RESEARCH IN RADIOBIOLOGY

Annual Report of Work in Progress
in the Internal Irradiation Program

Radiobiology Laboratory
University of Utah College of Medicine

Respectfully Submitted by
Webster S. S. Jee, Acting Director

March 31, 1978
Contract EY-76-C-02-0119

DISCLAIMER

This report was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor any agency Thereof, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.

DISCLAIMER

Portions of this document may be illegible in electronic image products. Images are produced from the best available original document.

TABLE OF CONTENTS

	Page
Group Leaders and Sections	5
Availability of Previous Reports	6
Current Census of the Beagle Colony	8
Preface to Injection Tables	9
Dosimetry	11
Injection Tables	
I. Toxicity Animals	14
A. Radium-226	14
B. Plutonium-239	26
C. Radium-228 (Mesothorium)	46
D. Thorium-228 (Radiothorium)	52
E. Strontium-90	58
F. Radium-224 (Quickradium)	64
G. Americium-241	68
H. Californium-252	76
I. Californium-249	80
J. Einsteinium-253	84
II. Test Animals	86
A. Radium-226	86
B. Plutonium-239	96
C. Radium-228 (Mesothorium)	114
D. Thorium-228 (Radiothorium)	116
E. Strontium-90	118
F. Radium-224 (Quickradium)	122
G. Americium-241	126
H. Lead-210	132
I. Californium-252	134
J. Californium-249	136
K. Curium-243/244	138
L. Einsteinium-253	140
M. Plutonium-237	142
N. Uranium-233	144
O. Uranium-238	146
P. Ancillary	148

TABLE OF CONTENTS (Continued)

<u>FEATURE ARTICLES</u>	Page
BONE SARCOMA INDUCTION IN BEAGLES BY LOW DOSES FROM ^{239}Pu and ^{226}Ra	158
DIFFERENCES IN THE INITIAL DEPOSITION OF Pu AND Ra IN THE SKELETON	161
REVISION OF SKELETAL DOSE CALCULATION IN BEAGLES INJECTED WITH 2.8 $\mu\text{Ci/kg}$ AT 3 MONTHS OF AGE	163
SERIAL STUDY OF ^{239}Pu RETENTION AND DISTRIBUTION IN THE JUVENILE BEAGLE	165
COMPARISON OF SOME SKELETAL EFFECTS OF ^{239}Pu ADMINISTERED AT 3 MONTHS VS. 17 MONTHS OF AGE IN BEAGLES	169
USE OF RIB BIOPSY SPECIMENS IN UNDERSTANDING SKELETAL KINETICS	186
MEASUREMENT OF TRABECULAR BONE CHARACTERISTICS OF LUMBAR VERTEBRAE, AND PROXIMAL FEMORA OF JUVENILE (3 MONTH OLD) BEAGLES	191
MEASUREMENTS OF LUMBAR VERTEBRAL AND PROXIMAL FEMORAL TRABECULAR BONE STRUCTURES IN ADULT BEAGLES	198
A CORRELATION BETWEEN INITIAL DEPOSITION OF Pu, TRABECULAR BONE CONTENT AND TUMOR FREQUENCY	211
THE MICRODISTRIBUTION AND RETENTION OF ^{239}Pu ON TRABECULAR SURFACES IN THE BEAGLE	216
THE RELATIONSHIP OF TRABECULAR BONE SURFACE AREAS, BONE TURNOVER RATES, AND INITIAL UPTAKE OF Pu AND Ra TO SITES OF OCCURRENCE OF OSTEOSARCOMA IN BEAGLES	220
PRELIMINARY SURFACE/VOLUME RATIOS AND BONE TURNOVER RATES OF TRABECULAR BONE IN YOUNG ADULT BEAGLES	224
QUANTITATIVE STUDIES OF BONE CELLS IN BEAGLES	231
STUDY OF SKELETAL CELL KINETICS OF YOUNG ADULT BEAGLES	234
COMPARISON OF BIOLOGIC ACTIVITY OF YOUNG ADULT HUMAN AND BEAGLE TRABECULAR BONE	237
HISTOLOGIC STUDY OF TRABECULAR BONE OF BEAGLE RIB	243
PLUTONIUM-INDUCED OSTEOSARCOMAS IN THE ST. BERNARD	245

TABLE OF CONTENTS (Continued)

<u>FEATURE ARTICLES</u> (Continued)	Page
EFFECT OF GONADECTOMY ON THE INCIDENCE OF PLUTONIUM-INDUCED BONE CANCER IN MICE	254
SEPARATION OF ^{224}Ra FROM ^{228}Th	260
EARLY RETENTION AND DISTRIBUTION OF INJECTED ^{224}Ra IN BEAGLES	263
RETENTION EQUATIONS AND REVISED SKELETAL DOSIMETRY FOR ^{241}Am IN BEAGLES	277
REVISED SKELETAL DOSIMETRY FOR BEAGLES INJECTED WITH ^{249}Cf or ^{252}Cf	283
THE EARLY DISTRIBUTION AND EXCRETION OF ^{233}U IN THE BEAGLE	287
DISTRIBUTION AND TRANSLOCATION OF PARTICULATE PLUTONIUM (HOT PARTICLE-SERIAL SACRIFICE STUDY)	291
A KINETIC MODEL FOR TRANSLOCATION OF PU-P FROM PHAGOCYtic ORGANS TO BONE	300
FURTHER STUDIES ON THE REMOVAL OF SYSTEMICALLY ABSORBED ^{109}Cd IN MICE USING A COMBINATION OF CHELATING AGENTS	305
CHELATION OF SYSTEMICALLY ABSORBED CADMIUM IN MICE WITH 2,3-DIMERCAPTOPROPANOL	314
Zn-DTPA SAFETY IN THE MOUSE FETUS	327
<u>ADDITIONS TO BIBLIOGRAPHY</u>	336

GROUP LEADERS AND SECTIONS

Radiobiology Laboratory,
University of Utah College of Medicine

Section	
<hr/>	
Acting Director	Professor Webster S. S. Jee
Bone	Webster S. S. Jee
Chemistry	Walter Stevens
Clinic and Pathology	Glenn N. Taylor
General Services	Webster S. S. Jee
Physics	Charles W. Mays

AVAILABILITY OF PREVIOUS REPORTS

Copies of our reports may be obtained from the National Technical Information Service, Springfield, Virginia. Paper copies are available at the indicated prices (add \$2.50 for overseas mailing). Microfiche copies are \$2.25 each.

Report	Date	Title	Cost
TID-7639	Jun 1954	Consultants Meeting	\$11.00
AECU-3418	Mar 1955	Annual Report	5.50
AECU-3109	Sep 1955	Semi-Annual Report	6.00
TID-16458	Mar 1956	Annual Report	7.00
TID-16459	Sep 1956	Semi-Annual Report	5.50
AECU-3522	Mar 1957	Annual Report	7.75
AECU-3583	Sep 1957	Semi-Annual Report	7.00
C00-215	Mar 1958	Annual Report	8.50
C00-216*	Mar 1958	Escape of Radon and Thoron	5.50
C00-217	Sep 1958	Semi-Annual Report	8.50
AECU-4112	Feb 1959	Radioactive Fallout	4.50
C00-218*	Mar 1959	Annual Report	8.75
C00-219*	Sep 1959	Semi-Annual Report	5.50
C00-220	Mar 1960	Research in Radiobiology	8.75
C00-221	Aug 1960	Interim Report of ⁹⁰ Sr	4.50
C00-222	Sep 1960	Research in Radiobiology	7.00
C00-223*	Mar 1961	Research in Radiobiology	5.00
C00-224*	Sep 1961	Research in Radiobiology	6.50
C00-225	Mar 1962	Research in Radiobiology	7.00
C00-226	Sep 1962	Research in Radiobiology	7.00
C00-227*	Mar 1963	Research in Radiobiology	9.00
C00-228*	Sep 1963	Research in Radiobiology	8.50
C00-119-229	Mar 1964	Research in Radiobiology	8.75
C00-119-230*	Jul 1964	(Superseded by C00-119-245)	5.00
C00-119-231*	Sep 1964	Research in Radiobiology	7.75
C00-119-232*	Mar 1965	Research in Radiobiology	8.75
C00-119-233*	Sep 1965	Research in Radiobiology	6.50
C00-119-234*	Mar 1966	Research in Radiobiology	11.00
C00-119-235	Sep 1966	Research in Radiobiology	7.00

* Also available on request from this laboratory.

AVAILABILITY OF PREVIOUS REPORTS (Con't.)

<u>Report</u>	<u>Date</u>	<u>Title</u>	<u>Cost</u>
C00-119-236*	Mar 1967	Research in Radiobiology	\$10.00
C00-119-237*	Mar 1968	Research in Radiobiology	7.75
C00-119-238*	Aug 1968	Rb in RBC, Plasma, and Urine	5.50
C00-119-239	Dec 1968	Cs, Rb, and K Metabolism	5.50
C00-119-240*	Mar 1969	Research in Radiobiology	10.25
C00-119-241*	Mar 1970	Retention and Dosimetry	7.75
C00-119-242*	Mar 1970	Research in Radiobiology	12.00
C00-119-243*	Jan 1971	Osteosarcoma Growth Dynamics	7.00
C00-119-244*	Mar 1971	Research in Radiobiology	12.00
C00-119-245*	May 1971	Radiobiology Safety Manual	5.00
C00-119-246*	Mar 1972	Research in Radiobiology	11.75
C00-119-247*	Oct 1972	Rb and Cs Metabolism	5.50
C00-119-248*	Mar 1973	Research in Radiobiology	11.75
C00-119-249*	Mar 1975	Research in Radiobiology	11.00
C00-119-250*	Mar 1975	Research in Radiobiology	9.00
C00-119-251*	Mar 1976	Research in Radiobiology	11.50
C00-119-252*	Mar 1977	Research in Radiobiology	10.00
C00-119-253*	Mar 1978	Research in Radiobiology	10.50

*Also available on request from this laboratory.

STATUS OF THE BEAGLE COLONY

as of 31 March 1978

NUCLIDE		NUMBER OF DOGS
^{253}Es	(einsteinium)	7
^{252}Cf	(californium)	30
^{249}Cf	(californium)	27
$^{243/244}\text{Cm}$	(curium)	0
^{241}Am	(americium)	91
^{239}Pu	(plutonium)	250
^{233}U	(uranium)	1
^{228}Th	(radiothorium)	1
^{228}Ra	(mesothorium)	0
^{226}Ra	(radium)	109
^{224}Ra	(quickradium)	59
^{90}Sr	(strontium)	0
Aging Controls		41
Unassigned		<u>201</u>
Total		817

PREFACE TO THE INJECTION TABLES

Tables I and II list the toxicity and test animals, respectively. Toxicity animals are those animals which are usually maintained until sacrifice becomes a clinical necessity; test animals may be sacrificed as needed for special studies.

Dogs are put into the toxicity study at graded injection levels. At each level, about half the dogs are male and half female. Litter mates are used whenever possible. Each animal receives the designated dose of one radionuclide in a single intravenous injection at approximately 17 months of age. At this age the skeleton is mature with all epiphyses fused except those of the ribs. Twelve such groups have been injected for each of the six radionuclides, ^{226}Ra , ^{239}Pu , ^{228}Ra , ^{228}Th , ^{90}Sr , and ^{241}Am . The present injection program involves ^{226}Ra and ^{239}Pu at lower dose levels, ^{249}Cf or ^{252}Cf , ^{224}Ra , and other animals receiving various radionuclides of current interest.

The five injection levels designated by integers are those specified at the early meetings of the consultants, and those designated by nonintegers have been added by the laboratory staff. Since those injection levels were originally specified in "retained" activities, the actual injections are four times the desired "retained" $\mu\text{Ci/kg}$ of ^{226}Ra , ^{228}Ra (Mesothorium), and ^{90}Sr , and 1.11 times the desired "retained" $\mu\text{Ci/kg}$ of ^{239}Pu , ^{228}Th (Radiothorium), ^{249}Cf , ^{252}Cf , and $^{243}/^{244}\text{Cm}$.*

* Since radioactive decay and excretion occur continuously, the term body retention is obviously meaningless unless the time after injection is specified. Our present measurements indicate that:

average	^{226}Ra retention = 0.25 at about 271 days
average	^{239}Pu retention = 0.90 at about 6 days
average	^{228}Ra retention = 0.25 at about 214 days
average	^{228}Th retention = 0.90 at about 6 days
average	^{90}Sr retention = 0.25 at about 134 days
average	^{241}Am retention = 0.90 at about 6 days
average	^{249}Cf retention = 0.90 at about 1 day
average	^{252}Cf retention = 0.90 at about 1 day
average	$^{243}/^{244}\text{Cm}$ retention = 0.90 at about 1 day
average	^{253}Es retention = 0.90 at about 1 day
average	^{224}Ra retention = 0.16 at about 6 days

are the same for all the radionuclides except ^{90}Sr , in which case they are greater by a factor of 10. Injection level 1 is the basis of the scheme, and is 10 times the maximum permissible concentration of ^{226}Ra in man. Level 1 = $10 \times \frac{0.1 \mu\text{Ci } ^{226}\text{Ra}}{70 \text{ kg man}} = 0.0143$ "retained" $\mu\text{Ci/kg}$. All other injection levels are simple multiples of level 1 as shown below.

