

October 2019

Evaluating Feline Release Criteria Following Iodine-131 Therapy For Hyperthyroidism

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EVALUATING FELINE RELEASE CRITERIA FOLLOWING IODINE-131 THERAPY FOR HYPERTHYROIDISM

A Thesis

Submitted to the Graduate Faculty of the
Louisiana State University and
Agricultural and Mechanical College
in partial fulfillment of the
requirements for the degree of
Master of Science

in

The Department of Physics and Astronomy

by
Anthony Ramon Davila
B.S., B.S., B.I.S., Louisiana State University, 2017
December 2019

This work is dedicated to my wife and my parents,
who have always supported me and believed in me.

ACKNOWLEDGEMENTS

I would first like to thank Dr. Wei-Hsung Wang, my graduate advisor and committee chair, not only for inspiring me to pursue health physics as a path of study but also for providing me with the support I needed to conduct my own research for the first time.

Next, I would like to thank Dr. Jon Fletcher for his expertise in veterinary medicine and his willingness to work with me on this research. His care for his patients and his passion for research are both admirable and infectious.

Of course, I would also like to thank the rest of my committee: Dr. Kenneth Matthews (co-chair) and Dr. Shane Stadler. They both provided valuable scientific insight that I would not have gathered on my own. Additionally, Dr. Matthews' radiation detection course is the reason I first become interested in medical and health physics.

I would be remiss to not also thank my peers from the Radiation Safety Office: Dr. Charles Wilson IV, Amin Hamideh, Jabari Robinson, and Daniel DiMarco who contributed constructive criticisms and aided in refining my thoughts.

Lastly, I would like to especially thank my wife Lexi, who always inspires and encourages me, and my parents Ruth and Francisco, who have always nurtured my love of math and science.

Without each and every one of these individuals, this endeavor would not have been possible.

This work was supported in part by a graduate fellowship from the Nuclear Regulatory Commission.

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ABSTRACT

Hyperthyroidism is a very common endocrine disorder in both humans and cats. Radioactive iodine ablation therapy is considered the gold standard; however, the patient becomes a radiation source and poses a potential radiological risk to others. The regulations governing when the patient can be released differ between human medicine and veterinary medicine. A human patient can receive up to 33 mCi of I-131 and be discharged the same day; yet a feline patient can receive a dose as low as 2 mCi and require multiple days of hospitalization. This discrepancy has not been satisfactorily addressed; and overly restrictive release criteria can place a burden on the veterinary staff, the patient, and the pet owner. In this study, administered activities and exposure rates are measured for hyperthyroid cats undergoing treatment at Louisiana State University Veterinary Teaching Hospital to determine if current criteria are too restrictive for releasing cats to their owners. Additionally, radioassays are performed on the surface of the cat, its excreta, and its environment to characterize the potential exposures to the pet owners. Annual total effective dose equivalents for the pet owners are calculated using the NRC's equation from NUREG-1556 Vol 9. The results of the assays show that minimal radioactivity is present. The results of the TEDE estimates indicate that the majority of cats can be released the same day of injection and that the resulting TEDE to the pet owner is unlikely to exceed 100 mrem, suggesting that current release criteria are overly conservative.

CHAPTER 1. INTRODUCTION

1.1. Iodine-131, Hyperthyroidism, and Radioactive Iodine Therapy

Iodine-131 (I-131) is a radioisotope of iodine with a physical half-life of 8.02 days; its primary decay emissions include a 606 keV β - particle with 89.6% abundance and a 364 keV γ -ray with 81.5% abundance (Knolls Atomic Power Lab 2010). I-131 is normally a health concern after the release of fission products during a nuclear accident, as most recently following the Fukushima Daiichi incident (Tokonami et al., 2012). I-131 emits energetic γ -rays that pose an external exposure hazard while the β - particles can cause internal exposures if inhaled or ingested. I-131's preferential uptake in the thyroid along with its biological half-life of 80 days in humans can irradiate the thyroid cells and potentially lead to thyroid cancer. However, the same properties that make I-131 a health concern also make it a valuable medical treatment. Any form of iodine that enters the body subsequently enters the blood stream as iodide. Once in the blood, iodide is actively transported from the blood into the thyroid's functional unit, the follicle (Leggett, 2010). The iodide is concentrated into the follicle's lumen where it is oxidized into iodine and incorporated into the protein thyroglobulin. Iodinated thyroglobulin is then moved back into the follicle cell and broken down into the thyroid hormones thyroxine (T4) and triiodothyronine (T3). After the thyroid hormones are secreted and broken down, iodine is eventually eliminated through the kidneys and urine, primarily, but also through saliva, feces, and sweat to a lesser extent. Medical professionals can use iodine's biological role to treat thyroid disorders, most commonly hyperthyroidism.

Hyperthyroidism is an common endocrinopathy characterized by an overactive thyroid and excessive production of T3 and T4 hormones (Ross, 2011). Hyperthyroidism,

however, is not exclusive to humans and also afflicts cats. In fact, hyperthyroidism is the most commonly diagnosed endocrinopathy in older felines (Peterson, 2006). While the underlying cause of feline hyperthyroidism is not definitively known, benign, adenomatous hyperplasia—an increased reproduction rate of non-cancerous thyroid cells—is the most common diagnosis (Peterson, 2012). The clinical signs for a cat with hyperthyroidism most commonly include weight-loss, increased appetite, and increased drinking and urination due to the role that the T3 and T4 hormones play in metabolism (Peterson et al., 2016).

The therapeutic options for feline hyperthyroidism are antithyroid medications, thyroidectomy, radioactive iodine ablation (RIA) treatment, and dietary therapy. Antithyroid medications require multiple daily administrations which can be difficult to do with feline patients. Even if the pill can be administered, some cats may not tolerate the side effects associated with the medication (Peterson, 2006). Most importantly, antithyroid medications are not curative. Dietary therapy is also non-curative, and the cat must maintain a strict iodine-deficient diet. Dietary therapy can also be difficult due to the dependence on the palatability of the low iodine food by the patient. Thyroidectomies, on the other hand, are a curative treatment option when successful. However, thyroidectomy carries the risks and complications associated with surgery and anesthesia (Peterson, 2006). Though they can be curative, thyroidectomies can also result in failure to remove all the hyperplastic tissue resulting in relapse.

Out of the available treatment options, RIA therapy is considered the treatment of choice by veterinarians (Carney et al., 2016). RIA is an effective and curative treatment for feline hyperthyroidism with a majority ($\geq 95\%$) of cases resolved with a single dose; RIA is considered safe with minimal side effects and no associated mortality (Carney et al., 2016).

RIA's efficacy is due to I-131's physical and biological characteristics. The hyperplastic thyroid tissue is hyperfunctional; therefore, the radioactive iodine becomes concentrated there. The β - particles deposit their energy locally resulting in the ablation of those hyperplastic tissues while sparing healthy nearby tissues (Carney et al., 2016). RIA has a high cost up front, but the biggest disadvantage to RIA is the mandatory hospitalization period following treatment which can last from 3 days to 4 weeks depending on the administered dose and the regional regulations (Carney et al., 2016; Peterson, 2006). This disadvantage to RIA is unique to treatment of feline hyperthyroidism and is not present in treating human hyperthyroidism.

1.2. Iodine-131 Release Criteria

In human medicine, the patient release criteria for I-131 treatments are regulated by 10 CFR 35.75 which establishes an annual total effective dose equivalent (TEDE) limit of 500 mrem to any individual and a 100 mrem limit above which instructions to maintain doses to others as low as reasonably achievable (ALARA) are required to be provided to the patient (CFR 2019b). NUREG-1556 Vol. 9 Rev. 2 provides guidance to medical use license holders including an equation to calculate TEDE and tables with activities and dose rates that are compliant with the 500 mrem and 100 mrem limits (NRC 2008). Table 1.1. summarizes the default release criteria for I-131. If a patient is administered an activity of 33 mCi or less, hospitalization is not required. If a patient is administered an activity greater than 7 mCi, the patient must be given radiation safety instructions. Alternatively, if the patient has a measured dose rate less than 7 mrem/hr hospitalization is not required; and instructions must be given for measured dose rates above 2 mrem/hr.

