Paper

Anisotropy of the Radiation Field Following Canine Sn-117m Treatment

Matthew G. Arno,[1] Jaime Simon,[2] Nigel Stevenson,[3] and John Donecker[3]

Abstract—**Tin-117m (^{117m}Sn) is used to treated dogs with osteoarthritic joints by radiosynoviorthesis. The internal conversion and Auger electrons emitted by the ^{117m}Sn provide the therapeutic effect. Sn-117m also emits gamma rays, of which the most significant is 158.6 keV. The external radiation field around a treated dog is of interest to limit the dose to the owners/caretakers of the dog. The dog's torso attenuates the radiation being emitted toward the opposite side of the dog's body. This leads to a radiation field that is significantly non-isotropic. This study characterizes the anisotropy of this field to permit maximum dose rate measurements to be used to calculate the dose to individuals in the vicinity of the dog. Measurements were made in nine directions and at two distances, 0.3 and 1.0 m, to characterize common distances and spatial orientations for human-dog interactions. From these measurements, the percent reduction in the average dose rate compared to the maximum dose rate was determined. From a radiation safety perspective, the important factor is the minimum amount of shielding effectiveness or percent reduction that can be expected. A reasonable measure for this value is the fifth percentile of the shielding effectiveness distribution. The fifth percentile shielding effectiveness measures are 27% and 21% at 0.3 and 1.0 m, respectively.**
Health Phys. 121(2):150–155; 2021

Key words: dose assessment; radiation protection; radiation therapy; radioisotope

INTRODUCTION

RADIOSYNOVIORTHESIS (RSO) to treat chronic pain and inflammation of osteoarthritis (OA) in dogs has been deployed in animal health due to the lack of treatments that veterinarians can turn to in cases where the primary and secondary line of treatments are found to be inadequate. Synovetin OA® is a colloid containing tin-117m (^{117m}Sn) that can be used to treat osteoarthritic dog joints, including the elbow, stifle (the equivalent of the human knee), and hip. The internal conversion and Auger electrons emitted by the ^{117m}Sn provide the therapeutic effect. Sn-117m also emits gamma rays, the most significant of which is 158.6 keV. The use of ^{117m}Sn radiosynoviorthesis in veterinary medicine is relatively new. As a new therapy modality, there are multiple effectiveness and safety concerns that need to be addressed. The patient safety aspects have been addressed previously (Srivastava 2007; Doerr et al. 2015; Stevenson et al. 2015; Aashish 2018; Lattimer et al. 2019). As ^{117m}Sn enters commercial use, radiation safety for members of the public must be addressed. The external radiation field around a treated dog is of interest in order to limit the dose to the owners/caretakers of the dog.

One of the concerns with this treatment is ensuring that dose limits for members of the public will be met. The initial attempt to license ^{117m}Sn using the same methodology as is used for ^{131}I therapy for cats was unsuccessful (US NRC 2018). The US Nuclear Regulatory Commission's (NRC) main concerns revolved around the relatively long effective half-life of ^{117m}Sn compared with ^{131}I as used in hyperthyroid therapy in cats, the need for confidence in the characterization of pet-human interactions, and the adequacy and compliance with behavior modification instructions. Effectively, the NRC's position was that the behavior of cats and dogs and their interactions with their owners is different and that dog-specific data was needed to demonstrate the ability to comply with public dose limits. Sn-117m colloid is different from many other unsealed radionuclides used due to its half-life, 13.6 d, and the lack of biological elimination. To demonstrate compliance with the public dose limits, time and motion studies are needed to prospectively calculate the dose to members of the public, of which the people that share a household with the dog are the critical group. Earlier human dose assessments had used relatively simple assumptions regarding interactions and the geometry of those interactions

[1]Foxfire Scientific, Arlington, TX; [2]IsoTherapeutics Group, LLC, Angleton, TX; [3]Exubrion Therapeutics, Buford, GA.

This work was funded by Exubrion Therapeutics®, Buford, GA. The authors declare no other potential conflicts of interest.

For correspondence contact: Matthew Arno, Foxfire Scientific, 4621 S Cooper St., Suite 131-332, Arlington, TX 76017, or email at **arno@foxfirescientific.com**.