Level 0.1	is	1/27	of level 1
Level 0.2	is	1/9	of level 1
Level 0.5	is	1/3	of level 1
Level 0.7	is	2/3	of level 1
Level 1.5	is	2	times level 1
Level 1.7	is	3	times level 1
Level 2	is	6	times level 1
Level 3	is	18	times level 1
Level 4	is	54	times level 1
Level 4.5	is	94	times level 1
Level 5	is	162	times level 1

The numbering system for the dogs has been built around the injection program and serves as a code to describe each dog's place in the experiment. The first letter tells the sex of toxicity animals (M = male, F = female). When the first letter is T, the dog is a test animal. M, F, or T is followed by a number which denotes chronological order of groups in the case of toxicity dogs and of individual test dogs.

Next comes a code letter for the radionuclide: R = ^{226}Ra , P = ^{239}Pu , M = ^{228}Ra , T = ^{228}Th , S = ^{90}Sr , J = ^{85}Sr , Q = ^{224}Ra , W = ^{241}Am , L = ^{210}Pb , G = ^{249}Cf , F = ^{252}Cf , C = $^{243/244}\text{Cm}$, E = ^{253}Es , K = ^{237}Pu , U = ^{233}U , V = ^{238}U , and A = Ancillary.

"A" following the regular dog number means that the dog is a replacement, "H" following the regular dog number means that the dog received its dose in more than one injection. "B", "C", or "D" denotes special assignment. "E" in the final position is used to denote that the dog listed is a St. Bernard. "P" in the final position indicates that the nuclide was injected in particulate form. "Y" in the final position indicates that the animal was injected as a juvenile. A plus (+) in the final position denotes that the animal was "old" when injected. Letters denoting a radionuclide may follow the final number,

in which case the letter indicates that two radionuclides were given. The injection level refers to the radionuclide appearing first in the identifying code.

Example: MIR5 is a male animal in the first radium group at the highest injection level.

Although MIR5, MIR4, MIR3, MIR2, MIR1, and MIR0 constitute a group and were injected at the same time, the tables are arranged according to injection level to facilitate comparison of all the R5 animals, all the R4 animals, etc.

The conditions listed in the injection tables under "Comments on Dead Dogs" present the lesions or factors that had the most prominent effect on the clinical status of the animal. For example, multiple rib fractures, which seldom produced symptoms, are not listed, even though their incidence was usually much higher than the crippling fractures involving the limb bones or mandible. The hematological changes have been omitted unless they were extreme. Increased rate of tooth loss, hepatic changes, eye lesions, and many other factors in the various syndromes have not been included because of space limitations. Over the years many soft tissue tumors have been removed surgically. In many instances, the conditions that have been listed were the reasons for sacrifice of the animal but they were not the immediate cause of death. Most of the animals were euthanized when death appeared imminent or when life could no longer be prolonged humanely.

DOSIMETRY

The injection tables include the calculated average dose in rads to the skeleton at death. ^{226}Ra , ^{228}Ra , ^{90}Sr , ^{241}Am , ^{249}Cf , and ^{252}Cf doses are calculated for each dog using its individually observed retention values: ^{239}Pu , ^{228}Th , and ^{224}Ra doses are based on our average skeletal retention equations. For our standard beagle, the following equations were used for the EFFECTIVE* skeletal retention at (t) days after injection:

*Effective retention is decreased both by radioactive decay and biological elimination.

$$^{226}\text{Ra} = 0.412e^{-0.558t} + 0.105e^{-0.0730t} + 0.196e^{-0.00488t} + 0.287e^{-0.000299t}$$

(5-level only)

$$^{226}\text{Ra} = 0.251e^{-0.982t} + 0.211e^{-0.269t} + 0.210e^{-0.0155t} + 0.177e^{-0.00204t} + 0.151e^{-0.000150t}$$

(lower levels)

$$^{222}\text{Rn}/^{226}\text{Ra} = 0.075 (1 - e^{-0.181t}) t^{0.158}$$

(All levels)

$$^{239}\text{Pu} \text{ (dose level 5)} = 0.07e^{-0.0011t} + 0.43$$

$$^{239}\text{Pu} \text{ (dose level 4)} = 0.11e^{-0.0011t} + 0.39$$

$$^{239}\text{Pu} \text{ (dose level 3)} = 0.15e^{-0.0011t} + 0.34$$

$$^{239}\text{Pu} \text{ (lower levels)} = 0.29e^{-0.0011t} + 0.21$$

$$^{228}\text{Ra} = 0.251e^{-0.982t} + 0.211e^{-0.269t} + 0.21e^{-0.0158t} + 0.177e^{-0.00237t} + 0.151e^{-0.000479t}$$

(pure at $t = 0$)

84% retention of in vivo produced ^{228}Th and daughters.

$$^{228}\text{Th} = 0.69e^{-0.00113t}$$

$$^{224}\text{Ra}/^{228}\text{Th} = 0.895$$

$$^{212}\text{Pb}/^{228}\text{Th} = 0.866$$

$$^{90}\text{Sr} = 0.36e^{-0.95t} + 0.29e^{-0.12t} + 0.10e^{-0.0092t} + 0.12e^{-0.0020t} + 0.13e^{-0.00022t}$$

$$^{241}\text{Am} \text{ (dose level 5)} = 0.359 + 0.157 (1 - e^{-0.0065t})$$

$$^{241}\text{Am} \text{ (dose level 4)} = 0.359 + 0.141 (1 - e^{-0.0029t})$$

$$^{241}\text{Am} \text{ (dose level 3)} = 0.359 + 0.076 (1 - e^{-0.0021t})$$

$$^{241}\text{Am} \text{ (lower levels)} = 0.359 + 0.015 (1 - e^{-0.0014t})$$

$$^{249}\text{Cf} = 0.498e^{-0.0000794t}$$

$$^{252}\text{Cf} = 0.498e^{-0.000791t}$$

$$^{224}\text{Ra} = 0.528 e^{-0.214t} - 0.228 e^{-9.01t}$$

with the effective retention of ^{224}Ra daughters of:

$$^{220}\text{Rn} \text{ and } ^{216}\text{Po} = 0.486 e^{-0.214t} - 0.276 e^{-4.65t}$$

$$^{212}\text{Pb} = 0.447 e^{-0.214t} - 0.336 e^{-2.40t}$$

$$^{212}\text{Bi} \text{ and } ^{212}\text{Po} + ^{208}\text{Tl} = 0.391 e^{-0.214t} - 0.350 e^{-2.38t}$$

Detailed retention data and dosimetric analysis have been presented in a special report, C00-119-241 (March 1970), supplemented by other reports in C00-119-252 (March 1977) and C00-119-253 (March 1978).

The skeletal doses in this report are based upon a wet skeleton which is 7.5% of the body weight at the time of injection (C00-119-246, pp. 167-192, 1972).

^{228}Ra doses deserve special comment. The dose from "pure" ^{228}Ra and its in vivo produced daughters is based on our best evaluation of 5.77 ± 0.02 yr for the ^{228}Ra half-period. The tabulated total doses include the contributions from ^{228}Th contamination in the injection solutions. For example, ^{228}Th contaminations of 0.6%, 3%, and 15%, respectively, account for 2.7%, 13%, and 42% of the total dose in rads at 1000 days. If injected ^{228}Th is 4 times more toxic rad-for-rad than is in vivo produced ^{228}Th , these injected ^{228}Th contaminations would account for 10%, 37%, and 74% of the total biological damage at 1000 days. Therefore, it may be desirable to use only results from the slightly contaminated (0.6% ^{228}Th) dogs in evaluation of ^{228}Ra toxicity.

TABLE I. CHRONIC TOXICITY ANIMALS (MAR. 31, 1978)

A. RADIUM - 226

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		INJECTED	D	MO	YR	
M001R0.0	558	8.03		20	4	53		3116
M002R0.0	487	14.6		16	11	53		3675
F003R0.0	601	11.4		10	3	54		2139
M004R0.0	461	11.0		7	4	54		5284
M005R0.0	460	6.57		22	6	54		4018
F006R0.0	483	8.43		27	7	54		3182
M007R0.0	511	11.0		24	8	54		3360
F008R0.0	638	8.21		21	12	54		3361
F009R0.0	700	11.7		11	4	55		1550
M010R0.0	522	10.9		27	7	55		4698
F011R0.0	544	10.2		20	12	55		4575
F012R0.0	501	8.68		17	1	56		4283
M013R0.0	515	12.3		4	3	64		4752
F014R0.0	536	10.8		23	10	64	4907	
M015R0.0	564	12.8		4	2	65		4372
F016R0.0	469	10.0		7	4	65		3677
M017R0.0	469	12.50		27	4	66	4356	
F018R0.0	497	12.00		25	5	66	4328	
F019R0.0	533	8.42		13	10	66	4187	
M020R0.0	536	9.70		29	12	66	4110	
F021R0.0	549	9.90		26	1	67	4082	
M022R0.0	533	12.1		22	3	67		3907
F031R0.0B	536	10.6		23	10	64		4458
F031R0.0C	536	9.88		23	10	64		4690
F031R0.0D	542	9.9		21	9	65	4574	
F032R0.0B	542	7.8		21	9	65	4574	
F032R0.0C	532	11.7		21	9	65	4574	
F032R0.0D	532	9.7		21	9	65	4574	
F033R0.0B	532	9.8		21	9	65		3670
F033R0.0C	496	9.50		25	5	66	4328	
F033R0.0D	496	11.80		25	5	66		3916
F034R0.0B	525	8.20		26	1	67	4082	
F034R0.0C	520	8.9		22	3	67	4027	
F034R0.0D	484	9.9		22	3	67		3185
F035R0.0B	502	9.41		1	2	68	3711	
F035R0.0C	502	9.38		1	2	68	3711	
F035R0.0D	552	8.86		9	1	69	3368	
F036R0.0B	467	10.1		2	7	68	3559	
F036R0.0C	467	9.17		2	7	68	3559	
F036R0.0D	467	9.08		2	7	68	3559	
F037R0.0B	801	11.1		20	5	69	3237	
F037R0.0C	501	10.4		23	9	70	2746	
F037R0.0D	501	10.9		23	9	70	2746	

A. RADIUM - 226

DOG NUMBER	COMMENTS ON DEAD DOGS
M001R0.0	SEMINOMA, LYMPHOSARCOMA
M002R0.0	TRANSITIONAL CELL CARCINOMA
F003R0.0	STATUS EPILEPTICUS
M004R0.0	CHRONIC INTERSTITIAL NEPHRITIS; THROMBOSIS
M005R0.0	OBTURATING PULMONARY EMBOLISM
F006R0.0	STATUS EPILEPTICUS
M007R0.0	STATUS EPILEPTICUS, NEPHRITIS
F008R0.0	PANCREATIC ADENOCARCINOMA
F009R0.0	AORTIC BODY TUMOR
M010R0.0	NEPHRITIS
F011R0.0	VAGINAL FIBROMA
F012R0.0	UNDETERMINED
M013R0.0	MALIGNANT MELANOMA (ORAL)
F014R0.0	
M015R0.0	CHRONIC PANCREATITIS; HYDROCEPHALUS
F016R0.0	EPIDERMOID CARCINOMA, LUNG CARCINOMA
M017R0.0	
F018R0.0	
F019R0.0	
M020R0.0	
F021R0.0	
M022R0.0	SEPTICEMIA
F031R0.0B	
F031R0.0C	BILIARY CALCULUS; VAGINAL LEIOMYOSARCOMA
F031R0.0D	
F032R0.0B	
F032R0.0C	
F032R0.0D	
F033R0.0B	MAMMARY CARCINOMA
F033R0.0C	
F033R0.0D	MAMMARY CARCINOMA
F034R0.0B	
F034R0.0C	
F034R0.0D	HEMANGIOSARCOMA (SOFT TISSUE)
F035R0.0B	
F035R0.0C	
F035R0.0D	
F036R0.0B	
F036R0.0C	
F036R0.0D	
F037R0.0B	
F037R0.0C	
F037R0.0D	