Table 1.1. Summary of default release criteria for I-131

TEDE Limit [mrem]	Activity [mCi]	Dose Rate [mrem/hr]
500	33	7
100	7	2

Adapted from NU-REG 1556 Vol 9 Rev 2

In veterinary medicine, the patient release criteria are regulated by 10 CFR 20.1301 which establishes an annual TEDE limit of 100 mrem and a limit of 2 mrem in any hour in any unrestricted area (CFR 2019a). NCRP 148 recommends a release criterion of 0.5 mR/hr at 1 meter; however, NUREG-1556 Vol. 7 Rev. 1, which provides guidance for academic and research license holders under which veterinary medicine falls, recommends more restrictive release criteria (NCRP 2004, NRC 2018). Its recommendation for release criteria is at least 4 days of hospitalization and a measured dose rate less than 0.25 mR/hr at 1 foot (approximately 0.023 mR/hr at 1 meter) (NRC 2018). Moreover, both sets of release criteria are factors more conservative than the 100 mrem release criteria (2 mrem/hr) from NUREG-1556 Vol. 9. The reasoning behind using more restrictive release criteria has not been elucidated by the Nuclear Regulatory Commission (NRC).

Furthermore, the standard administered activity in feline RIA is 4 mCi, which is nearly half the 7 mCi recommendation for exceeding 100mrem; and doses as low as 2 mCi have been proven effective in treating feline hyperthyroidism; yet these doses require hospitalization (Lucy et al., 2017). Meanwhile, doses used in treating human hyperthyroidism can range from 5 mCi to 30 mCi and require no hospitalization. (Ross, 2011; Sisson et al., 2011).

1.3. Motivation and Aims

The discrepancy between the release criteria can lead to confusing interpretations of the radiation risk. For example, this difference suggests that a cat administered 2 mCi

poses a greater risk than a human administered 33 mCi. One could argue the feline patient is not aware of its status as a radiation source and, therefore, cannot minimize exposure to others; however, the pet owner can follow instructions to keep their annual TEDE ALARA. NCRP Report No. 155 and Commentary No. 11 state that family members “should be distinct from members of the public” and their TEDE limits “should not be as restrictive” because they are willing to accept their radiation burden in exchange for psychological benefits (NCRP 2006, NCRP 1995). In NUREG 1492, a regulatory analysis of patient release criteria, the NRC acknowledges not only the economic costs to the hospital and patient from restrictive release criteria but also the psychological benefits to the patient from less restrictive criteria (NRC 1997). Pet owners are likely to face similar costs and benefits. A recent survey found that the biggest concern for most pet owners when considering RIA therapy for their cat was the hospitalization length—followed by travel distance and financial cost (Boland et al., 2014). This same survey revealed that 82% of owners thought their cat would be unhappy during its hospitalization and 65% of owners would miss their cat (Boland et al., 2014). An important initial step in analyzing the costs and benefits of different release criteria for feline patients and their owners is the assessment of dose to the pet owner.

The aim of this current study is to provide conservative TEDE estimates of the pet owner following their cat’s RIA therapy and characterize the potential exposures from the cat. A multitude of studies have already investigated the dose estimates to family members and members of the public, and they have been summarized in the Oak Ridge National Lab (ORNL) report pertaining to patient release (Dewji and Hertel, 2017). The report’s summary can be put simply: high doses or thyroid uptakes are typically associated with

failure to adhere to ALARA guidance. Additionally, numerous studies have been conducted to provide more accurate equations that use less assumptions and more patient-specific data or more realistic models (DeSantis and Chabot, 2001; Siegel et al., 2007; Willegaignon et al., 2007; Zanzonico et al., 2000). These equations typically provide less restrictive release criteria compared to the default values from NUREG-1556 Vol. 9. To provide conservative TEDE estimates, administered activities and exposure rates of feline patients were taken, along with other measurements to further characterize the radioactivity of the feline patient. Then, those measurements were used with an adapted version of the NRC's default equation in NUREG-1556 Vol. 9 to calculate the TEDE to the pet owner. The decision to use the default equation was based on a few reasons. First, while a couple of studies have developed biokinetic models for I-131 in hyperthyroid cats, agreed upon values for uptake fractions and effective half-lives for thyroidal and extrathyroidal compartments that could be used in patient-specific models are not currently available for felines (Chen et al., 2018; Hays et al., 1988). Second, the NRC should theoretically accept these TEDE estimates as showing compliance with the regulations because they were derived using their own equation. Third, the NRC default equation contains various conservative assumptions; therefore, actual TEDEs should be lower than the estimated TEDEs if the assumptions hold.

1.4. Conservative Assumptions in NRC Default Equation

The following assumptions that are found within the NRC's equation allow for conservative estimates for the TEDE. The equation assumes the maximally exposed person receives the dose from total decay. The equation contains an implicit assumption that 1 roentgen of exposure results in 1 mrem of TEDE. The equation uses the radiological half-life of I-131 and does not consider any voiding or biological elimination. Lastly, the

equation assumes the radioactivity of the patient is an unattenuated point source. Various studies have demonstrated that the point source model overestimates dose from nuclear medicine therapy patients (de Carvalho et al., 2011; Siegel et al., 2002; Sparks et al., 1998; Yi et al., 2013).

CHAPTER 2. MATERIALS AND METHODS

2.1. Radioactive Iodine Treatment at Louisiana Veterinary Teaching Hospital

All data was collected in accordance with Louisiana State University (LSU) Institutional Animal Care and Use Committee protocol #19-012. Data was collected using feline patients at the LSU Veterinary Teaching Hospital (LSUVTH) that underwent the I-131 ablation procedure. To be included in this study, the cat must have had a diagnosis of hyperthyroidism. Additionally the following exclusion criteria were used to limit the factors affecting the patients' iodine biokinetics: the cat could not have had a thyroidectomy, could not have had advance kidney disease, could not have been administered thyroid suppressing medication in the week prior to RIA treatment, and could not have had thyroid cancer.

After the pet owner has decided on RIA treatment, the cat is typically admitted to the LSUVTH on a Monday. The cat is housed inside a 70cm x 70cm x 70cm kennel in the iodine quarantine room for the entire duration of its stay. During its hospitalization, the cat is checked on twice daily and provided with fresh water and food and clean litter. Figure 2.1. shows a typical kennel set up.



Figure 2.1. Typical kennel set up for feline patient receiving RIA therapy. The cat is provided food water, and litter in a small tray. Additionally, the bottom of the kennel is lined with towels and absorbent urine pads.

The procedure routinely takes three days followed by two days of hospitalization.

On Monday, the cat undergoes a physical exam that involves palpation of the thyroid gland to identify the presence of any cervical mass and to assess the symmetry of the disorder.

The next day, Tuesday, a technetium-99m (Tc-99m) scan is performed to confirm the diagnosis and aid in determining the dose of I-131. On Wednesday, the cat is administered the sodium iodide I-131 solution via intrascapular subcutaneous injection, see Figure 2.2.

LSUVTH utilizes low dose RIA and typically prescribes doses ranging from 2 mCi to 3 mCi.



Figure 2.2. A cat receiving an intrascapular subcutaneous injection.
Source: <https://vcahospitals.com/know-your-pet/giving-injections-to-cats>

Following injection, a radiation survey of the room is performed in order to identify any potential contamination. The feline patient typically remains in quarantine until Friday when a survey of the cat is performed to determine if the 0.5 mR/hr at 1 m release criteria used by LSUVTH is satisfied. If the feline patient's exposure rate is below the criteria, the cat is released back into owner custody that afternoon. If the exposure rate does not meet the criteria, the patient remains hospitalized until the reading falls below the criteria so that the cat can be safely released back to the owner. After the cat is released, the owner must follow radiation safety instructions to minimize their exposure. Figure 2.3. shows the instructions provided to pet owners.

Follow-Up Care for Radioactive Iodine Treatment



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Home Care Instructions

Following discharge from the hospital, your cat poses very little risk to you, your family, and other pets. However, there is a low level of radioactivity that persists at the time of discharge. The radioactivity will decrease with time. The following precautions should be followed for the next 2 weeks after hospital discharge:

- The cat should be strictly confined indoors preferably in a bathroom or washroom.
- People should have limited contact with the cat except for brief periods needed for necessary care.
- Pregnant women and children under the age of 18 should have NO contact with the cat.
- Keep the litter box away from children and other pets. Use clumping litter, and wear rubber gloves when removing wastes from the litter box. The radioactive substance is excreted in the cat's urine and feces. The litter and waste should be kept in a separate bag from the household garbage and held in a garage or store room for 2 additional weeks prior to disposal.
- Wash your hands carefully after handling the cat, food dishes, or the litter box (urine and feces).

Figure 2.3. Home care instructions given to pet owners following their cats' RIA therapy. These instructions help keep the dose to the pet owner ALARA.