(*Manuscript accepted* 26 *February* 2021)
0017-9078/21/0

DOI: 10.1097/HP.0000000000001428

(Wendt et al. 2020). Additional refinement of those assumptions, both with regard to dose rate and the geometry of those interactions, was needed to address NRC's concerns. It should be noted that veterinary medicine is regulated under 10 CFR 30 rather than 10 CFR 35, and thus the public dose limits in 10 CFR 20 (or the Agreement State equivalents) apply to veterinary medicine in all states except Texas, which regulates veterinary medicine under Title 25 Texas Administrative Code Chapter 289 Rule 256 (Texas Administrative Code 2018), the Texas equivalent of 10 CFR 35.

One of the inputs to the time and motion study is the dose rate at various distances from the dog at which an individual might be located. Canine anatomy is such that the dog's joints are at the same height or lower than the dog's torso when in a standing position. In this position, the dog's torso attenuates the radiation being emitted toward the opposite side of the dog's body, above the dog, and at the other longitudinal end of the dog. In a seated position, this shielding effect is increased further. This leads to a radiation field that is significantly non-isotropic. This study was conducted to establish the characteristics of this non-isotropic field. Conceptually, a person positioned in the same plane in front of or on the left side of a dog treated in the left elbow will be directly exposed to radiation emitted from the elbow, while a person positioned behind, to the right, and above will be exposed to a lower dose rate due to the shielding effect of the interposed tissues between the elbow and the individual.

Attempting to quantify the orientation of a person with respect to a dog for a time and motion study is not feasible. It is a simpler task to quantify time at a particular distance regardless of orientation. For any given distance, 0.3 m, 1.0 m, etc., it can be assumed that a person will be in a variety of positions with respect to the dog. Therefore, an "average" dose rate at a particular distance becomes the relevant dose rate to use to calculate the individual's dose.

However, it is commonplace to use the maximum dose rate at a particular distance to determine release criteria and similar criteria. For instance, the criteria for the release of human patients based on dose rate is based on measured dose rates that are "no greater than," i.e., maximum measured dose rates (US NRC 2020a). Likewise, the transportation index is based on the maximum measured dose rate from a package as specified in 49 CFR 173.403 (US DOT 2004). This results in the need to determine the average dose rate to an individual based on the maximum measured dose rate. This can be expressed as a ratio or as a percentage reduction. This study was designed to provide this percentage reduction.

MATERIALS AND METHODS

This study has been conducted in two parts. The first portion of the study was done in support of an application for generic authorization for use of ^{117m}Sn to treat dog elbows that has been approved by the NRC for use in NRC-regulated states and in Agreement States as they see fit (US NRC 2020b). The second portion of the study was subsequently done to evaluate joints other than the elbow.

General methodology

For each of the study parts, the same basic methodology has been used. A series of measurements are taken at various orientations and distances to measure the dose rate from a treated joint and to simulate the various positions an individual may be in with respect to a dog. These net measurements are averaged and compared to the net maximum dose rate measured at the same distance. The orientations chosen were:

- Anterior (toward the head) to the treated joint at the height of the treated joint;
- Posterior (toward the rump) to the treated joint at the height of the treated joint;
- Laterally left from the treated joint at the height of the treated joint;
- Laterally right from the treated joint at the height of the treated joint;
- Anterior to the treated joint at a 45-degree angle upward;
- Posterior to the treated joint at a 45-degree angle upward;
- Laterally left from the treated joint at a 45-degree angle upward;
- Laterally right from the treated joint at a 45-degree angle upward; and
- Dorsal (above) to the treated joint.

Each of these measurements is performed at distances of 0.3 m and 1.0 m from the treated joint, resulting in a total of 18 measurements. If two joints are treated, the distance is measured from the nearest joint. The anterior, posterior, and dorsal measurements are taken along the dog's centerline. If the dog's size is such that 0.3 m is within the dog's body, the measurement is taken on contact in the indicated direction. The 45-degree upward angle was chosen to approximate the center of mass of a person standing next to (1-m distance) or kneeling beside (0.3-m distance) a dog.

A spectrum of dog sizes was selected to correspond to the range of typical dog sizes for which this treatment is offered. A minimum dog size of 4.5 kg is accepted for treatment with no maximum size, although the treatment dosage is the same for all dogs weighing more than 50 kg. The typical treated dog is in the 20- to 35-kg weight range.