A. RADIUM - 226

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DOSE TO SKELETON (RADS)
F038R0.0B	501	11.5		23 9 70	2746	
F042R0.0B	338	8.00		25 4 69		33
M101R0.0Y	92	4.65		1 4 75	1095	
M102R0.0Y	88	3.60		25 3 75	1102	
M103R0.0Y	93	4.38		24 4 75	1072	
F104R0.0Y	89	4.53		14 3 75	1113	
F105R0.0Y	88	4.51		25 3 75	1102	
F106R0.0Y	92	3.64		1 4 75	1095	
M107R0.0Y	93	4.32		8 3 77	388	
F108R0.0Y	93	4.22		16 3 77	380	
F109R0.0Y	88	2.92		19 1 78	71	
M013R0.2	529	9.77	0.00577	4 3 64	4518	23
F014R0.2	460	8.10	0.00836	23 10 64	3448	52
M015R0.2	504	10.8	0.00873	4 2 65	4102	36
F016R0.2	486	8.90	0.00665	7 4 65	4190	32
M017R0.2	494	11.80	0.00711	27 4 66	4356	
F018R0.2	497	9.30	0.00652	25 5 66	3387	21
F019R0.2	533	10.6	0.00785	13 10 66	3611	36
M020R0.2	546	11.4	0.00676	29 12 66	3493	25
F021R0.2	549	11.5	0.00687	26 1 67	3101	21
M022R0.2	533	12.9	0.00961	22 3 67	4027	
M013R0.5	529	11.0	0.0171	4 3 64	3676	57
F014R0.5	510	9.75	0.0220	23 10 64	4907	
M015R0.5	490	10.4	0.0263	4 2 65	4297	96
F016R0.5	500	11.4	0.0205	7 4 65	4141	97
M017R0.5	494	9.20	0.0215	27 4 66	4052	85
F018R0.5	496	9.10	0.0197	25 5 66	4328	
F019R0.5	533	10.0	0.0230	13 10 66	4187	
M020R0.5	536	13.2	0.0206	29 12 66	4110	
F021R0.5	538	8.80	0.0208	26 1 67	4082	
M022R0.5	520	12.3	0.0290	22 3 67	3192	89
M031R0.5B	508	11.40	0.021	27 4 66	4310	103
F031R0.5C	537	9.40	0.0235	22 12 65	4393	113
F031R0.5D	537	11.70	0.0238	22 12 65	4482	
M032R0.5B	496	13.40	0.0196	25 5 66	3219	60
F032R0.5C	519	10.10	0.0239	22 12 65	4180	102
F032R0.5D	509	10.10	0.024	22 12 65	3870	104

A. RADIUM - 226

DOG NUMBER	COMMENTS ON DEAD DOGS
F038R0.0B	
F042R0.0B	SPECIAL STUDY
M101R0.0Y	
M102R0.0Y	
M103R0.0Y	
F104R0.0Y	
F105R0.0Y	
F106R0.0Y	
M107R0.0Y	
F108R0.0Y	
F109R0.0Y	
M013R0.2	MALIGNANT MELANOMA (ORAL)
F014R0.2	MALIGNANT MELANOMA (ORAL)
M015R0.2	CIRCULATORY FAILURE
F016R0.2	LYMPHOSARCOMA
M017R0.2	
F018R0.2	LUNG CARCINOMA
F019R0.2	
M020R0.2	UNDIFFERENTIATED MALIGNANCY (SOFT TISSUE)
F021R0.2	MAMMARY CARCINOMA
M022R0.2	
M013R0.5	BILE DUCT CARCINOMA
F014R0.5	
M015R0.5	MELANOMA (ORAL)
F016R0.5	MAMMARY CARCINOMA; UTERINE CARCINOMA
M017R0.5	ORAL MELANOMA
F018R0.5	
F019R0.5	
M020R0.5	
F021R0.5	
M022R0.5	THYROID ADENOCARCINOMA
M031R0.5B	THYROID CARCINOMA; SPONDYLITIS
F031R0.5C	TRAUMA
F031R0.5D	
M032R0.5B	
F032R0.5C	SQUAMOUS CELL CARCINOMA (ORAL)
F032R0.5D	HEMANGIOSARCOMA (SPLEEN)

A. RADIUM - 226

DOG	INJECTION	AGE WEIGHT	INJECTED	DATE	DAYS SINCE	DOSE TO
NUMBER	(DAYS)	(KG)	(UCI/KG)	INJECTED	INJECTION	SKELETON
						(RADS)
M033R0.5B	497	12.90	0.0194	25	5 66	3848
F033R0.5C	527	10.60	0.0212	27	4 66	4356
F033R0.5D	527	8.70	0.0217	27	4 66	4356
M034R0.5B	496	10.50	0.0196	25	5 66	4328
F034R0.5C	524	9.90	0.0215	27	4 66	4322
F034R0.5D	508	9.70	0.0212	27	4 66	4356
M035R0.5B	536	10.4	0.0205	29	12 66	4110
F035R0.5C	532	9.00	0.0201	29	12 66	4110
F035R0.5D	532	10.2	0.0202	29	12 66	4110
M101R0.5Y	88	4.32	0.0186	25	3 75	1102
M102R0.5Y	93	4.44	0.0187	24	4 75	1072
M103R0.5Y	90	3.61	0.0192	6	5 75	1060
F104R0.5Y	88	4.09	0.0184	25	3 75	1102
F105R0.5Y	88	4.08	0.0184	25	3 75	1102
F106R0.5Y	93	3.60	0.0188	24	4 75	1072
M107R0.5Y	93	3.69	0.0191	8	3 77	388
M108R0.5Y	88	2.54	0.0185	19	1 78	71
F109R0.5Y	90	3.45	0.0177	9	3 78	22
M001R1.0	471	8.48	0.0618	20	4 53	5727
M002R1.0	627	10.0	0.0876	16	11 53	4054
F003R1.0	706	8.68	0.0576	10	3 54	3860
M004R1.0	414	8.60	0.0642	7	4 54	2038
M005R1.0	490	11.7	0.0436	22	6 54	3780
F006R1.0	483	7.23	0.0584	27	7 54	5260
M007R1.0	511	11.4	0.0651	24	8 54	3544
F008R1.0	861	8.98	0.0559	21	12 54	2988
F009R1.0	781	9.88	0.0521	11	4 55	4399
M010R1.0	523	11.5	0.0573	27	7 55	4003
F011R1.0	511	11.2	0.0522	20	12 55	5462
F012R1.0	501	9.71	0.0444	17	1 56	3978
M013R1.0	529	11.7	0.0527	4	3 64	3739
F014R1.0	510	10.5	0.0701	23	10 64	1729
M015R1.0	490	8.88	0.0797	4	2 65	893
F016R1.0	501	8.99	0.0611	7	4 65	4557
M017R1.0	494	11.40	0.0639	27	4 66	4356
F018R1.0	496	10.00	0.0589	25	5 66	3625
F019R1.0	526	11.6	0.0682	13	10 66	3612
M020R1.0	536	10.0	0.0610	29	12 66	4110
F021R1.0	525	8.10	0.0633	26	1 67	4082
M022R1.0	484	10.9	0.0861	22	3 67	4027
M001R1.0	227	4 53	5727			
M002R1.0	316	4054				
F003R1.0	201	3860				
M004R1.0	144	2038				
M005R1.0	149	3780				
F006R1.0	249	5260				
M007R1.0	223	3544				
F008R1.0	124	2988				
F009R1.0	132	4399				
M010R1.0	209	4003				
F011R1.0	200	5462				
F012R1.0	165	3978				
M013R1.0	218	3739				
F014R1.0	197	1729				
M015R1.0	109	893				
F016R1.0	223	4557				
M017R1.0	192	3625				
F018R1.0	275	3612				

A. RADIUM - 226

DOG NUMBER	COMMENTS ON DEAD DOGS
---------------	-----------------------

M033R0.5B	EPIDERMOID CARCINOMA (ORAL)
-----------	-----------------------------

F033R0.5C	
-----------	--

F033R0.5D	
-----------	--

M034R0.5B	
-----------	--

F034R0.5C	MAMMARY CARCINOMA
-----------	-------------------

F034R0.5D	
-----------	--

M035R0.5B	
-----------	--

F035R0.5C	
-----------	--

F035R0.5D	
-----------	--

M101R0.5Y	
-----------	--

M102R0.5Y	
-----------	--

M103R0.5Y	
-----------	--

F104R0.5Y	
-----------	--

F105R0.5Y	
-----------	--

F106R0.5Y	
-----------	--

M107R0.5Y	
-----------	--

M108R0.5Y	
-----------	--

F109R0.5Y	
-----------	--

M001R1.0	MELANOMA ORAL CAVITY
----------	----------------------

M002R1.0	SEMINOMA
----------	----------

F003R1.0	MAMMARY GLAND CARCINOMA
----------	-------------------------

M004R1.0	TRAUMA
----------	--------

M005R1.0	TRANSITIONAL CELL CARCINOMA; HYDRONEPHROSIS
----------	---

F006R1.0	NEPHRITIS
----------	-----------

M007R1.0	STATUS EPILEPTICUS
----------	--------------------

F008R1.0	LYMPHOSARCOMA
----------	---------------

F009R1.0	PNEUMONIA
----------	-----------

M010R1.0	FIBROSARCOMA (GINGIVA)
----------	------------------------

F011R1.0	MELANOMA (EYE); MAMMARY CARCINOMA
----------	-----------------------------------

F012R1.0	MELANOMA, GINGIVA
----------	-------------------

M013R1.0	PROSTATIC CYST
----------	----------------

F014R1.0	UNDETERMINED (NO NEOPLASIA)
----------	-----------------------------

M015R1.0	UNDETERMINED (NO NEOPLASIA)
----------	-----------------------------

F016R1.0	LYMPHOSARCOMA
----------	---------------

M017R1.0	
----------	--

F018R1.0	MAMMARY CARCINOMA
----------	-------------------

F019R1.0	OSTEOSARCOMA
----------	--------------

M020R1.0	
----------	--

F021R1.0	
----------	--

M022R1.0	
----------	--

A. RADIUM - 226

DOG INJECTION DATE DAYS SINCE INJECTION DOSE TO SKELETON (RADS)

NUMBER	AGE WEIGHT (KG)	INJECTED (UCI/KG)	DATE	DAYS SINCE INJECTION	DOSE TO SKELETON (RADS)
F03R1.0B	509	10.40	0.0712	22 12 65	3009
M10R1.0Y	88	4.09	0.0545	25 3 75	1402
M10R1.0Y	92	4.54	0.0546	1 4 75	1095
M10R1.0Y	90	3.03	0.0564	6 5 75	1060
F104R1.0Y	88	3.71	0.0541	25 3 75	1102
F105R1.0Y	92	4.70	0.0528	1 4 75	1095
F106R1.0Y	93	4.20	0.0557	24 4 75	1072
M107R1.0Y	93	4.12	0.0575	8 3 77	388
M108R1.0Y	88	2.52	0.0548	19 1 78	71
F109R1.0Y	90	3.61	0.0544	9 3 78	22

M001R1.7	523	9.98	0.137	17 1 56	4438
M002R1.7	598	7.85	0.163	30 11 56	1273
M002R1.7A	493	12.0	0.222	6 3 63	3254
F003R1.7	473	13.1	0.165	20 12 55	3267
M004R1.7	514	6.20	0.163	20 12 55	5495
M005R1.7	511	10.1	0.151	20 12 55	4107
F006R1.7	491	7.9	0.152	20 12 55	3432
M007R1.7	598	7.17	0.163	30 11 56	3142
F008R1.7	491	9.50	0.154	20 12 55	2577
F009R1.7	598	7.55	0.168	30 11 56	3914
M010R1.7	590	9.57	0.167	30 11 56	557
M010R1.7A	545	10.6	0.183	7 1 59	4903
F011R1.7	598	8.17	0.165	30 11 56	532
F012R1.7	590	8.95	0.167	30 11 56	2399
M101R1.7Y	92	4.19	0.163	1 4 75	1095
M102R1.7Y	93	5.45	0.167	24 4 75	1072
M103R1.7Y	90	2.84	0.167	6 5 75	1060
F104R1.7Y	88	3.65	0.159	25 3 75	1102
F105R1.7Y	88	3.66	0.158	25 3 75	1102
F106R1.7Y	93	3.62	0.180	24 4 75	1072
M107R1.7Y	93	3.77	0.166	16 3 77	8