2.2. Administered Activities and Exposure Rates

In this study, seven feline patient case studies were followed that spanned from February to May of 2019. One cat was subsequently removed from the study because a review of its medical history revealed that a thyroidectomy had been previously performed. Administered activities were calculated by measuring the syringe's activity before and after patient injection using

$$Q = A_f - A_0 \quad (\text{Equation 2.1})$$

where Q is the administered activity in mCi, A_f is the activity in the syringe after injection, and A_0 is the activity in the syringe before injection. The 108 cm exposure rate readings in mR/hr were taken immediately after injection (day 0) and repeated each subsequent day (day 1 and day 2) during their hospitalization using a Fluke 451B ion chamber survey meter with a closed beta slide, pictured in Figure 2.4. Feline patients were discharged on

day 2 in accordance with the regular veterinary practice if they met the release criteria and were not kept hospitalized for the purposes of this study as that would not be considered ethical.



Figure 2.4. Fluke 451B ion chamber survey meter used to perform exposure rate measurements in units of mR/hr.

To consistently perform the survey readings and reduce variability from distance, the cats were placed in a pet carrier to limit their movements. Tape was used to mark the 100 ± 1 cm distance from the front of the carrier. However, the cat thyroid was maximally located 8 ± 2 cm into the carrier from the front. Therefore, exposure rate readings were taken at 108 ± 2 cm. Exposure rates at one meter were then calculated using the inverse square law

$$X_1 = X_0 \frac{d_0^2}{d_1^2} \quad \text{(Equation 2.2.)}$$

where X_1 is the exposure rate at one meter, X_0 is the measured exposure rate at 108 cm, d_0^2 is the distance of the measured exposure rate, 108 cm, and d_1^2 is 100 cm. The inverse

square law was also used to calculate the distance at which the exposure rate increases to 2 mR/hr

$$d_2 = \sqrt{\frac{X_1 d_1^2}{X_2}} \quad \text{(Equation 2.3.)}$$

where d_2 is the distance at which the exposure rate increases to 2 mR/hr, d_1 is 100cm in distance, X_1 is the one-meter exposure rate, and X_2 is an exposure rate of 2 mR/hr. Figure 2.5. shows this experimental set-up. Additionally, five readings were taken at each survey. The mean exposure rate measurements were then fitted to an exponential curve to obtain an effective half-life of I-131 for each patient.



Figure 2.5. Experimental set-up for collection of exposure rate data. The distance between the blue tape is 100 ± 1 cm.

2.3. TEDE Estimates

TEDE estimates were calculated using administered activities and the exposure rates for each of the three days during the patient's hospitalization. The TEDE to the pet owner from each cat was calculated using an equation adapted from equation U.2. in

NUREG-1556 Vol. 9 Rev. 2

$$TEDE(\infty) = \frac{34.6\Gamma QT_{pE}}{r^2} \quad (\text{Equation 2.4.})$$

where TEDE is the estimated total effective dose equivalent in mrem from total decay, 34.6 is the product of the 24hr/d conversion factor and the total integration of decay (1.44), Γ is $0.22 \frac{mR \cdot m^2}{hr \cdot mCi}$ the specific gamma constant for I-131, Q is the administered activity in mCi, T_p is the physical half-life of 8.02 days, E is the occupancy factor, r is the distance in meters (2008). The TEDE was calculated using both the administered activities and the exposure rate measurements and using occupancy factors of both 0.25 and 1. NUREG 1556 Vol 9 uses an occupancy factor of 0.25 for radionuclides with half-lives greater than 1 day. In this study, an occupancy factor of 1 was also used to simulate a situation where the pet owner could feasibly be at home all day with the cat such as a retiree or someone who works from home. When calculating TEDE from exposure rates, the product ΓQ is replaced by the 1m exposure rates, X_1 .

$$TEDE(\infty) = \frac{34.6X_1T_{pE}}{r^2} \quad (\text{Equation 2.5.})$$

Implicit in both Equation 2.4. and Equation 2.5. is a 1 R=1 rem conversion factor. The committed effective dose equivalent estimates for the inhalation and ingestion pathways were calculated using equation B.3. from NUREG-1556 Vol. 9 Rev. 2.

$$CEDE = Q * 10^{-5} * DCF * 1000 \quad (\text{Equation 2.6.})$$

where CEDE is the committed effective dose equivalent in mrem, Q is the administered activity in mCi, 10^{-5} is the NRC's assumed fractional intake, DCF is the I-131 dose conversion factor from the EPA Federal Guidance Report No 11 for either inhalation or ingestion in rem/mCi, 1000 is for the conversion from rem to mrem (EPA 1988).

2.4. Excreted Activities

Urine and fecal samples were collected from the patients to measure the amount of radioactivity excreted. Urine samples were collected in the form of either urine-soaked litter or a urine-soaked pad. For simplicity, both forms will simply be referred to as urine samples. The urine and fecal samples were collected at each check-in, and the excreta were placed in rigid syringe packs for 12 mL syringes, pictured in Figure 2.6. The rigid syringe packs were initially used so that the samples' activities could be easily measured using a Biodex Atomlab 100 dose calibrator, shown in Figure 2.7. However, the rigid syringe packs limited the amount of sample that could be measured at once; so they were replaced with 16.5x14.9 cm² sealable zipper polyethylene sandwich storage bags for later samples due to the large amount of excreta that some patients produced. Urine pad samples were only collected when the staff determined urine was present based on visual and tactile inspection. The contaminated portion of the pad was removed with scissors to then be measured in the dose calibrator. Excreta samples were measured three times, and samples were grouped into 24-hour bins starting from time of injection. The excreta samples were decay corrected to the time of injection and used to calculate the ratio of the excreted

activity to the injected activity and multiplied by 100 to obtain the percent excreted activity.



(a)

(b)

Figure 2.6. Containers used to measure the activity of the excreta in the dose calibrator (a) Rigid syringe pack for a 12 mL syringe (b) Sealable zippered polyethylene sandwich storage bag



Figure 2.7. Biodex Atomlab 100 dose calibrator used to measure excreted activity.

2.5. Surface Contamination

Wipe tests were performed on the feline patients to detect any removable contamination on the cats' surfaces. A wipe test was performed on each patient before

injection and repeated once each day during its hospitalization. The methodology for the wipe tests was adapted from Chalmers et al, 2006. One wipe was used to survey from the dorsal midline at the base of the neck extending caudally to the base of the tail as well as laterally along the abdomen areas. Another wipe was used to survey all the paws on both the dorsal and palmar/plantar surfaces. The wipes used were 1 in² polystyrene wipes. The wipes were then measured using one-minute counting times in a Packard Cobra II Model 5002 gamma counter (Figure 2.8.a) and, subsequently, in a Beckman Model LS 6000LL liquid scintillation counter (LSC) (Figure 2.8.b). The net count rates were then converted to activity using each detectors' efficiency. Additionally, wipe tests were performed on the kennel interior, food bowl, and water bowl at the time of patient discharge. The wipe of the kennel interior covered the lower half of the three kennel walls along with the kennel floor.



(a)



(b)

Figure 2.8. (a) Packard Cobra II Model 5002 gamma counter used to detect the gamma activity present on the wipes. (b) Beckman Model LS 6000LL liquid scintillation counter used to detect activity from beta-minus radiation on the wipes.

2.6. Counter Efficiencies

To determine the efficiency of the gamma counter and LSC, six samples were prepared with a known radioactivity of iodine-131. A sodium iodide I-131 solution of 4 mCi/ml obtained by Cardinal Health was serially diluted to 0.1 $\mu\text{Ci}/\mu\text{L}$. Two microliter

drops were added to six polystyrene wipes, resulting in an activity of 0.2 μCi on each wipe. Three wipes were used to determine the efficiency of the gamma counter, and three were used to determine the efficiency of the LSC. The samples' count rates were measured using five-minute counting times at weekly intervals for 8 weeks. The measured count rates of the three samples were averaged and then divided by the expected disintegrations per minute, calculated using the known activity, to determine the counter's efficiency.

CHAPTER 3. RESULTS AND DISCUSSION

3.1. Injected Activities and Exposure Rates

The cats were treated with activities of carrier free sodium iodide I-131 in the range of 1.62 to 2.54 mCi with an average administered activity of 2.14 mCi. Mean exposure rates at 1 meter ranged from 0.23 to 0.46 mR/hr on day 0, from 0.19 to 0.43 mR/hr on day 1, and from 0.13 to 0.38 mR/hr on day 2. The values of the administered activities and the mean exposure rates are tabulated in Table 3.1. All administered activities were well below the NRC's calculated activity limit for exceeding 100 mrem TEDE of 7 mCi. Additionally, all mean exposure rates are well below the corresponding dose rate limit of 2 mrem/hr. These findings suggest that the TEDE to the pet owner should be well below 100 mrem if an occupancy factor of 0.25 at a distance of 100 cm are valid assumptions.