Elbow study

The elbow study was performed in 2019 as simulated treatments in support of a submission to the NRC (Arno 2020). A population of dogs of various sizes that could be injected with ^{117m}Sn was not available for various reasons. Therefore, to approximate the torso shielding effects from treated elbows, ^{117m}Sn sources

Fig. 1. Dog with ^{117m}Sn affixed to medial elbows.

were secured to the medial surface of the dog elbows, and radiation field measurements were obtained. The ^{117m}Sn sources consisted of tin-iodide solutions absorbed on blotter paper and double-bagged in plastic Ziploc-type pouches for contamination control. The active area of the blotter paper was approximately 1 cm X 2 cm with total activities of 125 MBq each, about 10% more than the maximum prescribed 111 MBq activity per elbow. Fig. 1 shows a dog with the sources taped to its elbows. Positioning of the sources in this manner is a good approximation for determining the radiation field at distances other than on contact.

Ten dogs ranging in size from a 5-kg dachshund to a 39-kg chocolate lab formed the dog population used in the study. All measurements were made with sources on each elbow to simulate a dog treated in both elbows. Dose rate measurements were made with a Ludlum 9DP (Ludlum Measurements, Sweetwater, TX) ion chamber. Two (0.3 and 1.0 m) fiberglass rods were used to ensure repeatability of the measurement distances. The rods were used to position the meter and then withdrawn for the actual measurement.

Stifle and hip study

The stifle and hip study was performed in 2020 using decapitated cadaver dogs so that actual injections of the ^{117m}Sn could be performed. Unlike the elbow study, measurements were taken after injection into a single joint (the left stifle or hip joint was always injected first) and into both of the same type of joint. Sixteen dog cadavers were used, eight each for the hip and stifle, ranging in size from 10 kg to 26 kg. The dog weights were based on the pre-decapitated weight.

Injections into the cadavers were performed by a licensed veterinarian in the same manner as would be used for a live dog. The cadaver was then suspended in a cargo sling from an A-frame to approximate a normal standing position as shown in Fig. 2. Dose rate measurements were

Fig. 2. Cadaver suspended in position for dose rate measurements.

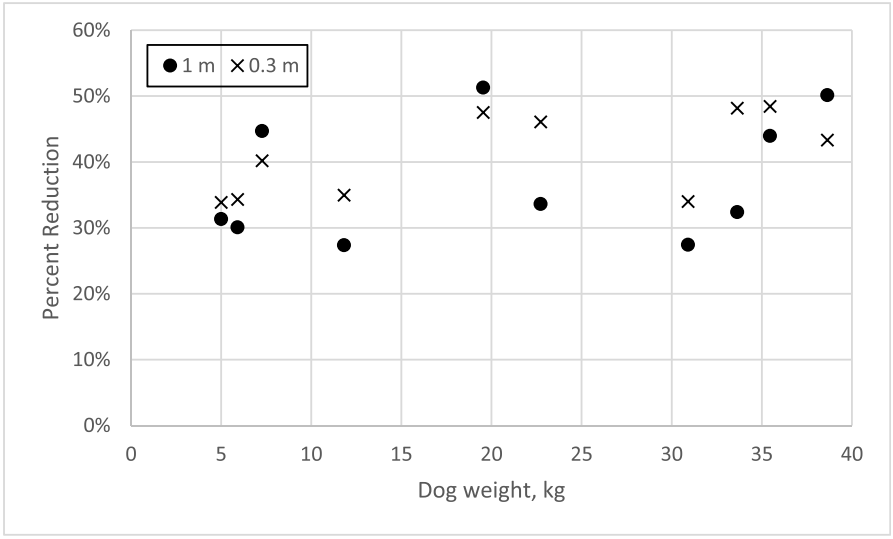

Fig. 3. Elbow average dose rate percent reduction from the maximum measured dose rate.

performed using a Ludlum Model 26-1 detector equipped with an ambient dose equivalent filter Ludlum Model 2002-1050. The use of the ambient dose equivalent filter allows the data to be collected in Sieverts instead of C kg^{-1} and dramatically reduces the over-response of the G-M pancake detector on the Model 26-1 to the 158.6 keV primary gamma ray from ^{117m}Sn when calibrated using a ^{137}Cs source. Wood dowels (0.3 and 1.0 m) were used to ensure repeatability of the measurement distances. The dowels were used to position the meter and then withdrawn for the actual measurement.