M001R2.0	471	8.74	0.382	20 4 53	3440
M002R2.0	592	8.21	0.387	16 11 53	3775
F003R2.0	541	8.53	0.347	10 3 54	4459
M004R2.0	414	10.5	0.361	7 4 54	325
M004R2.0A	420	10.6	0.306	11 4 55	4368
M005R2.0	461	11.5	0.267	22 6 54	4703
M001R2.0	1147				
M002R2.0	833				
M003R2.0	1163				
M004R2.0	252				
M004R2.0A	1523				
M005R2.0	1325				

A. RADIUM - 226

DOG
NUMBER

COMMENTS ON DEAD DOGS

F031R1.0B STATUS EPILEPTICUS
M101R1.0Y
M102R1.0Y
M103R1.0Y
F104R1.0Y
F105R1.0Y
F106R1.0Y
M107R1.0Y
M108R1.0Y
F109R1.0Y

M001R1.7 OBTURATING ABDOMINAL AORTA AND PULMONARY EMBOLISM
M002R1.7 LYMPHOSARCOMA
M002R1.7A FIBROSARCOMA (GINGIVA)
F003R1.7 MAMMARY GLAND CARCINOMA
M004R1.7 NEPHRITIS
M005R1.7 OSTEOSARCOMA
F006R1.7 PULMONARY CALCIFICATION (NO BONE TUMOR)
M007R1.7 BACTERIAL TOXEMIA, INTERSTITIAL CELL ADENOMA
F008R1.7 DRUG ALLERGY
F009R1.7 PYOMETRA
M010R1.7 TRAUMA
M010R1.7A UNDIFFERENTIATED MALIGNANCY (NON-SKELETAL); MELANOMA (EYE)
F011R1.7 MELANOMA (ORAL); THYROID CARCINOMA
F012R1.7 UNDETERMINED (NO BONE TUMOR)
M101R1.7Y
M102R1.7Y
M103R1.7Y
F104R1.7Y
F105R1.7Y
F106R1.7Y
M107R1.7Y ANESTHESIA ACCIDENT

M001R2.0 HEMANGIOSARCOMA (SPLEEN)
M002R2.0 OSTEOSARCOMA
F003R2.0 RETICULUM CELL SARCOMA (NON-SKELETAL)
M004R2.0 PERFORATED ILEUM
M004R2.0A OSTEOSARCOMA; VALVULAR ENDOCARDITIS
M005R2.0 OSTEOSARCOMA; ADRENAL CORTICAL CARCINOMA

A. RADIUM - 226

- 22 -

DOG	INJECTION	AGE WEIGHT (KG)	INJECTED (UCI/KG)	DATE	DAYS SINCE INJECTION	DOSE TO SKELETON (RADS)
-----	-----------	-----------------	-------------------	------	----------------------	-------------------------

F006R2.0	486	10.6	0.360	27	7 54	4615
M007R2.0	514	11.1	0.413	24	8 54	3425
F008R2.0	572	6.95	0.331	21	12 54	4781
F009R2.0	592	9.38	0.317	11	4 55	3998
M010R2.0	523	9.95	0.345	27	7 55	3569
F011R2.0	495	9.30	0.310	20	12 55	3297
F012R2.0	497	10.3	0.281	17	1 56	2948
M101R2.0Y	90	4.64	0.317	7	3 75	1120
M102R2.0Y	90	4.27	0.324	7	3 75	1120
M103R2.0Y	90	5.35	0.320	7	3 75	1120
F104R2.0Y	90	4.36	0.317	7	3 75	1120
F105R2.0Y	90	3.93	0.321	7	3 75	1120
F106R2.0Y	89	4.19	0.309	14	3 75	1113
M107R2.0Y	93	4.53	0.329	16	3 77	380
F109R2.0Y	88	2.79	.332	19	1 78	71

M001R3.0	473	8.91	1.20	20	4 53	2850
M002R3.0	470	9.02	1.21	16	11 53	2226
F003R3.0	386	7.74	1.11	10	3 54	2497
M004R3.0	412	11.7	1.16	7	4 54	1917
M005R3.0	461	13.0	0.846	22	6 54	2955
F006R3.0	486	9.75	1.14	27	7 54	1932
M007R3.0	514	12.3	1.29	24	8 54	2099
F008R3.0	542	7.76	1.03	21	12 54	2612
F009R3.0	551	8.02	0.987	11	4 55	2487
M010R3.0	525	10.1	1.06	27	7 55	1737
F011R3.0	495	12.9	0.938	20	12 55	1610
F012R3.0	497	11.4	0.883	17	1 56	1897
M101R3.0Y	93	4.41	1.01	24	4 75	1072
M102R3.0Y	93	5.40	1.01	24	4 75	1072
M103R3.0Y	90	2.94	1.08	6	5 75	1060
F104R3.0Y	88	3.74	1.02	25	3 75	1102
F105R3.0Y	93	4.51	1.02	24	4 75	1072
F106R3.0Y	90	3.25	1.07	6	5 75	1060
F107R3.0Y	88	2.46	1.05	19	1 78	71
F109R3.0Y	93	03.40	1.09	19	1 78	71
F501R3.0+	1787	10.4	0.806	10	6 75	1025
F502R3.0+	1918	8.26	0.972	22	9 76	555
F503R3.0+	1836	10.0	1.08	29	11 77	122

M001R4.0 471 9.08 3.51 20 4 53 1606 8767

A. RADIUM - 226

DOG NUMBER	COMMENTS ON DEAD DOGS
F006R2.0	EPIDERMOID CARCINOMA (TYMPANIC BULLA)
M007R2.0	OSTEOSARCOMA, CUSHING SYNDROME
F008R2.0	UNDIFFERENTIATED MALIGNANCY, SMALL INTESTINE
F009R2.0	MAMMARY CARCINOMA
M010R2.0	OSTEOSARCOMA
F011R2.0	OSTEOSARCOMA
F012R2.0	MAMMARY ADENOCARCINOMA
M101R2.0Y	
M102R2.0Y	
M103R2.0Y	
F104R2.0Y	
F105R2.0Y	
F106R2.0Y	
M107R2.0Y	
F109R2.0Y	

M001R3.0	OSTEOSARCOMA
M002R3.0	OSTEOSARCOMA
F003R3.0	OSTEOSARCOMA
M004R3.0	OSTEOSARCOMA
M005R3.0	OSTEOSARCOMA
F006R3.0	OSTEOSARCOMA
M007R3.0	OSTEOSARCOMA
F008R3.0	OSTEOSARCOMA
F009R3.0	OSTEOSARCOMA
M010R3.0	OSTEOSARCOMA
F011R3.0	PYOMETRITIS + SECONDARY PERITONITIS
F012R3.0	OSTEOSARCOMA
M101R3.0Y	
M102R3.0Y	
M103R3.0Y	
F104R3.0Y	
F105R3.0Y	
F106R3.0Y	
F107R3.0Y	
F109R3.0Y	
F501R3.0+	
F502R3.0+	
F503R3.0+	

M001R4.0	OSTEOSARCOMA
----------	--------------

A. RADIUM - 226

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE INJECTED			DAYS SINCE INJECTION		DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR	3/31/78	DEATH	
M002R4.0	470	9.53	3.55	16	11	53		1884	8200
F003R4.0	384	8.65	3.33	10	3	54		490	2944
F003R4.0A	598	7.20	3.10	30	11	56		1614	5140
M004R4.0	408	8.83	3.47	7	4	54		1518	8084
M005R4.0	461	13.2	2.42	22	6	54		1659	6007
F006R4.0	486	8.55	3.44	27	7	54		1939	9511
M007R4.0	453	9.55	3.88	24	8	54		1647	7792
F008R4.0	474	8.94	3.14	21	12	54		1324	6153
F009R4.0	542	08.53	3.02	11	4	55		1471	5460
M010R4.0	527	10.8	3.28	27	7	55		1553	10109
F011R4.0	491	10.4	2.84	20	12	55		1469	7031
F012R4.0	496	9.61	2.81	17	1	56		1435	5169
F501R4.0+	1787	10.5	2.50	10	6	75		303	1330
F502R4.0+	1933	9.09	2.96	22	9	76		555	
F503R4.0+	1836	10.9	3.44	29	11	77		122	
F504R4.0+	1735	7.93	1.98	10	1	78		80	
M001R5.0	473	9.87	10.5	20	4	53		908	19924
M002R5.0	470	8.85	10.8	16	11	53		1380	24095
F003R5.0	380	7.82	10.1	10	3	54		481	9529
M004R5.0	408	8.90	10.6	7	4	54		1091	21889
M005R5.0	458	10.9	10.1	22	6	54		1220	20577
F006R5.0	486	9.66	10.2	27	7	54		1015	20552
M007R5.0	453	8.85	11.9	24	8	54		1288	22277
F008R5.0	474	7.76	9.68	21	12	54		968	15419
F009R5.0	420	9.16	9.48	11	4	55		1288	21255
M010R5.0	527	10.7	10.2	27	7	55		825	14905
F501R5.0+	1827	12.8	10.2	16	8	77		227	
F502R5.0+	1812	9.65	9.97	29	11	77		122	
F503R5.0+	1819	10.8	6.31	10	1	78		80	

A. RADIUM - 226

DOG
NUMBER

COMMENTS ON DEAD DOGS

M002R4.0	OSTEOSARCOMA
F003R4.0	CANINE DISTEMPER
F003R4.0A	OSTEOSARCOMA
M004R4.0	OSTEOSARCOMA
M005R4.0	OSTEOSARCOMA
F006R4.0	OSTEOSARCOMA
M007R4.0	OSTEOSARCOMA
F008R4.0	OSTEOSARCOMA
F009R4.0	OSTEOSARCOMA
M010R4.0	OSTEOSARCOMA
F011R4.0	OSTEOSARCOMA
F012R4.0	OSTEOSARCOMA
F501R4.0+	PERITONITIS
F502R4.0+	
F503R4.0+	
F504R4.0+	

M001R5.0	OSTEOSARCOMA
M002R5.0	OSTEOSARCOMA
F003R5.0	CANINE DISTEMPER
M004R5.0	OSTEOSARCOMA
M005R5.0	OSTEOSARCOMA
F006R5.0	OSTEOSARCOMA
M007R5.0	OSTEOSARCOMA
F008R5.0	OSTEOSARCOMA
F009R5.0	OSTEOSARCOMA + ANEMIA
M010R5.0	OSTEOSARCOMA + FRACTURED MANDIBLE
F501R5.0+	
F502R5.0+	
F503R5.0+	

B. PLUTONIUM - 239

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE INJECTED			DAYS SINCE INJECTION 3/31/78	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR	DEATH	
M001P0.0	443	9.70		1	12	52		4003
F002P0.0	424	6.36		2	3	53		2755
M003P0.0	515	10.8		1	6	53		5362
M004P0.0	426	10.7		16	9	53		5138
F005P0.0	620	9.75		14	10	53		4088
F006P0.0	410	5.59		12	5	54		449
F007P0.0	515	6.90		25	10	54		5344
M008P0.0	585	10.9		15	3	55		4072
F009P0.0	574	11.0		9	9	55		3032
F010P0.0	658	11.0		22	11	55		3971
M011P0.0	602	10.3		24	4	56		3821
M012P0.0	630	10.9		29	5	56		4143
F013P0.0	517	9.47		4	3	64	5140	
F014P0.0	452	9.89		12	5	64		4105
M015P0.0	527	12.1		23	10	64		3750
M016P0.0	486	13.9		7	4	65	4741	
M017P0.0	551	12.2		18	11	66	3796	
F018P0.0	536	11.4		29	11	66	4140	
M019P0.0	536	13.1		29	11	66	4140	
F020P0.0	546	8.50		29	12	66		3748
M021P0.0	549	13.3		26	1	67	4082	
F022P0.0	489	10.6		25	5	67	3963	
M031P0.0B	452	11.8		12	5	64		1763
M031P0.0C	452	12.6		12	5	64		3629
M032P0.0B	452	11.2		12	5	64		4840
M032P0.0C	542	10.3		21	9	65	4574	
M033P0.0B	517	12.1		21	9	65	4574	
M033P0.0C	503	11.70		18	11	65		4164
M034P0.0B	525	13.5		26	1	67	4082	
M034P0.0C	484	12.7		22	3	67	4027	
M035P0.0B	484	12.5		22	3	67	4027	
M035P0.0C	484	13.1		22	3	67		3501
M036P0.0B	489	11.0		25	5	67		2525
M036P0.0C	485	12.2		25	5	67	3963	
M037P0.0B	507	11.7		22	6	67	3935	
M037P0.0C	493	10.4		22	6	67	3935	
M038P0.0B	529	10.7		16	11	67		3623
M038P0.0C	529	12.2		16	11	67		3382
M039P0.0B	503	10.7		21	12	67	3753	
M039P0.0C	503	10.1		21	12	67	3753	
M040P0.0B	484	10.3		30	7	68	3531	
M040P0.0C	552	11.4		9	1	69	3368	
M041P0.0B	560	9.49		17	1	69	3360	

