External Exposure of Veterinary Staffs and Pet Owners from Feline $^{99m}$Tc-MAG3 Renal Scintigraphy

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External exposure of veterinary staffs and owners in veterinary nuclear medicine was estimated by monitoring the surface dose rate (SDR) and ambient dose rate (ADR) from the feline renal patient ($n=20$) and controls (normal cats, $n=8$) during and after renal scintigraphy with $^{99m}$Tc-mercaptoacetyl triglycine (MAG3, dose 93–141 MBq/head). The highest SDR was at the ventral side of abdomen and its SDR-time course followed within the degradation curve with physical half-life ($6.01$ h) ADR demonstrated significant decrease up to about 100-fold by keeping distance from the patient at 100 cm. All cats showed acceptable SDR which was less than $115$ µSv/h in 24 h post injection, where cumulative SDR till infinity was less than $1$ mSv (=dose limit to the public). Urination had a conspicuous effect on SDR at 24 h ($0.38$–$9.6$ µSv/h) and all urinated cat showed less than 1/10 of the limit of the yearly external public exposure. These results satisfied current legislation in Japan, while the 24 h post-dose regulation was considered over-regulated in the case of sufficiently lower maximum SDR. From the perspective of overburdening animals, their owners, and veterinary clinics, it was considered desirable to determine criteria based on the maximum SDR for each patient.

Key Words: radiation exposure, radiation protection legislation, veterinary nuclear medicine, renal scintigraphy, cat, technetium-99m mercaptoacetyl triglycine ($^{99m}$Tc-MAG3)

1. Introduction

The radiation protection strategies in nuclear medicine need to concern the external radiation exposure from the radioactive patient to veterinary staffs and the public. There are few data available about the radiation exposure from the radioactive small animal patient.1–3) Veterinary staffs are frequently obtained to external radiation while performing nuclear medicine procedures such as preparing and administrating radiopharmaceuticals, restraining animal patient on the gamma-camera scanning table, removing the animal patient from the bed, and transporting and recovering post- sedated or anesthetized radioactive animal patient.

Chronic kidney disease (CKD) is a common clinical problem in older companion animals, and elderly cats are also commonly diagnosed with this CKD.4) Since insensitive outcomes for detecting kidney failure were evaluated from clinical sign and blood and urine profile, such as complete blood count (CBC), blood and urinary biochemistry profiles including electrolyte, blood urea nitrogen and creatinine.5) Radiography and ultrasonography are common exams evaluating the anatomical details of kidney; however, these procedures cannot describe a quantitative renal function. $^{99m}$Tc-mercaptoacetyl triglycine (MAG3) renal scintigraphy can provide not only the morphologic information but also the quantitative function of the individual kidney with-
out any invasion.\textsuperscript{6})

Japanese legislation restricts 24 h consignment of veterinary nuclear medical patients including dogs and cats if they receive 99m\textsuperscript{Tc}-labeled pharmacies not more than 150 MBq, and 48 h if animal injected above 150 MBq. This dose-dependent regulation was simply based on the calculation by physical half-life of 99m\textsuperscript{Tc} with no consideration of animal’s self-absorption, distribution, and excretion. On the other hands, obstructive uropathy may result in severer urinary retention in the body than in normal animal. Therefore, feline CKD patient may retain significantly higher radioactivity in renal scintigraphy.

In Japan, Kitasato University Veterinary Teaching Hospital (KUVTH) is the only hospital that performs veterinary nuclear medicine for dogs and cats. Therefore, an assessment of radiation exposure is needed to reduce the concerns of the veterinary staffs. This study aimed to measure dose rate to evaluate exposure to the personnel who are involved in feline renal scintigraphy by comparing the dose rate from renal patients and normal controls within 24 h post-injection. Appropriate positional relationship and distance between animal and the veterinary staffs, and the rationality of the 24 h detention period of patient in hospitals, and the risk assessment of owners will be discussed.

2. Materials and methods

2·1 Animals

Twenty-eight cats \{age 5.4±3.2 years (2 to 15 years old) with body weight 4.1±0.86 kg (2.2 to 5.5 kg)\} were monitored from June 2018 to Aug 2020. The breed of the cats included Scottish fold, American shorthair, Munchkin, Japanese, Maine coon, Siamese, and mix.