RESULTS

The results of the elbow study are presented in Fig. 3. The results of the stifle and hip study are presented in Figs. 4 and 5. The hypothesis prior to the studies was that there may be a difference in the average shielding depending on whether one or two joints are injected, the type of joint injected, and the subject mass. Examination of the data indicates no clear dependence on subject mass regardless of the joint type or number of joints injected. Any small dependence that might exist is indistinguishable from the scatter in the data. Only in the single case of subjects injected in both stifles was there indication of size dependence. Notably, injection in a single stifle resulted in the highest shielding effectiveness but without a size dependence.

Given the lower placement on the body, measured dose rates from the stifle are subject to more attenuation by the torso when measured at the 45-degree upward angle and thus result in the noted statistically significant difference at 30 cm. At 1 m, this difference is presumed to be diminished by the increased opportunity for shallow angle scattering.

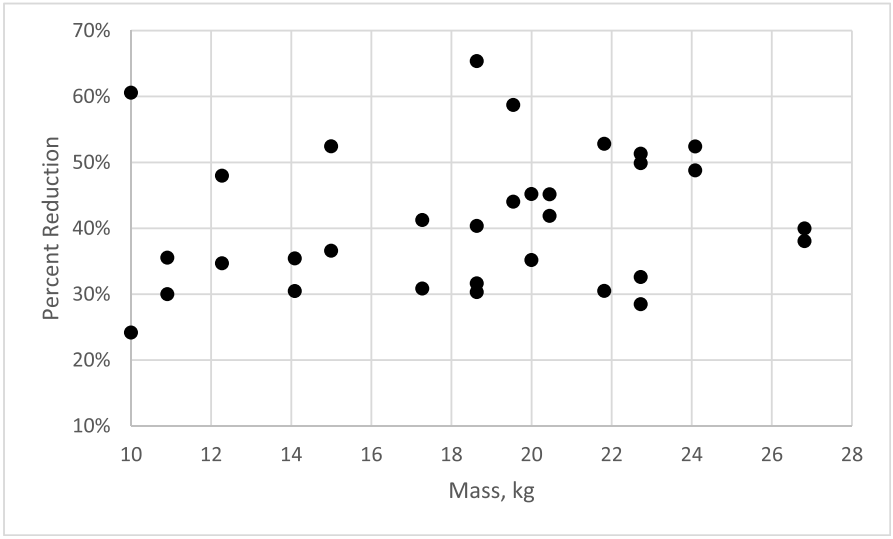

Fig. 4. Stifle and hip average dose rate percent reduction from the maximum measured dose rate, 0.3 m distance.

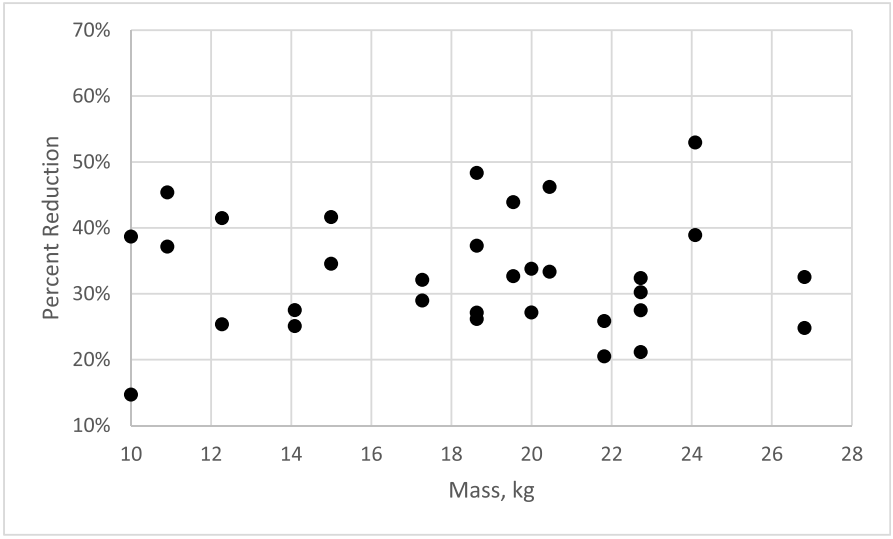

Fig. 5. Stifle and hip average dose rate percent reduction from the maximum measured dose rate, 1.0 m distance.