B. PLUTONIUM - 239

DOG NUMBER	COMMENTS ON DEAD DOGS:
M001P0.0	SPLENIC RUPTURE, METASTATIC SEMINOMA
F002P0.0	ANESTHETIC ACCIDENT
M003P0.0	PANCREATIC ADENOCARCINOMA
M004P0.0	THYROID CARCINOMA, NEPHRITIS
F005P0.0	ADRENAL CORTICAL CARCINOMA
F006P0.0	OBSTRUCTING PULMONARY EMBOLISM
F007P0.0	RHABDOMYOSARCOMA
M008P0.0	CIRCULATORY FAILURE
F009P0.0	PULMONARY EMBOLISM, NEPHRITIS
F010P0.0	LEUKEMIA
M011P0.0	FIBROSARCOMA (SPLEEN)
M012P0.0	TESTICULAR CARCINOMA
F013P0.0	
F014P0.0	SURGICAL SHOCK; PYOMETRA
M015P0.0	TRANSITIONAL CELL CARCINOMA
M016P0.0	
M017P0.0	
F018P0.0	
M019P0.0	
F020P0.0	PLEURAL EFFUSION
M021P0.0	
F022P0.0	
M031P0.0B	STATUS EPILEPTICUS; BILE DUCT OBSTRUCTION
M031P0.0C	MALIGNANT MELANOMA (ORAL)
M032P0.0B	CARDIAC INSUFFICIENCY
M032P0.0C	
M033P0.0B	
M033P0.0C	UNDETERMINED
M034P0.0B	
M034P0.0C	
M035P0.0B	
M035P0.0C	PARALYSIS (UNDETERMINED ETIOLOGY)
M036P0.0B	STATUS EPILEPTICUS
M036P0.0C	
M037P0.0B	
M037P0.0C	
M038P0.0B	TRANSITIONAL CELL CARCINOMA
M038P0.0C	PNEUMONIA
M039P0.0B	
M039P0.0C	
M040P0.0B	
M040P0.0C	
M041P0.0B	

B. PLUTONIUM - 239

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DOSE TO SKELETON (RADS)
M042P0.0	479	14.0		24 4 74	1437	
M042P0.0B	338	11.6		25 4 69		32
M043P0.0	479	13.8		24 4 74	1437	
M044P0.0	479	12.7		24 4 74	1437	
M045P0.0	497	11.5		29 8 74	1310	
M046P0.0	497	11.5		29 8 74	1310	
M047P0.0	497	11.3		29 8 74	1310	
M048P0.0	497	11.7		29 8 74	1310	
M081P0.0Y	105	7.10		9 3 72	2213	
F082P0.0Y	105	7.30		9 3 72	2213	
F083P0.0Y	91	3.97		25 4 72	2166	
F084P0.0Y	89	3.67		25 4 72	2166	
M086P0.0Y	91	4.37		25 4 72	2166	
F101P0.0Y	93	2.97		19 9 74	1269	
M102P0.0Y	89	4.65		21 11 74	1226	
F103P0.0Y	91	2.54		19 9 74	1269	
M104P0.0Y	89	4.68		26 11 74	1221	
M105P0.0Y	92	4.90		27 4 76	703	
F106P0.0Y	92	3.46		13 4 76	717	
M107P0.0Y	90	4.07		27 4 76	703	
F108P0.0Y	91	4.28		16 12 76	470	
M109P0.0Y	91	4.08		16 12 76	470	
F013P0.1	515	9.46	0.00068	4 3 64	4492	3
F014P0.1	452	10.3	0.00055	12 5 64	4503	2
M015P0.1	536	9.67	0.00071	23 10 64	4319	3
M016P0.1	501	12.0	0.00059	7 4 65	4146	2
M017P0.1	551	12.2	0.00057	8 11 66	4161	
F018P0.1	536	9.28	0.00070	29 11 66	4140	
M019P0.1	536	11.6	0.00063	29 11 66	4140	
F020P0.1	536	9.80	0.00075	29 12 66	3939	3
M021P0.1	538	11.3	0.00059	26 1 67	4082	
F022P0.1	489	9.8	0.00059	25 5 67	2968	2
M031P0.1B	517	12.2	0.00068	4 3 64	2760	2
F032P0.1B	549	10.4	0.00059	18 11 65	4516	
M033P0.1B	549	10.8	0.00079	18 11 65	4156	3
F034P0.1B	533	11.1	0.00058	8 11 66	3292	2
M035P0.1B	489	10.3	0.00059	25 5 67	3963	
F036P0.1B	493	9.79	0.00060	22 6 67	3600	4
M037P0.1B	493	11.3	0.00059	22 6 67	3935	
F038P0.1B	513	9.52	0.00057	21 12 67	1979	1

B. PLUTONIUM - 239

DOG NUMBER	COMMENTS ON DEAD DOGS
M042P0.0	
M042P0.0B	SPECIAL STUDY
M043P0.0	
M044P0.0	
M045P0.0	
M046P0.0	
M047P0.0	
M048P0.0	
M081P0.0Y	
F082P0.0Y	
F083P0.0Y	
F084P0.0Y	
M086P0.0Y	
F101P0.0Y	
M102P0.0Y	
F103P0.0Y	
M104P0.0Y	
M105P0.0Y	
F106P0.0Y	
M107P0.0Y	
F108P0.0Y	
M109P0.0Y	
F013P0.1	TRANSITIONAL CELL CARCINOMA; PERITONITIS
F014P0.1	CHONDROSARCOMA
M015P0.1	PANCREATIC DYSTROPHY
M016P0.1	EPIDERMOID CARCINOMA (FRONTAL SINUS)
M017P0.1	
F018P0.1	
M019P0.1	
F020P0.1	MAMMARY CARCINOMA
M021P0.1	
F022P0.1	ACCIDENTAL STRANGULATION
M031P0.1B	STATUS EPILEPTICUS
F032P0.1B	
M033P0.1B	BONE MARROW APLASIA
F034P0.1B	CHRONIC PANCREATITIS
M035P0.1B	
F036P0.1B	INHALATION PNEUMONIA
M037P0.1B	
F038P0.1B	TRAUMA

B. PLUTONIUM - 239

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DOSE TO SKELETON (RADS)
M039P0.1B	490	10.5	0.00058	21 12 67	3753	
M044P0.1B	500	10.9	0.00057	8 8 73	1696	
F044P0.1C	569	8.34	0.00072	2 12 70	2676	
M045P0.1B	504	13.5	0.00122	30 5 74	1401	
F045P0.1C	500	9.00	0.00051	8 8 73	1696	
M046P0.1B	504	13.2	0.00120	30 5 74	1401	
F046P0.1C	500	10.2	0.00057	8 8 73	1696	
F047P0.1	500	9.34	0.00051	8 8 73	1696	
F048P0.1	527	10.9	0.00120	30 5 74	1401	
F049P0.1	504	9.71	0.00124	30 5 74	1401	
F013P0.2	517	9.44	0.00206	4 3 64	3221	7
F014P0.2	516	7.44	0.00173	12 5 64	3983	7
M015P0.2	505	10.9	0.00201	23 10 64	4808	9
M016P0.2	500	11.4	0.00163	7 4 65	2841	5
M017P0.2	533	11.8	0.00171	8 11 66	4161	
F018P0.2	530	9.46	0.00200	29 11 66	4140	
M019P0.2	530	12.1	0.00198	29 11 66	4140	
F020P0.2	532	8.30	0.00224	29 12 66	4110	
M021P0.2	538	12.1	0.00181	26 1 67	4082	
F022P0.2	485	8.3	0.00176	25 5 67	3963	
M031P0.2B	515	10.7	0.00185	4 3 64	2640	5
F031P0.2C	452	11.9	0.00169	12 5 64	4971	8
F031P0.2D	429	9.35	0.00186	12 5 64	5071	
M032P0.2B	549	13.60	0.00178	18 11 65	3591	6
F032P0.2C	494	10.1	0.00183	4 2 65	3881	7
F032P0.2D	490	8.04	0.00193	4 2 65	4803	
M033P0.2B	513	14.50	0.00178	18 11 65	2776	5
F033P0.2C	549	12.50	0.00176	18 11 65	4516	
F033P0.2D	513	12.70	0.00178	18 11 65	4516	
M034P0.2B	533	12.7	0.00170	8 11 66	3934	7
F034P0.2C	533	11.5	0.00172	8 11 66	4161	
F034P0.2D	519	9.92	0.00167	8 11 66	4161	
M035P0.2B	489	11.2	0.00173	25 5 67	3963	
F035P0.2C	507	10.5	0.00175	22 6 67	2593	5
F035P0.2D	507	9.10	0.00175	22 6 67	3935	
M036P0.2B	479	12.9	0.00177	25 5 67	3963	
F036P0.2C	493	10.4	0.00177	22 6 67	3291	6
F036P0.2D	569	8.74	0.00146	16 11 67	3351	5
M037P0.2B	529	10.6	0.00149	16 11 67	2804	4
F037P0.2C	529	10.1	0.00150	16 11 67	3788	

B. PLUTONIUM - 239

DOG NUMBER	COMMENTS ON DEAD DOGS
---------------	-----------------------

M039P0.1B
M044P0.1B
F044P0.1C
M045P0.1B
F045P0.1C
M046P0.1B
F046P0.1C
F047P0.1
F048P0.1
F049P0.1

F013P0.2	INTESTINAL ILEUS
F014P0.2	ENTERITIS
M015P0.2	ATHEROSCLEROSIS
M016P0.2	ENCEPHALITIS
M017P0.2	
F018P0.2	
M019P0.2	
F020P0.2	
M021P0.2	
F022P0.2	
M031P0.2B	MELANOMA (ORAL)
F031P0.2C	PULMONARY THROMBO-EMBOLISM
F031P0.2D	
M032P0.2B	HEMANGIOSARCOMA (SPLEEN)
F032P0.2C	MAMMARY CARCINOMA; LUNG THROMBO-EMBOLISM
F032P0.2D	
M033P0.2B	PNEUMONIA
F033P0.2C	
F033P0.2D	
M034P0.2B	PROSTATIC CARCINOMA
F034P0.2C	
F034P0.2D	
M035P0.2B	
F035P0.2C	LUNG CARCINOMA
F035P0.2D	
M036P0.2B	
F036P0.2C	ENTERITIS
F036P0.2D	INTSTINAL PERFORATION
M037P0.2B	HEMANGIOSARCOMA (ABDOMINAL CAVITY)
F037P0.2C	

B. PLUTONIUM - 239

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DEATH	DOSE TO SKELETON (RADS)
F037P0.2D	529	7.14	0.00153	16 11 67	3788		
M038P0.2B	517	10.0	0.00152	16 11 67		3546	5
F038P0.2C	503	7.95	0.00211	21 12 67	3388		
F038P0.2D	499	9.08	0.00176	21 12 67		2880	5
M039P0.2B	542	11.6	0.00214	2 12 70	2676		
F039P0.2C	499	9.46	0.00173	21 12 67	3753		
F039P0.2D	499	9.34	0.00176	21 12 67		3401	6
M042P0.2B	504	9.42	0.00182	8 8 73	1696		
F042P0.2C	589	9.55	0.00176	4 9 69	3130		
M043P0.2B	497	11.0	0.00179	24 4 74	1437		
F043P0.2C	542	9.50	0.00239	2 12 70	2676		
M044P0.2B	540	11.6	0.00177	17 11 71		97	<<1
M044P0.2C	491	12.0	0.00188	24 4 74	1437		
M044P0.2D	488	11.6	0.00184	24 4 74	1437		
M045P0.2B	488	11.6	0.00184	24 4 74	1437		
M045P0.2C	482	11.4	0.00188	24 4 74	1437		
M046P0.2B	482	11.1	0.00179	24 4 74	1437		
F013P0.5	517	9.93	0.00540	4 3 64		2388	15
F013P0.5A	501	11.2	0.00495	23 9 70	2746		
F014P0.5	516	9.98	0.00493	12 5 64		4537	21
M015P0.5	505	8.41	0.00627	23 10 64		4588	28
M016P0.5	501	12.6	0.00521	7 4 65		4062	21
M017P0.5	533	13.4	0.00506	8 11 66	4161		
F018P0.5	530	8.98	0.00594	29 11 66	4140		
M019P0.5	530	11.9	0.00645	29 11 66		3829	24
F020P0.5	532	9.30	0.00553	29 12 66		3490	20
M021P0.5	538	9.80	0.00526	26 1 67	4082		
F022P0.5	485	8.1	0.00525	25 5 67	3963		
M025P0.5	509	9.70	0.00539	30 1 74	1521		
M026P0.5	509	9.96	0.00536	30 1 74	1521		
M031P0.5B	515	10.5	0.00549	4 3 64		1648	15
F031P0.5C	494	8.44	0.00572	4 2 65		2546	16
M032P0.5B	549	13.60	0.00546	18 11 65		227	14
F033P0.5B	503	10.10	0.00559	18 11 65		4509	24
M034P0.5B	530	12.5	0.00642	29 11 66		1920	14
F035P0.5B	501	9.54	0.00520	22 6 67	3935		
M036P0.5B	479	11.5	0.00527	25 5 67		3885	20
F037P0.5B	517	8.39	0.00454	16 11 67	3788		
M038P0.5B	517	10.5	0.00448	16 11 67		3497	35
F039P0.5B	490	10.9	0.00528	21 12 67	3753		