Based on results of general physical examination, complete blood count, and blood biochemistry including blood urea nitrogen (BUN), creatinine (Cr) and electrolytes, cats were grouped into a healthy normal control (C; \(n=8\)) and renal patients (R; \(n=20\)). The R group was categorized by already diagnosed as renal disease and to know if there is any improvement or progression of renal disease and had a serum creatinine concentration \(\geq 1.6\) mg/dL and at least one of the following: abnormal kidney on ultrasound, CT, or diluted urine (urine specific gravity (USG)<1.035) according to IRIS guidelines of the stage 2 CKD or higher. All owners were informed consent for the accordance of animal to participate in the renal scintigraphy protocol which was prepared in KUVTH. The cats of C and R with that information is listed in Tables 1 and 2.

This study has been approved by committee on experimental animal ethics in Kitasato University, School of Veterinary Medicine.

2·2 Scintigraphy

2·2·1 Drug preparation and sedation

Each cat was fasted at least 8 h before renal scintigraphy. The fluid intravenous transfusion was performed prior to scanning protocol to maintain normal hydration status owing to dehydration can lead to decrease blood volume and delay wash out the radiotracer, resulting in erroneous scintigraphy.\textsuperscript{7}) Alfaxan (Alfaxalone, Meiji Seika Pharma Co. Ltd., Tokyo) was injected into each cat with a 1 mg/kg bolus, followed by continuous infusion (0.1 mg/kg/min) from a plug placed in the cephalic vein, under ECG monitoring. Each injection dose of MAG3 (MAGscinti injection, Nihon Medi-Physics Co. Ltd., Tokyo) was measured by ionization chamber dose calibrator (IGC-8, Hitachi, Tokyo). Total injection dose to the animal was calculated by differences of pre- and post-injectable syringe with decay correction of 99m\textsuperscript{Tc} physical half-life (6.01 h).

2·2·2 Image acquisition

The source activity unshielded syringe of pre-injection and post-injection is routinely counted at 30 cm from the gamma camera system (Infinia\textsuperscript{8})
Hawkeye4, GE healthcare Japan, Tokyo), and a static image was acquired for 60 s with a matrix size of 256×256 pixels. The animal was placed in the left lateral recumbency on the imaging table where kidneys were at the centre of the camera. Dynamic frame acquisition was made immediately after MAG3 injected intravenously. The first dynamic phase was acquired for 5 min, 2 s per frame. The second dynamic phase was acquired for 15 min, 10 s per frame, with a matrix size of 128×128 pixels. The dynamic images were acquired in total for 20 min for 240 frames. The kidney depth image is a static image for 60 s on the left lateral recumbency with matrix size is 256×256 pixels. Based on the renogram, effective renal plasma flow (ERPF) of each cat was calculated.8)

2·3 Dose rate measurement
The trial was a randomized controlled clinical trial. After the completion of the renal scintigraphy, a semiconductor survey meter (PDR-303, Hitachi, Tokyo) was used for dose rate measurements at various body locations of cat at various distances within 24 h. The exposure rate measurement was recorded by one veterinarian member when the survey meter reading stabilized. The room background ambient dose rate (ADR) is 0.04±0.05 μSv/h. The external dose rates were measured at the surface of the head, thorax, and abdomen. The distance ADR were obtained at 50, 100 cm from a cat (Fig. 1). Each cat was measured SDR and ADR at post-scanning, during the daytime when veterinarian checked physical examination and changed training pad inside the cage (at least 2 times), and 24 h post-injection.

The radioactive decay correction for dose rate measurements at injection time and 24 h post-injection were calculated from measuring dose rate post-scanning and before getting out of the restricted area. In addition, the radiation dose after 24 h post-injection to infinity was calculated as external radiation exposure for public.

2·4 Statistics
Statistical analysis was performed using R Foundation for Statistical Computing software (R Version 3.5.1).9) are presented as mean±standard deviation (SD). A p-values are 2-tailed with statistical significance defined with p<0.05. Correlations among variables were determined by regression analysis and Pearson Correlation.

3. Results
The animals examined in this study are listed in Table 1 for C and Table 2 for R. The patients showed relatively higher BUN and Cr and lower USG, with sufficient reasons for scintigraphy as listed in Table 2. The injected dose of MAG3 was 107±7 MBq and 117±12 MBq (mean±sd.) for C and R, respectively (Tables 1, 2).