ANOVA tests reveal there is no significant difference between the shielding effectiveness of injecting one or two hips at either 0.3 m or 1 m (P values of 0.90 and 0.18, respectively). With the stifles, there is a statistically significant difference between the shielding effectiveness at 0.3 m but not at 1 m (P values of 0.005 and 0.37, respectively). Comparing the overall shielding effectiveness of the hip vs. the stifle at 0.3 m and 1 m results in P values of 0.0007 and 0.38, respectively. The datum that is significantly different is the case of 1 stifle injected and measured at 0.3 m; the shielding effectiveness in this case is noticeably higher than in the other cases.

A total of 12 cases were evaluated—three joint types at two distances and with one or two joints injected. Of these 12 cases, only one exhibited a significant difference as discussed above, and it exhibited a higher shielding effectiveness than the other cases. Due to the absence of a significant difference between joint type or number of joints injected for most of the cases, all the data were combined. Figs. 6 and 7 present the elbow data overlaid with the hip and stifle data at the 0.3- and 1.0-m distances. From a radiation safety perspective, the important factor is the minimum amount of shielding effectiveness that can be expected. A reasonable measure for this value is the fifth percentile of the shielding effectiveness distribution. The fifth percentile shielding effectiveness values are 27% and 21% at 0.3 and 1.0 m, respectively. The inclusion of the one stifle measured at the 0.3-m case has little impact on the determination of the fifth percentile given that it has a higher shielding effectiveness than the other cases

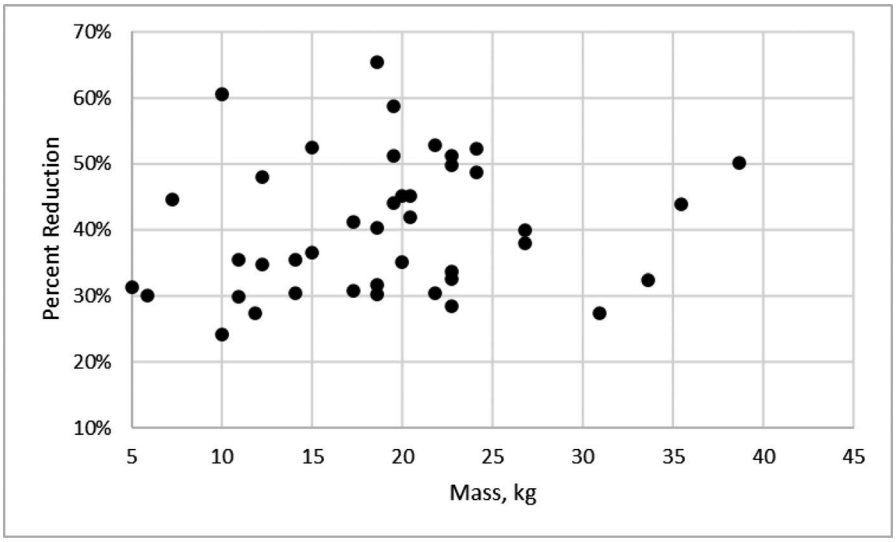

Fig. 6. All joints average dose rate percent reduction from the maximum measured dose rate, 0.3 m distance.

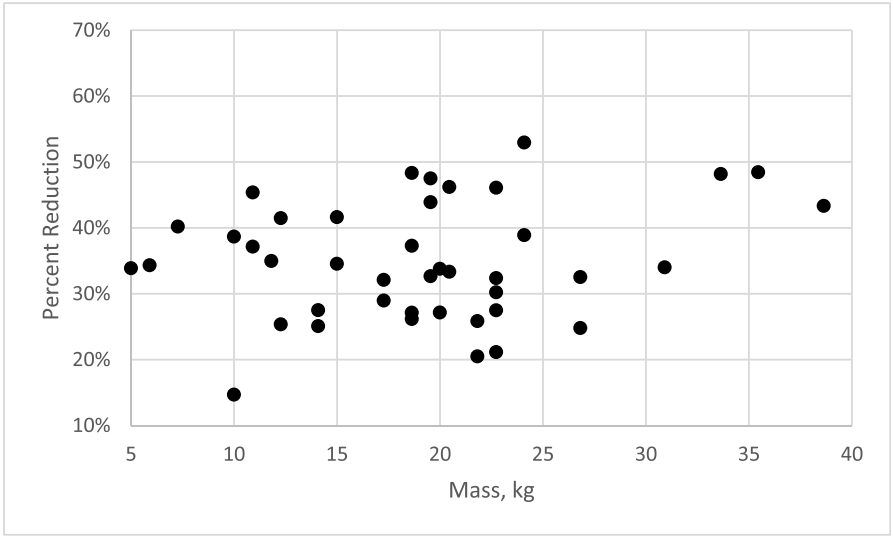

Fig. 7. All joints average dose rate percent reduction from the maximum measured dose rate, 1.0 m distance.

and permits single values for each distance to be used for future dose calculations.