Table 3.1. Administered activities and mean exposure rates at 1 meter.

Cat	Prescribed Activity [mCi]	Administered Activity [mCi]	Exposure Rate [mR/hr]		
			Day 0	Day 1	Day 2
1	2.25	1.79±0.06	0.24±0.02	0.20±0.02	0.14±0.01
2	2.94	2.48±0.08	0.47±0.02	0.43±0.01	0.34±0.01
3	2.25	1.62±0.05	0.28±0.04	0.22±0.01	0.21±0.01
4	2.50	1.92±0.06	0.23±0.02	0.19±0.01	0.13±0.01
5	3.00	2.46±0.08	0.43±0.02	0.41±0.01	0.38±0.01
6	3.00	2.54±0.08	0.36±0.02	0.38±0.01	0.30±0.01

The administered activity values are the difference in the measured activity of the syringe before and after patient injection. The exposure rate values are the calculated exposure rates for 1 meter based on the measured exposure rates at 108 cm. Values are reported as the mean value plus/minus their standard error.

The distances at which the exposure rate increases to 2 mR/hr ranged from 0.34 to 0.48m on day 0, 0.31 to 0.46m on day 1, and 0.25 to 0.44m on day 2. Instructions should be given to the pet owner warning against spending an appreciable amount of time at this distance or closer to the cat. These distances can be found in Table 3.2. Based on these

results, if a pet owner maintains a distance of at least half a meter, then they should likely not receive more than 2 mrem in any hour.

Table 3.2. Distance[m] at which the exposure rate increases to 2mR/hr.

Cat	2 mR/hr distance [m]		
	Day 0	Day 1	Day 2
1	0.35±0.02	0.31±0.02	0.26±0.01
2	0.48±0.01	0.46±0.01	0.41±0.01
3	0.37±0.02	0.33±0.01	0.32±0.01
4	0.34±0.02	0.31±0.01	0.25±0.01
5	0.46±0.01	0.45±0.01	0.44±0.01
6	0.43±0.01	0.44±0.01	0.39±0.01

Values are reported as the expected value plus/minus its standard error. A pet owner standing this distance from their pet for 1 hour would be exposed to 2 mR.

Figure 3.1. illustrates exposure rates over time. The exposure rates were fitted to an exponential curve to determine the effective half-life and, subsequently, to calculate the biological half-life. Effective half-lives ranged from 2.2 to 14 d and biological half-lives from -19 to 72 d. Those values are tabulated in Table 3.3. Cats 1, 2, and 4 have R^2 values over 0.90 indicating that the variation in the data is explained by an exponential model. Additionally, the effective half-lives of cats 1, 2, and 4 are in agreement with the current literature ranging from 2 to 4 days (Martin et al., 2015; Roberts et al., 2015). This agreement suggests that cats 1, 2, and 4 exhibit the expected feline biokinetics for iodine-131. Meanwhile, cats 3, 5, and 6 have unexpected biokinetics for iodine. Cat 5 had a high R^2 value, however, its effective half-life of 14 days is longer than expected. Similarly, cats 3 and 6 have longer than expected half-lives of 4.8 and 7.2 days, respectively. Cat 6's low R^2 value can be explained by its exposure rate increase from 0.36mR/hr on day 0 to 0.38 mR/hr on day 1, suggesting that cat 6 exhibits slow uptake. Effective half-lives less than or equal to 4 days are ideal as that signifies the feline patient is eliminating the I-131 faster than the I-131 decays, which would reduce the pet owners' exposure when in the vicinity of the cat.

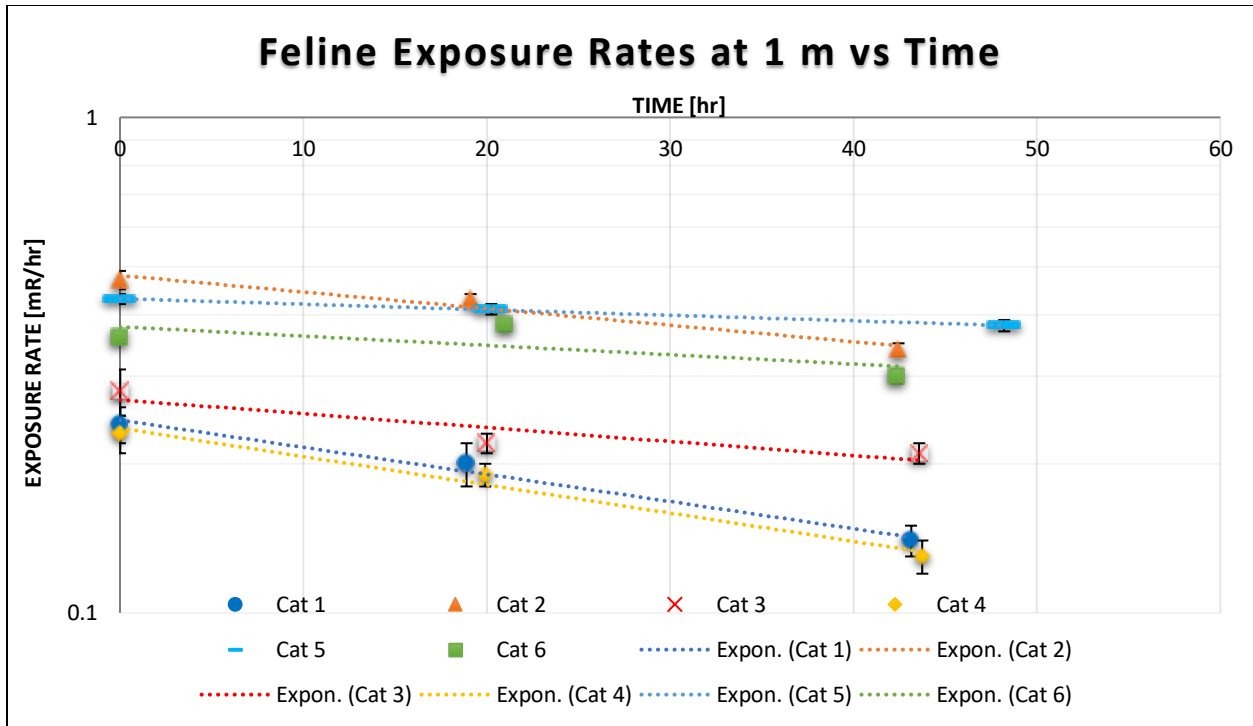


Figure 3.1. Semi-log plot of patients' exposure rates at 1 meter over time. The exposure rates were fitted to an exponential curve. Error bars signify plus/minus standard error.

Table 3.3. Effective half-lives and biological half-lives

Cat	T_E [d]	R^2	T_B [d]
1	2.2	0.99	3.0
2	3.6	0.95	6.5
3	4.8	0.85	12
4	2.1	0.99	2.8
5	14	0.99	-19
6	7.2	0.51	72

Effective half-lives (T_E) are listed in the second column with their respective coefficient of determination (R^2) in the third column. The last column contains the biological half-lives (T_B) calculated from the effective half-lives.

3.2. TEDE Estimates

The calculated TEDEs based on administered activity are tabulated in Table 3.4., while TEDEs based on measured exposure rates are tabulated in Table 3.5. The TEDE estimates using administered activity ranged from 25 to 39 mrem and from 99 to 155 mrem, for occupancy factors of 0.25 and 1, respectively. These estimates are also

represented graphically in Figure 3.2. As illustrated in Figure 3.2., the estimated TEDEs based on administered activity and an occupancy factor of 0.25 are well below the 100 mrem limit. Based on these results, all feline patients could have been released the day of injection without exceeding the pet owner’s annual limit. This result is expected given that all the administered activities are less than the NRC’s limit of 7 mCi. In the case of an occupancy factor of 1, for pet owners who are able to stay home with their cat all day, the estimated TEDEs for all but cat 3 exceed the 100 mrem. Only cat 3 could have been released the day of injection. Equation 2.4. can be solved empirically for the administered activity. Using an occupancy factor of 1 and TEDE limit of 100 mrem, administered activities would have to be below 1.64 mCi to release the patient the same day as injection. While low doses have been demonstrated to successfully treat feline hyperthyroidism by Lucy *et al*, this restrictive activity criteria can be circumvented by using measured dose rates as the release criteria (Lucy et al., 2017).

Table 3.4. TEDE estimates based on administered activity

Cat	Injected Activity [mCi]	TEDE [mrem]	
		E = 0.25	E = 1
1	1.79±0.06	27±1	109±4
2	2.48±0.08	38±1	152±5
3	1.62±0.05	25±1	99±3
4	1.92±0.06	29±1	117±4
5	2.46±0.08	38±1	150±5
6	2.54±0.08	39±1	155±5

Values are reported as expected value plus/minus standard error.