Abdominal ventral SDR was the highest at the body but there was no significance between C and R as shown in Fig. 2. Significantly higher SDR was observed at head and thorax of R than that of
Table 1 Normal cats examined $^{99m}$Tc-mercaptoacetyl triglycine (MAG3) renal scintigraphy

| No. | Age | Sex | BW (kg) | MAG3 Dose (MBq) | BUN (mg/dl) | Cr (mg/dl) | SDR$_0$ (μSv/h) | ERPF (ml/min/kg) |
|-----|-----|-----|---------|-----------------|-------------|-----------|----------------|------------------|
| 1   | 2.2 | M   | 4.1     | 114             | 27.6        | 20.8      | 1.57           | 210              |
| 2   | 3.2 | M   | 5.5     | 115             | 20.8        | 18.9      | 1.25           | 127              |
| 3   | 2.0 | F   | 4.2     | 111             | 26.6        | 24.3      | 1.35           | 382              |
| 4   | 5.0 | M   | 5.5     | 99              | 17.9        | 20.2      | 1.36           | 162              |
| 5   | 2.5 | F   | 4.8     | 105             | 21.6        | 24.0      | 1.86           | 152              |
| 6   | 8.1 | FS  | 3.8     | 115             | 30.0        | 21.7      | 1.48           | 324              |
| 7   | 9.6 | FS  | 3.4     | 104             | 30.8        | 26.3      | 1.37           | 224              |
| 8   | 7.8 | FS  | 4.2     | 97              | 23.2        | 24.7      | 1.17           | 240              |

mean 5.1 4.4 107 24.8 22.6 1.43 228 8.8

sd 3.0 0.8 7 4.6 2.6 0.21 88 2.2

All cats were mix breed, 1Sex; M; male, F; female, FS; female spayed, 2BUN; blood urea nitrogen, 3Cr; creatinine, 4SDR$_0$; Estimated abdominal surface dose rate at time 0 of MAG3 injection, 5ERP; Effective renal plasma flow (ml/min/kg), 6nd; not determined.

Fig. 2 Surface dose rate immediately after renal scintigraphy (Significant differences (*p<0.05)). Abdominal ventral surface was the highest at the body surface but there was no significance between normal control (C) and renal patient (R).

Table 2 Patient cats examined $^{99m}$Tc-mercaptoacetyl triglycine (MAG3) renal scintigraphy

| No. | Age | Breed | BW (kg) | MAG3 Dose (MBq) | BUN (mg/dl) | Cr (mg/dl) | USG | Reason for Scintigraphy | SDR$_0$ (μSv/h) | ERPF (ml/min/kg) |
|-----|-----|-------|---------|-----------------|-------------|-----------|-----|--------------------------|----------------|------------------|
| 1   | 9.3 | MC    | 4.6     | 141             | 30.6        | 29.6      | 1.011 | Renal pelvic dilatation with calculi | 324            | 7.9              |
| 2   | 9.4 | M     | 5.5     | 125             | 22.6        | 16.9      | 1.017 | Left kidney enlargement - obstructiv | 372            | 6.0              |
| 3   | 3.5 | F     | 3.9     | 136             | 34.8        | 26.0      | 1.016 | Bilateral hydronephrosis at time 0 | 246            | 5.4              |
| 4   | 2.1 | MC    | 4.2     | 93              | 22.5        | 29.2      | 1.035 | Bilateral hydronephrosis | 203            | 4.1              |
| 5   | 4.5 | MC    | 4.6     | 110             | 24.1        | 28.5      | 1.027 | Bilateral hydronephrosis | 191            | 2.1              |
| 6   | 4.9 | FS    | 4.2     | 88              | 28.6        | 24.2      | 1.015 | Bilateral hydronephrosis | 357            | 6.6              |
| 7   | 2.0 | FS    | 3.5     | 122             | 34.9        | 35.4      | 1.013 | Bilateral hydronephrosis | 355            | 7.7              |
| 8   | 4.1 | FS    | 3.1     | 93              | 29.6        | 192       | 1.091 | Bilateral hydronephrosis | 201            | 0.4              |
| 9   | 4.1 | FS    | 3.3     | 111             | 33.8        | 154       | 1.010 | Bilateral hydronephrosis | 182            | 6.7              |
| 10  | 6.1 | FS    | 3.2     | 121             | 37.8        | 50.2      | 1.080 | Bilateral hydronephrosis | 307            | 1.6              |
| 11  | 10.3| MC    | 5.5     | 110             | 20.0        | 24.5      | 1.008 | Bilateral hydronephrosis | 241            | 2.0              |
| 12  | 10.3| MC    | 4.3     | 117             | 27.2        | 24.0      | 1.006 | Bilateral hydronephrosis | 309            | 2.4              |
| 13  | 5.1 | MC    | 3.3     | 105             | 31.9        | 26.0      | 1.020 | Bilateral hydronephrosis | 281            | 1.9              |
| 14  | 15.0| F     | 2.2     | 119             | 54.2        | 41.5      | 1.006 | Bilateral hydronephrosis | 309            | 6.1              |
| 15  | 3.1 | MC    | 4.0     | 133             | 33.3        | 93.6      | 1.011 | Bilateral hydronephrosis | 220            | 2.2              |
| 16  | 4.6 | MC    | 4.3     | 108             | 25.1        | 33.8      | 1.011 | Bilateral hydronephrosis | 102            | 1.1              |
| 17  | 7.7 | FS    | 3.4     | 117             | 34.1        | 53.1      | 1.015 | Bilateral hydronephrosis | 231            | 1.5              |
| 18  | 3.2 | MC    | 4.7     | 123             | 26.4        | 31.6      | 1.020 | Bilateral hydronephrosis | 156            | 2.3              |
| 19  | 6.1 | MC    | 4.9     | 117             | 23.6        | 45.0      | 1.015 | Bilateral hydronephrosis | 138            | 2.4              |
| 20  | 4.1 | FS    | 2.8     | 117             | 42.2        | 42.1      | 1.020 | Bilateral hydronephrosis | 317            | 1.8              |

