RETENTION AND DOSIMETRY OF SOME INJECTED RADIONUCLIDES IN BEAGLES

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MARCH 1970

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TABLE OF CONTENTS

Preface.	1
Design and calibration of a total-body counting system for measuring radioactivity in Beagles.	2
Radium and mesothorium retention and skeletal dosimetry in Beagles.	25
Distribution of injected ^{226}Ra in the Beagle skeleton.	60
Fractional radon retention in bone.	69
Retention and skeletal dosimetry of injected ^{90}Sr in Beagles.	79
Distribution of injected ^{90}Sr in the Beagle skeleton.	97
Distribution and retention of injected ^{210}Pb in the Beagle. . .	105
Americium-241 retention in Beagles.	123
^{228}Th skeletal dosimetry and total-body ^{212}Bi retention in Beagles.	144

PREFACE

This report of the retention and skeletal dosimetry of radio-nuclide-injected dogs in the Beagle colony at the University of Utah's Radiobiology Division appears in the Laboratory's 20th anniversary year. Ours is a long-term project, designed to provide answers to specific questions in radiobiology which are becoming increasingly important with the continued development of the nuclear age.

The retention measurements and resulting dose and dose-rate calculations of the type given in this report are fundamental to an understanding of the relationship of internal irradiation and the observed biological effects. Our data are presented in detail so that they can be used by other investigators. We sincerely hope that this report may provide a means of obtaining some significant insights into the extremely important problems in human radiobiology which form the basis for our studies.

Support for this project has been provided entirely by the U. S. Atomic Energy Commission under contract AT(11-1)-119. Unfortunately, only a few of the many persons whose contributions were essential during the past 20 years could be named in the authorship and acknowledgments to individual articles.

Assistance with the production of this report was given by Nancy Peixhot, Cheryl Fisher, and Mary Rieben who did the manuscript typing, and by Barbara Staker, Julian Maack, Hal Pullum and other members of the Medical Illustration Service, University of Utah who did the graphic work. We are especially grateful to Professor Thomas F. Dougherty, Director of the Radiobiology Division, who provided the leadership and encouragement which made possible the completion of this report.

Ray D. Lloyd
March 1970

DESIGN AND CALIBRATION OF A TOTAL-BODY
COUNTING SYSTEM FOR MEASURING
RADIOACTIVITY IN BEAGLES

R. D. Lloyd, D. H. Taysum and C. W. Mays

Abstract: A positioner for holding dogs during total-body counting was designed. It was constructed so that when an animal is placed on his back, his midline is curved into a 33-cm radius arc, which approximates an isoresponse line for an 8 inch x 4 inch NaI(Tl) crystal positioned with its face at the center of curvature for this arc. Counter response is relatively independent of the location of an emitter at various points along the dog's midline. The positioner molds the animal to a uniform 15 cm lateral thickness so that body attenuation of photons is similar among adult beagles. Effects on counting rate of differences in position of dogs within its confines are small. Calibration was accomplished by counting in this positioner 8 dogs containing various radionuclides. Their body burdens were then determined by the radioactivity of their individual bones and tissues following autopsy.

INTRODUCTION

In order to calculate the radiation dose to the dogs in our colony from internally deposited radionuclides, the retention of administered radioactivity and its distribution within the body must be determined as a function of time after injection. For those nuclides which emit photon radiation in connection with their radioactive decay, serial external counting (total-body and partial body) can indicate the retention at many points in time for the same animal. During earlier days of this project, retention measurements were made with the canine total-body liquid scintillation counters K-9⁽¹⁾ and K-9 Bark II.^(2,3) Because of the limitations of liquid scintillation counters, we found it necessary to design and calibrate a new counting system.

DESIGN

Criteria. Requirements for the counting system included the following desirable criteria:

- (1) capability of distinguishing among various photon emitters;
- (2) adequate counting rates for dogs at relatively low injection levels;
- (3) minimum resolving time corrections at counting rates produced by dogs at high injection levels;
- (4) detector response relatively independent of the location of an emitter within a dog's body;
- (5) uniform photon attenuation within the bodies of dogs injected with the same nuclide;
- (6) insensitivity to poorly controllable variables such as animal size, accuracy of positioning, and dog movement during counting (respiration);
- (7) reliability and ruggedness under routine counting conditions;
- (8) provision for the safety, health, and comfort of the animals to be counted.

A design which appeared to meet many of these requirements incorporated a NaI(Tl) crystal 8 inches in diameter and 4 inches thick as the detector. This crystal was of large enough size that counting rates would be relatively high, it had operated reliably for a number of years under laboratory conditions, and its resolution of different photon emitters was adequate. If the dog were curved around the crystal so that his midline would conform to a line on which all points were counted with equal efficiency, counting rates would be somewhat independent of both dog length and the location

of activity along his body. Counting the dogs from the side also contributed to this effect. Since a dog is bilaterally symmetrical with respect to skeleton and major soft tissues*, as much of a given tissue is further from as is closer to the crystal along the dog's longitudinal axis. Counting rates could be increased by choosing an isoresponse line close to the detector, and resolving time corrections could be decreased with an isoresponse line further away. The effects of dog positioning and respiration would also be minimized at a greater distance from the crystal as would the effects of emitter location within the animal. If all dogs could be made to have the same lateral thickness, the attenuation of photons emitted from within the body would be similar for dogs containing the same radionuclide.

The concept ⁽⁴⁾ which emerged from all of these considerations was that of a curved box which would cause the body of an animal placed within it to conform to both a uniform lateral thickness and an isoresponse line with respect to the detector (Figure 1).

The isoresponse line. Circular arcs of various radii were constructed with their common center point at the center of the face of an 8 x 4 inch NaI(Tl) crystal. A line perpendicular to the crystal face connecting the arcs and the center point intersected each arc at a point designated "0°". Other points along the arc were marked at measured angles from the zero point. For example, on the 33 cm arc, points were established at 21° intervals such that they fell at -42°, -21°, 0°, +21° and +42° (Figure 2). A lucite cylinder 4.2 cm

* Even the liver is approximately centered when in this position, which is not the case in some other mammals including man.

Figure 1. A Beagle in the dog positioner or "Hound Holder". The anesthetized animal is placed on his back in the lucite box which curves his midline into an arc having a 33 cm radius. The box is positioned such that the dog's midline is 33 cm from the face of an 8 x 4 inch NaI(Tl) crystal, a full-size model of which is shown here. This counting arrangement was designed so that counter response would be relatively independent of the location of an emitter along the length of a dog. The positioner molds the animals to a uniform 15 cm lateral thickness to provide somewhat equal photon attenuation among the adult Beagles in the colony. The legs are fastened in a standard position with masking tape and the dog's head is centered in the "nose cone" trough in which the nose rests. A trachea tube is inserted to provide an open airway while the animal is being counted.

in diameter and 13 cm long containing a 2 cm diameter axial tunnel could be centered over each of these points as a source holder for a series of ampoules containing ^{241}Am , ^{90}Sr , ^{60}Co , and ^{226}Ra and which elevated the center of the radioactive solution to the same height as the crystal face center. These sources of photon radiation were each counted at all of the points marked along each arc, and their net counting rates were compared to that recorded at the point marked "0°". Table 1 lists the results of these measurements for the 33 cm arc which was chosen for the final design as a compromise between the requirements of adequate counting rates for low-level dogs and minimum resolving time corrections for dogs at higher levels.

Table 1. Relative counting rates of several emitters along an arc 33 cm from the center of the face of an 8 x 4 inch NaI(Tl) crystal (see Figure 2).

Nuclide	Photon Energy, MeV	Relative Counting Rate				
		-42°	-21°	0°	+21°	+42°
^{241}Am	0.06	0.974	0.956	1.00	0.964	0.936
^{90}Sr	0.05 to 0.30*	0.947	0.987	1.00	0.962	0.927
^{60}Co	1.17 and 1.33	0.980	0.997	1.00	0.996	0.988
^{226}Ra	0.32	0.997	0.993	1.00	0.981	0.970
	0.61	0.970	0.994	1.00	0.987	0.954
	1.76	1.00	1.00	1.00	0.996	0.997

* Bremsstrahlung photons.

Figure 2. Configuration used in the determination of the isoresponse line (see Table 1).

Data in Table 1 indicate that an isoresponse curve for the 8 x 4 inch NaI(Tl) crystal is approximated by a 33 cm arc having the center of the crystal face as its center of curvature. Therefore, this 33 cm arc satisfied the design criterion that the midline of the dog correspond to an isoresponse curve.

Positioner dimensions. The largest Beagle in our colony (as of 1963) was selected to provide an upper limit on size which the dog positioner would be required to accomodate (M2R0 = 14.6 kg at injection, 21.2 kg maximum weight, and 18.3 kg at the time of this study). It was found that this animal could just be contained within a box of minimum lateral width of 15 cm and of minimum length about 60 cm. A curved box was constructed of 1/4 inch thick lucite as thinner or more flexible walls tend to deform when a dog is inserted. Its dimensions were about 60 cm long by 15 cm wide by 30 cm high (Figure 3). All points midway between the front and rear curved walls lay on a cylindrical surface with a radius of curvature equal to 33 cm (Figure 1). An extended head and neck support (Nose Cone) was provided for the animal's head so that the neck could lie flat. This was to minimize constriction of the air passage in the anesthetized dog. The trough constructed in the extension also provided a convenient landmark for accurately positioning the animal's head, since his nose could be placed exactly in its center. Within the limits of normal-sized adult Beagles in our colony, the width of this positioner molds all the animals to a constant 15 cm thickness, providing similar photon attenuation from dog to dog. For counting, the box is positioned so that the dog's axial midline coincides with the 33 cm-radius arc, and the center of the crystal face coincides

Figure 3. Dimensions of dog positioner.

with the center of curvature of the arc, as illustrated in Figure 1. This dog positioner is affectionately known as the "Hound Holder".

Dog Safety. Since the animal and detector are enclosed within a steel shield for background suppression during counting, the dog's condition is continuously monitored via closed circuit television. While under anesthesia, a trachea tube is utilized to provide an open airway, to keep material (such as vomitus) out of the lungs, and to provide a ready means of breathing assistance in an emergency.

Effect of positioning errors. The error in a dog's counting rate due to differences in position within the hound holder was investigated. Four animals were counted repeatedly. After each count, the animal was completely removed from the positioner and then repositioned for the next count. Dog Tl8S6, a midget beagle weighing only 5.94 kg at injection, was so small that he could be moved along the arc and positioned against the front wall and against the back wall in turn, with room to spare. He was first counted in standard position (nose in nose cone, body centered between front and rear walls of positioner) for 10 minutes. Then the following 1 minute counts were made:

- (1) against front wall
- (2) against rear wall
- (3) tail against left wall; head out of head support
- (4) centered in positioner.

Results of all these measurements are exhibited in Table 2. In every case, the expected counting error (based only on counting statistics) was of the same order as the observed deviation from the average. It was concluded from these data that errors in a dog's counting rate as a result of small errors in positioning within the hound holder were insignificant.

Table 2. Effect of dog positioning on counting rate

Dog	Nuclide	Photon Energy, MeV	Trial No.	Background Counting Time, Min.	Counts Collected	Dog Counting Time, Min.	Net Counts Collected	% Deviation from average	Statistical Counting Error %
M9M2	^{228}Ra	0.93 (^{228}Ac)	1	10	775	10	21884	-0.4	± 0.7
			2			10	22039	+0.4	
		2.62 (^{208}Tl)	1	10	212	10	9738	+0.7	± 1.0
			2			10	9600	-0.7	
M4M2	^{228}Ra	0.93 (^{228}Ac)	1	5	385	5	4070	+0.8	± 1.7
			2			5	4076	+0.9	
		0.93	3			5	3899	-3.4	
		0.93	4			5	4150	+2.8	
		0.93	5			5	4060	+0.5	
		0.93	6			5	3974	-1.6	
		2.62 (^{208}Tl)	1	5	105	5	2093	-1.0	± 2.3
			2			5	2170	+2.6	
		2.62	3			5	2075	-1.8	
		2.62	4			5	2158	+2.1	
		2.62	5			5	2127	+0.6	
		2.62	6			5	2061	-2.5	
FLS4	^{90}Sr	0.05-0.50 ⁺	1	10	10924	2	36638	-3.6	± 0.5
			2			2	38527	+1.4	
			3			2	38833	+2.2	
			4			2	37961	-0.1	
Tl856	^{90}Sr	0.05-0.50 ⁺	1*	10	11043	10	1647515	-	± 0.2
			2*			1	164903	+0.1	
			3*			1	164176	+0.3	
			4*			1	165276	+0.4	
			5*			1	164309	-0.2	

⁺Bremsstrahlung photons.

*No. 1 = Standard position.

No. 2 = Against front wall.

No. 3 = Against rear wall.

No. 4 = Against left end.

No. 5 = Centered in positioner.

CALIBRATION

^{226}Ra , ^{228}Ra , and ^{228}Th . Six dogs with body burdens of ^{226}Ra or ^{228}Ra or ^{228}Th were counted in the hound holder immediately before autopsy. The total-body counting rate of each animal at the appropriate energy was compared to that of a known activity of the same emitter except that both a ^{228}Ra standard and a ^{228}Th standard were counted for the ^{228}Ra dogs so that the $^{228}\text{Ra} + ^{228}\text{Ac}$ spectrum could be separated from the ^{228}Th daughters spectrum of both the dogs and the ^{228}Ra standard. Each standard was in 10 ml of solution in a 10 ml ampoule inserted into the center of a lucite cylinder 8.2 cm in diameter and 11.3 cm long containing an axial tunnel 2 cm in diameter extending into the cylinder 7.1 cm. The lucite cylinder was in turn centered within a cylindrical polyethylene absorber 13.25 cm in diameter and 40 cm high having an axial tunnel which could just accomodate the lucite cylinder. This polyethylene cylinder, containing the lucite absorber and the ampoule, was centered against the rear wall of the hound holder for counting (Figure 4). The ratio of the counting rate of the dog to the counting rate per μCi of the standard gave the "apparent" μCi of emitter in the dog.

Immediately following death, the individual bones and the soft tissues of the animal were placed in #2 cans. The counting rate of each sample was compared to that of the appropriate ampoule standard centered in an identical can. As a standard for individual bones, the ampoule was surrounded in the can by styrofoam (density = 0.02 g/cm^3)*.

* The implicit assumption that the counting rate per μCi of a bone is equal, on the average, to the counting rate per μCi of an ampoule was verified by counting a representative sample ($\sim 1/2$) of the skeleton of dog TLM4.5 as described in this calibration study, then ashing the samples and determining their true activity by counting a known fraction of the dissolved ash in a 10 ml ampoule using ampoule standards. Activities derived by these counting methods agreed within a few percent.

Figure 4. Representation of an ampoule standard in the dog positioner showing its relationship to the crystal and absorbers during counting.

A plastic insert with a density near that of water was used for an absorber to surround the ampoule in the can as a standard for soft-tissue counting. The ratio of the counting rate of the bone or soft-tissue to the counting rate per μCi of the standard yielded the μCi of emitter in the part, while the sum of these values gave the "true" μCi of emitter in the total dog.

An individual total-body counting calibration factor, C_f , for each dog was calculated as

$$C_f = \frac{\text{"true" } \mu\text{Ci}}{\text{"apparent" } \mu\text{Ci}}$$

Since four of these animals had body burdens of ^{228}Ra , a separate calibration factor for the ^{228}Ra (^{228}Ac gamma-ray spectrum) and for the ^{228}Th daughters (^{208}Tl gamma-ray spectrum) could be calculated for each, so that the six dogs gave a total of ten calibration factors. Results are listed in Table 3.

Table 3. Calibration factors for the NaI crystal counter determined for the 6 animals used in this study.

<u>Nuclide</u>	<u>Dog</u>	<u>γ-ray Energy, MeV</u>	<u>Calibration Factor</u>
^{226}Ra	T61R4*	1.76	0.834
^{228}Th	F9T3	2.62	0.871
^{228}Ra	M9M2	0.93	0.907
	M9M2	2.62	0.876
^{228}Ra	F5M2	0.93	0.831
	F5M2	2.62	0.878
^{228}Ra	M9M3	0.93	0.852
	M9M3	2.62	0.821
^{228}Ra	M6M2	0.93	0.817
	M6M2	2.62	0.838
Average and Experimental S. D.			0.85 $\pm$ 0.03

* ^{214}Bi body content; bones and tissues were corrected for build-up of radon daughters between death and counting.

DOG POSITIONING IN K-9 BARK II

Figure 5. K-9 Bark II, a total-body counter for measuring the gamma-ray activity in living dogs. It was operated from 1957 to 1965 and was dismantled in 1968. Since the scintillator virtually surrounded the dog, the counting efficiency was high. Disadvantages which led to its abandonment were poor resolution and a high background. The scintillation liquid was 70 gallons of toluene with 5 g of *p*-terphenyl and 0.2 g of 1, 5-di[2-(5-phenyloxazolyl)] benzene (POPPOP) per liter.

Inspection of the data in Table 3 reveals that, of the four ^{228}Ra dogs, in 2 cases the calibration factor at 0.93 MeV is lower than the calibration factor at 2.62 MeV and in 2 cases it is higher. In addition, the average of the 4 calibration factors at 0.93 MeV (0.852) and the average of the 5 calibration factors at 2.62 MeV (0.854) differ by only 0.2%. Since no important effect of gamma-ray energy on the relative magnitude of the calibration factor was apparent, all the calibration factors were averaged. The average calibration factor was then used to correct the total-body counting results for all ^{226}Ra , ^{228}Ra , and ^{228}Th dogs counted in this configuration by multiplying the "apparent" μCi by 0.85. It was to be expected that the calibration factor would be less than 1.0 since the ampoule standards are actually counted farther from the crystal than is the effective center of radioactivity in the dog.

Because retention values for many dogs had been determined in the liquid scintillation counter*, K-9 Bark II,^(2,3) before the crystal counter was put into operation, and because some animals had been counted with both systems at different times, calibration of K-9 II was accomplished using techniques similar to those described for the crystal counter. Results are shown in Table 4. The average calibration factor of 0.94 was used to correct the "apparent" μCi measured for all ^{226}Ra and ^{228}Th dogs counted with K-9 II.

* K-9 Bark II was a cylinder 1 meter in length containing 70 gallons (265 liters) of liquid scintillator around an axial tunnel 7 inches (18 cm) in diameter in which the dog or standard was centered for counting. K-9 II was built in 1957 and dismantled in 1968 (Figure 5).

Table 4. Calibration factors* for the liquid scintillation counter K-9 II-determined for the 5 dogs in this study.

<u>Nuclide</u>	<u>Dog</u>	<u>Calibration Factor</u>
^{226}Ra	ML0R3 ⁺	0.966
^{226}Ra	M7R3 ⁺	0.916
^{226}Ra	T28R3H ⁺	1.029
^{226}Ra	T61R4 ⁺	0.877
^{228}Th	F9T3	0.921
Average and Experimental S. D. 0.94 ± 0.06		

* Ampoule standards used to determine "apparent" μCi in the intact dog were counted inside a laminated cylinder of untempered masonite 16.5 inches long and 5 inches in diameter.

+ ^{214}Bi body content; bones and tissues were corrected for build-up of radon daughters between death and counting.

^{90}Sr . Bremsstrahlung x-rays produced as a consequence of the radioactive decay of $^{90}\text{Sr} + ^{90}\text{Y}$ within the animal's body can be utilized to determine body burdens of ^{90}Sr .⁽³⁾ Since the production of x-ray photons as well as their attenuation depends on the absorber size and composition,^(5,6) great care must be taken to ensure that the phantom containing the ^{90}Sr standard matches exactly the atomic number, configuration, activity distribution, and dimensions of the animal. We believe that the most appropriate phantom for ^{90}Sr bremsstrahlung measurements in Beagles is a Beagle containing an accurately determined activity of ^{90}Sr distributed within his body in an identical fashion to that in the dogs being measured. Phantoms were prepared for this purpose which closely approximated the ideal phantom described above by injecting 2 Beagles with ^{90}Sr . They were then

Table 5. Two dogs prepared as ^{90}Sr standards for total-body counting.

Dog	Sex	Body Weight, kg	Injected $\mu\text{Ci}^{90}\text{Sr/kg}$	Days of Age at Injection	Days, Injection to Sacrifice
T13S4*	M	10.50	19.1	324	8
T20S4J	F ⁺	8.54	28.9	440	13

* T13S4 was christened "Sam McGee" after the most distinguished frozen corpse described in the literature.⁽⁷⁾

+ T20S4J, a pseudohermaphrodite, was originally named "Christine J." but for contemporary appearance could now be called "Myra B." ⁽⁸⁾ in view of its uncertain sex classification.

sacrificed after a delay of about 1 and 2 weeks to allow for the deposition in the skeleton of virtually all of the retained ^{90}Sr and were frozen. Table 5 lists some pertinent data on these 2 animals.

T13S4 was frozen in a prone position so that he could be inserted into the tunnel of K-9 II, and T20S4J was positioned in the hound holder for freezing so that this dog could serve as a ^{90}Sr standard for the NaI crystal counting system. The ^{90}Sr activity contained in each of these phantoms was determined and verified by a combination of methods.

Two beagles (M2S5A and M3S5) dying with osteosarcomas 1740 and 2256 days after the injection of about $100 \mu\text{Ci}^{90}\text{Sr/kg}$ were counted shortly before autopsy using T13S4 and T20S4J as ^{90}Sr standards. One member of each set of paired bones was obtained from each of these 2 long-term dogs following autopsy. For unpaired bones, such as vertebrae, sternum, etc., a measured weight fraction (about 1/2) was also obtained.

Samples were ashed in an electric muffle furnace at approximately 600° overnight. The ash from each bone was dissolved in con-

centrated nitric acid, transferred to calibrated flasks, and diluted to volume with 0.1N nitric acid after at least 5 rinsings of the crucible with concentrated nitric acid, followed by 0.1N nitric acid. Representative 1 ml samples of each solution were taken in duplicate and were weighed to determine their density. After a 3 week delay to allow the ^{90}Y daughter to achieve equilibrium with the ^{90}Sr parent, the samples were β -counted in a well-type plastic scintillator, ^(9, 10) comparing the counting rates obtained to that of an equilibrated ^{90}Sr standard in 1 ml of distilled water in a sealed polypropylene test tube 12 mm in diameter and 75 mm long, identical to those containing the samples. Activities of ^{90}Sr for each bone were then calculated, making appropriate corrections for the effect of solution density on counting rate ⁽¹¹⁾ and for the fraction of the total dissolved bone that each sample represented. Assuming that the ^{90}Sr content of the member of each set of paired bones not analysed was equal to that of the member that was analysed and that the ^{90}Sr concentration was uniform in the unpaired bones, estimates were made of the ^{90}Sr content of the bones not analysed. The ^{90}Sr activity in the total dog was then calculated as the sum of the individual bones, since by 1700 days post-injection virtually all of the retained ^{90}Sr is in the skeleton.⁽¹²⁾ Once the ^{90}Sr content of both M2S5A and M3S5 was established, the ^{90}Sr content of the 2 frozen ^{90}Sr standards T13S4 and T20S4J could be calculated, since these phantoms and each of the ashed dogs had been total-body counted intact, and ratios of their counting rates had been obtained. The expressions

$$\mu\text{Ci}^{90}\text{Sr in T13S4} = \frac{\text{T13S4 counting rate}}{\text{M2S5A or M3S5 counting rate per } \mu\text{Ci}}$$

$$\mu\text{Ci}^{90}\text{Sr in T20S4J} = \frac{\text{T20S4J counting rate}}{\text{M2S5A or M3S5 counting rate per } \mu\text{Ci}}$$

yielded the following results:

T13S4	via	M2S5A	=	110.52 μCi
T13S4	via	M3S5	=	110.92 μCi
T20S4J	via	M2S5A	=	97.90 μCi
T20S4J	via	M3S5	=	98.93 μCi

(^{90}Sr activities corrected to 8 July 1960).