B. PLUTONIUM - 239

DOG NUMBER	COMMENTS ON DEAD DOGS
---------------	-----------------------

F037P0.2D	
M038P0.2B	FLASMA CELL MYELOMA (HUMERUS)
F038P0.2C	
F038P0.2D	NEPHRITIS; PANCREATITIS
M039P0.2B	
F039P0.2C	
F039P0.2D	RHABDOMYOSARCOMA
M042P0.2B	
F042P0.2C	
M043P0.2B	
F043P0.2C	
M044P0.2B	SPECIAL STUDY
M044P0.2C	
M044P0.2D	
M045P0.2B	
M045P0.2C	
M046P0.2B	
F013P0.5	MAMMARY CARCINOMA
F013P0.5A	
F014P0.5	CHONDROSARCOMA (NOSE)
M015P0.5	AORTIC THROMBOEMBOLISM; THYROID CARCINOMA
M016P0.5	CHROMAPHOB ADENOMA
M017P0.5	
F018P0.5	
M019P0.5	OSTEOSARCOMA
F020P0.5	EPIDERMOID CARCINOMA (ORAL)
M021P0.5	
F022P0.5	
M025P0.5	
M026P0.5	
M031P0.5B	STATUS EPILEPTICUS
F031P0.5C	SPECIAL STUDY
M032P0.5B	SPECIAL STUDY
F033P0.5B	MAMMARY CARCINOMA
M034P0.5B	SPECIAL STUDY
F035P0.5B	
M036P0.5B	OSTEOSARCOMA
F037P0.5B	
M038P0.5B	UNDETERMINED
F039P0.5B	

B. PLUTONIUM - 239

DOG	INJECTION	AGE WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED	DAYS SINCE INJECTION	DOSE TO SKELETON (RADS)
M042F0.5B	542	13.1	0.00675	2 12 70	2676	
M042F0.5C	542	12.2	0.00668	2 12 70	2676	
F042F0.5D	542	9.71	0.00668	2 12 70	2676	
F043F0.5B	545	11.6	0.00484	3 10 69	3101	
F043F0.5C	537	10.7	0.00480	3 10 69	3101	
M043F0.5D	500	12.0	0.00546	8 8 73	1696	
M044F0.5B	445	11.5	0.00360	3 6 69	99	<1
F044F0.5C	504	8.48	0.00604	8 8 73	1696	
M045F0.5B	472	10.3	0.00350	3 6 69	42	<1
F045F0.5C	540	10.0	0.00516	17 11 71	35	<<1
M046F0.5B	484	11.8	0.00336	3 6 69	7	<<1
F046F0.5C	540	9.15	0.00516	17 11 71	7	<<1
M047F0.5	568	11.9	0.00524	8 8 74	1331	
M048F0.5	568	12.1	0.00546	8 8 74	1331	
F049F0.5	569	9.10	0.00537	8 8 74	1331	
F050F0.5	568	12.8	0.00541	8 8 74	1331	
M051F0.5	506	11.9	0.00552	29 8 74	1310	
M052F0.5	506	10.4	0.00549	29 8 74	1310	
M053F0.5	498	13.2	0.00515	29 8 74	1310	
M054F0.5	497	10.8	0.00551	29 8 74	1310	
F055F0.5	533	9.65	0.00547	17 10 74	1261	
F056F0.5	533	9.56	0.00552	17 10 74	1261	
F057F0.5	523	8.14	0.00524	17 10 74	1261	
F101F0.5Y	93	2.74	0.00617	19 9 74	1269	
M102F0.5Y	91	3.43	0.00618	19 9 74	1269	
F103F0.5Y	91	3.39	0.00611	19 9 74	1269	
M104F0.5Y	90	3.43	0.00525	27 4 76	703	
M105F0.5Y	89	4.17	0.00570	26 11 74	1221	
F106F0.5Y	89	4.51	0.00580	26 11 74	1221	
F107F0.5Y	94	3.53	0.00553	22 9 76	555	
M108F0.5Y	91	4.47	0.00484	16 12 76	470	
M110F0.5Y	90	4.48	0.00521	9 3 78	22	
F014F0.7	533	8.98	0.00947	22 7 69	3166	
M015F0.7	533	10.3	0.00941	22 7 69	3174	
M016F0.7	516	11.9	0.0102	4 9 69	3130	
M017F0.7	540	8.04	0.0103	3 10 69	3101	
F018F0.7	531	9.66	0.00942	22 7 69	3174	
M019F0.7	501	11.6	0.0104	23 9 70	3174	
F020F0.7	521	9.18	0.00926	22 7 69	3174	
M021F0.7	499	11.1	0.0104	23 9 70	2746	

1737

22

B. PLUTONIUM - 239

DOG NUMBER	COMMENTS ON DEAD DOGS
---------------	-----------------------

M042P0.5B

M042P0.5C

F042P0.5D

F043P0.5B

F043P0.5C

M043P0.5D

M044P0.5B SPECIAL STUDY

F044P0.5C

M045P0.5B SPECIAL STUDY

F045P0.5C SPECIAL STUDY

M046P0.5B SPECIAL STUDY

F046P0.5C SPECIAL STUDY

M047P0.5

M048P0.5

F049P0.5

F050P0.5

M051P0.5

M052P0.5

M053P0.5

M054P0.5

F055P0.5

F056P0.5

F057P0.5

F101P0.5Y

M102P0.5Y

F103P0.5Y

M104P0.5Y

M105P0.5Y

F106P0.5Y

F107P0.5Y

M108P0.5Y

M110P0.5Y

F014P0.7

M015P0.7

M016P0.7

M017P0.7

F018P0.7

M019P0.7 STRANGULATED HERNIA

F020P0.7

M021P0.7

B. PLUTONIUM - 239

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE INJECTED			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR		
F022P0.7	538	9.69	0.0108	4	9	69	3130	
F023P0.7	538	9.56	0.0108	4	9	69	3130	
F024P0.7	516	8.90	0.0110	4	9	69	3130	
M025P0.7	506	10.9	0.0117	8	8	73	1696	
M026P0.7	494	10.2	0.0112	20	9	73	1653	
M027P0.7	494	11.9	0.0116	20	9	73	1653	
F028P0.7	494	10.6	0.0110	20	9	73	1653	
F029P0.7	493	8.63	0.0113	20	9	73	1653	
F030P0.7	487	9.91	0.0113	20	9	73	1653	
M031P0.7	521	13.2	0.00956	4	12	73	1578	
M032P0.7	521	9.46	0.00967	4	12	73	1578	
M033P0.7	509	10.7	0.0103	30	1	74	1521	
M034P0.7	521	10.1	0.00979	4	12	73	1578	
F035P0.7	521	10.6	0.00981	4	12	73	1578	
F036P0.7	521	11.1	0.00999	4	12	73	1578	
M037P0.7	520	11.6	0.00999	4	12	73	1578	
F038P0.7	520	11.4	0.00995	4	12	73	1578	
F039P0.7	512	8.24	0.00969	4	12	73	1578	
M040P0.7	512	10.7	0.00990	4	12	73	1578	
M041P0.7	533	11.9	0.0105	30	1	74	1521	
M042P0.7	533	11.6	0.0106	30	1	74	1521	
M043P0.7	533	10.1	0.0106	30	1	74	1521	
F044P0.7	533	10.2	0.0105	30	1	74	1521	
M045P0.7	509	10.8	0.0104	30	1	74	1521	
F046P0.7	509	10.2	0.0105	30	1	74	1521	
F047P0.7	508	8.39	0.0103	30	1	74	1521	
M048P0.7	502	10.30	0.00910	5	3	74	1487	
M049P0.7	471	12.30	0.00990	5	3	74	1487	
F050P0.7	522	9.33	0.0112	29	8	74	1310	
F051P0.7	522	11.8	0.0105	29	8	74	1310	
M001P1.0	443	9.41	0.0150	1	12	52	4572	66
F002P1.0	422	6.85	0.0163	2	3	53	4810	74
M003P1.0	515	8.00	0.0165	1	6	53	4292	68
M004P1.0	608	9.97	0.0139	16	9	53	4549	60
F005P1.0	620	8.80	0.0142	14	10	53	1539	27
F005P1.0A	472	11.0	0.0168	3	9	58	3764	63
F006P1.0	410	7.38	0.0140	12	5	54	4292	58
F007P1.0	510	6.36	0.0167	25	10	54	3981	65
M008P1.0	453	10.6	0.0172	15	3	55	3367	5
F009P1.0	556	7.87	0.0168	9	9	55	2257	43

B. PLUTONIUM - 239

DOG
NUMBER

COMMENTS ON DEAD DOGS

F022P0.7
F023P0.7
F024P0.7
M025P0.7
M026P0.7
M027P0.7
F028P0.7
F029P0.7
F030P0.7
M031P0.7
M032P0.7
M033P0.7
M034P0.7
F035P0.7
F036P0.7
M037P0.7
F038P0.7
F039P0.7
M040P0.7
M041P0.7
M042P0.7
M043P0.7
F044P0.7
M045P0.7
F046P0.7
F047P0.7
M048P0.7
M049P0.7
F050P0.7
F051P0.7

M001P1.0 OSTEOSARCOMA
F002P1.0 CIRCULATORY FAILURE
M003P1.0 OSTEOSARCOMA
M004P1.0 BILE DUCT CARCINOMA
F005P1.0 COLITIS, ENTERITIS + SECONDARY HEPATIC NECROSIS
F005P1.0A THYROID CARCINOMA
F006P1.0 CARCINOMA OF COLON
F007P1.0 TRAUMA LYMPHADENOPHATHY
M008P1.0 OSTEOSARCOMA
F009P1.0 OSTEOSARCOMA

B. PLUTONIUM - 239

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DOSE TO SKELETON (RADS)
F010P1.0	641	12.00	0.0152	22 11 55	3649	56
M011P1.0	602	8.90	0.0157	24 4 56	5160	76
M012P1.0	629	9.67	0.0167	29 5 56	2374	44
M013P1.0	504	12.7	0.0153	3 9 58	5277	75
F014P1.0	533	10.4	0.0141	22 7 69	3174	
M015P1.0	516	12.8	0.0159	4 9 69	3130	
M016P1.0	516	10.6	0.0165	4 9 69	3130	
M017P1.0	537	10.9	0.0151	3 10 69	3101	
F018P1.0	531	9.89	0.0140	22 7 69	3174	
M019P1.0	501	9.82	0.0159	23 9 70	2746	
F020P1.0	521	10.4	0.0141	22 7 69	3174	
M021P1.0	499	10.0	0.0156	23 9 70	2746	
F022P1.0	521	9.04	0.0139	22 7 69	3174	
F023P1.0	538	11.2	0.0163	4 9 69	3130	
F024P1.0	516	10.4	0.0163	4 9 69	3130	
M025P1.0	504	11.0	0.0168	8 8 73	1696	
F101P1.0Y	93	2.23	0.0171	19 9 74	904	
M102P1.0Y	91	2.83	0.0171	19 9 74	904	
F103P1.0Y	89	3.56	0.0137	21 11 74	1226	
M104P1.0Y	89	5.14	0.0158	21 11 74	1226	
M105P1.0Y	91	5.19	0.0143	2 3 76	759	
F106P1.0Y	91	4.36	0.0142	2 3 76	759	
F107P1.0Y	92	4.46	0.0194	8 10 76	539	
F108P1.0Y	91	2.52	0.0146	16 12 76	470	
M109P1.0Y	90	3.78	0.0155	9 3 78	22	
F501P1.0+	1787	9.54	0.0158	10 6 75	1025	
F502P1.0Y	1830	11.4	0.0174	6 7 77	268	
M001P1.7	657	8.72	0.0475	26 6 56	3025	151
F002P1.7	527	8.62	0.0431	22 11 55	3430	150
M003P1.7	642	8.63	0.0495	26 6 56	3430	173
M004P1.7	673	8.37	0.0484	10 10 56	3312	165
F005P1.7	642	11.6	0.0493	26 6 56	2659	142
F006P1.7	642	10.3	0.0459	26 6 56	2221	116
F007P1.7	756	9.73	0.0481	10 10 56	3353	165
M008P1.7	673	13.6	0.0479	10 10 56	3282	162
F009P1.7	756	9.72	0.0485	10 10 56	2500	134
F010P1.7	739	10.6	0.0495	10 10 56	467	36
F010P1.7A	472	8.07	0.0457	3 9 58	4214	187
M011P1.7	599	11.6	0.0486	24 4 56	2777	145
M012P1.7	673	9.41	0.0491	10 10 56	2973	154

