0.986) | –0.423 ($p$ = 0.195) |
| 24 | 0.391 ($p$ = 0.299) | 0.277 ($p$ = 0.651) | 0.229 ($p$ = 0.474) | –0.145 ($p$ = 0.670) |
| 48 | 0.408 ($p$ = 0.275) | 0.238 ($p$ = 0.699) | 0.312 ($p$ = 0.323) | –0.141 ($p$ = 0.678) |

[1]Pearson's correlation coefficient.
[2]RAIU = radioiodine uptake measurement.
[3]T/S - thyroid/salivary uptake ratio.
[4]$p$ - probability value; correlation is significant if $p \leq 0.05$.

## DISCUSSION

The scintigraphic evaluation of feline thyroids in suspected cases of hyperthyroidism using $^{99m}TcO_4^-$ is well documented[4,6,10,13,15,16,20]. Two kinds of scintigraphic examinations are usually carried out on thyroidal tissue. These are qualitative scintigraphy, a pictorial presentation of functional thyroidal tissue, and a quantitative thyroid uptake measurement. Both $^{131}$I and $^{99m}TcO_4^-$ have been used for scintigraphic evaluations but their metabolism in thyroidal tissue is somewhat different[16]. $^{131}$I, like stable iodine, is actively trapped and concentrated by the thyroidal tissue and subsequently organified through incorporation into thyroglobulin[16]. $^{99m}TcO_4^-$ is similarly trapped and concentrated but not organified[16]. $^{99m}TcO_4^-$ is claimed to be the isotope of choice for scintigraphic procedures, with the exception of detecting differentiated thyroid metastases in postoperative thyroid cancer patients[6]. Technetium is inexpensive, relatively safe, well matched to gamma cameras because of its physical characteristics and will permit early imaging (20 min after administration)[2,19].

A number of techniques have been developed to determine thyroidal uptake. Using $^{99m}TcO_4^-$ and a scintillation camera the percentage uptake can be calculated by comparing the thyroidal activity, 20 min post-injection, to the activity in a vial containing $^{99m}TcO_4^-$ of known activity[13]. A relatively accurate estimation of uptake can be determined from the T\S of $^{99m}TcO_4^-$ at 20 min post-injection[4,17]. An additional method of determining thyroid uptake is the calculation of RAIU $^{131}$I using a TUS[11,15]. This system comprises a probe consisting of a single collimated sodium iodide crystal coupled to a single photomultiplier tube and accompanying electronics[17] (Fig. 1). The 24 h $^{131}$I uptake value is a well documented standard in thyroidal uptake determination[3,12,18]. The calculation of RAIU of $^{123}$I has also been described[9].

A point of consideration is the compatibility of $^{99m}TcO_4^-$ and $^{131}$I with the 2 aforementioned scintillation counting systems. The gamma camera is 95 % efficient in detecting the activity of $^{99m}TcO_4^-$, but only 28 % efficient for $^{131}$I. This is due to the poor sensitivity of the camera to detect the high-energy photons (364 keV) emitted by $^{131}$I. The thicker crystal of the uptake probe on the other hand is considerably more effective, demonstrating a 90 % detection efficiency for $^{131}$I[1].

In the present study, the poor initial uptake of $^{99m}TcO_4^-$ in the euthyroid cats differs markedly from thyroid uptake in humans where the thyroid in euthyroid individuals demonstrates a far greater initial activity[7,8]. The reason for this difference is not known. However, the poor initial uptake found in this study supports the findings of Nap *et al.*[14] that thyroidal uptake was maximal at 60 min after intravenous injection of $^{99m}TcO_4^-$. This raises questions about the validity of the recommendation that imaging should start at 20 min after intravenous infusion of the radionuclide[2,15,19]. Despite the relatively poor initial uptake, it was still possible to determine the T/S, and the ratio of 1.2:1 is similar to the results of Beck *et al.*[4], the scintigraphic imaging occurring

10–15 min after radionuclide injection. This differs from the findings of Nap *et al.*[14] that the salivary uptake was so poor that T/S could not be determined. It has been suggested that sedation or starvation may have been responsible for this discrepancy[7]. Medetomidine hydrochloride did not appear to affect the thyroidal uptake of $^{99m}TcO_4^-$ significantly in this small sample, as there was no difference in the uptake patterns for sedated and non-sedated animals. This drug normally causes a profound bradycardia and hypotension when given intravenously[21]. The differences in uptake patterns may be associated with the differences in activity of $^{99m}TcO_4^-$ given, namely: approximately 111 MBq in this study compared with 37 MBq[4] and 15 MBq[14]. The T/S determined from the delayed image in this study was 3.8:1. This together with the observations of Nap *et al.*[14] suggests that for T/S to be a reliable method of thyroidal uptake determination, thyroidal imaging should occur later than the suggested 20 min after radionuclide injection.

Mean RAIU started at 33 % at 1 h, declined to 20 % between 6 and 12 h, rose slightly to 22 % at 24 h, and finally dropped to 18 % at 48 h. This pattern contrasted with other uptake studies where the uptake started at a low level and increased gradually[11,19]. We believe that the initial peak in our study could have reflected circulating $^{131}I$ levels superimposed over thyroidal trapping and binding as described by Hays and Wesselossky[8]. This discrepancy between the studies could be explained by the longer sampling intervals used in the other studies. Different routes of administration (oral *v.* parenteral) may also influence this type of comparison[19]. The actual peak percentage uptake values in our study were marginally lower than those in comparative studies[11,19]. This may reflect the influence of dietary iodine, which is documented as having a profound effect on radioiodine metabolism[5,9,13].

It was interesting to note that 3 cats (Nos 9, 11 and 12) peaked at higher levels than the rest. These 3 cats were all neutered females. Owing to the relatively small number of animals in this study, we were not able to make statistical deductions from this finding and the significance (if any) is unknown. We are not aware of any veterinary publication intimating a sexual variation in radioiodine metabolism in the thyroids. One possible explanation is that these cats had autonomous thyroid nodules but were not yet clinically hyperthyroid. These would presumably have been seen on the scintigrams.

The RAIU picture for the single case of hyperthyroidism contrasts dramatically with that of the euthyroid group. In this case, there was a rapid increase in uptake, peaking at 77 % at 10 hours. Thereafter, there was a more gradual decrease. This pattern parallels that found by other investigators[9,11,19]. A noticeable difference was that this case peaked at 10 hours after administration, whereas in the studies by Sjollema *et al.*[19] and Hoenig *et al.*[9], peak uptake occurred at 24 h. The peak uptake in this cat was also somewhat higher than the mean peaks found in the aforementioned studies[9,11,19]. This single case supports the proposal by Sjollema *et al.*[19] that measurements made between 4 and 24 h reflect the thyroidal metabolism most accurately and therefore are to be preferred to measurements made after 24 h.

There was a significant correlation between the 10 h RAIU and the early T/S using the parotid/mandibular salivary complex. In addition, the 2 cats (Nos 11 and 12) with the greatest radioiodine uptake demonstrated higher activity peaks during the scintigraphic study.

In conclusion, the TUS functioned well, and provided results that were, as anticipated, similar to other published studies. The TUS is limited in that it is unable to demonstrate metastatic and ectopic thyroidal tissue or the laterality of a thyroidal lesion. RAIU is claimed to be a relatively insensitive diagnostic test for determining hyperthyroidism. We suggest $^{131}I$ and TUS may offer veterinary institutions and practitioners an opportunity to study thyroids at a fraction of the equipment cost required for a scintigraphic facility.

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