Therefore, the bremsstrahlung output of these 2 phantoms was equivalent to that of a Beagle injected with ^{90}Sr as a young adult with the activity distributed in the skeleton as it would be more than 4 years after injection and retaining about 110.7 μCi and 98.4 μCi , respectively.

All urine and feces produced by T20S4J between injection and sacrifice were collected and assayed for their ^{90}Sr content by bremsstrahlung counting. The injected activity minus the total activity excreted gave another estimate of the retained activity within the dog's body. This method of calculating the ^{90}Sr content of T20S4J yielded 98.61 μCi (corrected to 8 July 1960).

Three Beagles with body burdens of ^{90}Sr were counted in this laboratory along with T13S4 and T20S4J. The ^{90}Sr content of each of these 3 dogs was later determined by radiochemical techniques at the Radiobiology Laboratory, University of California at Davis. Calculated ^{90}Sr activities on 8 July 1960 in our 2 phantoms based on comparative bremsstrahlung counting and the Davis radiochemical assay were 108.4 μCi for T13S4 and 97.6 μCi for T20S4J.

Forty-two ^{90}Sr dogs from our colony were counted both in K-9 II and with the NaI crystal. These 2 counts on the same dog were com-

pleted within about a 15 minute time period. The ^{90}Sr content of each living dog was calculated using T13S4 as a standard and the K-9 II counting. Forty-two estimates of the activity of T20S4J were then obtained using the NaI counting data and the ^{90}Sr activity of each living dog derived from the K-9 II counting. The average of these values, corrected to 8 July 1960, was 97.6 μCi , indicating that a μCi in T13S4 is equivalent to a μCi in T20S4J within about 1%. The foregoing calibration data are summarized in Table 6. Note

Table 6. Calibration of the ^{90}Sr body content of T13S4 and T20S4J and verification of the results.

<u>Method</u>	<u>$\mu\text{Ci}^{90}\text{Sr}$ on 8 July, 1960</u>	
	<u>T13S4</u>	<u>T20S4J</u>
Calibration:		
via M2S5A	110.52	97.90
via M3S5	110.92	98.93
(Average)	(110.7)	(98.4)
Verification:		
injected-excreted ^{90}Sr	-----	98.61
via F26	118.88* and 107.03 ⁺	96.25
via D3F15	105.56* and 98.73 ⁺	93.93
via 13F	111.58 ⁺	102.65
via T13S4 and 42 ^{90}Sr dogs		97.63

* K-9 II counting

+ Counted 2 meters from the 8 x 4 inch NaI(Tl) crystal.

(F26 received ^{90}Sr by injection and D3F15 received dietary ^{90}Sr beginning in utero. Both dogs were from the University of California, Davis, Radiobiology Laboratory project and were made available for study through the courtesy of Dr. Marvin Goldman and Dr. Rocco J. Della Rosa. 13F received ^{90}Sr from a single, short-term inhalation exposure at the Lovelace Foundation Fission Product Inhalation project at Albuquerque, N. M., and was made available for study through the courtesy of Dr. Bruce B. Boecker.)

that the values for each dog obtained by comparison with animals receiving their ^{90}Sr as adults are in fairly good agreement, while the values obtained by comparison with the dog which received his ^{90}Sr in the diet all during the period of skeletal development may appear to be consistently low. Because the photon output per μCi is higher for ^{90}Sr fixed in cortical bone than in trabecular bone, the more uniformly labelled diet dog should have had a greater photon output per retained μCi than the animals exposed as adults.⁽¹²⁾ However, for use as standards for our ^{90}Sr -injected beagles, the values of 110.7 μCi and 98.4 μCi for T13S4 and T20S4J are considered to be verified by the ancillary studies reported in Table 6.

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✓ RADIUM AND MESOTHORIUM RETENTION AND SKELETAL DOSIMETRY IN BEAGLES

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Abstract: Radium retention has been determined in 125 Beagles injected with ^{226}Ra and in 78 Beagles injected with ^{228}Ra . The radionuclides were administered intravenously in a citrate buffer solution when the animals were about 1.5 years of age. Retention measurements now extend to more than 14 years after injection (for dogs nearly 16 years of age) so that future revision of the radium retention equations appears unlikely since the median survival time in our control beagles is about 11.3 years after injection (~ 12.7 years of age). Dogs injected with $10\ \mu\text{Ci } ^{226}\text{Ra/kg}$ had a higher retention than those receiving $3\ \mu\text{Ci } ^{226}\text{Ra/kg}$. This is interpreted as a consequence of radiation damage to the bone remodeling processes at high ^{226}Ra concentrations. Total-body retention of injected radium in the $10\ \mu\text{Ci/kg}$ dogs during the first 1400 days after injection was as if about 41% was retained with a biological half-time of 1 day, 10% with 10 days, 20% with 142 days, and 29% with 2318 days. Radium retention during the first 5200 days by animals receiving lower ^{226}Ra injections of $3\ \mu\text{Ci/kg}$ or less and by animals injected with ^{228}Ra was as if about 25% was retained with a biological half-time of 1 day, 21% with 3 days, 21% with 43 days, 18% with 347 days, and 15% with 4621 days. The average skeletal radiation dose rate and cumulative radiation dose were calculated for Beagles receiving ^{226}Ra or ^{228}Ra injections using the appropriate retention equation. Allowance was made in the ^{226}Ra calculations for the changing skeletal retention of ^{222}Rn and its radioactive daughters; and in the ^{228}Ra calculations for the diminution of ^{228}Ra activity by radioactive decay as well as for the ingrowth and skeletal retention of ^{228}Th and its radioactive daughters. Radiation dose parameters for each dog were adjusted by his individual retention measurements.

RETENTION

One hundred twenty-five Beagles averaging about 17.7 months of age (excluding 1 dog 7.8 years old) were injected with $0.0436\text{--}25.1\ \mu\text{Ci } ^{226}\text{Ra/kg}$ and seventy-eight Beagles

averaging 17.9 months of age were injected with 0.0159-10.6 μCi $^{228}\text{Ra}/\text{kg}$. All injections were made into the cephalic vein of the forelimb, with the radioactivity in a sodium citrate-citric acid buffer solution (pH 3.5). Details of the experimental design, injection procedure, and veterinary care have been reported. ⁽¹⁾

The retention of ^{226}Ra or ^{228}Ra was measured in each of the animals by gamma-ray counting. Detectors used in total-body counting of ^{226}Ra -injected dogs were the liquid scintillation canine counters K-9 ⁽²⁾ and K-9 Bark II ^(3,4) or a NaI (Tl) crystal counter, ⁽⁴⁾ the last of which was also used to measure the retention of ^{228}Ra dogs.

Since the principal gamma-rays escaping the bodies of dogs containing ^{226}Ra are due to the radon daughters ^{214}Pb (Ra B) and ^{214}Bi (Ra C), their ^{222}Rn content was actually obtained by total-body counting. Radium body burdens were calculated from the body radon content and the Rn/Ra ratio for the appropriate time after injection using the expression ⁽⁵⁾

$$\text{Rn/Ra} = 0.075 t^{0.158} \left(1 - e^{-0.181t} \right)$$

at t days after ^{226}Ra injection. We believe that this indirect method of determining the ^{226}Ra body content is more accurate than the direct method of coupling body ^{222}Rn measurements with the measurement of ^{222}Rn exhalation. Breath radon determinations evaluate the rate of radon escape in the expired air, which may vary considerably over short spans of time. This can introduce inaccuracies into calculation of the body radium content.

The gamma-ray spectrum of a dog injected with ^{228}Ra contains contributions from the γ -emitting daughters of ^{228}Th (the most important of which is ^{208}Tl) as well as from ^{228}Ac , the γ -emitting daughter of ^{228}Ra . When the contributions from these two sources are separated, not only can estimates be made of the ^{228}Ra body burden, but the body content of ^{212}Bi , considered to be in equilibrium with its 3-minute half-period daughter, ^{208}Tl , can also be determined.

When the ^{226}Ra retention data (Table 1) were examined, it became obvious that dogs at the 5 level (10 $\mu\text{Ci/kg}$ injected) retained a much greater fraction of their injected radium than did the dogs at lower levels. Therefore, data for these animals were analyzed separately. A semi-log plot of the ^{226}Ra retention of all animals at the 5-level was made (Figure 1). Points representing serial measurements of the same dog were connected to form "streamlines" of the individual retentions. A curve representing the average retention was drawn so as to pass near the center of the data while still remaining approximately parallel to the slopes of the individual stream lines. Data for dogs of non-standard injection age were not considered in fitting the curve. The equation of this line indicates that total-body retention of injected radium in the Beagle at the 5-level was as if about 41.2% was retained with a biological half-time of 1.2 days, 10.5% with 9.5 days, 19.6% with 142 days, and 28.7% with 2318 days. No 5-level dog survived more than 1380 days after injection, so this equation should not be extrapolated beyond about 4 years.

Retention data for dogs injected with ^{226}Ra at the lower 1, 1.7,

2, 3, and 4 levels (0.04-3.88 $\mu\text{Ci/kg}$) were grouped together for analysis (Figure 2). The retention equation shown in Figure 2 was obtained in a similar fashion to that described for the 5-level. It indicates that the total-body retention of injected ^{226}Ra at lower levels in the Beagle is as if about 25% was retained with a biological half-time of 0.71 days, 21% with 2.6 days, 21% with 43 days, 18% with 347 days, and 15% with 4621 days.

We interpret the higher retention in the 5-level (10 $\mu\text{Ci/kg}$) dogs as a radiation damage effect in the bone remodeling processes at these relatively high ^{226}Ra concentrations. It has been shown (6) that cellular activity and consequent bone remodeling are diminished in our 5-level animals. This higher fractional retention in dogs with relatively high body burdens of ^{226}Ra conforms to the "Matthew Effect" first proclaimed in a very old and much quoted reference: "For to every one who has will more be given, and he will have abundance; but from him who has not, even what he has will be taken away." (Matthew 25:29, Revised Standard Version).

If radiation damage effects are not too severe, the equation for biological retention derived from one radium isotope, such as ^{226}Ra , should fit the observed retention of another radium isotope such as ^{228}Ra . In Figure 3, the measured ^{228}Ra retention in the mesothorium-injected dogs is compared with the retention function for the lower level ^{226}Ra animals. The equation appears to be an adequate representation of the data, and so this comparison provides an independent check of the ^{226}Ra retention equation.

DOSIMETRY

²²⁶Ra. The alpha particle plus recoil energy produced by each ²²⁶Ra disintegration is 4.86 MeV, while the resulting alpha plus beta plus recoil energy from ²²²Rn and its radioactive daughters ²¹⁸Po, ²¹⁴Pb, ²¹⁴Bi, and ²¹⁴Po totals 20.36 MeV. (7) If the Beagle skeleton is 10% of the dog's injection weight, then the mean skeletal dose rate $\frac{dD}{dt}$ from the injection of 1 μ Ci ²²⁶Ra/kg of which a fraction B deposits in bone and releases E MeV per disintegration to the skeleton is (8)

$$\frac{dD}{dt} = 0.512 \ B \ E \ \frac{\text{rads}}{\text{day}}$$

then

$$\left(\frac{dD}{dt}\right)_{\text{Ra alone}} = (0.512) \ (Ra) \ (4.86) \ \frac{\text{rads}}{\text{day}} = 2.488 \ (Ra) \ \frac{\text{rads}}{\text{day}}$$

and

$$\left(\frac{dD}{dt}\right)_{\text{Rn + dau}} = (0.512) \ (Ra) \ \left(\frac{Rn}{Ra}\right) \ (20.36) \ \frac{\text{rads}}{\text{day}} = 10.424 \ (Ra) \ \left(\frac{Rn}{Ra}\right) \ \frac{\text{rads}}{\text{day}}$$

where Ra is the fractional radium retention and Rn/Ra is the radon to radium ratio in the skeleton at t days after injection.

The sum of these two expressions is the total dose rate in rads per day:

$$\left(\frac{dD}{dt}\right)_{\text{Ra + Rn + dau}} = 2.488 \ (Ra) + 10.424 \ (Ra) \ \left(\frac{Rn}{Ra}\right)$$

The fractional radium retention (Ra) is given for any time t after injection by the appropriate retention equation (5-level or lower-level), and the radon to radium ratio (Rn/Ra) can be determined from ⁽⁵⁾

$$Rn/Ra = 0.075 t^{0.158} (1 - e^{-0.181 t})$$

The dose rate for other than a 1 μ Ci/kg injection is found by multiplying by the actual injected μ Ci ²²⁶Ra/kg. Cumulative average skeletal dose in rads can be adequately approximated by a numerical integration of all daily dose rates, in rads per day, from zero to t days after injection. We have adjusted the calculated radiation dose to each animal for his individual retention measurements.

These calculations ignore the contribution to the skeletal dose rate and dose from ²¹⁰Pb and its radioactive daughters ²¹⁰Bi and ²¹⁰Po (total energy = 5.72 MeV). Assuming no loss of ²¹⁰Pb from the skeleton, we calculate that during the first 10 years after injection, the ²¹⁰Pb activity in bone averages about 0.4% of the injected ²²⁶Ra activity. The cumulative skeletal radiation dose from ingrown ²¹⁰Pb for the first 10 years is calculated to be about 1.7% that from ²²⁶Ra plus ²²²Rn and daughters through ²¹⁴Po. During the first 20 years, the ²¹⁰Pb dose would be about 5.6% of that from ²²⁶Ra plus ²²²Rn-²¹⁴Po. These two estimates of ²¹⁰Pb dose may be unrealistically high, however, as they are based on the assumption of no ²¹⁰Pb excretion. This underestimation of the total dose by about 2%-6% has been somewhat compensated for in the cumulative dose calculated for the long-

term animals by an equivalent 3% overestimation of the ^{226}Ra activity in our original ^{226}Ra γ -ray standard with which most of the injection solutions were compared for evaluation. This was a result of assuming $1 \mu\text{g } ^{226}\text{Ra} = 1 \mu\text{Ci}$, while the actual relationship is $1 \mu\text{g } ^{226}\text{Ra} = 0.97 \mu\text{Ci}$. In any case, the total effect of these two opposing sources of error probably amounts to only a very few percent in the dosimetry of our long-term ^{226}Ra -injected dogs.

^{228}Ra . When the biological retention equation for ^{226}Ra at the lower levels is used for the ^{228}Ra dogs (Figure 3), it must be corrected for the radioactive decay of ^{228}Ra to obtain the effective retention for purposes of dosimetry. For a 5.77 year half-period, ⁽⁹⁾ the effective retention of ^{228}Ra in our Beagles becomes

$$\text{Ret}_{\text{eff}} = 0.25 e^{-0.982 t} + 0.21 e^{-0.269 t} + 0.21 e^{-0.0158 t} + \\ + 0.18 e^{-0.00237 t} + 0.15 e^{-0.000479 t}$$

The average beta particle energy deposited by each disintegration of $^{228}\text{Ra} + ^{228}\text{Ac}$ is 0.42 MeV, while the resulting alpha + beta + recoil energy from ^{228}Th and its radioactive daughters ^{224}Ra , ^{220}Rn , ^{216}Po , ^{212}Pb , ^{212}Bi , ^{212}Po and ^{208}Tl totals 33.24 MeV. ⁽⁷⁾ If the Beagle skeleton is 10% of the dog's injection weight, then the mean skeletal dose rate $\frac{dD}{dt}$ from the injection of $1 \mu\text{Ci } ^{228}\text{Ra}/\text{kg}$ of which a fraction B deposits in bone and releases E MeV per disintegration to the skeleton is ⁽⁸⁾

$$\frac{dD}{dt} = 0.512 B E \frac{\text{rads}}{\text{day}}$$

$$\frac{dD}{dt} \bigg|_{^{228}\text{Ra} + ^{228}\text{Ac}} = 0.512 (\text{MsTh}) (0.42) \frac{\text{rads}}{\text{day}} = 0.215 (\text{MsTh}) \frac{\text{rads}}{\text{day}}$$

$$\frac{dD}{dt} \bigg|_{^{228}\text{Th} \rightarrow ^{208}\text{Pb}} = 0.512 (\text{Bi}) (33.24) \frac{\text{rads}}{\text{day}} = 17.019 (\text{Bi}) \frac{\text{rads}}{\text{day}}$$

where (MsTh) is the fractional ^{228}Ra retention and Bi is the body ^{212}Bi content relative to retained ^{228}Ra at $\underline{t}$ days after injection.

The sum of these two expressions is the total mean skeletal dose rate in rads per day:

$$\frac{dD}{dt} \bigg|_{^{228}\text{Ra} \rightarrow ^{208}\text{Pb}} = 0.215 (\text{MsTh}) + 17.019 (\text{Bi})$$

The fractional ^{228}Ra retention (MsTh) is given for any time $\underline{t}$ after injection by the effective ^{228}Ra retention equation. Small losses of ^{220}Rn ⁽¹⁰⁾ in the breath and ^{224}Ra ⁽¹¹⁾ in excreta occur in ^{228}Ra -burdened dogs. Almost no losses of ^{228}Th occur. ⁽¹¹⁾ Therefore, the body content of ^{212}Bi is only slightly less than the body ^{228}Th content. If the simplifying assumption is made that these excess losses have a minor effect, then at any time after injection the ^{228}Th produced by the radioactive decay of ^{228}Ra in the skeleton can be considered approximately equal to the measured body content of ^{212}Bi which is also produced by the radioactive decay of injected ^{228}Ra . The relationship between the body ^{228}Th activity and the injected ^{228}Ra activity as a function of time $\underline{t}$ (given on page 33 of Reference 12) is:

$$^{228}\text{Th} = ^{228}\text{Ra})_0 \left(\frac{\lambda_2}{\lambda_2 - \lambda_1} \right) (e^{-\lambda_1 t} - e^{-\lambda_2 t})$$

where $^{228}\text{Ra})_0$ = initial ^{228}Ra activity

λ_1 = effective decay constant of ^{228}Ra

λ_2 = effective decay constant of ^{228}Th
(if no excretion of ^{228}Th is assumed, then

λ_2 = the radioactive decay constant = 0.0009936 / day)

If the ^{228}Th resulting from ^{228}Ra decay is calculated separately for each component of the effective retention equation of ^{228}Ra , the sum of these separate calculations is the retained ^{228}Th from ^{228}Ra decay assuming no biological loss of ^{228}Th from its sites of production. After subtraction of the body ^{212}Bi produced by ^{228}Th in the injection solution, ⁽¹³⁾ the measured ($^{212}\text{Bi}/^{228}\text{Ra}$) in the dog is divided by the calculated ($^{228}\text{Th}/^{228}\text{Ra}$) to obtain a ($^{212}\text{Bi}/^{228}\text{Th}$) ratio, which is an indication of the retention of the daughters of in vivo-produced ^{228}Th . Results of 136 measurements between 1963 and 1969 of 47 living dogs at 294 to 3899 days after injection gave an average ($^{212}\text{Bi}/^{228}\text{Th}$) ratio of 0.84 with a standard deviation of 0.01. No dependence of this ($^{212}\text{Bi}/^{228}\text{Th}$) ratio upon time after injection was apparent from the data. Since the fractional retention of the in vivo-produced ^{228}Th daughters was relatively uniform from dog to dog and did not appear to change significantly with time, the value of the body ^{212}Bi content could be calculated for ^{228}Ra -injected dogs using the ^{228}Ra effective retention equation, the theoretical ($^{228}\text{Th}/^{228}\text{Ra}$) ratio and the 84% retention of daughters.

The mean skeletal dose rate for other than a 1 $\mu\text{Ci/kg}$ injection

is found by multiplying by the actual injected $\mu\text{Ci/kg}$. Cumulative average skeletal dose from injected ^{228}Ra and its daughters produced in vivo can be approximated by a numerical integration of all the daily dose rates from zero to t days after injection. Radiation doses from ^{228}Th and daughters in the injection solution must be determined separately and added to the ^{228}Ra dose to obtain totals. We have adjusted the calculated dose to each animal for his individual retention measurements.

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Figure 1. Radium retention in beagles at the 5-level (10 μCi $^{226}\text{Ra/kg}$ injected).

Figure 2. Radium retention in beagles at the lower levels (0.04-3.88 $\mu\text{Ci } ^{226}\text{Ra/kg}$ injected).

Figure 3. Radium retention in beagles injected with ^{228}Ra (mesothorium).

Table 1. Retention of injected ^{226}Ra in beagles indicated by total-body gamma-ray counting of the retained daughters of ^{222}Rn and corrected for the time-dependent Rn/Ra ratio (see p.). Body retention measurements were made with liquid scintillation counters (K9 or K9II), or crystal counter (NaI) or were calculated from the measurement of the ^{226}Ra content of individual bones and tissues after autopsy *.