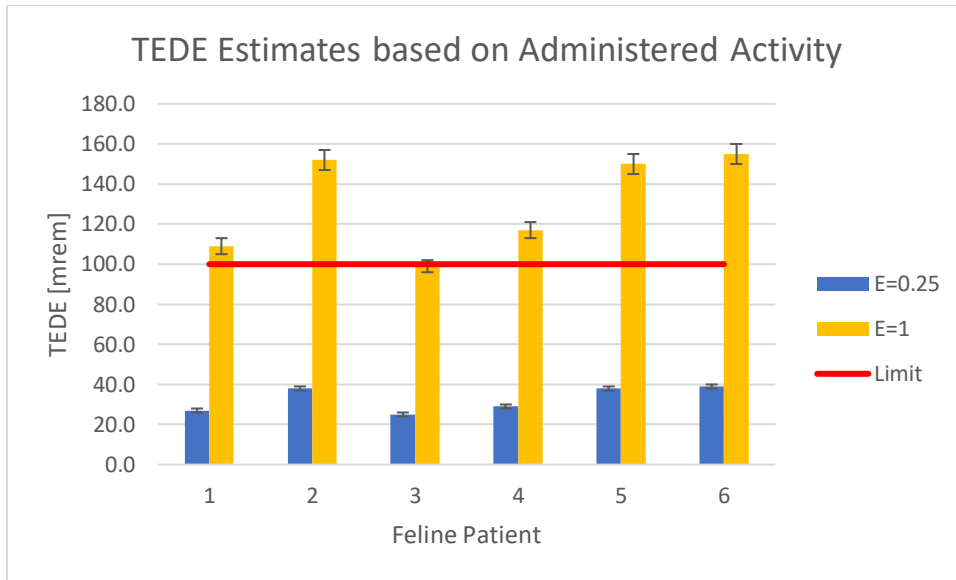


Figure 3.2. TEDE estimates based on administered activity. Error bars indicate plus/minus one standard error.

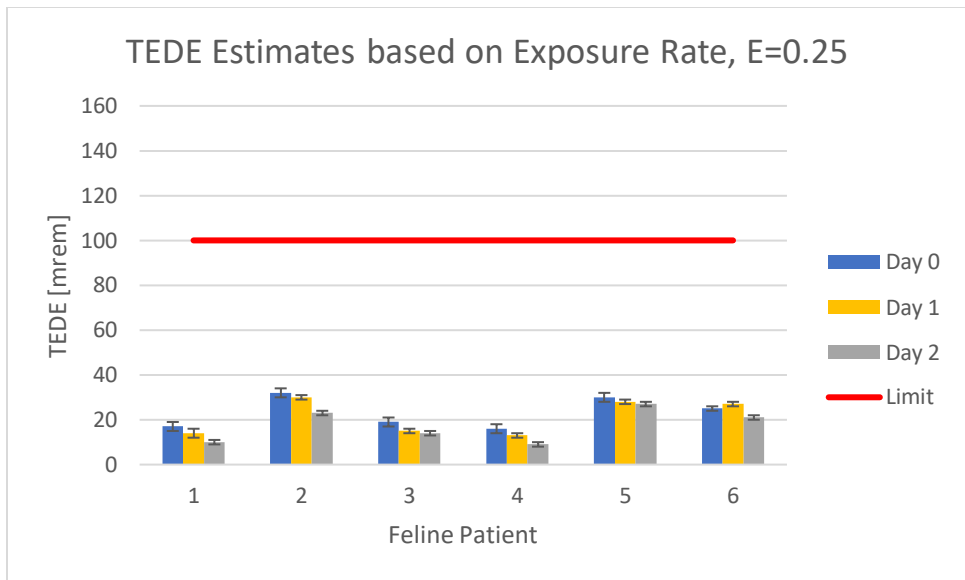
The TEDE estimates using exposure rates and 0.25 occupancy ranged from 16 to 32 mrem, 13 to 30 mrem, and 9 to 27 mrem for days 0, 1 and 2, respectively, and are illustrated in Figure 3.3.a. Again, the TEDE estimates using an occupancy factor of 0.25 are well below the 100 mrem limit. This result is expected since all the measured exposure rates are below the NRC's limit of 2 mrem/hr, again suggesting that all feline patients could have been released on day 0 without exceeding the pet owner's annual limit. The TEDE estimates using exposure rates and an occupancy factor of 1 ranged from 65 to 130 mrem, 52 to 120 mrem, and 36 to 107 mrem, for days 0, 1, and 2, respectively. These estimates are illustrated in Figure 3.3.b. Like Equation 2.4., Equation 2.5. can also be solved analytically. The dose rate that corresponds to a 100 mrem limit and occupancy factor of 1 is 0.36 mrem/hr. And indeed, this is evident in the results. Four of the cats could have been released on day 0, while cats 2 and 5 were not suitable for release until day 2. These results show the advantage of dose-rate-based release criteria over activity-based release criteria. While using the activity-based release criteria with an occupancy factor of 1, none of the

cats could have been released on injection day. In contrast, the dose-rate-based criteria could have allowed 4 out of 6 cats to be released on injection day. Further support for the use of dose-rate-based criteria comes from a previous studies that failed to find a linear relationship between measured exposure rates and administered activity (Feeney et al., 2003; Weichselbaum et al., 2003). Other studies have also established that the measured dose rate is typically less than the calculated dose rate due to patient specific parameters such as self-shielding and biokinetics (Siegel et al., 2002; Yi et al., 2013). Therefore, using measured dose rates for release criteria is recommended because the TEDE estimates provided are more realistic compared to those calculated using administered activities, while still maintaining the conservatism of the NRC's equation.

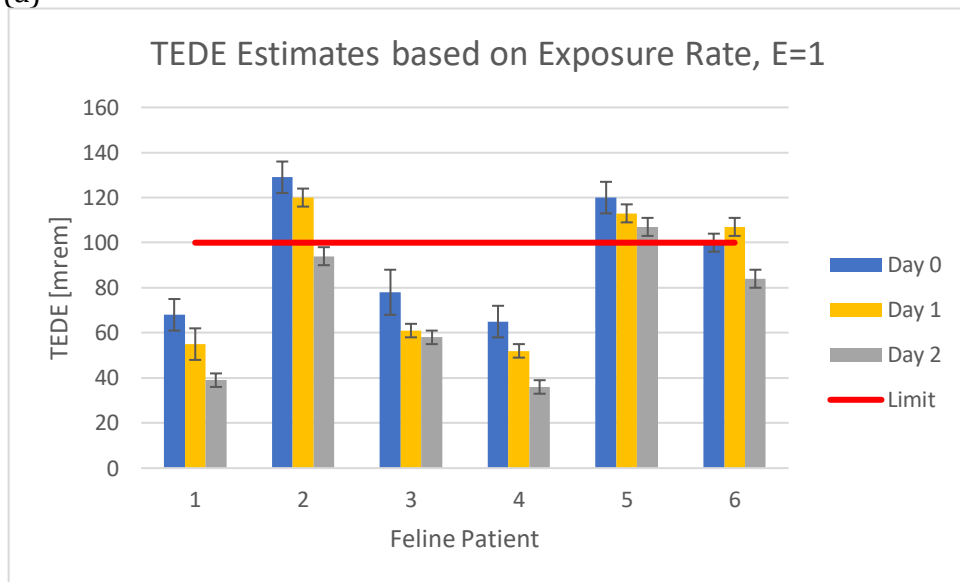
Table 3.5. TEDE estimates based on measured exposure rates

Cat	Exposure Rate [mR/hr]			TEDE [mrem]					
				E = 0.25			E = 1		
	Day 0	Day 1	Day 2	Day 0	Day 1	Day 2	Day 0	Day 1	Day2
1	0.24±0.02	0.20±0.02	0.14±0.01	17±2	14±2	10±1	68±7	55±7	39±3
2	0.47±0.02	0.43±0.01	0.34±0.01	32±2	30±1	23±1	129±7	120±4	94±4
3	0.28±0.04	0.22±0.01	0.21±0.01	19±2	15±1	14±1	78±10	61±3	58±3
4	0.23±0.02	0.19±0.01	0.13±0.01	16±2	13±1	9±1	65±7	52±3	36±3
5	0.43±0.02	0.41±0.01	0.38±0.01	30±2	28±1	27±1	120±7	113±4	107±4
6	0.36±0.02	0.38±0.01	0.30±0.01	25±1	27±1	21±1	100±4	107±4	84±4

Values are reported as expected value plus/minus uncertainty.