CONCLUSION

Performance of a public dose assessment for situations for which there are not accepted generic parameters, such as occupancy factors for different adjoining room types in a medical setting, can be complex. Often, a prospective time and motion study is required. Such a study requires characterization of the radiation field being emitted from the radiation source; determination of the behavior of both the source (the dog) and the receptor (an individual); and the distances and times associated with those behaviors. This study provides the input necessary for the first category of necessary information. That characterization has been distilled to a form usable as an input into the remainder of the public dose assessment.

Acknowledgments—The authors would like to thank Brian Poteet of Cypress, TX, for his assistance in performing this study.

This work was funded by Exubrion Therapeutics®, Buford, GA.

REFERENCES

Arno MG. Evaluation of potential dose to members of the public from treatment of dogs with Synovetin OA™ containing Sn-117m [online]. 2020. Available at ***https://adamswebsearch2.nrc.gov/webSearch2/main.jsp?AccessionNumber=ML20142A295***. Accessed 1 October 2020.

Aashish CG. On the investigation of radionuclides used in radiosynoviorthesis. Lubbock, TX: Texas Tech University; 2018. Thesis.

Doerr CA, Stevenson NR, Gonzales GR, Simon J, Bendele A, Srivastava SC, Strauss HW. Homogeneous Sn-117m colloid radiosynovectomy results in rat models of joint disease. J Nucl Med 3(Suppl):1243; 2015.

Lattimer JC, Selting KA, Lunceford JM, Holland JR, Simon J, Stevenson NR, Doerr CA. Intraarticular injection of a Tin-117m radiosynoviorthesis agent in normal canine elbows causes no adverse effects. Vet Radiol Ultrasound 60:567–574; 2019.

Srivastava SC. The role of electron-emitting radiopharmaceuticals in the palliative treatment of metastatic bone pain and for radiosynovectomy: applications of conversion electron emitter Tin-117m. Brazilian Arch Biol Technol 50:49–62; 2007.

Stevenson NR, Lattimer JC, Selting KA, Gonzales GR, Doerr CA, Bendele A, Simon J, Srivastava SC. Abstract S6-03: homogeneous Sn-117m colloid—a novel radiosynovectomy agent. World J Nucl Med 14(Suppl 1):S15–S68; 2015.

Texas Administrative Code. Medical and veterinary use of radioactive material; Texas regulations for control of radiation. Final/Adopted. Austin, TX: Texas Register; 43:6029–6418; 2018.

US Department of Transportation. Hazardous material regulations; compatibility with the regulations of the International Atomic Energy Agency; final rule. Washington, DC: US DOT00; 40 CFR 173.403, 69 FR 3670–3673; 2004.

US Nuclear Regulatory Commission. Response to technical assistance request dated 4/27/2018. New Haven, CT: Central Hospital for Veterinary Medicine; 2018. Available at ***https://adamswebsearch2.nrc.gov/webSearch2/main.jsp?AccessionNumber=ML1819A440***. Accessed 27 November 2018.

US Nuclear Regulatory Commission. Release of patients administered radioactive material. Washington, DC: US Government Printing Office; Regulatory Guide 8.39; 2020a.

US Nuclear Regulatory Commission. Technical evaluation report for the exubrion therapeutics proposed license application template for the release of dogs following treatment with a tin-117m colloid. Washington, DC: US NRC; 2020b. Available at ***https://adamswebsearch2.nrc.gov/webSearch2/main.jsp?AccessionNumber=ML20269A277***. Accessed 1 December 2020.

Wendt RE III, Selting KA, Lattimer JC, Wong J, Simon J, Stevenson NR, Stearns SD. Radiation safety considerations in the treatment of canine skeletal conditions using ^{153}Sm, ^{90}Y, and ^{117m}Sn. Oper Radiat Safety 118:702–710; 2020.