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{226}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
M1R1	471	0.0618	2503	8.8	K9II
			3026	8.5	K9II
			5168	5.1	NaI
M2R1	627	0.0876	2272	8.3	K9II
			2816	8.5	K9II
F3R1	706	0.0576	2702	5.4	K9II
			3408	5.5	K9II
			3408	4.4	NaI
M5R1	490	0.0436	2026	12.5	K9II
			2600	11.9	K9II
			3306	9.1	NaI
F6R1	483	0.0584	1987	10.2	K9II
			2565	10.2	K9II
			3272	10.8	K9II
			3272	8.4	NaI
			4704	7.9	NaI
M7R1	511	0.0651	1927	11.9	K9II
			2537	11.0	K9II
F8R1	861	0.0559	1803	7.6	K9II
			2418	8.9	K9II
			2988	7.7	K9II
F9R1	781	0.0521	1190	8.9	K9II
			2319	6.5	K9II
			3018	7.5	K9II
			3018	5.5	NaI
			3760	6.3	NaI
M1OR1	523	0.0573	1574	10.5	K9II
			2212	13.2	K9II
			3654	9.2	NaI

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{226}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
F11R1	511	0.0522	1463	8.4	K9II
			2066	11.1	K9II
			2767	10.2	K9II
			2767	8.7	NaI
			3508	7.4	NaI
			4193	7.2	NaI
F12R1	501	0.0444	1386	12.2	K9II
			2040	11.6	K9II
			2743	10.4	K9II
			2743	10.2	NaI
			3480	11.3	NaI
M13R1	529	0.0527	139	32.0	K9II
			139	30.2	NaI
			512	24.4	NaI
			1202	19.8	NaI
F14R1	510	0.0701	279	31.2	NaI
			470	24.2	NaI
M15R1	490	0.0797	176	27.0	NaI
			866	20.4	NaI
F16R1	501	0.0611	805	15.1	NaI
			1617	8.6	NaI
M17R1	494	0.0639	420	20.0	NaI
			1232	13.3	NaI
F18R1	496	0.0589	393	20.4	NaI
			1204	11.6	NaI
F19R1	526	0.0682	253	24.8	NaI
			1063	14.7	NaI
M20R1	536	0.061	175	30.2	NaI
			986	16.5	NaI
F21R1	525	0.0633	151	20.8	NaI
			958	9.8	NaI
M22R1	484	0.0861	98	40.3	NaI
			904	23.0	NaI
F31R1B	501	0.0712	547	17.3	NaI
			1359	13.4	NaI

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{226}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
T41R1	899	0.0487	63	24.6	K9II
M1R1.7	523	0.137	1501	10.1	K9II
			2024	9.9	K9II
			2744	8.4	NaI
			3479	8.8	NaI
			4166	7.2	NaI
M2R1.7	598	0.163	1162	8.4	K9II
			1273	8.3	K9II
M2R1.7A	493	0.222	139	35.9	K9II
			139	37.0	NaI
			874	25.2	NaI
			1561	22.2	NaI
F3R1.7	473	0.165	2052	12.0	K9II
			2758	11.4	NaI
			2758	11.1	NaI
M4R1.7	514	0.163	1508	15.9	K9II
			2052	9.7	K9II
			2759	9.8	K9II
			2759	8.7	NaI
			3507	8.5	NaI
			4193	7.0	NaI
M5R1.7	511	0.151	1480	14.0	K9II
			2054	14.1	K9II
			2760	11.9	K9II
			2760	11.4	NaI
			3507	11.6	NaI
F6R1.7	491	0.152	1476	14.6	K9II
			2054	14.5	K9II
			2761	13.9	K9II
			2761	13.7	NaI
M7R1.7	598	0.163	1098	10.5	K9II
			1708	10.6	K9II
			2418	9.7	K9II
			2418	9.0	NaI
F8R1.7	491	0.154	1430	14.0	K9II
			2054	14.4	K9II
			2577	14.3	K9II

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{226}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
F9R1.7	598	0.168	1183	7.2	K9II
			1720	7.0	K9II
			2420	6.6	K9II
			2420	5.7	NaI
			3162	4.8	NaI
			3848	6.8	NaI
M10R1.7A	545	0.183	314	14.7	K9II
			952	13.7	K9II
			1652	11.3	K9II
			1652	10.8	NaI
			2394	9.8	NaI
			3080	8.9	NaI
F11R1.7	598	0.165	3900	8.6	NaI
			1077	7.7	K9II
			1720	7.3	K9II
			2425	7.0	K9II
			2425	6.2	NaI
			3162	4.4	NaI
F12R1.7	590	0.167	3847	5.1	NaI
			1068	9.0	K9II
T43R1.7	963	0.145	1722	8.9	K9II
			64	27.4	K9II
M1R2	471	0.382	419	20.9	K9
			470	19.1	K9
			606	18.1	K9
			697	14.0	K9
			878	15.4	K9
			906	15.6	K9
			1030	20.4	K9
			2503	8.6	K9II
			3026	8.8	K9II
			3440	9.9	K9II
M2R2	592	0.387	277	16.8	K9
			400	14.7	K9
			470	14.6	K9
			669	11.4	K9
			809	11.5	K9
			2272	5.8	K9II
			2816	5.4	K9II
			3521	5.2	NaI

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{226}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
F3R2	541	0.347	8	42.5	K9
			14	48.2	K9
			22	45.1	K9
			36	37.4	K9
			128	28.3	K9
			293	21.1	K9
			370	20.3	K9
			2158	8.2	K9II
			2702	8.6	K9II
			3408	8.3	K9II
			3408	7.6	NaI
M4R2	414	0.361	8	66.9	K9
			29	63.4	K9
			110	36.9	K9
			168	33.0	K9
			272	29.6	K9
			359	28.5	K9
			1761	15.6	K9II
M4R2A	420	0.306	158	30.4	K9
			2305	15.9	K9II
			3012	13.9	NaI
M5R2	461	0.267	3	52.4	K9
			16	50.9	K9
			36	44.0	K9
			203	31.0	K9
			426	25.1	K9
			565	26.5	K9
			2026	15.2	K9II
			2600	15.2	K9II
			3307	13.5	K9II
			3307	13.2	NaI
			4053	13.2	NaI
F6R2	486	0.360	2	82.3	K9
			13	52.5	K9
			276	29.0	K9
			388	28.6	K9
			1987	12.9	K9II
			2565	13.1	K9II
			3275	12.2	K9II
			3275	11.6	NaI
			4018	9.1	NaI

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci }^{226}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
M7R2	514	0.413	255	22.9	K9
			360	20.0	K9
			455	17.2	K9
			1927	9.4	K9II
			2537	10.1	K9II
			3425	10.0	K9II
			3425	9.1	NaI
F8R2	572	0.331	366	24.6	K9
			1803	10.8	K9II
			2418	10.3	K9II
			3129	9.3	K9II
			3129	9.2	NaI
			3871	8.7	NaI
			4557	8.1	NaI
F9R2	592	0.317	186	20.5	K9
			1190	10.6	K9II
			2319	8.8	K9II
			3018	8.0	K9II
			3018	8.1	NaI
			3761	7.2	NaI
M10R2	523	0.345	1574	15.6	K9II
			2212	16.7	K9II
			3278	14.2	NaI
F11R2	495	0.310	1003	18.2	K9II
			1463	12.0	K9II
			2066	13.7	K9II
			2767	11.6	K9II
			2767	11.7	NaI
F12R2	497	0.281	1386	13.5	K9II
			2040	14.5	K9II
			2744	12.6	K9II
			2744	12.2	NaI
			2948	12.6	K9II
			2948	12.3	NaI
M1R3	473	1.20	419	17.6	K9
			470	19.0	K9
			606	17.9	K9
			697	17.9	K9
			1030	16.7	K9
			2503	9.1	K9II

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{226}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
M2R3	470	1.21	277	19.9	K9
			400	17.7	K9
			470	17.4	K9
			809	14.3	K9
			2226	7.8	K9II
F3R3	386	1.11	8	44.7	K9
			14	54.8	K9
			22	52.1	K9
			36	50.4	K9
			57	46.9	K9
			128	35.9	K9
			293	27.8	K9
			370	25.7	K9
			2158	10.2	K9II
M4R3	412	1.16	8	63.4	K9
			29	55.5	K9
			110	39.8	K9
			168	36.4	K9
			272	32.4	K9
			359	29.5	K9
			1917	16.2	K9II
M5R3	461	0.846	3	61.5	K9
			16	58.6	K9
			36	50.9	K9
			203	35.7	K9
			565	28.0	K9
			2026	16.0	K9II
			2955	12.9	K9II
F6R3	486	1.14	2	87.4	K9
			13	54.0	K9
			276	32.6	K9
M7R3	514	1.29	225	30.8	K9
			455	27.9	K9
			1927	15.0	K9II
			2099	17.6	K9II
			2099	17.1	*
F8R3	542	1.03	150	30.7	K9
			366	21.4	K9
			1803	10.0	K9II
			2430	9.9	K9II
			2612	9.4	K9II

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{226}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
F9R3	551	0.987	186	28.3	K9
			1190	14.3	K9II
			2319	9.8	K9II
			2487	9.9	K9II
M10R3	525	1.06	1574	15.4	K9II
			1737	19.1	K9II
			1737	19.6	*
F12R3	497	0.883	1386	15.5	K9II
T32R3	471	1.13	66	28.5	K9II
			121	26.1	K9II
			185	24.0	K9II
			233	21.2	K9II
			282	24.0	K9II
			337	20.0	K9II
			486	19.8	K9II
			586	18.8	K9II
			899	17.0	K9II
			1585	14.1	NaI
T33R3	471	1.15	66	36.5	K9II
			121	32.5	K9II
			185	29.2	K9II
			233	22.0	K9II
			282	21.8	K9II
			337	25.0	K9II
			486	23.9	K9II
			586	22.0	K9II
			904	19.6	K9II
			1581	16.5	NaI
T34R3	470	1.12	1822	14.2	NaI
			66	32.3	K9II
			121	27.4	K9II
			185	26.5	K9II
			233	19.2	K9II
			282	21.3	K9II
			337	21.4	K9II
			486	19.8	K9II
			586	19.6	K9II
			899	18.5	K9II
T35R3J	670	0.951	1581	15.6	NaI
			8	55.6	*

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{226}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
T44R3	938	0.937	68	24.9	K9II
T46R3	810	0.928	69	36.1	K9II
T63R3	559	0.899	36 36	39.4 37.7	K9II NaI
T64R3	551	0.919	63 63	28.0 29.2	K9II NaI
T65R3	551	0.922	70 70	34.2 34.1	K9II NaI
T66R3	549	0.904	132 132	23.9 23.5	K9II NaI
T67R3	549	0.898	134 134	28.7 27.6	K9II NaI
T68R3	549	0.917	175 548 1227	19.9 14.9 12.2	NaI NaI NaI
T69R3	499	0.919	175 548	27.4 16.5	NaI NaI
T70R3	499	0.922	175 548 1227	34.3 26.1 22.9	NaI NaI NaI
M1R4	471	3.51	419 470 606 697 1030	31.1 27.5 23.9 23.1 19.6	K9 K9 K9 K9 K9
M2R4	470	3.55	277 400 470 809 1884	25.8 24.1 22.6 19.3 12.8	K9 K9 K9 K9 *
F3R4	384	3.33	8 14 22 36 57 128 293 370	40.2 53.6 51.4 49.7 45.9 37.1 31.5 29.4	K9 K9 K9 K9 K9 K9 K9 K9

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci }^{226}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
F3R4A	598	3.10	1162	12.5	K9II
M4R4	408	3.47	8	69.4	K9
			29	52.8	K9
			110	40.2	K9
			168	36.4	K9
			272	33.8	K9
			359	31.6	K9
M5R4	461	2.42	3	70.6	K9
			16	62.0	K9
			36	55.3	K9
			203	34.8	K9
			565	28.9	K9
F6R4	486	3.44	2	87.0	K9
			13	54.1	K9
			276	34.1	K9
			1943	16.3	K9II
M7R4	453	3.88	255	24.9	K9
			455	21.6	K9
			1647	14.0	K9II
F8R4	474	3.14	150	36.6	K9
			366	26.2	K9
F9R4	542	3.02	186	26.3	K9
			1190	15.6	K9II
M10R4	527	3.28	1553	21.2	K9II
F11R4	491	2.84	1463	18.1	K9II
F12R4	496	2.81	1386	14.0	K9II
T15R4	672	3.11	1864	11.1	K9II
			2127	10.8	K9II
T36R4	695	2.99	244	30.5	K9II
			925	17.1	K9II
			925	16.3	NaI
			1154	15.6	K9II
			1154	15.4	NaI
T37R4	695	3.00	244	23.2	K9II
			922	10.8	K9II
			922	10.7	NaI

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{226}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
T38R4	695	3.02	244	27.8	K9II
			925	13.8	K9II
			925	13.4	NaI
			1503	10.1	NaI
T57R4	501	2.72	14	39.2	K9II
T58R4	496	2.41	61	44.3	K9II
T59R4	496	2.57	63	38.0	K9II
T60R4	490	2.33	117	31.2	K9II
T61R4	490	2.70	342	29.7	K9II
			342	28.3	NaI
			371	27.4	K9II
			371	27.4	NaI
T62R4	490	2.68	342	25.1	K9II
			342	24.0	NaI
M1R5	473	10.5	419	32.8	K9
			470	33.3	K9
			606	28.9	K9
			697	29.4	K9
			878	27.0	K9
			906	26.7	K9
M2R5	470	10.8	277	32.8	K9
			400	29.0	K9
			470	27.1	K9
			669	24.0	K9
			809	23.3	K9
			1380	18.7	*
F3R5	380	10.1	8	42.5	K9
			14	51.3	K9
			22	49.4	K9
			36	45.8	K9
			57	44.0	K9
			128	38.5	K9
			293	34.1	K9
			370	32.0	K9

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{226}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
M4R5	408	10.6	8	64.4	K9
			29	50.9	K9
			110	40.6	K9
			168	38.2	K9
			272	35.8	K9
			359	33.7	K9
			527	31.2	K9
			1091	24.0	*
M5R5	458	10.1	3	61.8	K9
			16	54.6	K9
			36	49.2	K9
			203	33.6	K9
			426	27.2	K9
			565	25.8	K9
F6R5	486	10.2	2	83.9	K9
			13	49.8	K9
			276	35.7	K9
			388	33.3	K9
			1017	29.2	*
M7R5	453	11.9	255	27.6	K9
			360	26.8	K9
			455	24.8	K9
F8R5	474	9.68	150	36.8	K9
			366	26.6	K9
			968	20.8	*
F9R5	420	9.48	186	36.2	K9
			1190	22.6	K9II
T1R5	995	10.3	372	17.8	K9
			422	20.3	K9
			455	20.2	K9
			526	18.5	K9
			834	14.2	K9
			1071	13.4	K9
T2R5	919	4.39	380	19.4	K9
			474	18.3	K9
			484	19.3	K9
			791	14.3	K9
			1155	12.1	K9
			1368	12.1	*

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{226}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
T3R5	1465	4.76	380	13.0	K9
			413	12.4	K9
			428	11.6	K9
			428	11.6	*
T4R5	459	10.6	1	82.6	*
T12R5	397	9.72	225	25.4	*
T13R5	397	9.76	188	26.7	*
T16R5	604	9.68	12	44.2	*
T29R5	474	10.4	10	48.7	K9II
			66	38.6	K9II
			121	34.6	K9II
			185	34.7	K9II
T30R5	474	10.4	10	49.1	K9II
			66	38.2	K9II
			121	36.3	K9II
T31R5	471	10.4	66	38.4	K9II
			121	36.5	K9II
			185	34.6	K9II
			233	32.2	K9II
			282	27.9	K9II
			303	31.6	K9II
T49R5	485	7.54	5	84.6	NaI
T50R5	485	7.46	15	68.5	NaI
T51R5	418	8.48	54	53.6	K9II
			54	54.1	NaI
			92	50.9	K9II
			92	50.4	NaI
T52R5	418	8.57	15	56.0	NaI
T53R5	418	8.50	33	57.2	K9II
			33	53.2	NaI
T55R5	417	8.61	33	49.4	K9II
			33	45.8	NaI

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{226}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
T56R5	417	8.61	40	49.5	K9II
			40	45.6	NaI
			90	45.6	K9II
			90	44.3	NaI
T48R6	2842	25.1	49	31.8	*

Table 2. Retention of injected ^{228}Ra and ^{212}Bi content in beagles measured by total-body gamma-ray counting using a NaI(Tl) crystal counter or calculated from the measurement of the ^{228}Ra content of individual bones.*

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{228}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION OF ^{228}Ra	OBSERVED $^{212}\text{Bi}/^{228}\text{Ra}$
F1M0.5	492	0.0173	392	15.4	0.412
			1113	10.8	0.960
			1788	9.4	1.325
			2617	8.2	1.309
F2M0.5	492	0.0173	393	24.1	0.377
			1395	16.1	1.157
			2224	14.3	1.423
M3M0.5	493	0.0199	330	23.1	0.375
			1049	16.3	0.910
			1725	15.0	1.120
			2554	12.5	1.595
M4M0.5	475	0.0199	330	23.9	0.387
			1049	18.3	0.886
			1725	15.2	1.272
			2555	15.8	1.280
M5M0.5	534	0.0172	296	22.6	0.297
			1014	14.4	0.844
			1689	12.7	1.155
			2519	11.4	1.466
M6M0.5	510	0.0171	297	22.5	0.300
			1014	15.0	0.963
			1689	12.9	1.184
			2519	12.4	1.376
F7M0.5	492	0.0172	395	24.6	0.415
			1113	17.9	0.885
			1787	16.0	1.046
			2617	13.8	1.380
F8M0.5	654	0.0159	1258	12.8	1.000
			1973	9.3	1.481
			2647	9.8	1.236
			3474	8.7	1.525
M9M0.5	485	0.0170	1224	13.9	0.957
			1939	13.6	1.305
			2612	13.1	1.273
			3439	11.7	1.430

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{228}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION OF ^{228}Ra	OBSERVED $^{212}\text{Bi}/^{228}\text{Ra}$
M10M0.5	492	0.0174	400 1114 1786 2618	24.3 17.1 16.8 14.6	0.407 0.902 1.062 1.346
F11M0.5	505	0.0202	338 1053 1723 2551	23.4 16.1 13.5 12.9	0.350 0.817 1.219 1.285
M12M0.5	510	0.0165	304 1018 1688 2519	22.7 16.8 14.9 11.6	0.296 0.914 1.082 1.602
F1M1	718	0.0463	2952	7.3*	
F1M1A	590	0.0512	294 1015 1690 2516	19.5 13.2 11.3 9.7	0.329 0.837 1.145 1.544
F2M1	459	0.0324	3180 3899	10.7 10.8	1.585 1.507
M3M1	575	0.0589	2715 3154 3157	11.7 11.9 11.6*	1.462 1.496
M4M1	601	0.0481	2403 3121 3796	5.8 5.6 4.6	1.539 1.448 1.560
F5M1	658	0.0490	2354 3747	8.7 6.5	1.389 1.603
M6M1	521	0.0468	2306 3025	14.8 13.0	1.337 1.621
F7M1	534	0.0489	2159	11.1*	
F8M1	654	0.0491	1258 1973 2647	13.8 12.2 11.4	1.034 1.348 1.452

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{228}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION OF ^{228}Ra	OBSERVED $^{212}\text{Bi}/^{228}\text{Ra}$
M9M1	485	0.0504	1224	16.3	1.034
			1938	14.1	1.262
			2612	13.5	1.378
			3439	12.6	1.354
M10M1	492	0.0501	400	22.2	0.405
			1114	16.3	0.859
			1786	13.4	1.140
F11M1	505	0.0613	338	27.0	0.329
			1051	18.1	0.908
			1723	17.3	1.130
			2551	14.0	1.380
M12M1	528	0.0498	304	23.4	0.310
			1018	14.6	0.899
			1688	12.7	1.199
			2516	11.5	1.340
F1M1.7	510	0.151	294	19.9	0.303
			1015	15.2	0.851
			1690	12.5	1.237
			2516	11.0	1.397
F2M1.7	560	0.183	2383	12.2*	
M3M1.7	576	0.180	2709	10.9	1.456
			2709	10.0*	
M4M1.7	601	0.143	2403	8.2	1.462
F5M1.7	658	0.141	2354	11.2	1.386
			3072	10.4	1.480
M6M1.7	521	0.144	2306	6.9	1.374
			3024	6.0	1.547
F7M1.7	534	0.146	2267	12.0	1.311
			2646	12.0*	
F8M1.7	654	0.148	1259	10.5	1.095
			1973	8.6	1.313
M9M1.7	485	0.149	1224	16.8	0.998
			1939	14.2	1.279
			2611	12.6	1.379

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{228}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION OF ^{228}Ra	OBSERVED $^{212}\text{Bi}/^{228}\text{Ra}$
M10M1.7	492	0.124	400	29.8	0.404
			1114	16.3	0.933
			1786	20.9	1.169
			2614	18.3	1.361
F11M1.7	505	0.179	338	25.2	0.343
			1051	19.6	0.868
			1723	17.6	1.140
			2551	15.6	1.326
M12M1.7	524	0.153	304	22.4	0.322
			1018	16.6	0.834
			1688	17.5	1.128
			2516	13.4	1.325
F1M2	676	0.276	1780	9.3*	
F2M2	517	0.194	965	10.4*	
M3M2	576	0.358	619	22.0*	
M4M2	601	0.282	2282	12.4*	
F5M2	509	0.295	2358	9.1	1.402
			2688	8.3	1.478
			2688	9.2*	
M6M2	502	0.306	2306	12.0	1.276
			2674	13.9	1.373
F7M2	534	0.298	2239	13.2	1.326
			2239	11.6*	
F8M2	654	0.300	1261	12.9	0.969
			1973	10.6	1.304
M9M2	630	0.302	1226	15.0	0.936
			1254	14.4	0.964
			1254	14.7*	
M10M2	430	0.311	400	25.6	0.399
			1114	20.8	0.902
			1786	19.7	1.132

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{228}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION OF ^{228}Ra	OBSERVED $^{212}\text{Bi}/^{228}\text{Ra}$
F11M2	505	0.381	338	14.9	0.357
			1053	10.7	0.833
			1723	9.7	1.159
			2551	8.5	1.360
M12M2	524	0.306	304	25.7	0.308
			1018	19.6	0.854
			1688	17.5	1.111
F1M3	519	0.858	918	16.8*	
F2M3	460	0.612	1856	14.2*	
M3M3	579	0.965	1185	20.8*	
M4M3	601	0.916	1176	15.2*	
F5M3	531	0.940	1869	10.0*	
M6M3	502	0.953	1421	13.0*	
F7M3	534	0.907	1463	21.7*	
F8M3	633	0.950	1259	13.4	0.964
			1447	16.1*	
M9M3	630	0.918	1224	12.4	0.982
			1570	13.8	1.068
			1570	16.8*	
M10M3	581	1.00	400	20.4	0.419
			1114	16.4	0.923
F11M3	499	1.19	338	21.6	0.336
			1053	17.4	0.867
M12M3	510	0.987	304	20.8	0.347
			1018	17.8	0.831
F1M4	510	2.60	841	20.7*	
F2M4	460	1.86	778	19.3*	
M3M4	579	3.37	418	24.4*	
M3M4A	494	2.64	1063	22.0*	

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{228}\text{Ra/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION OF ^{228}Ra	OBSERVED $^{212}\text{Bi}/^{228}\text{Ra}$
M4M4	609	2.47	896	14.9*	
F5M4	509	2.67	1064	16.8*	
M6M4	502	2.66	1121	17.1*	
F7M4	544	2.67	1253	13.7*	
T1M4.5	529	4.23	314	28.5*	
T2M4.5	463	4.27	775	19.7*	
F2M5	460	5.46	780	22.5*	
M3M5	579	10.4	688	27.5*	
M4M5	482	7.89	561	22.9*	
F5M5	658	8.48	770	20.3*	
M6M5	580	8.67	792	13.2*	
F7M5	494	8.92	966	24.8*	
T3M5	579	10.6	700	29.7*	

*Calculated from gamma-ray counting of individual bones.

✓ DISTRIBUTION OF INJECTED ^{226}Ra IN THE BEAGLE SKELETON

Charles W. Mays, Ray D. Lloyd, and David R. Atherton

Abstract: The ^{226}Ra content of individual bones from 9 adult Beagles dying 1-2099 days after the injection of 0.163-10.6 $\mu\text{Ci } ^{226}\text{Ra/kg}$ was determined by gamma-ray counting. Bones were sealed in cans and frozen. About 24% of the retained skeletal radium was in the head and neck, 30% in the rib cage and thoracic and lumbar spine, 19% in the forelimbs and shoulder girdle, 23% in the hindlimbs and hip girdle, and 2% in the tail. The fraction of retained skeletal radium accounted for by some bones appeared to be dependent upon time after injection. This relationship was statistically significant for thoracic vertebrae (negative slope) and for cervical vertebrae, hindpaws, and forepaws (positive slope). In no case did the absolute value of the calculated slope exceed 1% of the retained total skeletal radium per year. There was a significant difference between the animals injected with about 10 $\mu\text{Ci/kg}$ and those given less ^{226}Ra in the relative distribution of retained activity in bones containing much trabecular or much cortical bone at burden times of more than one month, which is attributed to radiation damage of the bone remodeling processes in the high-level dogs.

INTRODUCTION

A previous report ⁽¹⁾ summarized the average bone-by-bone distribution of radium in the skeletons of 4 Beagles injected with ^{226}Ra in citrate buffer as young adults. The number of animals for which these measurements have been made now totals 9, and data for each dog as well as new averages are given.

METHODS

Individual bones obtained at autopsy were defleshed, centered in #2 cans, sealed, and frozen. The gamma-ray counting rate of each sample was compared with that of a National Bureau of Standards equilibrated ^{226}Ra standard in a glass ampoule, centered inside an

identical can. The detector used was either a liquid scintillation counter or an 8 inch x 4 inch NaI(Tl) crystal. Counting of most bones was delayed for at least a month after sealing to ensure secular equilibrium between ^{226}Ra and its daughters. Some samples were counted at least twice during the first 3 weeks after sealing, and their ^{226}Ra activity was calculated from the ingrowth of ^{222}Rn daughters.