(a)



(b)

Figure 3.3. (a) TEDE estimates based on measured exposure rates using an occupancy factor of 0.25. Error bars indicate plus/minus one standard error. (b) TEDE estimates based on measured exposure rates using an occupancy factor of 1. Error bars indicate plus/minus one standard error.

The CEDE estimates ranged from 0.53 to 0.84 mrem for the inhalation pathway and 0.86 to 1.35 mrem for the ingestion. CEDE estimates for each pathway and their sums are tabulated in Table 3.6. NUREG-1556 Vol. 9. recommends neglecting CEDE if it makes up less than 10% of the TEDE. The CEDE is 5.6% for all cats and, therefore, can be ignored. The fact

that the CEDE was 5.6% of the TEDE for all cats is due to the fixed nature of the TEDE and CEDE equations used. When a ratio of CEDE to TEDE is calculated, the administered activity term Q cancels out, leaving a ratio of 0.056 which is independent of the administered activity. Given the already low doses administered to feline patients, these findings reinforce that the dose contribution from internal exposures is negligible especially compared to dose contributions from external exposures.

Table 3.6. Committed Effective Dose Equivalent from inhalation and ingestion pathways

Cat	Administered Activity [mCi]	CEDE [mrem]			%TEDE*
		Inhalation	Ingestion	Cumulative	
1	1.79±0.06	0.59±0.02	0.95±0.03	1.54±0.04	5.6
2	2.48±0.08	0.82±0.03	1.32±0.04	2.14±0.05	5.6
3	1.62±0.05	0.53±0.02	0.86±0.03	1.39±0.03	5.6
4	1.92±0.06	0.63±0.02	1.02±0.03	1.65±0.04	5.6
5	2.46±0.08	0.81±0.03	1.30±0.04	2.11±0.05	5.6
6	2.54±0.08	0.84±0.03	1.35±0.04	2.19±0.05	5.6

Values are reported as the expected value plus/minus its standard error.

*%TEDE calculated as the ratio of the CEDE estimates and TEDE estimates based on administered activities and an occupancy factor of 0.25

3.3. Excreted Activities

The percent total excreted activity for the feline patients ranged from 1.09% to 9.25% in the first 24-hours and from 2.32% to 16.54% in the second 24-hours. Table 3.7. lists the percent excreted activity for the urine-soaked litter, urine pads, feces, the total for each day, and the 48hr total. The total percent excreted after 48 hours ranged from 3.41% to 24.50% which is lower than results from previous studies that found at least 50% of activity excreted in the first 48 hours (Feeney et al., 2003; Lamb et al., 2013; Martin et al., 2015).

This part of the experiment was not without difficulties. Excrement samples were initially collected using rigid syringe packs (pictured in Figure 2.7.). Rigid syringe packs

were initially chosen because they allowed for easy measurement of the sample's activity in the dose calibrator. However, the rigid syringe packs were deemed inefficient due to the restrictive sample amount that could be collected compared to the amount of excreted material to be analyzed. Starting with cat 4, the packs were replaced with polyethylene sandwich bags. The polyethylene sandwich bags allowed for greater amounts of excreta to be measured within the dose calibrator. Another difficulty was the inconsistent urine and feces production of the patients. Some patients did not produce feces within a given 24-hr period. On some occasions, the patients spilled contaminated litter outside of the tray. On others, patients would not contain their urine production within the litter tray although this loss was partly mitigated by the urine pads. Although the % activity excreted was lower than expected, % activity excreted in urine was higher than % activity excreted in feces for any given cat in either 24-hr period. This result is expected due to the fact that iodine clears out the body predominantly through the kidneys (Leggett, 2010).

Table 3.7. Percent activity excreted

Cat	% Activity Excreted								
	1st 24 hours				2nd 24 hours				Cumulative Total
	Litter	Pad	Feces	Total	Litter	Pad	Feces	Total	
1	0.64±0.02	*	0.60±0.02	1.24±0.03	2.71±0.09	*	**	2.71±0.09	3.95±0.09
2	1.58±0.05	*	**	1.58±0.05	3.86±0.12	*	**	3.86±0.12	5.44±0.13
3	1.09±0.03	*	**	1.09±0.03	2.22±0.07	*	0.10±0.00	2.32±0.07	3.41±0.08
4	9.25±0.39	*	0.04±0.00	9.29±0.39	9.51±0.40	*	**	9.51±0.40	18.80±0.56
5	7.50±0.24	0.46±0.02	**	7.96±0.24	8.04±0.26	5.05±0.16	3.45±0.11	16.54±0.32	24.50±0.40
6	4.17±0.13	*	**	4.17±0.13	4.27±0.14	*	1.48±0.05	5.75±0.15	9.92±0.20

Values are reported as the expected value plus/minus its uncertainty.

*Urine-pad activity was measured if visual or tactile inspection indicated the presence of urine.

** Some feline patients did not produce fecal samples throughout the 24-hour period.

3.4. Surface Contamination

The wipe tests done before injection were all within background, but wipes from day 1 and day 2 detected removable radioactivity on the surface of the patients. Figure 3.4. and Figure 3.5. show the surface activity from the gamma counter measurements and LSC measurements, respectively. Surface contamination on day 1 ranged from 0.16 to 0.52 nCi on the body and from 0.08 to 0.80 nCi on the paws based on the gamma counter and its efficiency. Surface contamination ranged from 0.20 to 0.46 nCi on the body and from 0.08 to 0.73 nCi on the paws based on the LSC and its efficiency. The presence of removable contamination is expected given that iodine can be eliminated from the body through the salivary glands. When the patient grooms themselves, they deposit the radioactive iodine from the saliva onto their surface. However, cross-contamination from contaminated litter could potentially contribute to the removable contamination found on the surface of the patient, especially on the paws. Regardless of the source of the removable contamination, our data shows that the activities are below 1 nCi. Additionally, our data shows that Day 2 activities were significantly lower than or equal to Day 1 activities, but never significantly higher.

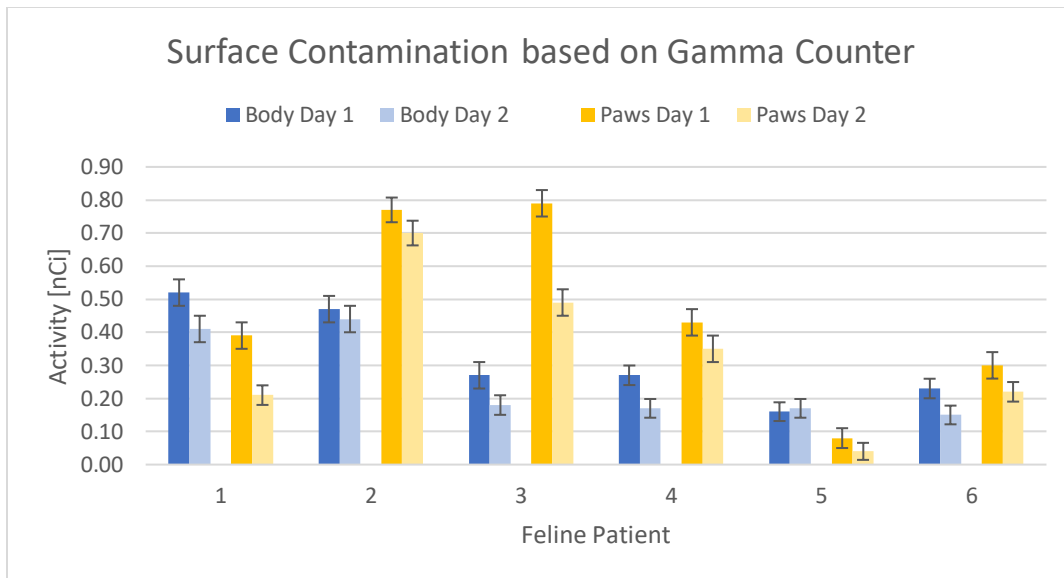


Figure 3.4. Surface Activity on feline patient based on gamma counter measurements. The blue columns indicate the surface activity of the body, while gold columns indicate activity for the paws. Error bars indicate plus/minus one standard deviation.