B. PLUTONIUM - 239

DOG
NUMBER

COMMENTS ON DEAD DOGS

F010P1.0 MAMMARY CARCINOMA
M011P1.0 THYROID CARCINOMA
M012P1.0 CHRONIC PANCREATITIS
M013P1.0 SENILITY, HYDROCEPHALUS

F014P1.0

M015P1.0

M016P1.0

M017P1.0

F018P1.0

M019P1.0

F020P1.0

M021P1.0

F022P1.0

F023P1.0

F024P1.0

M025P1.0

F101P1.0Y

M102P1.0Y

F103P1.0Y

M104P1.0Y

M105P1.0Y

F106P1.0Y

F107P1.0Y

F108P1.0Y

M109P1.0Y

F501P1.0+

F502P1.0Y

M001P1.7 OSTEOSARCOMA
F002P1.7 OSTEOSARCOMA
M003P1.7 CHROMOPHOBE ADENOMA OF PITUITARY, PROSTATE CARCINOMA
M004P1.7 OSTEOSARCOMA
F005P1.7 OSTEOSARCOMA
F006P1.7 OSTEOSARCOMA
F007P1.7 OSTEOSARCOMA
M008P1.7 OSTEOSARCOMA
F009P1.7 OSTEOSARCOMA
F010P1.7 ACUTE ENTERITIS
F010P1.7A OSTEOSARCOMA
M011P1.7 BILE DUCT CARCINOMA
M012P1.7 LEUKEMIA

B. PLUTONIUM - 239

DOG NUMBER	INJECTION			DATE			DAYS SINCE	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	INJECTED	INJECTION	3/31/78 DEATH		
				D	MO	YR		
M013P1.7	504	10.60	0.0473	3	9	58	4375	200
F101P1.7Y	93	2.34	0.0543	19	9	74	1269	
M102P1.7Y	91	2.97	0.0545	19	9	74	1269	
F103P1.7Y	89	3.84	0.0453	21	11	74	1226	
M104P1.7Y	93	3.40	0.0488	27	4	76	703	
M105P1.7Y	90	4.06	0.0485	27	4	76	703	
F106P1.7Y	89	4.20	0.0529	26	11	74	1221	
F107P1.7Y	93	3.91	0.0477	24	9	76	553	
M108P1.7Y	92	4.32	0.0473	8	10	76	539	
F501P1.7+	1725	10.0	0.0456	24	6	75	1011	
F502P1.7+	1732	10.0	0.0416	16	12	75	836	
F503P1.7+	1826	10.2	0.0519	13	5	76	687	
F504P1.7+	1831	11.2	0.0527	6	7	77	268	
M001P2.0	443	7.61	0.0853	1	12	52	2985	268
F002P2.0	422	7.73	0.112	2	3	53	2780	334
M003P2.0	485	10.5	0.0940	1	6	53	3185	310
M004P2.0	608	9.84	0.0862	16	9	53	2948	268
F005P2.0	594	8.12	0.0846	14	10	53	2423	228
F006P2.0	417	7.54	0.0902	12	5	54	2947	281
F007P2.0	485	8.40	0.0996	25	10	54	2093	240
M008P2.0	406	9.73	0.0957	15	3	55	1761	203
F009P2.0	552	9.72	0.101	9	9	55	2014	237
F010P2.0	551	7.94	0.0968	22	11	55	2912	299
M011P2.0	599	10.3	0.0961	24	4	56	1617	191
M012P2.0	622	9.98	0.100	29	5	56	2284	258
F101P2.0Y	91	2.60	0.0981	19	9	74	1269	
M102P2.0Y	91	2.85	0.106	19	9	74	1269	
M103P2.0Y	93	4.27	0.0904	2	3	76	759	
F104P2.0Y	92	3.12	0.0904	13	4	76	717	
M105P2.0Y	90	4.10	0.0963	27	4	76	703	
F106P2.0Y	91	2.81	0.0961	27	4	76	703	
F107P2.0Y	94	3.22	0.0980	22	9	76	555	
M108P2.0Y	91	3.69	0.0834	16	12	76	470	
F501P2.0+	1787	10.2	0.0903	10	6	75	1025	
F502P2.0+	1757	10.2	0.0908	5	3	76	756	
F503P2.0+	1743	8.44	0.110	5	3	76	756	

M001P3.0	418	8.00	0.261	1	12	52	1476	579
----------	-----	------	-------	---	----	----	------	-----

B. PLUTONIUM - 239

DOG NUMBER	COMMENTS ON DEAD DOGS.
---------------	------------------------

M013P1.7	CHONDROSARCOMA
----------	----------------

F101P1.7Y	
-----------	--

M102P1.7Y	
-----------	--

F103P1.7Y	
-----------	--

M104P1.7Y	
-----------	--

M105P1.7Y	
-----------	--

F106P1.7Y	
-----------	--

F107P1.7Y	
-----------	--

M108P1.7Y	
-----------	--

F501P1.7+	
-----------	--

F502P1.7+	
-----------	--

F503P1.7+	
-----------	--

F504P1.7+	
-----------	--

M001P2.0	OSTEOSARCOMA
----------	--------------

F002P2.0	OSTEOSARCOMA
----------	--------------

M003P2.0	OSTEOSARCOMA
----------	--------------

M004P2.0	OSTEOSARCOMA
----------	--------------

F005P2.0	OSTEOSARCOMA
----------	--------------

F006P2.0	OSTEOSARCOMA
----------	--------------

F007P2.0	SQUAMOUS CELL CARCINOMA (FRONTAL SINUS)
----------	---

M008P2.0	ASPIRATION PNEUMONIA
----------	----------------------

F009P2.0	OSTEOSARCOMA
----------	--------------

F010P2.0	OSTEOSARCOMA
----------	--------------

M011P2.0	OSTEOSARCOMA
----------	--------------

M012P2.0	OSTEOSARCOMA
----------	--------------

F101P2.0Y	
-----------	--

M102P2.0Y	
-----------	--

M103P2.0Y	
-----------	--

F104P2.0Y	
-----------	--

M105P2.0Y	
-----------	--

F106P2.0Y	
-----------	--

F107P2.0Y	
-----------	--

M108P2.0Y	
-----------	--

F501P2.0+	
-----------	--

F502P2.0+	
-----------	--

F503P2.0+	
-----------	--

M001P3.0	OSTEOSARCOMA
----------	--------------

B. PLUTONIUM - 239

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR		
F002P3.0	422	6.85	0.312	2	3	53	1947	886
M003P3.0	485	8.74	0.291	1	6	53	1604	695
M004P3.0	608	8.51	0.292	16	9	53	1950	830
F005P3.0	650	8.22	0.288	14	10	53	1504	650
F006P3.0	415	8.38	0.282	12	5	54	1617	678
F007P3.0	485	9.00	0.314	25	10	54	1627	760
M008P3.0	406	9.73	0.300	15	3	55	177	782
F009P3.0	552	7.67	0.300	9	9	55	1894	831
F010P3.0	533	8.94	0.298	22	11	55	1547	689
M011P3.0	599	10.5	0.309	24	4	56	1198	569
M012P3.0	622	10.2	0.308	29	5	56	1659	758
M081P3.0Y	91	4.03	0.320	25	4	72	2166	
M086P3.0Y	89	3.29	0.319	25	4	72	2166	
M089P3.0Y	89	4.23	0.312	25	4	72	2166	
F101P3.0Y	91	2.88	0.332	19	9	74	1269	
M102P3.0Y	93	3.93	0.316	27	4	76	703	
F103P3.0Y	92	3.54	0.269	13	4	76	717	
M104P3.0Y	92	4.65	0.317	27	4	76	703	
M105P3.0Y	91	3.86	0.312	27	4	76	703	
F106P3.0Y	91	4.22	0.315	1	6	76	668	
F107P3.0Y	93	3.69	0.295	24	9	76	553	
M108P3.0Y	90	3.56	0.283	16	12	76	470	
F501P3.0+	1718	10.3	0.290	17	6	75	1018	
F502P3.0+	1739	9.56	0.298	23	12	75	829	
M001P4.0	443	7.61	0.823	1	12	52	1724	2215
F002P4.0	568	8.65	1.03	2	3	53	1556	2521
M003P4.0	485	9.36	0.929	1	6	53	1198	1784
M004P4.0	566	8.74	0.974	16	9	53	1066	1678
F005P4.0	650	7.05	0.872	14	10	53	1245	1736
F006P4.0	420	9.26	0.811	12	5	54	1357	1749
F007P4.0	485	8.45	0.963	25	10	54	1198	1850
M008P4.0	651	9.22	0.887	15	3	55	1157	1650
F009P4.0	552	8.58	0.960	9	9	55	1343	2050
F010P4.0	527	6.48	0.868	22	11	55	1241	1723
M011P4.0	596	9.56	0.927	24	4	56	1288	1904
M012P4.0	598	11.4	0.838	29	5	56	1463	1938
M001P5.0	418	8.86	2.67	1	12	52	1324	5873

B. PLUTONIUM - 239

DOG
NUMBER

COMMENTS ON DEAD DOGS:

F002P3.0 OSTEOSARCOMA
M003P3.0 OSTEOSARCOMA
M004P3.0 OSTEOSARCOMA
F005P3.0 OSTEOSARCOMA
F006P3.0 OSTEOSARCOMA
F007P3.0 OSTEOSARCOMA
M008P3.0 OSTEOSARCOMA
F009P3.0 OSTEOSARCOMA
F010P3.0 OSTEOSARCOMA
M011P3.0 OSTEOSARCOMA
M012P3.0 OSTEOSARCOMA
M081P3.0Y
M086P3.0Y
M089P3.0Y
F101P3.0Y
M102P3.0Y
F103P3.0Y
M104P3.0Y
M105P3.0Y
F106P3.0Y
F107P3.0Y
M108P3.0Y
F501P3.0+
F502P3.0+

M001P4.0 OSTEOSARCOMA
F002P4.0 OSTEOSARCOMA
M003P4.0 OSTEOSARCOMA
M004P4.0 OSTEOSARCOMA
F005P4.0 OSTEOSARCOMA
F006P4.0 OSTEOSARCOMA
F007P4.0 OSTEOSARCOMA
M008P4.0 OSTEOSARCOMA
F009P4.0 OSTEOSARCOMA
F010P4.0 OSTEOSARCOMA
M011P4.0 OSTEOSARCOMA
M012P4.0 OSTEOSARCOMA