RESULTS AND DISCUSSION

Table 1 lists the results of the measurements for all 9 dogs in the study, 4 of which (T4R5, T16R5, F8R5, and M2R5) provided the ^{226}Ra distribution data reported in Reference 1. Also tabulated are the averages and experimental standard deviations. All data are given in terms of percent of retained skeletal radium. The averages exhibited in Table 1 are similar to the radium skeletal distribution values reported previously. Averages in both reports are compared in Table 2.

A test of the linear relationship between percent retained skeletal radium in each bone and time after injection was made. Equations were fit to the data with the aid of a Univac 1108 computer by the method of least squares, and the resulting slopes were tested for significance using F values. Table 3 lists the results of these calculations. Although 4 of the slopes were significantly different from zero based on the F test, none of them exceeded an absolute value of 1% of the retained skeletal radium per year.

Animals at the 5-level ($10\mu\text{Ci/kg}$ injected) retain a greater fraction of their injected ^{226}Ra than dogs at lower levels

($\leq 3\mu\text{Ci/kg}$). ⁽²⁾ A group comparison test was therefore made of the values shown in Table 1 for each bone using two 5-level dogs (F8R5 and M2R5) and the five lower-level dogs (T28R3, M2R1.7, M10R3, M2R4, and M7R3) as the two groups. This was done in an attempt to determine if an impairment of bone remodeling, and therefore loss of skeletal radium, could be found. The 2 animals in the study which survived less than one month after injection were not considered because the radiation damage effects on radium retention could probably not be seen at these early times. ⁽³⁾

It might be expected that a relatively higher initial concentration of ^{226}Ra in parts of the skeleton with a large proportion of trabecular bone would be observed; this would be followed by a gradual relative increase in those parts with a larger proportion of cortical bone as remodeling proceeds in the lower-level dogs. If radiation damage effects were to be detected at the 5-level, concentrations may remain high in the trabecular bone and low in cortical bone as a consequence of interference with remodeling. Table 4 exhibits the results of the group comparison tests. In 8 of the 18 tests the means of the two groups were found to be significantly different at the 0.05 level. However, the 5-level animals had a relative mean greater than the lower levels for the fairly trabecular lumbar vertebrae and for the extremely trabecular sternum, while the 5-level values were lower for the radius, ulna, fibula, and tibia, which contain much cortical bone. The skull and upper teeth as well as the mandible and lower teeth showed decreased averages for the 5-level dogs. Animals at the 5-level characteristically lose teeth

while lower-level dogs retain their teeth much better. This effect is illustrated by data in Table 1. The two 5-level animals dying 1 and 12 days after injection had values for skull and upper teeth near the average for all nine dogs, while values for F8R5 (which lost 6 upper and 7 lower teeth before death) and M2R5 (which lost 12 upper and 6 lower teeth before death) are both much lower. This trend is also suggested by data for mandible and lower teeth. These observed differences may be accounted for in part by tooth loss at the 5-level.

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Table 1.

Distribution of skeletal radium in 9 Beagles injected with ^{226}Ra as young adults. Data shown are percent of skeletal radium values. All dogs were males except F8R5.

DOG	T4R5	T16R5	T28R3	F8R5	M2R1.7	M2R5	M1OR3	M2R4	M7R3	AVERAGE	STANDARD DEVIATION
DAYS AGE AT INJ.	459	604	512*	474	598	470	525	470	514	514	
DAYS INJ. TO DEATH	1	12	247*	968	1273	1380	1737	1884	2099	1067	
INJ. $\mu\text{Ci } ^{226}\text{Ra/kg}$	10.6	9.68	1.11	9.68	0.163	10.8	1.06	3.55	1.29	----	
BONE											
Forepaws	3.66%	2.51%	2.09%	2.62%	3.28%	3.15%	4.05%	4.65%	3.28%	3.25% $\pm$ 0.82	
Radii	2.07	1.7	1.99	1.35	2.44	1.73	2.50	2.28	2.27	2.04 $\pm$ 0.38	
Ulnae	2.04	1.69	1.98	1.34	2.34	1.71	2.76	2.29	2.04	2.02 $\pm$ 0.42	
Humeri	7.70	7.54	5.71	7.54	7.66	7.99	6.33	7.60	4.61	6.96 $\pm$ 1.19	
Scapulae	4.54	4.98	4.63	4.58	3.46	5.11	4.10	4.49	5.06	4.55 $\pm$ 0.52	
Hindpaws	4.80	3.01	3.07	3.27	5.04	4.15	5.39	5.12	4.51	4.26 $\pm$ 0.94	
Fibulae	0.35	.37	0.48	.33	0.38	.33	0.55	0.51	0.47	.42 $\pm$ 0.08	
Tibiae	4.43	3.99	3.93	3.51	6.22	3.50	5.48	5.07	4.86	4.55 $\pm$ 0.93	
Femura	7.95	6.33	5.91	7.32	8.88	6.76	5.75	----	6.38	6.91 $\pm$ 1.08	
Pelves	6.05	6.91	6.54	6.02	5.64	9.17	5.88	7.08	6.59	6.65 $\pm$ 1.08	
Skull + upper teeth	12.05	12.10	13.73	6.94	15.30	10.21	13.17	12.58	17.70	12.64 $\pm$ 3.03	
Mand. + lower teeth	4.03	4.59	6.60	3.13	7.08	4.88	7.50	5.85	6.42	5.56 $\pm$ 1.51	
Ribs	10.03	12.77	10.12	9.70	7.18	9.68	12.13	7.49	8.24	9.70 $\pm$ 1.93	
Sternum	5.30	3.28	1.85	5.20	1.10	4.12	0.78	----	1.53	2.90 $\pm$ 1.82	
Cerv. vert.	4.53	4.57	5.76	6.73	7.75	5.20	6.03	6.87	8.67	6.23 $\pm$ 1.43	
Thor. vert.	10.58	9.20	13.35	10.69	6.13	9.88	5.96	6.83	6.94	8.84 $\pm$ 2.53	
Lumb. vert.	6.87	11.67	8.81	10.18	7.70	10.65	5.24	7.59	6.36	8.34 $\pm$ 2.14	
Tail	0.97	2.87	1.39	0.96	0.89	1.76	1.85	1.36	1.79	1.54 $\pm$ 0.62	
Other	2.05	----	2.06	----	2.06	----	4.55	----	2.30	(1.71) $\pm$ ----	
Ret.Skel.Ra [†] /Inj. Ra	(82.6%)	(44.2%)	(23.8%)	(20.8%)	(8.3%)	(18.7%)	(19.6%)	(12.8%)	(11.3%)		

*Received six ^{226}Ra injections during 280 days; AGE at mid-injection and DAYS mid-injection to death.

[†]Residual Ra in skeleton.

Table 2. Average distribution of skeletal radium for 4 dogs (Ref. 1) and for 9 dogs (Table 1). Data shown are percent of retained skeletal radium values.

Bone or Bone Group	This Report	Previous Report
Forepaws	3.25%	3.01%
Radii	2.26	1.73
Ulnae	2.24	1.70
Humeri	6.96	7.74
Scapulae	4.55	4.83
Hindpaws	4.26	3.83
Fibulae	0.46	0.31
Tibiae	5.00	3.91
Femura	6.91	7.13
Pelves	6.65	7.08
Skull + upper teeth	12.64	10.38
Mand. + lower teeth	5.56	4.18
Ribs	9.70	10.62
Sternum	2.90	4.50
Cerv. Vert.	6.23	5.29
Thor. Vert.	8.84	10.15
Lumb. Vert.	8.34	9.90
Tail	1.54	1.81
Other	1.71	1.90

Table 3. Results of regression analyses of the relationship between percent of retained skeletal radium and time after injection for bones of the 9 dogs included in this study and their statistical significance.

<u>Bone</u>	<u>Slope, % Ra/yr</u>	<u>Intercept at t = 0</u>	<u>Level of Significance</u>
Forepaws	0.211	2.63%	0.10
Radii	0.0800	1.81	
Ulnae	0.0787	1.79	
Humeri	- 0.159	7.42	
Scapula	- 0.0268	4.63	
Hindpaws	0.254	3.52	0.10
Fibulae	0.0183	0.37	
Tibiae	0.188	4.00	
Femurs	- 0.0553	7.06	
Pelves	0.0606	6.47	
Skull + upper teeth	0.433	11.37	
Mand. + lower teeth	0.317	4.63	
Ribs	- 0.427	10.95	
Sternum	- 0.418	4.00	
Cerv. vent.	0.472	4.85	0.025
Thor. vent.	- 0.826	11.25	0.050
Lumb. vert.	- 0.462	9.69	
Tail	- 0.0251	1.61	

Table 4. Results of group comparison tests of percent retained skeletal radium in bones of 5-level (10 μ Ci/kg injected) versus lower level (< 3 μ Ci/kg injected) dogs dying more than 1 month after injection.

<u>Bone</u>	<u>5-level mean</u>	<u>lower level mean</u>	<u>"t" value</u>	<u>Level of Significance</u>
Forepaws	2.88	3.47	0.80	
Radii	1.54	2.30	4.22	0.01
Ulna	1.52	2.28	3.02	0.05
Humerus	7.76	6.38	1.42	
Scapula	4.84	4.35	1.05	
Hindpaws	3.71	4.63	1.25	
Fibula	0.33	0.48	3.14	0.05
Tibia	3.50	5.11	2.57	0.05
Femurs	7.04	6.73	0.28	
Pelves	7.60	6.35	1.33	
Skull & upper teeth	8.58	14.50	3.35	0.05
Mand. & lower teeth	4.00	6.69	4.06	0.01
Ribs	9.69	9.03	0.42	
Sternum	4.66	1.32	6.91	0.01
Cerv. Vert.	5.96	7.02	1.06	
Thor. Vert.	10.28	7.84	1.05	
Lumb. Vert.	10.42	7.14	3.17	0.05
Tail	1.36	1.46	0.27	

FRACTIONAL RADON RETENTION IN BONE

Charles W. Mays, Ray D. Lloyd, and Marvin A. Van Dilla

Abstract: Radon-to-radium ratios have been measured in bones of 49 Beagles dying 5 to 2988 days after the intravenous injection of ^{226}Ra . The expression $\text{Rn/Ra} = 7.5\%t^{0.158} (1 - e^{-0.181t})$ at t days describes the dependence of the Rn to Ra ratio in these bones upon time after administration. This equation also appears valid for dogs that received their radium in 6 equal injections spaced over a period of 280 days, when t is considered as time after mid-injection. Comparison of results for dogs with those reported for mice, rats, chinchillas, and humans suggests that skeletal Rn/Ra ratios as a function of time may be somewhat species independent.

INTRODUCTION

Radioactive ^{222}Rn is produced directly by the radioactive decay of ^{226}Ra . The physical half-period of radon is 3.82 days, and its noble gas properties preclude any important chemical reaction under physiological conditions. When ^{226}Ra decays in the skeleton the resulting ^{222}Rn will (a) decay within bone, or (b) diffuse into the circulation from which most of the radon will be exhaled. Alpha-particles emitted by ^{222}Rn and its radioactive daughters outside the body do not contribute to the animal's radiation dose. Therefore, skeletal dosimetry depends upon the Rn/Ra ratio as well as the Ra retention within bones as a function of time after administration.

METHODS

The 49 dogs included in this study each had been given an intravenous injection of ^{226}Ra in a citrate buffer 5-2988 days earlier. The ^{222}Rn content of bones containing ^{226}Ra was determined by gamma-ray counting shortly after sacrifice, correcting for the buildup of

the γ -emitting daughters of ^{222}Rn following death. Radium activities within each of the samples were subsequently measured. For some animals, the entire skeleton was analyzed, and in such cases the average skeletal Rn/Ra ratio was obtained. For others, the average Rn/Ra ratio for the left humerus and third lumbar vertebra was used to represent the skeletal average since the average of these 2 bones was similar to the skeletal average in dogs for which the entire skeleton was assayed.

The radon retention values were arranged by increasing order of time from injection to death. An equation was then fit to these data by the method of least squares with the aid of an IBM 7044 digital computer.

RESULTS AND DISCUSSION

Table 1 lists the measured Rn/Ra ratios at death for the 49 animals in this study. These ratios are shown as a function of time after injection in Figure 1. No strong dependence of the fractional radon retention on the relative injected activity is apparent.

The skeletal radon retention value of 10% for T10R5 (Table 1 and shown as an "X" in Figure 1) was not used in the least squares calculation upon which the fractional radon retention equation was based. This point was significantly lower than values of other dogs at a similar time after injection; the value of 13.8% for T11R5 (a littermate which was also injected at 43 days of age and was also sacrificed 49 days later) appeared to be in agreement with values for other dogs; and the observed radon/radium ratio in the humerus of T10R5 (12.2%) was much higher than its skeletal average of 10%.

Table 1.

Observed fractional radon retention in
bones of 49 beagles injected with ^{226}Ra .

DOG	INJECTED $\mu\text{Ci Ra/kg}$	DAYS AGE AT INJ.	BURDEN DAYS	OBSERVED % Rn/Ra			HUMERUS AND 3RD LUM. V. AVERAGE
				SKELETON	HUMERUS	3RD LUM. V.	
T49R5	7.54	485	5	----	6.4	5.8	6.1
T16R5	9.68	604	12	9.2	9.9	8.7	---
T57R4	2.72	501	14	----	9.8	9.3	9.6
T52R5	8.57	418	15	----	9.8	9.5	9.6
T50R5	7.46	485	15	----	11.5	9.9	10.7
T55R5	8.61	417	33	----	12.9	12.1	12.5
T53R5	8.50	418	33	----	13.5	13.3	13.4
T63R3	0.90	559	36	----	13.9	14.5	14.2
T71R5	9.23	4025	42	----	14.9	13.9	14.4
T10R5	1.98	43	49	10.0	12.2	----	----
T11R5	1.91	43	49	13.8	----	----	----
T8R5	1.92	290	58	----	13.7	----	----
T9R5	1.94	2276	58	----	13.8	----	----
T58R4	2.41	496	61	----	14.5	13.9	14.2
T59R4	2.57	496	63	----	14.4	13.7	14.0
T41R1	0.05	899	63	----	14.8	----	----
T43R1.7	0.14	963	64	----	15.7	15.2	15.4
T44R3	0.94	938	68	----	15.2	15.3	15.2
T46R3	0.93	810	69	----	15.3	15.7	15.5
T14R5	3.17	674	72	13.5	----	----	----
T56R5	8.61	417	90	----	14.9	14.5	14.7
T51R5	8.48	418	92	----	15.2	14.6	14.9
T13R5	9.76	397	188	16.2	16.9	15.9	----
T12R5	9.72	397	225	17.4	18.4	16.8	----
T31R5	10.40	471	303	----	18.6	18.7	18.6
T3R5	4.76	1467	428	20.7	----	----	----
F3R4	3.33	384	490	19.8	----	----	----
M1R5	10.50	473	908	24.0	----	----	----
F8R5	9.68	474	968	21.6	22.5	22.5	----
F6R5	10.20	486	1015	21.7	21.2	21.7	----
M4R5	10.60	408	1091	23.7	23.2	21.7	----
T36R4	2.99	695	1154	----	23.8	23.4	23.6
M2R1.7	0.16	598	1273	23.3	----	----	----
T2R5	4.39	919	1368	25.0	26.7	23.7	----
M2R5	10.80	470	1380	22.6	23.5	23.5	----
F12R4	2.81	496	1435	----	23.4	23.5	23.4
F9R4	3.02	542	1470	----	25.2	23.0	24.1
F11R3	0.94	495	1610	----	22.8	22.5	22.6
M7R4	3.88	453	1647	----	24.1	22.6	23.4
M10R3	1.06	525	1737	23.7	24.6	23.7	----
T33R3	1.15	471	1822	----	29.6	25.0	27.3
M2R4	3.55	470	1884	24.7	25.9	23.6	----
M7R3	1.29	514	2099	25.7	25.4	24.0	----
T15R4	3.11	672	2127	----	26.1	24.6	25.4
M2R3	1.21	470	2226	----	24.0	----	----
F12R1.7	0.17	590	2399	----	26.1	25.0	25.6
F9R3	0.99	551	2487	----	23.7	25.6	24.6
F8R1.7	0.15	491	2577	----	23.8	23.5	23.6
F8R3	1.03	542	2612	----	25.8	----	----
F8R1	0.06	861	2988	----	27.5	----	----

This difference is much greater than that for any of the 11 other dogs in Table 1 for which comparable measurements were made. The determination of the ^{222}Rn content of the total dog, T10R5, made at about the time of autopsy, may well have been in error.

Fractional radon retention in bone increases with increasing time after injection, and, in general, the relationship appears to follow a power function of time. This may reflect a progressive "burial" of the retained radium atoms in relatively inaccessible bone sites. The exponential term in the equation accounts for the ingrowth of ^{222}Rn following the deposition of radon-free, freshly injected ^{226}Ra in bone. This effect is no longer important by a few weeks after injection.

Since the rate constant in the exponential term (0.181/day) equals the radioactive decay constant of radon, the implication is that a slowly changing amount of radium is producing that radon which is retained. This radium may be rather tightly locked into bone. The more rapidly eliminated radium may produce radon that is not well retained, due to bone remodeling or location in regions of small, immature bone crystals from which radon diffusion is easy. Other explanations are possible.

Table 2 compares the measured fractional radon retention in some bones from Beagles given ^{226}Ra in 6 equal injections over a period of 280 days with the theoretical Rn/Ra calculated from the equation which was generated from the data of the dogs receiving a single injection. Time after injection (t) in each case was considered to be days after mid-injection (which was 140 days after the first injection). The close agreement suggests that this equation may

Figure 1. Radon to radium ratios in bones of dogs sacrificed at various times after ^{226}Ra injection (log-log plot).

Table 2. Fractional Radon Retention in Bones of 8 Beagles that Received Their ^{226}Ra in 6 Injections Over a Period of 280 Days.

Dog	Total injected $\mu\text{Ci } ^{226}\text{Ra/kg}$	Days age at mid inj.	Days mid inj. to death	Calculated % Rn/Ra*	Observed % Rn/Ra			
					Skeleton	Humerus	3rd Lum.V.	Hum + 3rd LV Average
T21R5H	10.8	521	246	17.9	----	17.5	17.1	17.3
T28R3H	1.15	512	247	17.9	19.0	19.8	20.2	19.3
T22R5H	10.0	521	447	19.7	----	19.6	18.8	19.2
T17R5H	10.5	523	1007	22.4	----	23.4	23.0	23.2
T18R5H	11.4	523	1086	22.6	----	23.3	21.8	22.6
T25R4H	3.56	519	1169	22.9	----	22.3	21.5	21.9
T20R5H	10.8	523	1190	23.0	----	----	22.5	22.5
T26R4H	3.62	519	1640	24.2	----	23.4	23.0	23.2

* % Rn/Ra = $7.5\% t^{0.158} (1 - e^{-0.181t})$ at $\pm$ days after mid-injection

also be valid for animals receiving multiple injections, at least when the time after mid-injection exceeds the duration of injections.

Retained ^{226}Ra activities in our radium-injected dogs are characteristically determined by dividing their ^{222}Rn content (measured by total-body counting) by the appropriate Rn/Ra ratio calculated from the equation shown in Figure 1. We believe that this indirect procedure yields more accurate results than the direct method of adding the measured total-body radon retention to the exhaled radon, determined by analysis of the expired air. Radon exhalation must be calculated from the measured rate of radon escape in the breath, which can fluctuate significantly over short spans of time. This can produce inaccurate estimates of the exhaled radon, resulting in errors of calculated total-body radium content.

Figure 2 displays some Rn/Ra measurements reported for mammalian species other than dogs and compares them with the equation representing the fractional radon retention in our Beagles (Figure 1). The close agreement among these 5 species suggests that the fractional radon retention in the mammalian skeleton is somewhat species independent. Perhaps, as proposed previously ⁽¹⁰⁻¹²⁾ this is a result of uniformities in the bone crystal dimensions among many species.

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Figure 2. Comparison of fractional radon retention among five mammalian species (log-log plot). Data for species other than the dog were taken from References 1-9. Mouse data of Reference 1 are averages of 4 animals except for the last 6 points, 5 of which are averages of 2 mice, and the final one for a single animal. Mouse data of Reference 2 show one point per animal as is also true of the chinchilla data of Reference 3. The 49 human measurements reported in Reference 9 were grouped by year after exposure and were averaged to obtain 13 data points.

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RETENTION AND SKELETAL DOSIMETRY OF INJECTED ^{90}Sr IN BEAGLES

Ray D. Lloyd, Charles W. Mays and Glenn N. Taylor

Abstract. The retention of ^{90}Sr has been determined by total-body counting in a group of 96 Beagles given 0.517 to 302 $\mu\text{Ci } ^{90}\text{Sr}/\text{kg}$ body mass by intravenous injection at about 1.4 years of age. Retention measurements now extend to nearly 5000 days (13.5 years) after administration. Total-body retention of injected ^{90}Sr was as if about 36% was retained with a biological half-time of 1 day, 29% with 6 days, 10% with 76 days, 12% with 365 days, and 13% with 4621 days. Using this retention function, the average skeletal radiation dose rate and cumulative skeletal radiation dose from $^{90}\text{Sr} + ^{90}\text{Y}$ were calculated. Allowance was made in the calculations for the effects on dose and dose rate of skeletal mass, diminution of ^{90}Sr concentration by radioactive decay, the escape of β -energy from bone, and the measured retention of each individual dog.

INTRODUCTION

Preliminary reports^(1, 2, 3, 4) of the biological retention of injected ^{90}Sr by Beagles in our colony have appeared previously. This report includes all of the retention data in the earlier versions plus measurements for an additional 2 years beyond the most recent of these.⁽⁴⁾ Since total-body retention values now extend to about 5000 days post-injection (nearly 15 years of age for dogs 1.4 years old at injection), future revision of the retention equation reported herein appears unlikely.

RETENTION

Ninety-six Beagles each were given a single intravenous injection of ^{90}Sr in a citrate buffer solution at about 1.4 years of age. Injected activities ranged from 0.515 to 302 $\mu\text{Ci } ^{90}\text{Sr}/\text{kg}$ body mass (Table 1). Details of experimental design, injection procedure, and

veterinary care have been reported.⁽⁵⁾ For most of the animals, measurements of retained activity were made by total-body bremsstrahlung counting several times after injection, and all dogs were counted at least once. Detectors employed in total-body counting were a liquid scintillation counter (K-9 Bark II) and a large NaI(Tl) crystal. These detectors, their calibration procedures, and counting techniques are described in References 1, 6, and 7.

All retention values were plotted on a single graph (Figure 1). Points representing measurements for the same dog were connected to form "stream lines" of the individual retentions, which are shown by the light lines in the figure. A curve representing the average retention of all dogs in the study was then fit through the data so as to pass near the center of all the points while remaining approximately parallel to the slopes of the individual stream lines. This average retention curve is indicated by the heavy line in Figure 1.

We have elected to represent the biological retention of injected ^{90}Sr in the Beagle by a sum of exponential terms; however, other equations may fit the retention data at least as well. Results of all measurements are given in Table 1 so that the interested reader can use them to derive other retention functions.

The equation of the average retention curve shown in the figure indicates that the total-body retention of injected ^{90}Sr in these dogs was as if 36% was retained with a biological half-time of 0.73 days, 29% with a half-time of 5.8 days, 10% with 76 days, 12% with 365 days, and 13% with 4621 days. The similarity of this retention function for ^{90}Sr in the Beagle to the retention function for ^{226}Ra

Table 2. Comparison of ^{90}Sr and ^{226}Ra Retention equations.