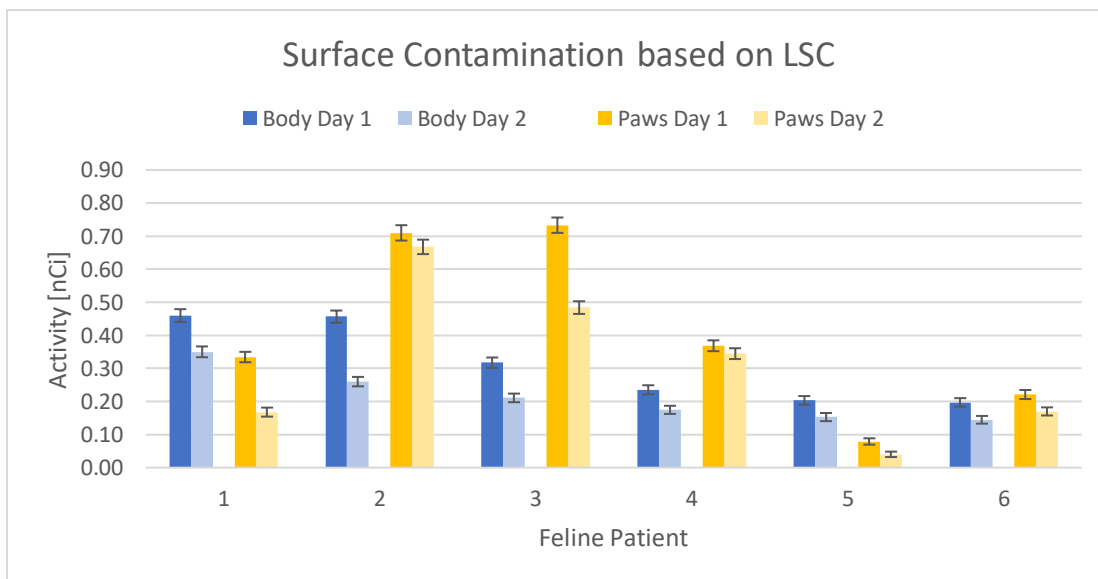


Figure 3.5. Surface activity on feline patient based on LSC measurements. The blue columns indicate the surface activity of the body, while gold columns indicate activity for the paws. Error bars indicate plus/minus one standard deviation.

Aside from the cat's surface, any surface that could become contaminated and subsequently touched by the pet owner was of interest. Food and water bowls were assayed as well as the kennel interior. Activities on these other surfaces are shown in Figures 3.6. and 3.7. for the gamma counter and LSC, respectively. Activities on the kennel

interior ranged from 0.08 nCi to 4.84 nCi based on measurements from the gamma counter while they ranged from 0.07 nCi to 3.89 nCi based on LSC measurements. Activities on the food bowl and water bowl ranged from 0.01 nCi to 0.20 nCi and 0.03 nCi to 0.17 nCi, respectively, for the gamma counter. For the LS counter, activities on the food and water bowls ranged from 0.04 nCi to 0.19 nCi and 0.03 nCi to 0.14 nCi, respectively. The food and water bowls had negligible activities whereas the kennel interior had activities elevated above background. However, the reason for the elevated activities is unclear and is not present for all the patients. The little contamination present on the bowls was likely from any saliva transfer when the patient was eating and drinking. Contamination inside the kennel may be from the patient rubbing against the walls or floor; however, the activities on the surface of the cat were lower than those found on the kennel interior. The elevated activities could more likely be explained by urine contamination from improper use (or lack of use) of the litter tray.

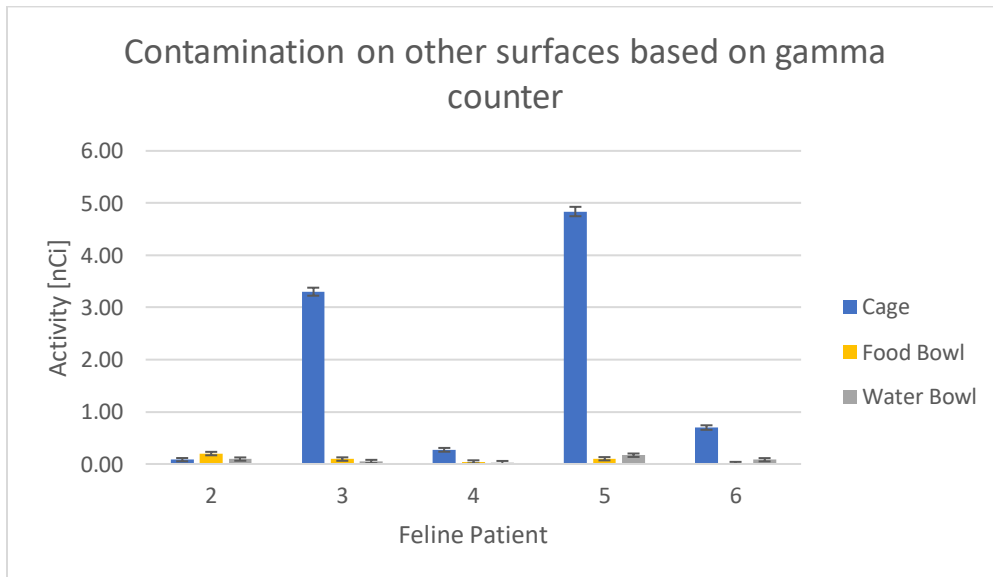


Figure 3.6. Contamination on other surfaces based on gamma counter measurements. Error bars indicate plus/minus one standard deviation.

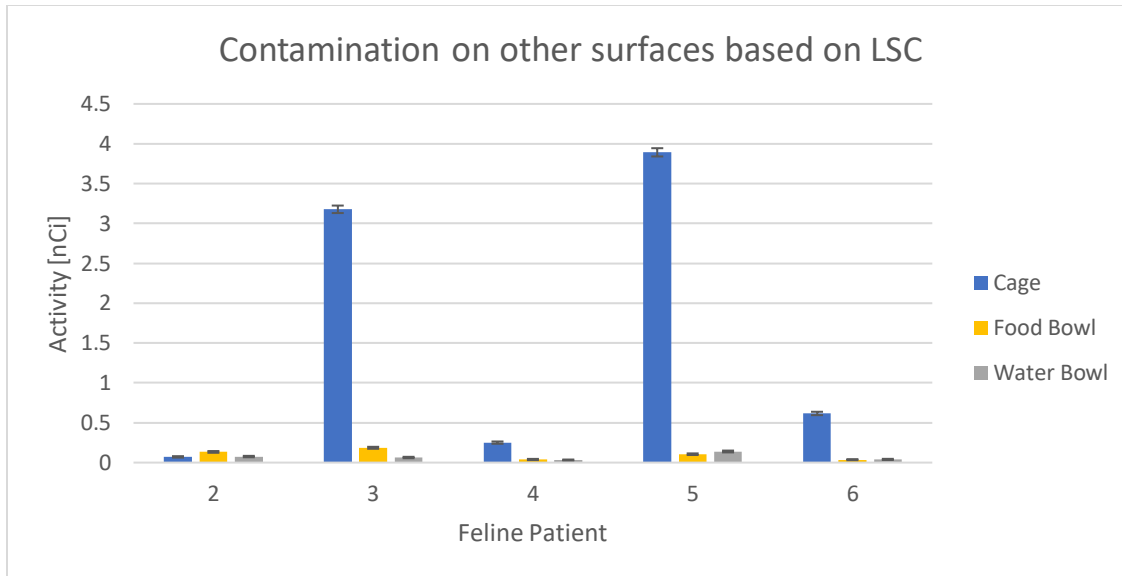


Figure 3.7. Contamination on other surfaces based on LSC measurements. Error bars indicate plus/minus one standard deviation.

3.5. Counter Efficiencies

Figures 3.8. and 3.9. show the measured count rates as a function of time along with their efficiencies for the gamma counter and LSC, respectively. As illustrated in Figure 3.8., the count rates obtained with the gamma counter are well fitted to an exponential curve. The same result is apparent in Figure 3.9. apart from the first data point. The explanation for this deviant data point is likely that the activity was saturating the LSC resulting in increased dead time, which would also explain why that data point has the lowest efficiency. For the gamma counter, an efficiency of 0.3 was used when calculating activities from the counting data. An efficiency of 0.3 was decided upon because the magnitudes of the measured count rates of the last data point are comparable to those measured on the surface of the patient. Following similar logic, an efficiency of 0.66 was used for determining activities using counting data from the LSC.