mean 6.0 4.0 117 30.9 53.4 3.68 1.015 252 3.7

ds 3.4 0.9 12 8.0 44.1 3.65 0.008 78 2.4

1Sex: M; male, MC; male castrated, F; female, FS; female spayed, 2Breed: SF; Scottish fold, AS American shorthair cat M: Munchkin J: Japanese cat MC: Maine coon, SM: Siamese cat, 3BUN; blood urea nitrogen, 4Cr; creatinine, 5USG; urinary specific gravity, 6SDR$_0$; Estimated abdominal surface dose rate at time 0 of MAG3 injection, 7ERP; Effective renal plasma flow (ml/min/kg), 6nd; not determined.
Effect of distance from the surface of abdomen on the ambient dose rate (ADR) immediately after scintigraphy. C: Normal control, R: renal patient. ADR decreased 30–100 fold at 50–100 cm from the patient.

There was good exponential correlation between corrected SDR per injected dose per body weight (cSDR) and body weight regardless of the renal health status (Fig. 4B). This implies the relationship that cSDR will decrease as the patient body weight or volume increases. However, although there was about 6 times higher cSDR in the lowest body weight cat compared to the heaviest one, actual SDR was in the range between 100–400 µSv/h and did not show correlation to the body weight (Fig. 4A).

The time course of abdominal SDR in 28 cats after MAG3 injection is shown in Fig. 5. The estimated SDR at injection time 0 was in the range of 100–400 µSv/h, and most of their degradation profile appeared within the slope of physical half-life (6.01 h). Urination within 24 h appeared drastically decreasing SDR, by factor 10 or more. Although there was a tendency that renal patients show higher SDR than normal controls, the overall SDR exposure from time t to infinity in all cats urinated within 24 h were below 1/10 of 1 mSv which is the limit to the public exposure. The urinated 5 cats out of 8 normal, and 4 cats out of 16 urinated cats were estimated to be less than 1/100 of 1 mSv, whereas non-urinated cats in 24 h was higher SDR than 1/10 of 1 mSv.

4. Discussion

Some studies concern the radiation exposure from nuclear medicine procedure to the veterinary staffs.1–3, 10–13) There is no report on the dose rate concerning feline scintigraphy. Our results of the exposure rates measured from personnel-patient interaction with various locations (Fig. 2) and dis-
stances (Fig. 3) provided the opportunity to evaluate approximate dose rate from healthy cat and cat with renal disease in renal scintigraphy. Our measured dose rates indicated some of the influential factors for occupational radiation exposure from personnel-patient interaction.

Based on our results, most influential factors from radioactive patients include the time after injection (Fig. 4A), body part and its distance, and urination of patients (Fig. 5).

The relatively highest SDR was at the surface of the abdomen compared with thorax and head (Fig. 2). This is likely since intravenously administered MAG3 is distributed throughout the body but is rapidly excreted by kidneys.14

From the data in Figs. 4A and 5, the occupational radiation dose will be the highest during the scintigraphy and the dose may not be influenced by the renal condition.

All results of comparing radiation exposure between non-urinating cats and urinated cats within 24 h demonstrated the significant decrease in abdominal SDR through urination (Fig. 5), which were contributed by the significant reduction of radioisotope eliminated out of the body. This result agreed with Gültekin et al.15 who reported the effective micturition of radioactive patients under routine examinations including thyroid scintigraphy, whole-body bone scintigraphy, myocardial perfusion scintigraphy, and renal scintigraphy. Additionally, not only the significant decrease of SDR from urinated cat in Fig. 5 also supported the higher SDR retained in non-urinating cat will give the chance to veterinary staffs to receive more radiation. Therefore, observation of urination before getting out of the restricted area is the key to reduce external exposure of the owner and public.