	^{90}Sr		$^{226}\text{Ra}^*$	
	%	$T_{1/2}$, days	%	$T_{1/2}$, days
First component	36	0.73	25	0.71
Second component	29	5.8	21	2.6
Third component	10	76	21	43
Fourth component	12	365	18	347
Fifth component	13	4621	15	4621
Equivalent Biological $T_{1/2}^+$		654		765

* See Reference 8

+ Weighted average of all component half-times.

in the Beagle⁽⁸⁾ (lower levels) reflects the similarity of skeletal deposition and total excretion between these two alkaline earth elements.^(9, 10) Although the equivalent biological half-time for Sr is shorter than that for Ra (Table 2), the half-time of the longest-lived component appears to be equal to that of Ra. John Marshall has suggested⁽¹¹⁾ that the final exponential may be an indication of the remodeling rate of cortical bone. Thus, in the mature Beagle skeleton, the half-time for remodeling of cortical bone may be about 4621 days or 13 years.

DOSIMETRY

Each decay of the $^{90}\text{Sr} + ^{90}\text{Y}$ pair releases an average of 1.13 MeV, ⁽¹²⁾ 79% of the β -energy from $^{90}\text{Sr} + ^{90}\text{Y}$ in a Beagle skeleton is absorbed by the skeleton,⁽¹³⁾ $1\mu\text{Ci} = 3.2 \times 10^9$ disintegrations per day (by definition), and $1\text{ rad} = 6.25 \times 10^7$ MeV/gram.⁽¹⁴⁾ If 10% of a Beagle's body weight at injection is skeleton, then, for $1\mu\text{Ci/kg}$

body injected, the average skeletal dose rate would be

$$\left(\frac{1\mu\text{Ci}}{100\text{ g}}\right)\left(\frac{3.2 \times 10^9 \text{ dis/day}}{\mu\text{Ci}}\right)\left(\frac{1.13 \text{ MeV}}{\text{dis}}\right)\left(\frac{0.79 \text{ MeV absorbed}}{1.0 \text{ MeV produced}}\right)\left(\frac{1 \text{ rad}}{6.25 \times 10^4 \text{ MeV/g}}\right)$$

$$= 0.457 \text{ rad/day to the skeleton}$$

(if all injected Sr concentrates in the skeleton with 100% retention).

The instantaneous average skeletal dose rate at some time t after injection, when the retention is less than 100%, can be estimated for a $1 \mu\text{Ci/kg}$ injection by solving the ^{90}Sr retention equation (Figure 1) for the desired time t , and multiplying the result by $0.457 e^{-\lambda_{\text{Sr}} t}$ rad/day, which corrects for the radioactive decay of ^{90}Sr and converts to rads/day. The symbol λ_{Sr} is the radioactive decay constant of $^{90}\text{Sr} = 6.85 \times 10^{-5}/\text{day}$.⁽¹⁵⁾ The cumulative average skeletal dose from injection to time t can be determined for a $1 \mu\text{Ci/kg}$ injection by integrating the equation for instantaneous dose rate, between the limits 0 and t . Both the cumulative dose and dose rate are multiplied by the injected $\mu\text{Ci}^{90}\text{Sr/kg}$ to obtain values for a particular animal. These values are then multiplied by the average ratio of the dog's measured retention and the retention calculated from the equation shown in Figure 1 for each time of measurement to correct for individual differences in retention.

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Figure 1. Retention of injected ^{90}Sr by 96 Beagles in this study.

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Table 1. Retention of injected ^{90}Sr in beagles measured by total-body bremsstrahlung counting with a liquid scintillation counter (K9II) or a crystal counter (NaI).

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{90}\text{Sr/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
F1S1A	521	0.588	2718	7.6	NaI
			3444	6.6	NaI
			4130	3.8	NaI
			4941	3.4	NaI
M2S1	567	0.606	2719	6.0	NaI
			3444	6.2	NaI
			4130	4.1	NaI
M3S1	493	0.572	2147	9.9	NaI
			2869	9.0	NaI
			3555	7.7	NaI
			4366	8.1	NaI
F4S1	525	0.560	2114	10.8	NaI
			2835	9.2	NaI
			3521	8.2	NaI
			4332	9.0	NaI
M5S1	555	0.532	2080	8.3	NaI
M6S1	466	0.581	1893	16.6	NaI
			2612	13.5	NaI
			3296	13.9	NaI
			4109	11.5	NaI
F7S1	524	0.517	1725	10.5	NaI
			2444	8.7	NaI
			3128	9.0	NaI
			3941	7.4	NaI
F8S1	483	0.697	1539	8.0	NaI
			2256	6.6	NaI
F9S1	549	0.534	1457	9.9	NaI
			2172	8.1	NaI
			2852	8.1	NaI
M10S1	522	0.558	1410	10.3	NaI
			2124	9.3	NaI
			2803	8.8	NaI
			3628	5.9	NaI

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{90}\text{Sr/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
F11S1	543	0.550	1377	10.6	NaI
			2089	8.3	NaI
			2768	8.1	NaI
			3593	6.8	NaI
M12S1	607	0.559	1315	9.9	NaI
			2025	8.7	NaI
F1S1.7	526	1.78	667	18.1	K9II
			685	17.7	K9II
			1956	10.9	K9II
			2718	10.2	K9II
			2718	10.1	NaI
			3444	9.3	NaI
			4130	8.0	NaI
			4941	7.8	NaI
M2S1.7	567	1.84	645	19.9	K9II
			685	17.6	K9II
			1956	9.5	K9II
			2719	9.3	NaI
			3444	8.5	NaI
			4130	7.6	NaI
M3S1.7	493	1.69	15	41.5	K9II
			1388	9.6	K9II
			2147	10.2	K9II
			2147	8.2	NaI
			2869	8.0	NaI
			3555	6.9	NaI
			4366	7.0	NaI
F4S1.7	522	1.68	10	39.8	K9II
			21	29.4	K9II
			38	27.9	K9II
			59	28.4	K9II
			142	25.0	K9II
			1354	8.9	K9II
			2114	8.7	K9II
			2114	6.7	NaI
			2835	6.4	NaI
			3521	6.0	NaI
			4332	6.2	NaI
M5S1.7	560	1.60	14	35.6	K9II
			21	33.9	K9II
			1326	8.6	K9II

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{90}\text{Sr/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
M5S1.7A	493	1.78	147	27.8	NaI
			868	18.1	NaI
			1552	16.4	NaI
			2364	14.4	NaI
M6S1.7	466	1.72	1137	15.6	K9II
			1892	14.5	K9II
			1892	13.9	NaI
			2612	12.0	NaI
			3296	11.9	NaI
			4109	9.5	NaI
F7S1.7	488	1.60	976	8.2	K9II
			1725	10.5	K9II
			1725	9.5	NaI
			2444	7.5	NaI
			3128	7.1	NaI
F8S1.7	472	2.03	787	10.7	K9II
			1539	11.7	K9II
			1539	9.8	NaI
F9S1.7	549	1.62	709	14.9	K9II
			1457	13.4	K9II
			1457	13.9	NaI
			2172	11.6	NaI
			2852	10.8	NaI
			3668	8.9	NaI
M10S1.7	519	1.66	443	19.1	K9II
			660	15.5	K9II
			1410	12.6	NaI
			2803	11.1	NaI
F11S1.7	543	1.68	317	12.3	K9II
			632	11.4	K9II
			1377	9.3	K9II
			1377	10.2	NaI
			2089	8.8	NaI
			2768	8.7	NaI
M12S1.7	607	1.68	244	18.9	K9II
			1315	11.3	NaI
			2025	9.5	NaI
			2703	9.4	NaI
			3529	8.2	NaI

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{90}\text{Sr/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
F1S2	502	3.70	1059	10.0	K9II
			1077	10.4	K9II
			2348	6.5	K9II
			3110	4.9	K9II
			3110	5.5	NaI
M2S2	567	3.42	645	18.7	K9II
			685	17.2	K9II
			1956	8.0	K9II
			2719	6.9	NaI
M3S2	494	3.39	15	42.6	K9II
			1388	9.9	K9II
			2147	9.3	K9II
			2147	9.1	NaI
			2869	8.4	NaI
F4S2	522	3.41	3555	7.8	NaI
			10	37.6	K9II
			21	32.0	K9II
			38	24.2	K9II
			59	27.3	K9II
			142	24.2	K9II
			1354	10.5	K9II
			2114	12.9	K9II
			2114	11.3	NaI
			2835	9.9	NaI
M5S2	560	3.24	3521	9.6	NaI
			4332	8.9	NaI
			14	44.0	K9II
			21	37.0	K9II
			1326	8.8	K9II
M6S2	466	3.50	2080	7.6	K9II
			2080	8.3	NaI
			1137	11.6	K9II
			1892	11.8	K9II
			1892	11.2	NaI
F7S2	488	3.19	2612	9.7	NaI
			3296	9.4	NaI
			4109	7.5	NaI
			976	8.5	K9II
			1725	8.4	K9II
			1725	8.6	NaI
			2444	7.6	NaI
			3128	7.6	NaI

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{90}\text{Sr/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
F8S2	465	4.14	787	8.7	K9II
			1539	9.7	K9II
			1539	10.0	NaI
			2256	8.5	NaI
			2939	8.0	NaI
			3752	7.0	NaI
F9S2	473	3.28	709	15.8	K9II
			1457	12.1	K9II
			1457	13.4	NaI
			2172	12.0	NaI
M10S2	508	3.34	443	18.0	K9II
			660	14.3	K9II
			1410	9.8	K9II
			1410	11.3	NaI
			2124	9.5	NaI
			2803	9.0	NaI
F11S2	543	3.41	317	14.4	K9II
			632	12.1	K9II
			1377	10.3	K9II
			1377	9.3	NaI
			2089	9.5	NaI
			2768	8.9	NaI
			3593	7.8	NaI
M12S2	607	3.49	244	17.6	K9II
			569	13.6	K9II
			1315	11.9	K9II
			1315	11.6	NaI
			2025	9.4	NaI
			2703	8.9	NaI
			3529	8.1	NaI
T16S2	604	3.27	9	38.0	K9II
T21S2.5J	363	8.30	13	47.7	NaI
F1S3	468	11.6	1059	18.4	K9II
			1077	18.9	K9II
			2348	11.8	K9II
			3110	8.2	K9II
			3110	9.1	NaI
			4522	7.9	NaI

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{90}\text{Sr/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
M2S3	565	11.6	645	16.4	K9II
			685	18.7	K9II
			1956	9.9	K9II
			2719	9.7	K9II
			2719	9.6	NaI
			3444	8.9	NaI
			4130	8.6	NaI
M3S3	494	10.8	15	41.7	K9II
			1388	10.5	K9II
			2147	9.7	NaI
			2869	8.8	NaI
			3555	8.1	NaI
			4366	7.5	NaI
F4S3	527	10.6	10	40.2	K9II
			21	29.2	K9II
			38	26.9	K9II
			59	25.6	K9II
			142	22.9	K9II
			1354	9.0	K9II
			2114	6.7	K9II
			2114	7.2	NaI
			2835	6.4	NaI
M5S3	557	10.1	14	42.7	K9II
			21	38.4	K9II
			1326	10.2	K9II
			2081	9.3	K9II
			2081	9.3	NaI
			3485	8.2	NaI
M6S3	466	10.9	1137	13.7	K9II
			1892	13.2	K9II
			1892	12.8	NaI
			2612	11.1	NaI
			3296	11.0	NaI
			4109	9.6	NaI
F7S3	486	10.1	976	10.4	K9II
			1728	9.8	K9II
			1728	10.0	NaI
			2444	8.9	NaI
			3128	8.0	NaI
			3941	6.9	NaI

DOG.	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{90}\text{Sr/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
F8S3	465	12.9	787	11.3	K9II
			1542	11.4	K9II
			1542	10.7	NaI
			2256	11.0	NaI
			2939	10.0	NaI
			3752	9.6	NaI
F9S3	468	10.1	709	15.1	K9II
			1457	13.9	K9II
			1457	14.1	NaI
			2172	12.3	NaI
			2852	11.4	NaI
			3668	10.2	NaI
M10S3	519	10.3	443	18.4	K9II
			1410	14.1	NaI
			2124	13.2	NaI
			2803	11.9	NaI
F11S3	541	10.8	317	7.4	K9II
			632	6.2	K9II
			1377	4.7	K9II
			1377	4.9	NaI
			2089	4.2	NaI
			2768	3.9	NaI
M12S3	605	10.2	244	13.5	K9II
			569	10.6	K9II
			1315	8.6	K9II
			1315	8.7	NaI
			2025	7.6	NaI
			2703	7.0	NaI
			3529	6.2	NaI
T12S3	593	10.5	5	50.5	K9II
F1S4	468	33.3	1059	14.9	K9II
			1077	15.0	K9II
			2348	9.4	K9II
			3682	7.0	NaI
M2S4	567	32.6	645	20.7	K9II
			685	21.1	K9II
			1956	11.7	K9II
M3S4	593	32.1	15	29.8	K9II
			1388	9.2	K9II
			2147	8.3	K9II
			2147	8.3	NaI

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{90}\text{Sr/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
F4S4	528	32.1	10	51.4	K9II
			21	37.3	K9II
			38	39.0	K9II
			59	36.2	K9II
			142	28.6	K9II
			1354	11.3	K9II
			2114	10.9	K9II
			2114	10.9	NaI
			2835	9.6	NaI
			3521	9.1	NaI
			4332	7.8	NaI
M5S4	562	30.6	14	42.6	K9II
			21	37.9	K9II
			1326	10.3	K9II
			2080	9.7	NaI
			2801	8.4	NaI
			3485	8.2	NaI
			4298	6.7	NaI
M6S4	504	32.7	1038	13.5	K9II
			1794	11.8	K9II
			1794	12.0	NaI
			2513	10.7	NaI
			3197	10.3	NaI
F7S4	478	30.9	976	13.1	K9II
			1728	13.6	K9II
			1728	13.0	NaI
			2444	11.7	NaI
			3128	10.8	NaI
			3941	9.5	NaI
F8S4	465	40.6	787	18.9	K9II
			1540	14.8	K9II
			1540	16.0	NaI
F9S4	468	30.6	709	14.0	K9II
			1457	13.0	K9II
			1457	12.8	NaI
			2172	11.2	NaI
			2852	10.1	NaI
			3668	9.2	NaI
M10S4	517	31.3	443	15.7	K9II
			660	14.5	K9II
			1410	10.9	K9II
			1410	11.4	NaI
			2124	10.1	NaI
			2803	9.5	NaI
			3628	8.7	NaI

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{90}\text{Sr/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
F11S4	542	32.7	317	13.1	K9II
			632	10.5	K9II
			1377	9.1	NaI
			2089	8.6	NaI
M12S4	605	32.3	244	14.9	K9II
			569	11.3	K9II
			1315	9.6	K9II
			1315	9.8	NaI
			2025	8.4	NaI
			2703	8.0	NaI
			3529	7.3	NaI
T13S4	324	19.1	8	55.5	K9II
T20S4J	440	28.9	13	35.0	NaI
F1S4.5	530	64.2	14	27.6	NaI
			99	18.5	NaI
			442	12.2	NaI
			1268	8.1	NaI
M2S4.5	530	63.6	14	27.6	NaI
			99	19.1	NaI
			442	12.7	NaI
			1268	8.8	NaI
M3S4.5	530	63.8	14	32.0	NaI
			99	23.0	NaI
			442	15.4	NaI
			1269	10.4	NaI
F4S4.5	530	64.5	14	35.8	NaI
			99	25.0	NaI
			442	17.8	NaI
			1269	13.2	NaI
M5S4.5	496	61.3	14	36.8	NaI
			99	28.0	NaI
			442	21.0	NaI
M6S4.5	496	63.8	14	31.2	NaI
			99	22.8	NaI
			442	16.3	NaI
			1269	11.9	NaI

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{90}\text{Sr/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
F7S4.5	511	64.5	14	33.7	NaI
			99	24.4	NaI
			442	17.3	NaI
			1269	12.6	NaI
F8S4.5	511	64.5	14	35.4	NaI
			99	25.5	NaI
			442	17.7	NaI
F9S4.5	511	64.0	14	35.3	NaI
			99	25.5	NaI
			442	17.6	NaI
M10S4.5	496	60.9	14	42.8	NaI
			99	33.6	NaI
			442	24.1	NaI
			1269	18.5	NaI
F11S4.5	496	63.8	14	30.6	NaI
			99	21.0	NaI
			442	14.6	NaI
			1269	11.3	NaI
M12S4.5	485	63.7	14	36.5	NaI
			99	26.2	NaI
			442	18.7	NaI
			1269	14.6	NaI
M2S5A	545	96.6	898	13.4	K9II
			1661	11.2	NaI
			1743	12.1	K9II
M3S5	507	102	10	49.5	K9II
			21	35.0	K9II
			38	37.4	K9II
			59	34.5	K9II
			142	30.0	K9II
			1354	13.7	K9II
			2114	11.9	K9II
			2114	11.7	NaI
			2256	11.0	K9II
			2256	11.0	NaI
F4S5	528	105	21	28.2	K9II
			38	29.9	K9II
			59	25.4	K9II
			142	22.3	K9II
			1354	8.6	K9II

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{90}\text{Sr/kg}$	DAYS AFTER INJECTION	% BIOLOGICAL RETENTION	DETECTOR
M5S5	621	95.2	14 21	42.2 38.6	K9II K9II
M6S5A	462	94.2	912	19.5	K9II
F7S5	478	92.7	976	17.0	K9II
F8S5	535	90.5	1078 1469	14.4 12.9	K9II K9II
F9S5	459	93.5	709 1457 1457	15.0 13.7 13.9	K9II K9II NaI
M10S5	517	95.9	443 660 990	15.9 14.1 13.6	K9II K9II K9II
F11S5	542	102	317 632 1377 1377	15.1 12.5 11.3 11.0	K9II K9II K9II NaI
M12S5	606	99.2	244	18.8	K9II
T14S5	542	96.1	9	34.4	K9II
T15S5	595	98.4	30	24.2	K9II
T22S5	545	99.0	157	18.9	NaI
T23S5	545	100	157	22.2	NaI
T17S6	670	295	14	28.1	K9II
T18S6	670	302	552 1281	8.1 6.9	NaI NaI
T19S6	670	284	23	16.3	K9II

✓ DISTRIBUTION OF INJECTED ^{90}Sr IN THE BEAGLE SKELETON

Ray D. Lloyd and Charles W. Mays

Abstract: The ^{90}Sr content of individual bones from two dogs dying 1740 and 2256 days after the injection of about 100 μCi $^{90}\text{Sr}/\text{kg}$ was determined by β -counting. Bones were ashed and dissolved in nitric acid. Counting was done with a well-type plastic scintillator. Distribution of the retained ^{90}Sr was about 35% of the skeletal ^{90}Sr in the head and neck, about 21% in the rib cage and thoracic and lumbar spine, about 20% in the forelimbs and shoulder girdle, about 23% in the hind limbs and hip girdle, and about 1% in the tail. Comparison of the $^{90}\text{Sr}/\text{Ca}$ ratios in bone samples from a dog dying 14 days after injection and of bone samples from a dog sacrificed 9 days after injection with those in corresponding bone samples from a dog dying 1448 days after injection showed that, for dogs injected as young adults, cortical bone initially takes up injected ^{90}Sr less avidly than does trabecular bone. Since cortical bone turns over more slowly, this marked difference in labelling is not seen at times long after injection.

INTRODUCTION

A previous report⁽¹⁾ has tabulated the bone-by-bone distribution of ^{239}Pu , ^{228}Th , and ^{226}Ra in the skeletons of Beagle dogs injected with the radionuclide in citrate buffer as young adults. Data for ^{90}Sr were not then available. The prediction was made, however, that the distribution of ^{90}Sr , when measured, would be similar to that found for Ra. The work reported herein completes the distribution study for the 5 toxicity radionuclides being investigated by this laboratory. The distribution of ^{90}Sr was found to be more dissimilar to that of Pu or Th than of Ra.

METHODS

Bones used in the ^{90}Sr distribution study were obtained at autopsy from two male Beagles (M2S5A and M3S5) dying with osteosarcomas 1740 and

2256 days, respectively, after the injection of about 100 μCi $^{90}\text{Sr}/\text{kg}$. For each animal, one member of each set of paired bones was analysed. For unpaired bones, such as vertebrae, sternum, etc., a measured weight fraction (about 1/2) was taken for analysis.

Samples were ashed in an electric muffle furnace at approximately 600°C overnight. The ash from each bone was dissolved in concentrated nitric acid, transferred to calibrated flasks, and diluted to volume with 0.1N nitric acid after at least 5 rinsings of the crucibles with concentrated followed by 0.1N nitric acid. Representative 1 ml samples of each solution were taken in duplicate and were weighed to determine their density. After a 3 week delay to insure that the ^{90}Y daughter was in equilibrium with the ^{90}Sr parent, the samples were β -counted in a well-type plastic scintillator,^(2,3) comparing the counting rates obtained to that of an equilibrated ^{90}Sr standard in 1 ml of distilled H_2O in a sealed polypropylene test tube 12 mm in diameter and 75 mm long, identical to those containing the samples. Activities of ^{90}Sr for each bone were then calculated, making appropriate corrections for the effect of solution density on counting rate⁽⁴⁾ and for the fraction of the total dissolved bone that each sample represented.

The 3rd lumbar vertebra and left humerus were also obtained from two other Beagles injected with about 100 μCi $^{90}\text{Sr}/\text{kg}$. These two humeri were sectioned into 8 pieces as were the humeri reported on page 123 of Reference 1. Bone samples were similarly obtained from a Beagle dying 14 days after the injection of 295 μCi $^{90}\text{Sr}/\text{kg}$. The ^{90}Sr content of each of these samples was determined in an identical

fashion described for M2S5A and M3S5. The Ca content of each piece was assumed to be 39.4% of the ashed weight.⁽⁶⁾

RESULTS AND DISCUSSION

Table 1 lists the results for the two dogs whose skeletons were half-ashed. Data reported in Table 1 pertain only to skeletal ^{90}Sr in Beagles injected as young adults more than 4 years previously. Animals receiving ^{90}Sr in their diet or those injected with ^{90}Sr shortly before ^{90}Sr assay would exhibit different ^{90}Sr distribution patterns than shown in Table 1.

Table 1. Percent of skeletal ^{90}Sr in the various bones of two beagles injected with ^{90}Sr at about 1 1/2 years of age dying with bone tumors 1740 and 2256 days later. M2S5A contained about 107 μCi and M3S5 contained about 99.2 μCi at death.

Bone	M2S5A	M3S5	Average
	1740 days after injection	2256 days after injection	
Forepaws	2.99 %	3.45 %	3.22 %
Radii	2.21	2.86	2.54
Ulnae	2.39	3.71	3.05
Humeri	6.75	6.88	6.82
Scapulae	4.75	5.10	4.92
Hindpaws	4.37	4.88	4.62
Fibulae	0.69	0.60	0.64
Tibiae	5.18	4.48	4.83
Femora	6.45	7.16	6.80
Pelves	5.10	6.59	5.84
Skull	16.75	17.07	16.91
Mandibles	7.25	7.62	7.44
Teeth	2.56	2.72	2.64
Ribs	9.65	8.41	9.03
Sternum	1.62	0.58	1.10
Cerv. Vert.	7.38	8.36	7.87
Thor. Vert.	6.21	5.09	5.65
Lumb. Vert.	4.75	2.65	3.70
Sacrum	0.98	0.54	0.76
Tail	1.33	0.98	1.16
Os Penis*	0.64	0.26	0.45

*Males only

Beagles exposed to a diet containing a constant $^{90}\text{Sr}/\text{Ca}$ ratio beginning in utero maintain a "uniform" $^{90}\text{Sr}/\text{Ca}$ label in the total skeleton from about 100 days of age until the end of feeding.⁽⁶⁾ The percent skeletal ^{90}Sr in each bone would therefore be equal to the percent skeletal calcium. A summary of bone by bone skeletal weights from 12 low level ^{239}Pu beagles (averaging 10 rads total skeletal radiation dose) compiled by Atherton, Stover, and Bruenger,⁽⁷⁾ allowed the calculation of the percent skeletal calcium in each bone or bone group (Table 2). No important differences are evident between

Table 2. Percent of skeletal ^{90}Sr in various bone groups of long term injection beagles (see Table 1) compared with the distribution calculated for a uniform $^{90}\text{Sr}/\text{Ca}$ label.