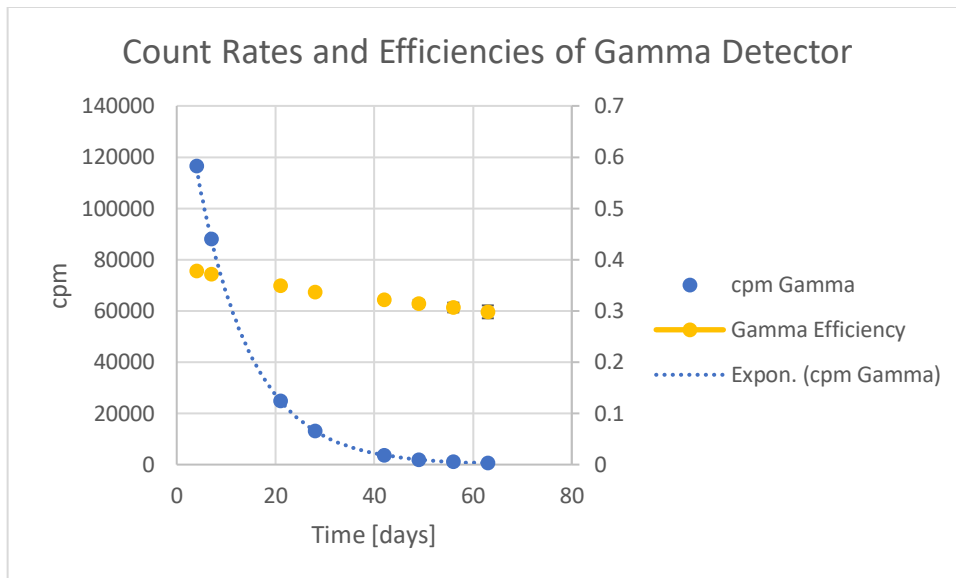


Figure 3.8. Count rates and efficiencies from gamma counter. Error bars indicate plus/minus one standard deviation.

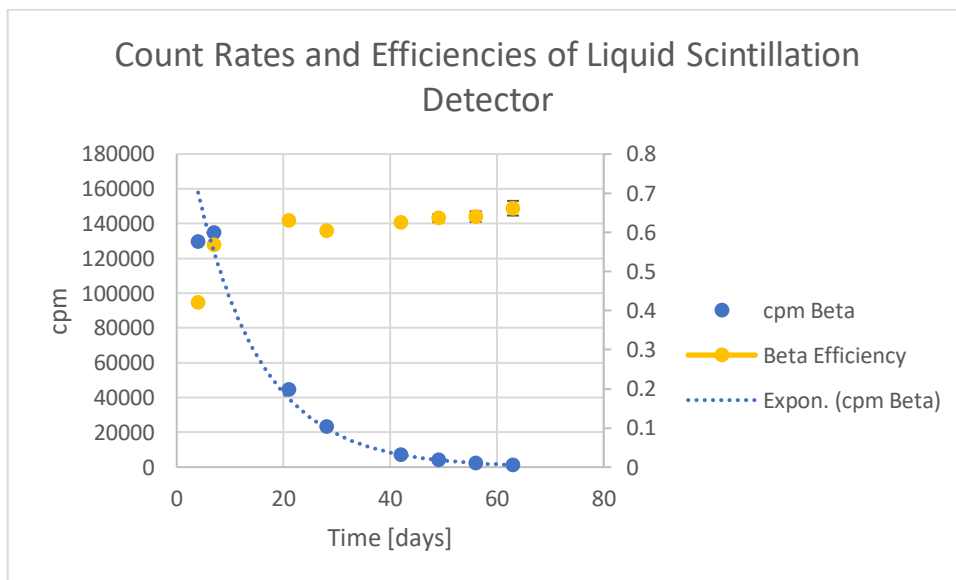


Figure 3.9. Count rates and efficiencies from LSC. Error bars indicate plus/minus one standard deviation.

CHAPTER 4. CONCLUSIONS

4.1. Key Findings

The present study characterized several aspects of radiation exposure to the pet owner from their cat. Half of the cats had effective half-lives consistent with the literature of less than 4 days. Effective half-lives in this range are preferable because the radioactivity is eliminated so the exposure to the pet owner from the cat itself is reduced. Additionally, if the pet owner is greater than half a meter away, then the received dose should not exceed 2 mrem in any hour for cats that were administered activities no greater than 2.54 mCi.

The main elimination pathway of iodine in cats is through the urine as evidenced by the urine samples' containing the highest amounts of radioactivity. Radioactivity was also found, though in smaller amounts, on the surface of the cat and its environment. This radioactivity is suspected to come from contamination from saliva, but urine contamination is also possible. Typically, surface contamination was present at levels below 1 nCi; however, some exceptions were found on the surface of the inside of the cage. The elimination pathway behind the elevated activity inside the cage is unknown but suspected to be from urine contamination.

Aside from characterizing the sources of exposure, this study provides conservative estimates of TEDE to the pet owner following their cats' RIA therapy. Using the NRC's default equations, this study demonstrated that the CEDE is always less than 10% of the TEDE and can be neglected. With an occupancy factor of 0.25 at a distance of 100 cm, calculated TEDEs to the pet owners were well below the 100 mrem limit; and the feline patients could, in theory, have been safely sent home the day of injection with home care instructions for the owner. Even when using the more conservative occupancy factor of 1,

the majority of the patients could have been sent home the day of injection without the pet owners' TEDE exceeding 100 mrem. These results coupled with the conservatism built into the equation suggest that the actual TEDE to the pet owner is not likely to exceed 100 mrem for administered activities below 2.54 mCi assuming the pet owner does not blatantly disregard the home care instructions.

4.2. Limitations

This study had several limitations in its design, the first being its small sample size. A larger sample size would allow for more accurate generalizations to be drawn from the data and would reduce the effects of any possible outliers. One result of the small sample size is a limited administered activity range. The standard dose for treating feline hyperthyroidism is 4 mCi; LSUVTH prescribes a maximum of 3 mCi. The highest administered activity in the study is 2.54 mCi, meaning that our TEDE, effective half-life, excreted activity, and surface contamination data may not be applicable for administered activities above 2.54 mCi. In addition to small sample size, short collection time is another limitation. Data was only collected over the two days which is short compared to the 8-day physical half-life of I-131. Ideally, data would have been collected over a longer period of time; but patients could not have been held past when they met the release criteria for ethical reasons. Other limitations are the previously mentioned issues with collecting urine and feces samples. The container used to hold the samples and measure them in the dose calibrator was changed partway through the experiment. This change makes comparing samples across all patients difficult without knowing the affect the containers had on the measured activity in the dose calibrator. Additionally, some excreted activity was lost due to poor containment within the litter pan. Lastly, cat movement during exposure rate

measurements was a source of uncertainty. Though steps were taken to minimize this effect, feline patients did not necessarily stay still during data collection, causing fluctuations in the exposure rate readings.

4.3. Future Work

The conservative TEDE estimates presented here could provide the preliminary groundwork for analyzing the costs and benefits of less restrictive release criteria for feline patients. Another factor that should be addressed in detail are the economic costs on veterinary hospitals and pet owners when more restrictive release criteria are used. Moreover, the present study addresses TEDE estimates to the pet owner when they have one cat that receives RIA therapy. However, cats have relatively short lives compared to humans; therefore, a single pet owner can have multiple cats throughout their lifetime that receive RIA therapy. A single pet owner can also have multiple cats at the same point in time that require the treatment. These such circumstances should be considered in any future cost-benefit analysis

Another aspect of feline patient release that should be addressed in depth in future studies is managing the cat's biological waste. The activities present in the litter at the time of release would be high enough to set off radiation detectors at the local landfill. Pet owners are already given instructions to hold waste for 2 weeks so that the radiation decays away. However, no methodology has been presented to keep doses ALARA while handling and storing the waste.

This study provides insight on the radioactive characteristics of a cat during hospitalization; repeating these measurements on a cat that is released to its owner the same day as injection would be interesting to see if any significant changes in the data

occur when the cat is in its home environment. Cats during hospitalization may be less likely to eat and drink, and therefore, less likely to urinate and defecate. Cats may not groom themselves as much when hospitalized. Conversely, they may groom excessively. Once at home a cat may not spend time in close contact with a contaminated litter box. All these factors can affect how the radioactivity is excreted from the cat and affect its potential to spread contamination.

Moreover, TEDE estimates that account for patient attenuation, source geometry, fractional uptakes, and effective half-lives could further help illuminate whether feline release criteria are too restrictive. Measurements of pet owner thyroid burden after the cat has been home for some time could also provide insight into the TEDE received by pet owners.

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VITA

Anthony Davila was born in Metairie, Louisiana in 1993. He grew up in the New Orleans area and attended Jesuit High School where he first learned to love science. He graduated from there in 2011 and enrolled in Louisiana State University. He spent the next six years studying various disciplines and in 2017 received a Bachelor of Science in physics, a Bachelor of Science in biochemistry, and a Bachelor of Interdisciplinary Studies. Anthony decided to remain at LSU to pursue a Master of Science degree from the Medical Physics and Health Physics program in the Department of Physics and Astronomy.

Upon successful completion of his degree requirements, Anthony anticipates graduating in December 2019. He hopes to gain employment as a health physicist in the New Orleans area.