The International Commission on Radiological Protection (ICRP) and legislation dose limits of Japan set rules of occupational annual dose limit of 50 mSv which averaged 20 mSv per year over a defined period of 5 years and the public annual dose limit of 1 mSv.16, 17

Based on the results in Fig. 3, since the renal scintigraphy is done within 1 h after MAG3 injection, cat is housed in carrier and moved into the cage and following overnight patient care would be additional 1 h at most, the total external dose from the cat would be estimated not more than 25 μSv/case (the maximum dose rate was less than 12 μSv/h×2h) at average distance of 50 cm from the patient. The radiology staffs in KUVTH, where veterinary nuclear medicine is performed at most 60 cases per year and external exposure as to effective dose is usually less than 1 mSv/month and never exceed 5 mSv/year.

One of several factors influencing cumulative staff exposure is the personnel-patient interaction to locations, distances, times, and intervals of work after injection. Our results suggest the proper position receiving the least external radiation exposure in this...
protocol is standing near the head of the patient. The lowest SDR from at the head is due to characteristics of specific biodistribution of the radiopharmaceutical.

Most times that staff approached the patient were post-scanning time and before going home. In our routine protocol, we take care of the sedated patient on the table keeping a distance from the patient mostly greater than 50 cm. The average working time since administrating radioisotope until putting the patient into a cage is $38 \pm 13$ min when calculating the staff radiation dose at 50 cm from the renal patient was $4.5 \pm 1.7 \mu$Sv per renal scintigraphy study.

In a routine scintigraphy, veterinary staff spends a short time at 50 cm distances to animal patients per case where the occupational exposure will be much lower than the assumed cumulative dose per day and the regulatory limits. Our assuming of the caseload per day of veterinary staff will be overestimated, it depends on the contact length and the working habits of each staff member. Furthermore, the effectiveness of the lead apron for $^{99m}$Tc radioisotope most be beneficial during close radioactive patient contact in imaging procedure.\textsuperscript{18, 19} Staff members should concern the routine steps of the procedure, monitoring the radiation dose by using dosimeter, use of the additional lead apron, and working with the ALARA concept to negligible levels of radiation exposure. The optimal working result in handling more caseloads than assuming.

Regarding public exposure, our results represented the renal function does have little influence on external radiation from the nuclear patient and urine at 24 h post-injection (Fig. 5). Nevertheless, micturition affects SDR and ADR from the patient to the pet owner. In other words, as far as the patient urinates, the less the owner receives the radiation exposure. In this study, some cats showed significantly lower SDR within 20 h of MAG3 injection (Fig. 5), which was 10 times lower than the yearly dose limit to public (1 mSv). This survey monitoring to the nuclear patients will be the evidence and elucidate the rationality to release restrains of patients from restricted area and may enable to relax current regulations.

In conclusion, this study satisfied current legislation concerning radiology personnel and pet owners who are involved in MAG3 renal scintigraphy in Japan. And the 24 h post-dose restriction of the patient was considered over-regulated in the case of a sufficiently lower maximum SDR. From the perspective of overburdening animals, their owners, and veterinary clinics, it was considered desirable to determine the restriction criteria based on the maximum SDR for each patient.

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要　旨

猫における$^{99m}$TcMAG3 腎シンチグラフィに関わる人の放射線防護評価

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$^{99m}$Tc-mercaptoacetyl triglycine (MAG3) 投与量93–141MBq/頭）による腎シンチグラフィでの猫（腎疾患20例および正常例8例）の表面線量率（SDR）と空間線量率（ADR）のモニタリングから、核医学検査時獣医スタッフと飼い主に対する外部被ばく線量を推定した。最も高い SDR は腹部側表面であり、その SDR 時間経過は、物理的半減期（6.01h）の減衰曲線未満であった。ADR は、患者からの平均距離を100cmに保つことにより、SDR に対し1/100 の有意な減少を示した。猫は投与後24 時間で115µSv/h 未満（物理学的半減期に満たず）で累積 SDR は1mSv つまり公衆への線量限度）未満となる管理区域内外への退出許容可能な SDR を示した。MAG3 投与後の排尿は24 時間以内の SDR (0.38–9.6µSv/h) に顕著な影響を及ぼし、排尿したすべての猫は投与後24 時間以内に年間の公衆に対する線量限度の1/10 未満を示した。これらの結果は日本の現在の法令基準を十分に満たしていたが、最大 SDR が十分に低い場合では、投与後24 時間の管理区域内での保管という規定が適切であると見なされた。動物、その飼い主、および動物病院の負担軽減の観点から、各患者の最大 SDR に基づいて管理区域内への退出基準を決定することが望ましいと考えられた。