<u>Bone or bone group</u>	<u>Long term injection dogs</u>	<u>Calculated uniform $^{90}\text{Sr}/\text{Ca}$ dogs</u>
Head	26.99 %	26.7 %
Cerv. Vert.	7.87	7.6
Thor. Vert.	5.65	6.1
Lumb. Vert.	4.46	6.0
Tail	1.16	0.9
Paws	7.84	10.0
Radii	2.54	2.7
Ulnae	3.05	2.9
Humeri	6.82	6.2
Tib + Fib	5.47	6.4
Femora	6.80	6.6
Pelves	5.84	5.3
Scapulae	4.92	3.9
Ribs	9.03	8.4
Sternum	1.10	0.3

the calculated uniform label and measured long-term injection animals. Data shown in Table 3, however, indicate that initial uptake of ^{90}Sr by cortical bone is less than that in trabecular bone. Long after injection,

Table 3. Ratios of $\mu\text{Ci } ^{90}\text{Sr/gCa}$ in the humerus and 3rd lumbar vertebra of 2 beagles injected with ^{90}Sr .

<u>Bone sample</u>	T14S5 9 days after the injection of <u>$96.1 \mu\text{Ci } ^{90}\text{Sr/kg}$</u>	F4S5 1448 days after the injection of <u>$105 \mu\text{Ci } ^{90}\text{Sr/kg}$</u>
Humerus Sections		
H-1 (proximal epiphysis)	2.49	0.59
H-2 (proximal epiphyseal line)	3.41	0.54
H-3 (proximal metaphysis)	2.86	0.84
H-4 (proximal diaphysis)	1.69	0.46
H-5 (mid-diaphysis)	1.36	0.53
H-6 (distal diaphysis and metaphysis)	1.72	0.75
H-7 (distal epiphyseal line)	2.27	0.75
H-8 (distal epiphysis)	<u>1.78</u>	<u>0.66</u>
Total Humerus	2.18	0.66
<u>3rd lumbar vertebra</u>	2.80	0.59

the trabecular bone is relatively more lightly labelled than initially, reflecting its more rapid turnover compared with cortical bone. Note that in the 9 day dog, T14S5, sections H-5, H-6, and H-4, the three least trabecular sections, have the lowest $^{90}\text{Sr/Ca}$ ratio, while the more trabecular humerus sections and the very trabecular 3rd lumbar vertebra have higher $^{90}\text{Sr/Ca}$ ratios. This light labelling of cortical bone is no longer evident in the 1448 day dog, F4S5.

Differential labelling of cortical and trabecular bone soon after injection is further illustrated by the $^{90}\text{Sr}/\text{Ca}$ ratios in some bones of T17S6 (Table 4). This dog died 14 days after the injection of 295 μCi $^{90}\text{Sr}/\text{kg}$. Bone samples containing a preponderance of trabecular bone are

Table 4. Ratios of μCi $^{90}\text{Sr}/\text{gCa}$ in some bone samples of T17S6, 14 days after the injection of 295 μCi $^{90}\text{Sr}/\text{kg}$ compared with corresponding ratios for two long-term injection dogs (Table 1).

<u>Bone sample</u>	<u>T17S6 (14 days post injection)</u>	<u>M2S5A (1740 days post injection)</u>	<u>M3S5 (2256 days post injection)</u>
Sternum	11.13	0.89	0.55
Rib	6.28		
3rd Lumbar Vertebra	6.00	0.65	0.51
Femur	4.84	0.63	0.58
Humerus	4.36	0.71	0.56
Tibia	3.94	0.61	0.45
Fibula	3.92		0.54
Ulna	3.32	0.53	0.63
Radius	3.27	0.52	0.57
Calvarium	3.27	0.74	0.69
Metatarsals	3.07	0.46	0.48
Metacarpals	2.94	0.43	0.53
Humerus Shaft	2.89		
Canine Teeth	1.48		
Molar Teeth	1.35		0.33

heavily labelled, while those containing a preponderance of cortical bone are only lightly labelled. Comparison of the relative $^{90}\text{Sr}/\text{Ca}$ ratios in various bones of the short-term dog T17S6 with those of the two long-term dogs M2S5A and M3S5 indicates that the initial marked difference in ^{90}Sr labelling between cortical and trabecular bone is not nearly as pronounced several years after injection.

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✓ DISTRIBUTION AND RETENTION OF INJECTED ^{210}Pb IN THE BEAGLE

R. D. Lloyd, C. W. Mays, D. R. Atherton
and F. W. Bruenger

Abstract: ^{210}Pb was administered to 10 young adult Beagles as an intravenous injection in a citric acid sodium citrate buffer solution at pH 3.5. Retention was determined by total-body counting of the 47 keV γ -ray. Total excreta collections from 3 dogs for the first 3 weeks after injection were assayed intact by γ -ray counting. About 3/4 of the excreted ^{210}Pb appeared in the feces. The fraction of the injected activity still in the circulating blood was about 0.40 at 1 day, 0.14 at 1 week, and 0.03 at 1 month. By 1 hour following injection, red cells had more than 99% of the ^{210}Pb in the blood. Preliminary results indicate that during the first 700 days, 36% of the injected Pb is retained in the dog with a biological half time of 4 days, 43% with 33 days, and 21% with 990 days. One dog sacrificed 28 days after injection had about 63% of the retained Pb in the skeleton, 20% in the liver, 8% in the blood and 9% in other soft tissues. Liver had the highest ^{210}Pb concentration of any tissue measured, 1.6 times that in the skeleton.

INTRODUCTION

Lead (Pb) contamination is becoming increasingly important in the pollution of the environment.^(1, 2, 3, 4, 5) Moreover, the residual body content of radioactive lead (^{210}Pb) has been investigated as a method of assessing the past exposure of uranium miners to ^{222}Rn and its radioactive daughters.^(6, 7, 8, 9, 10) Metabolic studies of Pb in large mammals are necessary so that these two problems can be more clearly understood.

Previous reports^(11, 12) have described the complications inadvertently introduced into our ^{224}Ra studies by the use of a ^{210}Pb -contaminated ^{228}Th solution from which some of the ^{224}Ra was produced. The radiotoxicity of ^{210}Pb must be established so that the biological

effects of ^{210}Pb radiation can be distinguished from those of the ^{224}Ra radiation. This is particularly important because of the German experience with ^{224}Ra -injected humans ⁽¹³⁾ and the consequent necessity for evaluating the dosimetry of ^{224}Ra to establish its toxicity relative to ^{226}Ra and other internally-deposited emitters.

METHODS

Three male Beagles aged 522 days (T1L5, T2L5, and T3L5) were each given an intravenous injection of ^{210}Pb in a sodium citrate-citric acid buffer solution (pH 3.5), and ^{210}Pb was similarly administered to seven other Beagles (2 males and 5 females), aged 502 to 515 days, as an inadvertent contaminant in their ^{224}Ra injection solution ^(11, 12) as summarized in Table 1.

Table 1. Beagles injected with ^{210}Pb .

<u>Dog</u>	<u>Sex</u>	<u>Age Days</u>	<u>Weight kg</u>	<u>Injected $\mu\text{Ci}^{210}\text{Pb}$</u>	<u>Injected $\mu\text{Ci}^{210}\text{Pb/kg}$</u>
T1L5	M	522	9.78	104.6	10.7
T2L5	M	522	9.16	98.0	10.7
T3L5	M	522	9.78	104.6	10.7
T15Q4	M	515	12.7	46.1	3.63
T16Q2	F	515	9.36	3.86	0.412
T17Q2	F	515	10.2	4.22	0.414
T18Q2	M	502	9.68	3.94	0.407
T19Q1	F	515	11.8	0.746	0.0632
T20Q1	F	515	10.4	0.653	0.0628
T21Q1	F	502	9.08	0.540	0.0595

Blood samples were obtained from T1L5, T2L5 and T3L5 by venipuncture on 4 occasions during the first day, beginning at 30 minutes after injection, and at various intervals thereafter for the first

72 days. Whole blood was separated into plasma and red cell fractions, and their ^{210}Pb content was determined using Knothole, a side-well NaI(Tl) detector.⁽¹⁴⁾

All urine and feces were collected from T1L5, T2L5 and T3L5 for the first 3 weeks after injection. Urine samples in 1 liter capacity polyethylene bottles were treated with 40 ml of concentrated HCl to ensure that the ^{210}Pb would remain in solution. Volumes were adjusted to 1 liter with distilled water. Feces samples were sealed in #2 cans after the addition of enough formalin and distilled water to fill the can. Counting rates of urine samples at 47 keV were compared with the counting rate of a known activity of ^{210}Pb dissolved in 960 ml of distilled water in a polyethylene bottle, identical to those containing the samples, to which 40 ml concentrated HCl had been added. The counting rates of feces samples at 47 keV were compared with that of a known ^{210}Pb activity dispersed in 480 ml of solution in a #2 can. Samples were placed between two 8 x 4 inch NaI(Tl) crystals for counting.⁽¹⁵⁾ Total-body retention was determined by gamma-ray counting using the 47 keV photon associated with the radioactive decay of ^{210}Pb . The dog was placed in a low-background counting chamber with 12 inch thick steel walls, and radioactivity measurements were made with a NaI(Tl) crystal 8 inches in diameter and 4 inches thick. The anesthetized dog was placed on his back in a lucite box which curved his body along a 33 cm-radius arc and which positioned his midline at a distance of 33 cm from the center of the crystal face. This box molded the animals to a uniform maximum lateral thickness of 15 cm so that photon self-absorption would

be relatively uniform from dog to dog. A ^{210}Pb standard in 10 ml of solution in a glass ampoule was also counted in the dog positioner inside of a lucite and polyethylene cylinder 13.25 cm in diameter to simulate the average absorption of gamma-radiation by a dog's body.⁽¹⁶⁾

One animal, T2L5, was sacrificed 28 days after injection. The dog was exsanguinated and then perfused with physiological saline solution. This procedure eliminated most of the ^{210}Pb within organs and tissues which was associated with blood. Individual bones, organs and tissues were assayed for their ^{210}Pb content by gamma-ray counting. The detectors used were either Knothole or a pair of 8 x 4 NaI(Tl) crystals. Corrections were made for the differences in counting rates between ampoule standards and samples of differing photon self-absorption. As a check on the accuracy of our γ -ray analysis, two bones from T2L5, the left humerus and the third lumbar vertebra, were γ -counted using the 8 x 4 inch NaI(Tl) crystals, and then they were subjected to wet ashing and radiochemical analysis using techniques described in Reference 12. By γ -counting, with correction for photon absorption, the percent of the injected ^{210}Pb found in the left humerus and in the third lumbar vertebra appeared to be 0.721% and 0.299%, respectively. Values obtained by radiochemical analysis were 0.719% and 0.296%, in excellent agreement with the values for the intact bones.

RESULTS AND DISCUSSION

^{210}Pb in the blood. By 1 hour following injection, more than 99% of the ^{210}Pb in the blood was associated with the red cell fraction, a

Table 2. Persistence of ^{210}Pb in the circulating blood of 3 Beagles following ^{210}Pb injection.

Time after injection	Percent of injected ^{210}Pb in the circulating blood		
	T1L5	T2L5	T3L5
0.5h	50.3 %	47.1 %	53.5 %
1.0h	51.3	49.0	52.1
3.0h	53.1	51.0	56.7
6.5h	52.6	53.8	57.7
1d	38.4	39.6	43.0
2d	28.2	31.8	35.0
3d	22.6	24.8	27.3
7d	12.6	13.7	15.0
13d	6.8	7.5	8.6
21d	4.66	5.72	5.69
27d	3.04	3.19	3.67
36d	2.05		2.01
55d	0.80		1.11
72d	0.480		0.625

condition maintained for at least 72 days. Table 2 lists the calculated percent of the injected ^{210}Pb in the circulation at various times after injection. The total blood volume of each animal used in these calculations was based upon the relationship of blood volume and body weight for Beagles in our colony (94.4 ml blood/kg body) given in Reference 17.

^{210}Pb excretion. Results of the excreta analysis are shown in Table 3. Also exhibited are percent total-body retention values obtained by subtracting the cumulative excretion (and removal of activity in blood samples) from 100%. The excretion of ^{210}Pb in these

Table 3.

Average urinary and fecal excretion by T1L5, T2L5, and T3L5 for the first 21 days after ^{210}Pb injection. Retention calculated via loss of ^{210}Pb by excretion and blood samples is shown in the last column.

Days after injection	% Injected ^{210}Pb in urine	% Cumulative urinary excretion	% Injected ^{210}Pb in feces	% Cumulative fecal excretion	% Cumulative total excretion	% Injected ^{210}Pb removed in blood samples	% Cumulative removed in blood	% Total cumulative loss	100 % Minus loss (retention)
1	2.19	2.19	4.22	4.22	6.41	2.84	2.84	9.25	90.75
2	1.10	3.29	3.68	7.90	11.19	0.36	3.20	14.39	
3	1.63	4.92	3.97	11.87	16.79	0.27	3.47	20.26	79.74
4	0.51	5.43	3.29	15.16	20.59			24.06	
5	0.93	6.36	2.17	17.33	23.69			27.16	
6	0.68	7.04	2.01	19.34	26.38			29.85	
7	0.52	7.56	1.30	20.64	28.20	0.16	3.63	31.83	68.17
8	0.51	8.07	1.68	22.32	30.39			34.02	
9	0.52	8.59	1.65	23.97	32.56			36.19	
10	0.45	9.04	1.21	25.18	34.22			37.85	
11	0.37	9.41	1.06	26.24	35.65			39.28	
12	0.32	9.73	0.74	26.98	36.71			40.34	
13	0.31	10.04	0.86	27.84	37.88	0.09	3.72	41.60	
14	0.24	10.28	1.41	29.25	39.53			43.25	56.75
15	0.20	10.48	1.47	30.72	41.20			44.92	
16	0.19	10.67	0.88	31.60	42.27			45.99	
17	0.24	10.91	0.72	32.32	43.23			46.95	
18	0.21	11.12	0.62	32.94	44.06			47.78	
19	0.24	11.36	0.60	33.54	44.90			48.62	
20	0.21	11.57	1.65	35.19	46.76			50.48	
21	0.16	11.73	0.78	35.97	47.70	0.06	3.78	51.48	48.52
Total		11.73		35.97	47.70				
% of total excretion		25 %		75 %	100 %				

animals was predominantly fecal. About 75% of the ^{210}Pb excreted in the first 3 weeks after injection appeared in the feces. Except for day 1 when 66% of the total excretion was in the feces and for days 4, 14, 15, 16, 20, and 21 when the fecal excretion was between 82% and 89% of the total, values for individual days fell between 70% and 77%.

In a different study by Bell and Gilliland,⁽¹⁸⁾ four 1 1/2 year old Beagles and three adult mongrel dogs were injected intravenously with ^{210}Pb (chemical form not stated). Total-body retention values were calculated from the measurement of ^{210}Pb in the excreta. The authors stated that "faecal excretion accounted for less than 1% of the total urinary plus faecal ^{210}Pb excretion." Tabulated retention of the injected Pb (their Table I) averaged about 91.6% at about one week. The cumulative excretion was claimed to have been 8% at the end of the first year and 10% after two years, making the alleged retention at these two points in time 92% and 90%, respectively.

Black⁽¹⁰⁾ exposed 6 female Beagles to ^{210}Pb via inhalation in a radon-enriched atmosphere. Retention was determined by excreta analysis. The proportion of the total ^{210}Pb elimination which was excreted in the feces ranged between 67% at 21 days and 90% at 630 days post exposure. Calculated total-body retention was about 26-32% at 1 year and about 12-15% at 2 years after exposure. Following an initial rapid loss of activity, the retention between about 300 and 800 days after exposure had a biological half-time of about 330 days.

The striking differences in excretion and calculated retention between the study of Stuart⁽¹⁰⁾ and that of Bell and Gilliland⁽¹⁸⁾ has been attributed by Cohen and Howells⁽¹⁹⁾ to the difference in mode of administration. Comparison of data from both studies with

our results (Table 3) shows that the retention and excretion of ^{210}Pb by our Pb-injected dogs were remarkably different from the injected dogs of Reference 18 but quite similar to the dogs of Reference 10 which were exposed by inhalation.

Because of the similarities in retention and excretion of our citrate-injected dogs and Black's inhalation-exposed dogs,⁽¹⁰⁾ we believe that not all ^{210}Pb excreted in the feces was accounted for in the studies reported by Bell and Gilliland,⁽¹⁸⁾ resulting in both an inaccurate estimate of fecal-to-total excretion and incorrectly high estimates of total-body retention. Moreover, retention values derived from excreta measurements for animals in our studies were monitored independently by total-body counting and by tissue analysis. Retention values of Black's animals, calculated from excretion data, agreed with those obtained at autopsy. In the studies of Bell and Gilliland,⁽¹⁸⁾ however, tissue analysis at sacrifice failed to verify the retention calculated from excreta measurements. Determination of stable Pb excretion for human subjects, cited by Black,⁽¹⁰⁾ agrees with his dog data and with our dog data. Aub⁽²⁰⁾ reported the retention of 50%-60% at 120 days with a subsequent biological half-time of about 346 days for dogs injected with ^{210}Pb . These results agree closely with those of Black.

^{210}Pb distribution. At 28 days after injection, the skeleton of T2L5 contained 63% of the retained ^{210}Pb . Liver had 20%, the blood had 8% and the other soft tissues had 9% of the retained ^{210}Pb (Table 4). The concentration of ^{210}Pb activity in the liver was about 1.6 times higher than that in the skeleton, about 3 times higher than in the kidneys, about 16 times higher than in the spleen, about 8 times

Table 4. Distribution of ^{210}Pb in the organs and tissues of T2L5 at 28 days after injection.

Part	Weight, g	% of injected ^{210}Pb	% injected ^{210}Pb per gram
Forepaws	56*	0.378 %	0.0067
Radii	30	0.289	0.0096
Ulnae	33	0.351	0.0106
Humeri	60	1.457	0.0243
Scapulae	54	1.050	0.0194
Hindpaws	61*	0.529	0.0087
Tibias + Fibulas	63	0.901	0.0143
Femurs	68	1.255	0.0185
Pelves	67	1.381	0.0206
Maxillae	167	3.068	0.0184
Mandibles	69	1.004	0.0146
Calvarium	33	0.345	0.0105
Ribs	174*	2.694	0.0155
Sternum	43	0.792	0.0184
Cerv. Vert.	94	1.315	0.0140
Thor. Vert.	111	4.059	0.0366
Lumb. Vert.	118	2.530	0.0214
Tail	35	0.275	0.0079
Patallae	8	0.019	0.0024
Total Skeleton	1344	23.7	0.0176
Liver	270	7.540	0.0279
Kidneys	49	0.445	0.0091
Spleen	24	0.041	0.0017
Muscle	3947	0.533	0.0001
Pelt	1573	1.629	0.0010
G.I. Tract	520	0.296	0.0006
Blood ⁺	911	3.190	0.0035
Testes	27	0.005	0.0002
Brain	83	0.040	0.0005
Heart	87	0.007	0.0001
Lungs + Trachea	77	0.073	0.0009
Prostate	10	<0.003	----
Eyes	15	<0.003	----
Pancreas	27	0.068	0.0025
Salivary	10	0.003	0.0003
Aorta	9	<0.003	----
Bladder	9	<0.003	----
Thymus	2.42	0.0004	0.0002
Adrenal	0.76	0.0003	0.0004
Pituitary	0.04	0.00003	0.0008
Parathyroids	0.005	0.00002	0.0040
Tonsil	0.88	0.00035	0.0004
Lymph Nodes	12.66	0.00968	0.0008
Thyroid	0.74	0.00071	0.0010
Total Soft Tissue ⁺	7666	13.9	0.0018
Total Dog	9010	37.6	0.0042

*Not defleshed

⁺Animal sacrificed by exsanguination. About 2500 ml saline was then used to flush the circulatory system.

higher than in the blood, about 15 times higher than in the combined soft tissue, and about 7 times higher than in the whole dog. Concentration measurements at 840 days after exposure reported by Black (Table 1 of Reference 10) indicate a much more uniform soft tissue distribution as well as a greater fraction of the retained activity in the skeleton (80-90%).

Measurement of total-body ^{210}Pb . The net counting rates at 47 keV of T1L5, T2L5, and T3L5, soon enough after injection that no loss of ^{210}Pb had occurred, averaged about 3% higher than the net counting rates of ampoule standards containing duplicates of their respective ^{210}Pb injected activities. Subsequently, it appeared as if the total-body counting rate per retained μCi was progressively decreasing during the first 3 weeks after injection. Such an effect could be accounted for by the assumption that as ^{210}Pb left the blood and soft tissue and became deposited in bone, the attenuation of the 47 keV photons was increased. Clearly, a calibration factor was required which, (a) matched the total-body counting results to the excretion results for the first 21 days after injection, (b) matched the total-body counting results of T2L5 on day 28 to the total ^{210}Pb content of the bones and soft tissues of T2L5 at sacrifice, and (c) accounted for the changing photon attenuation postulated for the first few weeks after injection without also predicting incredible values at long times after injection. The expression which was chosen to represent such a calibration factor and which gave a reasonable fit to the data was:

$$CF = 0.97 + 0.2068 (1 - e^{-0.2266t})$$

where CF = the calibration factor to be applied to the dog's total-body net counting rate at t days after injection.

Retention values calculated using results of total-body counting and this calibration factor were slightly lower than those based on excreta analysis. The retention value for T2L5 on day 28 similarly calculated was slightly higher than the retention value based on the analysis of individual bones, organs, and tissues of T2L5. Overall agreement is reasonable, however, and if some excreted ^{210}Pb had not been measured because of inadvertent losses of excreta, or if some retained ^{210}Pb had not been measured in the tissues of T2L5 because of the omission of some tissues from the counting schedule, the agreement would have been even better. Our experience has been that a dog's true retention is characteristically never underestimated by excreta measurements and is characteristically never overestimated by the analysis of individual bones and soft tissues.

The results of total-body counting for all 10 animals included in this study, corrected by the appropriate calibration factor, are reported in Table 5 and are displayed in Figure 1. We have elected to represent the total-body retention of injected ^{210}Pb in these dogs by a sum of exponentials. The expression chosen to describe the retention of a typical Beagle was

$$\% \text{ } ^{210}\text{Pb retention} = 36e^{-0.189t} + 43e^{-0.0212t} + 21e^{-0.0007t}$$

as shown in Figure 1.

In fitting this curve, an attempt was made to have it pass through

the average of the points representing the retention data parallel to the slopes of the lines connecting the serial measurements of the individual animals. Because the values for the 1-level dogs were probably least reliable, those for the higher levels were assigned larger weighting factors in obtaining averages. Allowance was also made for the projected retention of T1L5 and T3L5 at times greater than 300 days. This equation indicates that the retention of injected Pb in these Beagles is equivalent to 36% being retained with a biological half-time of about 4 days, 43% with 33 days, and 21% with 990 days, resulting in an equivalent biological half-time* of about 224 days. We anticipate the revision of the retention equation as more data are collected.

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* Weighted average of all component half-times.

Table 5. Retention of injected ^{210}Pb in beagles as determined by total-body counting.

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{210}\text{Pb/kg}$	DAYS AFTER INJECTION	PERCENT BIOLOGICAL RETENTION
T1L5	522	10.7	1	85.0
			3	76.2
			7	64.8
			14	50.9
			21	44.6
			28	37.8
			73	24.2
			218	14.6
T2L5	522	10.7	1	90.4
			3	75.9
			7	67.9
			14	53.6
			21	45.9
			28	40.1
T3L5	522	10.7	1	88.6
			3	78.6
			7	69.7
			14	55.0
			21	47.2
			28	41.3
			73	27.7
			218	17.0
T15Q4	515	3.63	35	43.0
			67	33.0
			99	27.1
			187	22.6
			357	18.3
			503	16.1
			585	16.1
			727	14.8
T16Q2	515	0.412	67	25.9
			99	22.6
			187	19.8
			357	17.0
			503	13.2
			585	12.2
			727	10.9

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{210}\text{Pb/kg}$	DAYS AFTER INJECTION	PERCENT BIOLOGICAL RETENTION
T17Q2	515	0.414	67	32.5
			99	26.3
			187	22.3
			357	20.8
			503	15.4
			585	14.9
			727	13.4
T18Q2	502	0.407	67	32.2
			99	27.8
			187	23.4
			357	20.4
			503	14.8
			585	15.7
			727	11.2
T19Q1	515	0.0632	67	31.8
			99	26.2
			187	21.2
			357	19.4
			503	18.0
			585	16.9
			733	15.2
T20Q1	515	0.0628	67	31.5
			99	25.4
			187	23.6
			357	16.2
			503	15.5
			585	14.3
			733	12.1
T21Q1	502	0.0595	67	32.1
			99	28.3
			187	28.1
			357	20.4
			503	18.7
			585	18.8
			733	16.2

Figure 1. Biological retention of injected ^{210}Pb in Beagles. Measured retention values are indicated by circles, and serial measurements of the same dog are connected by lines. The curve representing average retention for all dogs was fit through the data parallel to the slopes of the lines representing the retention of individual animals. An attempt was made to have the average retention curve pass near the center of all the measurements at a given time after injection, except that the values for the higher level dogs were considered to be most reliable, and allowance was made at times greater than 200 days post-injection for the projected lower retention of T1L5 and T3L5.

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^{241}Am

AMERICIUM-241 RETENTION IN BEAGLES

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Abstract: Forty-eight adult beagles were injected with 0.00179 to 4.49 $\mu\text{Ci } ^{241}\text{Am/kg}$ body mass. Retained activity in the living animals was evaluated via the 60 keV gamma-ray using a combination of total-body and partial-body counting to determine the proportion in the liver and in non-liver tissue. Soon after injection, about 50% and 40%, respectively, of the administered ^{241}Am was deposited in the liver and non-liver tissue (mainly skeleton). In the animals injected with 0.00179 to 0.305 $\mu\text{Ci/kg}$ the liver and non-liver burdens decreased slowly each with a biological half-time of about 10 years during the first 850 days. Two dogs injected with about 2.80 $\mu\text{Ci/kg}$ exhibited a sharp decrease in liver retention beginning about 100 days after injection accompanied by an increase in non-liver ^{241}Am . Both showed extreme degenerative liver changes at death 401 and 448 days after injection. Similar but more slowly progressing effects were observed in the retention of ^{241}Am by two animals injected with about 0.904 $\mu\text{Ci/kg}$. At even longer times after injection, corresponding effects were noted in the lower level dogs. Excreta collections from four dogs during the first three weeks after injection showed that 7/8 of the excretion was urinary and that nearly 3/4 of the total ^{241}Am excreted during this period appeared in the first day's collection. Evaluation of the activity of individual bones, organs, and tissues of six animals autopsied 1 to 448 days after injection showed that although ^{241}Am was distributed in many soft tissues, the liver and skeleton were the principal deposition sites; however, americium concentration in the thyroid gland was higher than in the skeleton and was higher than in any other soft tissue except the liver. Autoradiography showed that ^{241}Am was deposited close to the location of the functioning thyroid cells. The kidney also had a relatively high concentration of activity, selectively deposited in the glomeruli.

INTRODUCTION

Modern nuclear technology is finding ^{241}Am to be useful in a variety of ways. Also, contemporary reactor plutonium contains ^{241}Am as an impurity. In fact, the gamma-ray emission from ^{241}Am has been used to locate ^{239}Pu deposits in humans accidentally exposed to such a

plutonium + ^{241}Am mixture⁽¹⁾. As total reactor output increases and as ^{241}Am is utilized to a larger extent, it appears that increasing exposures of humans to this nuclide can be expected. An evaluation of the metabolism and long-term effects of internally deposited ^{241}Am , therefore, needs to be made.

The metabolism and radiotoxicity of injected ^{239}Pu in beagles has been studied at this laboratory since 1952^(2,3,4,5). Seven liver tumors (including at least two carcinomas) have been observed in beagles injected 7 to 13 years earlier with 0.0139 to 0.0968 $\mu\text{Ci } ^{239}\text{Pu/kg}$ ⁽⁶⁾. However, most animals injected with these or greater amounts have died with bone tumors. Perhaps their consequently abbreviated survival times did not allow liver tumors to become evident. It has been observed in rats that ^{241}Am deposits in the liver and in the skeleton, as does plutonium, but that the proportion in the liver is greater with ^{241}Am ^(7,8). The appearance of liver disease (including liver tumors) and bone cancer is expected following the injection of ^{241}Am in beagles. If the higher uptake by the liver constitutes a "protective" effect on the skeleton and thereby extends the time to death from bone cancer, it is speculated that ^{241}Am -burdened beagles might exhibit a significant incidence of liver tumor especially at relatively low ^{241}Am levels.

This pilot study was designed to provide a comparison between the metabolism of ^{241}Am and ^{239}Pu , to evaluate the relative hazard of ^{241}Am as an internal emitter, and to gain an insight into the importance of liver degeneration, liver tumors, bone cancer and other effects as end-points following ^{241}Am deposition.

3

METHODS

Forty-eight adult beagles from our colony averaging 506 days of age* were each given a single intravenous injection of ^{241}Am in a citric acid-sodium citrate buffer solution at pH 3.5. Injected activities ranged from 0.02 to 52.1 $\mu\text{Ci } ^{241}\text{Am}$ (0.00179 to 4.49 $\mu\text{Ci } ^{241}\text{Am/kg}$ body mass) as shown in Table 1. The ^{241}Am activity subsequently deposited in their skeletons and in their livers was determined by a combination of total-body counting and partial-body counting, using the 60 keV gamma-ray.

For counting, the anesthetized animal was placed, backbone down, in a lucite box which curved his midline into an arc having a 33 cm radius (Fig. 1). The box was positioned such that the dog's midline was 33 cm from the face of an 8 x 4 inch NaI(Tl) crystal. This counting arrangement was designed so that detector response would be relatively independent of the location of an emitter along the length of a dog. It had been previously determined that a point source of photon radiation placed anywhere on the hemi-spherical surface 33 cm from the center of this crystal face was counted with almost equal efficiency. The lucite container molded the animals to a constant 15 cm thickness to provide somewhat equal photon absorption from dog to dog, regardless of size, within the size limits of our adult beagles. Both the animal and the detector were housed during the counting period in a low-background steel room constructed of 12 inch thick plate.

A lead (Pb) shield 20 cm high, 18 cm wide, and 1.5 cm thick was interposed between the crystal and the animal's liver during partial-

*The ages ranged between 467 and 561 days except for 2 short term sacrifice animals aged 393 and 858 days at injection.

Table 1. Beagles injected with ^{241}Am .

<u>Level</u>	<u>Average weight at injection kg</u>	<u>Average injected $\mu\text{Ci/kg}$</u>	<u>Number of dogs injected</u>
5.5*	11.0	4.49	3
5**	11.3	2.80	3
4	10.3	0.909	6
3	11.2	0.305	6
2	11.6	0.0956	6
1.7	9.76	0.0482	6
1 ⁺	10.4	0.0162	6
0.5	10.5	0.00536	6
0.2	11.8	0.00179	6

*Dogs sacrificed at 1, 7, and 8 days after injection for ^{241}Am distribution studies.

**One dog sacrificed 22 days after injection for ^{241}Am distribution studies; two dogs died of radiation effects at 401 and 448 days after injection (see Results and Discussion section).

⁺One dog died by accidental strangulation 232 days after injection.

body counting. It had been determined radiographically that a shield of this size would effectively screen off the liver (Fig. 1). Calculation of the ^{241}Am activity in the liver and in the skeleton was based on the assumptions that ^{241}Am in the liver was counted with the same efficiency as ^{241}Am in the total-body, and that the liver burden was equal to the total-body burden minus (1) the ^{241}Am in the body not covered by the Pb shield, and (2) the ^{241}Am in the non-liver tissue covered by the Pb shield. Five beagles containing ^{241}Am were counted with and without this liver shield shortly before sacrifice. The liver was excised and placed in a 1 liter capacity polyethylene bottle, and the liver counting rate at 60 keV was compared with that of a known activity of ^{241}Am in

an identical bottle. Livers and standards were counted between two 8 x 4 inch NaI(Tl) crystals. The ^{241}Am standards had been diluted with distilled water to approximate the volume of liver sample so that photon self-absorption would be similar. Contribution of non-liver ^{241}Am to the counting rate of the intact animal with and without the liver shield could then be calculated using the measured activity in the liver. It was found for these animals that the percent of non-liver ^{241}Am shielded from the crystal could be approximated by the expression:

$$\% \text{ shielded} = 58.1 - (0.43) L$$

$$36 \text{ cm} \leq L \leq 43 \text{ cm}$$

where "L" = the length (cm) of the dog measured from the cranial angle of the scapula to the base of the tail (see Fig. 1).

This equation was used to calculate the proportion of the non-liver ^{241}Am covered by the shield for each ^{241}Am dog so that the partial-body counting results could be appropriately corrected. Most of the non-liver ^{241}Am is in the skeleton.

Total excreta collections were made from four of the dogs for 21 days post-injection. Calibration of the total-body counter was accomplished by using the ^{241}Am body burden computed as injected activity minus that excreted.

Individual bones, organs, and tissues of six dogs were evaluated for their ^{241}Am content using the same method described for excised livers. Not only was the distribution of activity determined for each animal, but the calibration of the total-body counter previously obtained by excreta subtraction was also verified by summing the ^{241}Am content in the individual organs.

RESULTS AND DISCUSSION

Table 2 shows the results of the gamma-ray assay of excreta collections from four dogs. The excretion of ^{241}Am in these animals was predominantly urinary. Cumulative (urine/total) excretion ratios averaged 0.871 for the entire 21-day period and 0.964 for the first day. Nearly 75% of the total ^{241}Am excreted during this 3 week period was found in the first day's collection. Estimated cumulative radiation doses (alpha + recoil energy = 5.57 MeV/ ^{241}Am disintegration) for this 21 day period averaged about 75 rads to the skeleton and about 300 rads to the liver for the two 5-level dogs and about 25 and 80 rads for the two 4-level animals.

Table 2. Percent of injected ^{241}Am excreted by four beagles (T1W5, T2W5, T3W4, T4W4).

<u>Days after injection</u>	Percent of injected ^{241}Am (average of all 4 dogs)			
	<u>Urine</u>	<u>Feces</u>	<u>Urine + Feces</u>	<u>Urine + Feces cumulative total</u>
0-1	8.027	0.267	8.294	8.294
1-2	0.340	0.506	0.846	9.140
2-3	0.336	0.144	0.480	9.620
3-7	0.507	0.328	0.835	10.455
7-14	0.327	0.139	0.466	10.921
14-21	0.174	0.059	0.233	11.154
Total	9.711	1.443	11.154	
% of total excretion	87.1%	12.9%	100%	

Retention values calculated from total-body and partial-body counting for the long-term animals are listed in Table 5 and are shown in Figs. 2 and 3 for the long-term animals. Dogs at the intermediate injection levels (0.0162 to 0.305 $\mu\text{Ci/kg}$) showed an initial deposit of about 50% and

40% of the injected ^{241}Am in the liver and non-liver tissue, respectively, followed by a slow decrease thereafter. However, the two animals at the 5-level (2.80 $\mu\text{Ci/kg}$) that survived over a year showed a markedly different retention pattern. Before about 100 days post injection, the retention curves for the 5-level dogs were roughly parallel to those of the intermediate levels. Then the total activity in the liver began to decrease sharply after the accumulation of about 1000-1500 rads to the liver. This was accompanied by an increase of ^{241}Am retention in non-liver tissue. These same trends were observed until the death of the animals at 401 and 448 days after injection. It appeared that during the last year of life ^{241}Am was leaving the liver and at least part was redepositing mainly in the skeleton. We interpret these observations as being indicative of radiation damage to the liver. Estimated liver doses at death were about 5500 rad (T1W5) and 7600 rad (T2W5). At sacrifice, both dogs were moribund with extreme liver degeneration accompanied by portal hypertension and ascites related to marked alteration of the general vascular architecture of the liver. Kidney damage may have also been contributory. Average skeletal doses at death were estimated at about 1600 and 1700 rads.

Table 3 lists the results of activity concentration measurements made on liver samples obtained serially from one of these 5-level dogs. Coupled with the observation that the liver weight at death for both of

Table 3. Concentration of ^{241}Am in the liver of T1W5.

<u>Source</u>	<u>Days after injection</u>	<u>% administered ^{241}Am kg of liver</u>
Biopsy	41	201
Biopsy	245	134
Autopsy	401	150

these dogs was about half the normal value, (144 g for T1W5 and 146 g for T2W5) these data suggest that the americium was tightly bound in the liver and that its accelerated loss resulted mainly from the release of activity from that liver tissue which was destroyed. Consequently, even though the total activity of ^{241}Am was reduced to less than half of the initial value, the activity concentration and therefore the average dose rate remained relatively unchanged.

The 2 to 3 month delay between injection and the sharp divergence of retention curves of the 5 - and intermediate - level animals could be a reflection of the time required to accumulate sufficient radiation dose to kill the liver cells either directly or at cell division.

Data for the 4-level animals ($0.9 \mu\text{Ci/kg}$) also shown in Figs. 2 and 3 suggest that an effect similar to that exhibited by the 5-level animals may have occurred. However, this effect seems to have been less dramatic and delayed toward longer post-injection times. Estimated liver doses at 300 days post injection were about 1100 rads. These two dogs presently have significant liver injury as determined by liver function tests⁽⁹⁾ with about 3400 rads liver dose and 1100 rads average skeletal dose at 896 days after injection.

Non-liver retention values for the 1, 2, and 3-level dogs after about 700 days post-injection indicate that the effect seen at the 5- and 4-levels may also have occurred but at a much later time. The accompanying sharp decline in liver retention, however, is not evident.

Evaluation of the ^{241}Am activity of individual bones, organs and tissues of the six sacrifice animals showed that americium was distributed in many soft tissues in addition to the primary deposition sites of liver

and skeleton and that activity in paired bones was similar. Results are summarized in Table 4. Note that tissues other than the liver and skeleton account for only a minor proportion of the retained activity. A few soft tissues such as muscle, pelt, and kidneys were found to contain as much as 1 to 2% of the injected americium. In general, soft tissues other than the liver did not appear to be important reservoirs of total-body ^{241}Am . A comparison of the liver and skeleton values for the two dogs which died with liver damage with those of healthy animals sacrificed soon after injection emphasizes the redistribution of activity from liver to skeleton in the long-term, high-level animals.

The thyroid contained about 0.05% of the administered ^{241}Am in all six dogs, while the amount in the adrenals, testes, and brain was even smaller. There is an apparent increase in americium deposition in the spleen for the two long-term dogs as compared with the short-term animals. This may be in part a consequence of the observed marked loss of activity from the liver.

It is of interest to consider the concentration of activity in these tissues. Of special significance is the thyroid: only the liver had a higher concentration. Autoradiography⁽¹⁰⁾ of the sectioned thyroid revealed that ^{241}Am activity was located within the interfollicular region (Fig. 4). Those cells which are fundamental to thyroid function are within α -particle range of the ^{241}Am deposit. No obvious differences were observed in the pattern of ^{241}Am deposition in the thyroids of dogs sacrificed 1 to 22 days after injection compared to those sacrificed at 401 and 448 days. This finding may require the thyroid to be considered a critical organ for ^{241}Am as an internal hazard if human thyroid

Table 4. Distribution of injected ^{241}Am in beagles.

Organ or Tissue	4* dogs sacrificed 1-22 days after injection		2** dogs dying 401 and 448 days after injection	
	% injected ^{241}Am kg tissue	% of injected ^{241}Am	% injected ^{241}Am kg tissue	% of injected ^{241}Am
Liver	178.59	48.68	125.04	18.13
Thyroid	55.07	0.048	106.97	0.050
Skeleton	27.05	28.75	41.70	47.95
Kidneys	15.59	0.65	18.03	1.21
Dura Mater	8.50	0.012	not measured	
Lymphatic tissue	8.46	0.049§	16.58	0.071§
Trachea	7.10	0.090	29.31	0.28
Aorta	4.84	0.025	5.15	0.048
Lung	4.56	0.35	4.89	0.39
Larynx	3.29	0.12	6.40	0.23
Salivary Glands	3.22	0.012	not measured	
Adrenals	3.15	0.0028	3.40	0.0060
Pituitary	2.60	0.00018	13.84	0.0010
Prostate	1.86	0.014	5.10	0.026
Spleen	1.51	0.028	16.52	0.072
Eyes	1.25	0.015	1.39	0.016
G.I. Tract	1.23	0.60	0.83	0.31
Heart	0.81	0.071	1.73	0.13
Urinary Bladder	0.78	0.0040	not measured	
Testes	0.77	0.0090	1.01	0.014
Pelt	0.76	1.72	0.98	1.45
Pancreas	0.52	0.010	0.63	0.014
Muscle	0.28	1.20§	0.64	1.66§
Fat	0.090	0.020§	not measured	
Thymus	<0.41	<0.0020	not measured	
Brain	<0.02	<0.001	0.10	0.008
Average Total-body Concentration	7.76		7.17	
Total ^{241}Am Content of Measured Tissues		82.5		72.1
Total-body ^{241}Am Content Via Total- body Counting		86.0		78.1

*3 dogs = 4.49 $\mu\text{Ci/kg}$, 1 dog = 2.80 $\mu\text{Ci/kg}$ **2 dogs = 2.80 $\mu\text{Ci/kg}$

§Incomplete Sample

deposition is similar to that in the dog. The kidney also had a relatively high concentration and may prove to be an additional critical organ. Autoradiographs of kidney tissue showed that ^{241}Am deposits in the glomeruli (Fig. 5). Abnormal urinalysis findings for the two long-term 4-level dogs indicate possible kidney damage. Kidney function and thyroid function are being studied in detail in beagles containing ^{241}Am .

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Figure 1. This illustration shows the way in which a dog is positioned for counting in the lucite box, the positioning of the Pb shield over the liver for partial-body counting, and the determination of the distance "L" used in Eq. (1).

Figure 2. Liver retention of injected ^{241}Am . Triangles represent the 5-level dogs ($2.8 \mu\text{Ci/kg}$ injected), squares represent the 4-level dogs ($0.9 \mu\text{Ci/kg}$), and circles represent the 1, 2, and 3-level dogs (0.02 to $0.3 \mu\text{Ci/kg}$). Average differences between individual measurements for the two 5-level dogs and their mean were about 5% of the value shown at each point, while the differences for the two 4-level dogs averaged about 7.5%. The average deviation from the mean value for the six 1, 2, and 3-level dogs was about 9%. The final two measurements at the 5-level each represent only one dog. The lower initial retention of the two 4-level dogs is tentatively ascribed to random variability in uptake by the liver. Data for the lower-level dogs before 100 days after injection were estimated from measurements of other animals at the same injection levels.

Figure 3. Retention of injected ^{241}Am in non-liver tissue including skeleton. Triangles represent the 5-level dogs ($2.8 \mu\text{Ci/kg}$ injected) squares represent the 4-level dogs ($0.9 \mu\text{Ci/kg}$), and circles represent the 1, 2, and 3-level dogs (0.02 to $0.3 \mu\text{Ci/kg}$). Average differences between individual measurements for the two 5-level dogs and their mean were about 3% of the value shown at each point, while the differences for the two 4-level dogs averaged about 1.5%. The average deviation from the mean value for the six 1, 2, and 3-level dogs was about 5%. The final two measurements at the 5-level each represent only one dog. Data for the lower-level dogs before 100 days post-injection were estimated from measurements of other animals at the same injection levels.

Figure 4. Autoradiograph of T15W5.5 thyroid. The ^{241}Am is concentrated in the interfollicular region within α -particle range of functioning thyroid cells.

Figure 5. Autoradiograph of T2W5 kidney showing selective deposition of ^{241}Am in the glomerulus.

Table 5. Retention of injected ^{241}Am in the liver and in non-liver tissue of beagles as measured by total-body and partial-body counting.

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{241}\text{Am/kg}$	DAYS AFTER INJECTION	% RETENTION IN LIVER	% RETENTION IN NON-LIVER TISSUE
T1W5	517	2.78	0	53.4	57.3
			1	53.7	44.1
			2	50.3	44.4
			3	50.8	45.5
			7	50.5	45.8
			14	50.4	44.9
			21	51.9	44.1
			41	49.9	44.5
			189	41.7	48.6
			401	22.8	62.0
T2W5	517	2.83	0	47.2	53.8
			1	47.6	43.6
			2	45.3	42.3
			3	47.3	40.5
			7	43.2	43.5
			14	45.4	41.2
			21	43.3	42.2
			41	44.7	42.3
			189	42.0	44.0
			448	13.4	58.0
T3W4	517	0.897	0	45.0	59.9
			1	46.5	46.5
			2	44.1	44.8
			3	43.7	45.3
			7	42.9	47.1
			14	43.9	46.7
			21	46.7	46.4
			41	44.9	43.5
			189	43.6	45.3
			365	35.5	44.1
			540	26.3	49.7
			644	25.0	49.9
			742	23.2	47.0
			772	24.4	49.2
			896	19.4	51.3

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{241}\text{Am/kg}$	DAYS AFTER INJECTION	% RETENTION IN LIVER	% RETENTION IN NON-LIVER TISSUE
T4W4	517	0.911	0	35.7	61.9
			1	39.6	46.7
			2	42.6	45.5
			3	36.8	46.4
			7	36.6	49.1
			14	34.7	49.6
			21	37.9	47.2
			41	33.7	46.2
			189	36.9	47.5
			365	34.6	42.0
			540	35.3	45.7
			644	26.5	47.8
			742	23.8	47.0
			772	27.8	47.0
			896	23.4	48.9
T5W3	561	0.305	103	55.2	39.1
			187	54.8	38.7
			461	49.6	39.5
			565	50.7	38.1
			854	42.4	37.2
			1089	40.1	42.0
T6W3	561	0.310	103	53.5	38.7
			187	54.1	37.3
			461	42.2	41.3
			565	41.1	40.4
			854	36.2	42.5
			1089	36.6	43.8
T7W2	561	0.0952	103	52.9	39.3
			187	50.4	39.0
			461	50.0	38.2
			565	51.0	36.4
			854	45.2	38.1
			1089	49.2	38.7
T8W2	561	0.0957	103	39.9	44.1
			187	42.5	40.3
			461	38.6	38.7
			565	45.2	36.3
			854	37.3	37.4
			1089	40.2	38.2

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{241}\text{Am/kg}$	DAYS AFTER INJECTION	% RETENTION IN LIVER	% RETENTION IN NON-LIVER TISSUE
T9W1	517	0.016	98	46.2	41.5
			187	51.0	40.5
			461	52.1	38.0
			565	46.9	39.2
			854	49.1	33.0
			1091	49.0	36.6
T10W1	517	0.0162	98	48.2	49.2
			187	48.7	39.2
			461	49.6	34.8
			565	56.0	35.8
			854	51.8	34.1
			1091	45.1	38.8
T11W0.5	526	0.00532	78	54.6	46.5
			194	56.8	37.1
T12W0.5	526	0.00539	75	36.5	42.8
			194	54.7	36.0
T13W0.2	526	0.00179	75	60.5	46.9
			194	50.7	29.8
T14W0.2	526	0.00178	70	59.4	37.2
			194	56.6	34.2
T15W5.5	858	4.53	1	48.7	38.1
T16W5	461	2.78	22	53.9	38.2
T17W4	523	0.924	7	59.3	40.2
T18W3	523	0.307	7	58.3	43.5
T19W2	513	0.097	7	52.9	39.4
T20W1	513	0.0161	7	47.1	44.6
T21W1	513	0.0166	7	52.0	44.0
T22W1	487	0.0164	7	51.4	44.5
T23W0.5	487	0.0053	7	48.7	46.7
T24W0.2	477	0.00181	7	50.3	48.9

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{241}\text{Am/kg}$	DAYS AFTER INJECTION	% RETENTION IN LIVER	% RETENTION IN NON-LIVER TISSUE
T25W4	473	0.927	259	48.4	44.8
T26W3	473	0.31	253	46.6	40.7
T27W2	473	0.0961	253	54.4	36.1
T28W1	472	0.0158	259	61.4	36.6
T29W0.5	472	0.00548	259	56.3	38.2
T30W0.5	472	0.00538	259	49.4	38.8
T32W5.5	560	4.46	3	45.9	35.7
			7	45.9	31.8
T33W5.5	395	4.47	3	46.2	38.1
			8	46.2	33.5
T34W4	477	0.893	7	53.9	35.1
T35W4	477	0.902	7	55.6	40.6
T36W3	477	0.305	7	56.3	38.8
T37W3	468	0.294	7	58.7	38.9
T38W2	477	0.0945	7	55.7	39.4
T39W2	468	0.0948	7	30.5	59.5
T40W0.5	467	0.00528	7	67.7	39.8
T41W0.2	467	0.0018	7	71.3	38.0
T42W1.7	495	0.0484	9	40.6	44.4
T43W1.7	492	0.0481	9	46.6	39.7
T44W1.7	492	0.0473	9	44.6	50.0
T45W1.7	492	0.0486	9	55.2	40.0
T46W1.7	484	0.0479	9	61.5	34.9
T47W1.7	484	0.0486	9	47.9	42.1

^{228}Th SKELETAL DOSIMETRY AND TOTAL-BODY ^{212}Bi
RETENTION IN BEAGLES

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Abstract: Total-body retention of ^{212}Bi , a radioactive daughter of ^{228}Th , has been measured for burden times of up to 7.9 years by gamma-ray counting in a group of 84 Beagles injected intravenously with $0.00159\text{--}2.76\ \mu\text{Ci}\ ^{228}\text{Th}/\text{kg}$ in a citrate buffer at an average age of about 1.4 years. In 14 animals sacrificed 1-1511 days after injection, about 84% of the retained ^{228}Th was in the skeleton, 4% in the liver, 2% in the kidneys, 3% in the pelt, and 2% in the GI tract, with some dependence of relative distribution upon time after injection. Radiation doses and dose rates from ^{228}Th and its daughters in the skeleton were calculated based on the assumptions that (a) following an initial deposition of about 69% of the injected ^{228}Th in bone, (b) the biological half-time of this radionuclide in the skeleton was about 13.6 years, (c) the $^{224}\text{Ra}/^{228}\text{Th}$ ratio in the dog was 0.895, (d) the corresponding $^{212}\text{Bi}/^{228}\text{Th}$ ratio was 0.866, and (e) that these ratios were independent of time after injection.

RETENTION

Each of eighty-four Beagles averaging 524 days of age was given a single intravenous injection of $0.00159\text{--}2.76\ \mu\text{Ci}\ ^{228}\text{Th}/\text{kg}$ in a citric acid sodium citrate buffer solution (pH 3.5). Details of the injection procedure, experimental design and veterinary care of these dogs have appeared in a previous publication. ⁽¹⁾ Their body ^{212}Bi content was determined by total-body gamma-ray counting. Measurements extend to nearly 2900 days (7.9 years) after injection. Detectors used for total-body counting were the liquid scintillation counters K-9 ⁽²⁾ and K-9 Bark II ^(3,4) or a NaI crystal counter. ⁽⁴⁾

The gamma radiation escaping from the body of a dog injected with

radiothorium is principally due to the daughters of $^{228}\text{Th}^*$. Most prominent above about 0.4 MeV are the ^{208}Tl gamma-rays. Since its physical half-period is only 3.1 minutes, ⁽⁵⁾ the ^{208}Tl activity resulting from ^{228}Th decay within the body is controlled by the activity of its 60.6 minute ⁽⁵⁾ half-period parent, ^{212}Bi . The ^{212}Bi activity is not in equilibrium with the ^{228}Th because of losses of ^{220}Rn (thoron) in the breath ⁽⁶⁾ and ^{224}Ra ⁽⁷⁾ in the excreta in excess of ^{228}Th elimination. Therefore, the ratio of the net ^{208}Tl counting rate of a ^{228}Th -injected dog and the corresponding counting rate of an identical phantom containing a duplicate of the injected ^{228}Th activity (with its daughters in secular equilibrium) at t days after injection is

$$\frac{\text{body } ^{212}\text{Bi}}{\text{injected } ^{228}\text{Th } e^{-\lambda_{\text{Th}} t}}$$

where λ_{Th} is the ^{228}Th decay constant, 0.0009936 per day. ⁽⁸⁾

It was reported previously ⁽⁹⁾ that the ratio of skeletal ^{212}Bi (skeletal ^{212}Pb) to skeletal ^{228}Th is about 0.866 and that the ratio of skeletal ^{224}Ra to skeletal ^{228}Th is about 0.895. Both ratios appear to be independent of time after injection. These determinations, which were made on fifteen humeri and about a dozen 3rd lumbar verte-

brae, have been confirmed by subsequent measurements of about half the skeleton of each of 6 dogs as shown in Table 1.

Table 1. Relationship of ^{224}Ra and ^{212}Pb to their Parent in the skeletons of dogs injected with ^{228}Th . The injection tables in each of this laboratory's annual reports (e.g. C00-119-240) give detailed information about the dogs.

Dog	Days after injection	$^{224}\text{Ra}/^{228}\text{Th}$	$^{212}\text{Pb}/^{228}\text{Th}$
M4T4	793	0.94	0.88
M4T3	801	0.97	0.90
T7T3	910	0.88	0.83
T8T3	1043	0.94	0.85
M4T2A	1222	0.85	0.76
F3T2	1511	*	0.89
Average		0.916	0.852
Ratios from Ref. 9		0.895	0.866

* Not measured

Biological retention of injected ^{228}Th in the skeleton at t days after injection can be described by the expression ⁽¹⁰⁾

$$^{228}\text{Th retention} = 0.69 e^{-0.00014 t}$$

which accounts for an average of about 84% of the retained ^{228}Th from 1 to 1500 days after injection (Table 2).

Table 2. Distribution of ^{228}Th in Beagles at various times after injection. The injection tables in each of this laboratory's annual reports (e.g. C00-119-240) give detailed information about the dogs.

Dog	Days post injection	Biol. retention (fractional)	Skeleton	Pelt	GI Tract	Liver	Kidneys	Other*
T9T3	1	0.914	74.2	6.1	3.1	3.7	3.9	9.0
T10T3	8	0.916	80.6	4.1	1.7	4.2	3.7	5.7
T1T5	23	0.888	73.0	7.6	1.7	5.5		12.2
T5T5	65	0.828	78.6			7.8	1.3	12.3
T2T5	77	0.875	74.8	3.4	2.5	3.5	4.1	11.7
M2T5	97	0.809	79.7			7.1	1.4	11.8
T4T5	113	0.819	83.4			5.2	1.2	10.2
M1T5	212	0.804	88.0			3.2	1.3	7.5
M4T4	793	0.871	94.7	1.5	0.8	1.1	0.8	1.1
M4T3	801	0.697	93.3	1.3	0.7	2.0	1.0	1.7
T7T3	910	0.616	89.0	2.2	1.5	2.2	1.3	3.8
T8T3	1043	0.718	85.0	1.7	1.3	1.6	1.4	9.0
M4T2A	1222	0.707	92.8	1.8		2.1	0.7	2.6
F3T2	1511	0.583	89.1	3.4		2.3		5.2

* Includes all tissues not listed for a particular dog.

Results of total-body counting for the determination of body ^{212}Bi are listed in Table 3. Figure 1 is a graphical representation of these data in which is also shown the skeletal ^{212}Bi equation for Beagles from Reference 9. At long times after injection, body ^{212}Bi and skeletal ^{212}Bi should be nearly equal, but soon after injection, body ^{212}Bi should be larger than skeletal ^{212}Bi because of a higher relative soft tissue deposition. In general, the skeletal ^{212}Bi curve appears to be somewhat higher not lower than the body ^{212}Bi measurements at early times. Most of the total-body counting involved animals at the lower levels while data used in obtaining the skeletal ^{212}Bi equation were from high-level dogs. Perhaps the difference is a consequence of a radiation damage effect on the bone remodeling processes similar to that observed with ^{239}Pu (11) and ^{226}Ra (12) in Beagles where dogs at higher levels retain a greater fraction of their injected radionuclide than those at lower levels. Retention functions given in Reference 7 and 10 were based in part on measurements of excretion, and thus probably over-estimate retention by a small amount.

The skeletal ^{212}Bi equation indicates a biological half-time of 13.6 years, about 7-fold greater than the physical half-period of the ^{228}Th parent. This indicates that changes in the dose rate are chiefly governed by physical decay rather than biological elimination.

DOSIMETRY OF SKELETAL ^{228}Th

Each disintegration of ^{228}Th deposits 5.50 MeV of alpha plus

recoil energy, while the corresponding energy resulting from ^{224}Ra decay is 5.77 MeV. The total alpha plus recoil plus beta energy delivered by the resulting daughters of ^{224}Ra (^{220}Rn , ^{216}Po , ^{212}Pb , ^{212}Bi , ^{212}Po and ^{208}Tl) totals 22.0 MeV. Assuming a 69% skeletal deposition ⁽¹⁰⁾ of a 1 μCi ^{228}Th /kg injection in a dog whose skeleton is 10% of his body weight, the average skeletal dose rate $\underline{t}$ days later from ^{228}Th alone is

$$\left(\frac{dD}{dt}\right)_{^{228}\text{Th}} = 0.512 (5.50) (0.69 e^{-0.00113 t}) \frac{\text{rads}}{\text{day}}$$

(the exponential term accounts for both the radioactive decay and biological elimination of ^{228}Th). Since the time-independent $^{224}\text{Ra}/^{228}\text{Th}$ ratio is about 0.895, ⁽⁹⁾ the dose rate from ^{224}Ra alone at $\underline{t}$ days after injection would be

$$\left(\frac{dD}{dt}\right)_{^{224}\text{Ra}} = 0.512 (5.77) (0.895) (0.69 e^{-0.00113 t}) \frac{\text{rads}}{\text{day}}$$

Allowing for the $^{212}\text{Bi}/^{228}\text{Th}$ ratio of 0.866, ⁽⁹⁾ the corresponding dose rate from the daughters of ^{224}Ra at $\underline{t}$ days after injection is

$$\left(\frac{dD}{dt}\right)_{^{220}\text{Rn} \rightarrow ^{208}\text{Pb}} = 0.512 (22.0) (0.866) (0.69 e^{-0.00113 t}) \frac{\text{rads}}{\text{day}}$$

The total dose rate is then equal to the sum of the 3 separate dose rate equations:

$$\left(\frac{dD}{dt}\right)_{^{228}\text{Th} \rightarrow ^{208}\text{Pb}} = 0.512 (5.50 + 5.16 + 19.05) (0.69 e^{-0.00113 t}) \frac{\text{rads}}{\text{day}}$$

and the cumulative average skeletal dose in rads from injection to t days later can be approximated by a summation of all the daily dose rates from zero to t . Radiation doses and dose rates were calculated for specific animals by multiplying the values calculated for a 1 $\mu\text{Ci/kg}$ injection by the $\mu\text{Ci } ^{228}\text{Th/kg}$ actually injected. Adjustments can also be made for the measured ^{212}Bi retention of each animal.

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Figure 1. Total-body content of ^{212}Bi in Beagles shown as percent of injected ^{228}Th (corrected for radioactive decay). Also plotted is the skeletal ^{212}Bi equation from Reference 9.

Table 3. Body ^{212}Bi retention measurements of Beagles injected with ^{228}Th made by total-body gamma-ray counting using the liquid scintillation counters K9⁽²⁾ and K9 Bark II^(3,4) or a Na I crystal detector.⁽⁴⁾

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{228}\text{Th/kg}$	DAYS AFTER INJECTION	$\frac{\text{BODY } ^{212}\text{Bi} \times 100}{\text{INJECTED } ^{228}\text{Th} e^{-\lambda t}}$	DETECTOR
M1T5	480	2.76	1	83	K-9
			2	68	K-9
			3	55	K-9
			4	57	K-9
			7	49	K-9
			11	53	K-9
			38	57	K-9
			70	56	K-9
			113	61	K-9
M2T5	483	2.63	2	73	K-9
			6	60	K-9
			23	63	K-9
			28	60	K-9
			57	65	K-9
			91	66	K-9
T2T5	501	2.56	1	78	K-9
			2	62	K-9
			3	55	K-9
			4	55	K-9
			11	57	K-9
			26	61	K-9
			38	61	K-9
			70	61	K-9
T4T5	455	2.59	2	72	K-9
			6	61	K-9
			23	64	K-9
			57	63	K-9
			91	72	K-9
T5T5	455	2.32	2	67	K-9
			6	55	K-9
			23	60	K-9
			57	58	K-9
			64	70	K-9
			65	65	K-9

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci}^{228}\text{Th/kg}$	DAYS AFTER INJECTION	$\frac{\text{BODY}^{212}\text{Bi} \times 100}{\text{INJECTED}^{228}\text{Th} e^{-\lambda t}}$	DETECTOR
M1T4	480	0.882	1	67	K-9
			2	59	K-9
			3	51	K-9
			4	56	K-9
			7	49	K-9
			11	52	K-9
			21	54	K-9
			38	52	K-9
			70	51	K-9
			113	61	K-9
			122	58	K-9
			212	59	K-9
			330	60	K-9
			407	64	K-9
			541	67	K-9
M2T4	480	0.916	589	64	K-9
			640	63	K-9
			2	74	K-9
			6	62	K-9
			23	60	K-9
			57	66	K-9
			91	66	K-9
F3T4	461	0.800	168	70	K-9
			303	71	K-9
			52	58	K-9
T3T4	429	0.870	1	74	K-9
			2	57	K-9
			3	52	K-9
			4	48	K-9
			11	51	K-9
			26	52	K-9
			70	48	K-9
			109	50	K-9
			211	50	K-9
			541	58	K-9
			807	59	K-9

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci}^{228}\text{Th/kg}$	DAYS AFTER INJECTION	$\frac{\text{BODY}^{212}\text{Bi} \times 100}{\text{INJECTED}^{228}\text{Th} e^{-\lambda t}}$	DETECTOR
T6T4	591	0.884	3	52	K-9
			7	51	K-9
			10	51	K-9
			15	53	K-9
			17	52	K-9
			21	54	K-9
			24	55	K-9
			29	55	K-9
			178	61	K-9
			210	62	K-9
M1T3	314	0.301	1	77	K-9
			2	70	K-9
			7	64	K-9
			21	64	K-9
			70	58	K-9
			113	63	K-9
			212	61	K-9
			330	61	K-9
			407	56	K-9
			541	63	K-9
			827	58	K-9
M2T3	458	0.301	2	78	K-9
			6	58	K-9
			23	54	K-9
			57	58	K-9
			91	56	K-9
			168	55	K-9
			303	38	K-9
F3T3	471	0.272	52	55	K-9
M5T3	571	0.269	561	65.0	K-9II
F6T3	451	0.282	227	59.0	K-9II
			1156	58.1	NaI
M7T3	427	0.266	199	47.7	K-9II
			861	59.3	NaI
M8T3	494	0.313	96	63.0	K-9II
F9T3	511	0.298	61	55.3	K-9II

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci } ^{228}\text{Th/kg}$	DAYS AFTER INJECTION	$\frac{\text{BODY } ^{212}\text{Bi} \times 100}{\text{INJECTED } ^{228}\text{Th} e^{-\lambda t}}$	DETECTOR
F10T3	508	0.280	33 971	59.9 62.1	K-9II NaI
F11T3	518	0.290	404	60.2	NaI
F12T3	459	0.320	371	56.0	NaI
T7T3	591	0.298	3 7 10 15 17 21 24 29 178 210 910	52 50 49 48 49 51 50 49 51 47 49.8	K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9II
M1T2	491	0.0976	1 2 3 7 21 70 113 212 330 407 491 541 589 827	81 61 55 54 56 52 58 54 55 54 59 51 54 53	K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9
M2T2	483	0.0875	2 6 23 57 91 168 303	76 58 56 54 62 48 52	K-9 K-9 K-9 K-9 K-9 K-9 K-9
F3T2	474	0.0908	52 1140	55 48.1	K-9 K-9II

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci}^{228}\text{Th/kg}$	DAYS AFTER INJECTION	$\frac{\text{BODY}^{212}\text{Bi} \times 100}{\text{INJECTED}^{228}\text{Th} e^{-\lambda t}}$	DETECTOR
M4T2	553	0.0900	903	50.6	K-9II
M5T2	598	0.0848	561	56.8	K-9II
F6T2	451	0.0879	227	56.7	K-9II
M7T2	517	0.0881	199 1015	41.4 53.8	K-9II NaI
M8T2	533	0.0981	96 1078	56.5 48.9	K-9II NaI
F9T2	527	0.0979	61 1104	56.8 47.8	K-9II NaI
F10T2	508	0.0919	33	54.6	K-9II
F11T2	518	0.0904	404	52.8	NaI
F12T2	464	0.100	371	49.2	NaI
M1T1.5	699	0.0289	2 23 57 91 168 303 498 903 1809 2894	70 51 54 49 49 47 45 46.7 46.7 43.6	K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9II K-9II K-9II
M2T1.5	458	0.0293	1613 2522	43.2 48.2	K-9II K-9II
F3T1.5	609	0.0303	52 247 1140	49 41 39.4	K-9 K-9 K-9II
M4T1.5	591	0.0299	103 110 123 1228 2143	47 61 54 38.4 40.2	K-9 K-9 K-9 K-9II K-9II

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci}^{228}\text{Th/kg}$	DAYS AFTER INJECTION	$\frac{\text{BODY}^{212}\text{Bi} \times 100}{\text{INJECTED}^{228}\text{Th} e^{-\lambda t}}$	DETECTOR
M5T1.5	593	0.0286	561 1624	47.5 45.8	K-9II NaI
F6T1.5	489	0.0292	227 1266	57.9 45.5	K-9II NaI
M7T1.5	517	0.0292	199	52.4	K-9II
M7T1.5A	521	0.0311	393	48.7	NaI
M8T1.5	494	0.0324	96 1136	61.0 46.8	K-9II NaI
F9T1.5	527	0.0306	61 1104	56.1 51.6	K-9II NaI
F10T1.5	508	0.0295	33 1076	57.7 51.9	K-9II NaI
F11T1.5	518	0.0305	404	55.0	NaI
F12T1.5	465	0.0329	371	48.7	NaI
M1T1	493	0.0146	1 3 7 21 70 113 212 330 407 491 541 589 827 1845 2754	86 62 60 58 56 61 55 50 42 55 50 45 35 52.7 51.1	K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9 K-9II K-9II
M2T1	699	0.0146	903 1809 2847	48.1 46.2 24.1	K-9II K-9II NaI

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci}^{228}\text{Th/kg}$	DAYS AFTER INJECTION	$\frac{\text{BODY}^{212}\text{Bi} \times 100}{\text{INJECTED}^{228}\text{Th} e^{-\lambda t}}$	DETECTOR
F3T1	723	0.0145	1812 2848	47.4 47.4	NaI K-9II
M4T1	699	0.0146	903 1809 2848	46.1 49.4 45.3	K-9II K-9II NaI
M5T1	513	0.0146	136 1044 2082	45.2 40.5 34.0	K-9II K-9II NaI
F6T1	489	0.0150	227 1266	56.1 48.2	K-9II NaI
M7T1	532	0.0147	199 1240	57.7 45.0	K-9II NaI
M8T1	533	0.0166	96 1136	55.3 41.1	K-9II NaI
F9T1	527	0.0160	61 1104	53.0 45.4	K-9II NaI
F10T1	508	0.0150	33 1076	54.7 55.9	K-9II NaI
F11T1	521	0.0154	404	45.5	NaI
F12T1	472	0.0167	371	47.7	NaI
M1T0.5	699	0.00496	2845	43.6	K-9II
M2T0.5	455	0.00490	2 168 303	76 56 53	K-9 K-9 K-9
F3T0.5	659	0.00485	2271	38.2	K-9II
M4T0.5	516	0.00540	2137	31.4	K-9II
M5T0.5	513	0.00522	136 1044 2082	47.2 38.9 42.2	K-9II K-9II NaI

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci}^{228}\text{Th/kg}$	DAYS AFTER INJECTION	$\frac{\text{BODY}^{212}\text{Bi} \times 100}{\text{INJECTED}^{228}\text{Th} e^{-\lambda t}}$	DETECTOR
F6T0.5	489	0.00510	227 1266	53.4 45.8	K-9II NaI
M7T0.5	532	0.00491	199 1240	56.4 46.3	K-9II NaI
M8T0.5	533	0.00562	96 1136	57.6 45.4	K-9II NaI
F9T0.5	569	0.00529	61 1104	53.4 46.8	K-9II NaI
F10T0.5	508	0.00510	33 1076	57.6 51.6	K-9II NaI
F11T0.5	530	0.00518	404	47.4	NaI
F12T0.5	492	0.00567	371	49.5	NaI
M1T0.2	682	0.00164	818	45.4	NaI
M2T0.2	682	0.00166	820	42.7	NaI
F3T0.2	478	0.00163	820	55.1	NaI
M4T0.2	478	0.00166	810	44.1	NaI
M5T0.2	625	0.00162	561	55.3	K-9II
M5T0.2A	530	0.00173	388	44.3	NaI
F6T0.2	489	0.00176	227 1266	59.6 44.3	K-9II NaI
M7T0.2	532	0.00159	199 1240	68.6 52.2	K-9II NaI
M8T0.2	494	0.00189	96 1136	61.8 44.9	K-9II NaI
F9T0.2	569	0.00171	61 1104	39.5 41.6	K-9II NaI

DOG	DAYS OF AGE AT INJECTION	INJECTED $\mu\text{Ci}^{228}\text{Th/kg}$	DAYS AFTER INJECTION	$\frac{\text{BODY}^{212}\text{Bi} \times 100}{\text{INJECTED}^{228}\text{Th} e^{-\lambda t}}$	DETECTOR
F10T0.2	508	0.00170	33 1076	64.7 48.2	K-9II NaI
F11T0.2	530	0.00171	404	57.6	NaI
F12T0.2	492	0.00190	371	42.4	NaI