M001P5.0 OSTEOSARCOMA

B. PLUTONIUM - 239

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DOSE TO SKELETON (RADS)
F002P5.0	1151	8.75	3.30	2 3 53	1576	8575
M003P5.0	515	8.10	3.00	1 6 53	499	2577
M004P5.0	566	9.18	3.17	16 9 53	1562	8167
F005P5.0	691	8.77	2.77	14 10 53	2059	9292
F006P5.0	407	7.90	2.57	12 5 54	1194	5121
F007P5.0	482	8.33	2.99	25 10 54	1491	7368
M008P5.0	497	9.55	2.69	15 3 55	1192	5351
F009P5.0	552	9.45	2.73	9 9 55	1145	5226
M081P5.OY	94	4.60	2.68	1 3 72	1161	5199
F082P5.OY	94	4.80	2.66	1 3 72	1295	5729
F083P5.OY	94	4.00	2.66	1 3 72	1442	6349
F084P5.OY	94	3.55	2.68	1 3 72	1259	5618
F085P5.OY	94	4.15	2.64	1 3 72	1134	5007
M086P5.OY	93	3.75	2.95	25 4 72	1345	6588
F087P5.OY	93	4.15	2.93	25 4 72	1119	5486
F088P5.OY	93	3.65	2.96	25 4 72	1227	6054
M089P5.OY	93	3.79	2.92	25 4 72	1443	6820
M090P5.OY	93	4.38	2.97	25 4 72	1137	5647
M091P5.OY	91	3.78	2.90	25 4 72	1491	7360
M092P5.OY	91	3.82	2.87	25 4 72	1616	8160

B. PLUTONIUM - 239

DOG NUMBER	COMMENTS ON DEAD DOGS
F002P5.0	OSTEOSARCOMA + FRACTURED MANDIBLE
M003P5.0	LIVER DEGENERATION + ASCITES
M004P5.0	OSTEOSARCOMA
F005P5.0	OSTEOSARCOMA, LIVER DEGENERATION + HEPATIC HEMORRHAGE
F006P5.0	OSTEOSARCOMA
F007P5.0	OSTEOSARCOMA + CRIPPLING FRACTURE
M008P5.0	GINGIVITIS
F009P5.0	OSTEOSARCOMA, EPISTAXIS + CIRCULATORY COLLAPSE
M081P5.0Y	OSTEOSARCOMA
F082P5.0Y	OSTEOSARCOMA
F083P5.0Y	OSTEOSARCOMA, FIBROSARCOMA (SOFT TISSUE)
F084P5.0Y	OSTEOSARCOMA
F085P5.0Y	OSTEOSARCOMA
M086P5.0Y	OSTEOSARCOMA
F087P5.0Y	OSTEOSARCOMA
F088P5.0Y	OSTEOSARCOMA
M089P5.0Y	OSTEOSARCOMA
M090P5.0Y	OSTEOSARCOMA
M091P5.0Y	OSTEOSARCOMA
M092P5.0Y	OSTEOSARCOMA

* F502P2+ and F503P2+ were given tracer ($\sim 0.24 \mu\text{Ci}$) ^{237}Pu in the same injection solution containing their ^{239}Pu .

C. RADIUM - 228 (MESOTHORIUM)

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DOSE TO SKELETON (RADS)
F001M0.0	732	7.33		4 1 54	3451	
F002M0.0	545	6.94		29 11 54	6155	
M003M0.0	579	13.0		13 3 56	5056	
M004M0.0	601	10.3		15 1 57	4816	
F005M0.0	671	11.2		5 3 57	4581	
M006M0.0	492	7.56		23 4 57	4934	
F007M0.0	395	8.71		4 6 57	1414	
F007M0.0A	594	10.9		15 1 63	3624	
F008M0.0	654	11.6		9 3 60	5009	
M009M0.0	575	12.4		13 4 60	413	
M010M0.0	581	13.3		17 7 62	2991	
F011M0.0	475	9.31		18 9 62	3248	
M012M0.0	695	10.0		22 12 60	4810	
F001M0.5	492	9.47	0.0173	17 7 62	5460	92
F002M0.5	492	9.15	0.0173	17 7 62	3689	124
M003M0.5	493	10.8	0.0199	18 9 62	4697	147
M004M0.5	475	12.8	0.0199	18 9 62	4193	159
F005M0.5	534	7.83	0.0172	23 10 62	3958	107
M006M0.5	510	10.3	0.0171	23 10 62	3019	95
F007M0.5	492	8.87	0.0172	17 7 62	4997	148
F008M0.5	654	12.6	0.0159	9 3 60	4208	93
M009M0.5	485	11.9	0.0170	13 4 60	5321	141
M010M0.5	492	10.6	0.0174	17 7 62	4567	147
F011M0.5	505	7.82	0.0202	18 9 62	4033	140
M012M0.5	510	10.6	0.0165	23 10 62	3920	111
F001M1.0	718	7.75	0.0463	4 1 54	295	261
F001M1.0A	590	8.07	0.0512	23 10 62	4292	292
F002M1.0	459	8.25	0.0324	29 11 54	5267	284
M003M1.0	575	13.8	0.0589	13 3 56	3157	408
M004M1.0	601	9.90	0.0481	15 1 57	4260	175
F005M1.0	658	8.80	0.0490	5 3 57	4565	256
M006M1.0	521	10.6	0.0468	23 4 57	3402	363
F007M1.0	534	9.89	0.0489	4 6 57	2159	199
F008M1.0	654	12.4	0.0491	9 3 60	3886	320
M009M1.0	485	10.1	0.0504	13 4 60	4670	429
M010M1.0	492	9.43	0.0501	17 7 62	2966	284
F011M1.0	505	8.91	0.0613	18 9 62	5673	

C. RADIUM - 228 (MESOTHORIUM).

DOG NUMBER	COMMENTS ON DEAD DOGS
F001M0.0	PURULENT MENINGOENCEPHALITIS
F002M0.0	UNDETERMINED; SENILITY
M003M0.0	BRAIN INFARCTION
M004M0.0	VALVULAR ENDOCARDITIS; MYOCARDIAL INFARCTION
F005M0.0	MAMMARY CARCINOMA
M006M0.0	NEPHRITIS
F007M0.0	STATUS EPILEPTICUS
F007M0.0A	PNEUMONIA
F008M0.0	AORTIC THROMBOEMBOLISM
M009M0.0	VIRUS PNEUMONIA
M010M0.0	MALIGNANT MELANOMA (ORAL)
F011M0.0	ASPIRATION PNEUMONIA
M012M0.0	PULMONARY THROMBOEMBOLISM; TRANSITIONAL CELL CARCINOMA
F001M0.5	THROMBO-EMBOLISM PORTAL VEIN
F002M0.5	CHRONIC PANCREATITIS
M003M0.5	AORTIC THROMBO-EMBOLISM
M004M0.5	UNDIFFERENTIATED SARCOMA (NON-SKELETAL)
F005M0.5	UNDETERMINED
M006M0.5	MALIGNANT MELANOMA (EYE)
F007M0.5	PNEUMONIA; MELANOMA (EYE)
F008M0.5	BACTERIAL ENTERITIS
M009M0.5	AORTA THROMBO-EMBOLISM
M010M0.5	KIDNEY DEGENERATION; AORTA THROMBOEMBOLISM
F011M0.5	BILE DUCT OBSTRUCTION; EYE MELANOMA
M012M0.5	STATUS EPILEPTICUS
F001M1.0	SARCOMA (SPLEEN)
F001M1.0A	KIDNEY DEGENERATION
F002M1.0	OSTEOSARCOMA
M003M1.0	OSTEOSARCOMA
M004M1.0	PNEUMONIA; PANCREATITIS
F005M1.0	MALIGNANT MELANOMA (EYE)
M006M1.0	EPIDERMOID CARCINOMA (PENIS)
F007M1.0	SARCOMA (HEART)
F008M1.0	MALIGNANT MELANOMA (EYE)
M009M1.0	VALVULAR ENDOCARDITIS
M010M1.0	MALIGNANT MELANOMA (EYE)
F011M1.0	MAMMARY CARCINOMA

C. RADIUM - 228 (MESOTHORIUM)

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DOSE TO SKELETON (RADS)
M012M1.0	528	9.27	0.0498	23 10 62	3786	308
F001M1.7	510	7.52	0.151	23 10 62	4265	956
F002M1.7	560	9.90	0.183	13 3 56	2383	977
M003M1.7	576	11.0	0.180	13 3 56	2709	964
M004M1.7	601	8.94	0.143	15 1 57	2864	565
F005M1.7	658	12.8	0.141	5 3 57	3234	833
M006M1.7	521	10.0	0.144	23 4 57	3424	524
F007M1.7	534	10.2	0.146	4 6 57	2646	800
F008M1.7	654	10.8	0.148	9 3 60	2486	515
M009M1.7	485	12.6	0.149	13 4 60	2799	896
M010M1.7	492	10.1	0.124	17 7 62	3101	997
F011M1.7	505	10.7	0.179	18 9 62	3325	1347
M012M1.7	524	9.28	0.153	23 10 62	3017	957
F001M2.0	676	7.60	0.276	4 1 54	1780	1160
F002M2.0	517	8.25	0.194	29 11 54	965	264
M003M2.0	576	11.0	0.358	13 3 56	619	473
M004M2.0	601	9.88	0.282	15 1 57	2282	1377
F005M2.0	509	8.30	0.295	5 3 57	2688	1237
M006M2.0	502	12.4	0.306	23 4 57	2674	1843
F007M2.0	534	10.1	0.298	4 6 57	2239	1419
F008M2.0	654	12.4	0.300	9 3 60	2386	1237
M009M2.0	630	9.99	0.302	13 4 60	1254	748
M010M2.0	430	11.2	0.311	17 7 62	2373	1931
F011M2.0	505	7.03	0.381	18 9 62	2878	1461
M012M2.0	524	9.47	0.306	23 10 62	2471	1992
F001M3.0	519	10.4	0.858	4 1 54	918	2444
F002M3.0	460	6.70	0.612	29 11 54	1856	2767
M003M3.0	579	10.4	0.965	13 3 56	1185	3285
M004M3.0	601	10.2	0.916	15 1 57	1176	2123
F005M3.0	531	8.51	0.940	5 3 57	1869	2864
M006M3.0	502	9.09	0.953	23 4 57	1421	2541
F007M3.0	534	9.94	0.907	4 6 57	1463	4193
F008M3.0	633	11.8	0.950	9 3 60	1447	2877
M009M3.0	630	9.83	0.918	13 4 60	1570	3036

C: RADIUM - 228 (MESOTHORIUM)

DOG
NUMBER COMMENTS ON DEAD DOGS

M012M1.0 LYMPHATIC LEUKEMIA

F001M1.7 OSTEOSARCOMA
F002M1.7 OSTEOSARCOMA
M003M1.7 OSTEOSARCOMA
M004M1.7 CARCINOMA SMALL INTESTINE
F005M1.7 OSTEOSARCOMA
M006M1.7 OSTEOSARCOMA
F007M1.7 OSTEOSARCOMA
F008M1.7 OSTEOSARCOMA
M009M1.7 OSTEOSARCOMA
M010M1.7 OSTEOSARCOMA
F011M1.7 OSTEOSARCOMA
M012M1.7 UNKNOWN

F001M2.0 OSTEOSARCOMA
F002M2.0 INTESTINAL HEMORRHAGE
M003M2.0 PNEUMONIA
M004M2.0 OSTEOSARCOMA
F005M2.0 OSTEOSARCOMA
M006M2.0 OSTEOSARCOMA
F007M2.0 CHRONIC PANCREATITIS
F008M2.0 OSTEOSARCOMA
M009M2.0 OSTEOSARCOMA
M010M2.0 OSTEOSARCOMA
F011M2.0 OSTEOSARCOMA
M012M2.0 OSTEOSARCOMA

F001M3.0 OSTEOSARCOMA
F002M3.0 OSTEOSARCOMA
M003M3.0 OSTEOSARCOMA
M004M3.0 OSTEOSARCOMA
F005M3.0 OSTEOSARCOMA
M006M3.0 OSTEOSARCOMA
F007M3.0 OSTEOSARCOMA
F008M3.0 OSTEOSARCOMA
M009M3.0 OSTEOSARCOMA

C. RADIUM - 228 (MESOTHORIUM)

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE			DAYS SINCE INJECTION 3/31/78	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR		
M010M3.0	581	10.4	1.00	17	7	62	1575	3091
F011M3.0	497	11.0	1.19	18	9	62	1395	3289
M012M3.0	510	12.9	0.987	23	10	62	1638	3153
F001M4.0	510	7.56	2.60	4	1	54	841	7485
F002M4.0	460	6.95	1.86	29	11	54	77	3029
M003M4.0	579	9.65	3.37	13	3	56	418	2393
M003M4.0A	494	7.34	2.64	4	6	57	1063	7472
M004M4.0	609	7.84	2.47	15	1	57	896	3573
F005M4.0	507	9.63	2.67	5	3	57	1064	5811
M006M4.0	502	9.49	2.66	23	4	57	1121	6379
F007M4.0	544	8.40	2.67	4	6	57	1253	6181
F001M5.0	494	7.77	8.11	4	1	54	232	5139
F002M5.0	460	7.35	5.46	29	11	54	780	10221
M003M5.0	579	8.87	10.4	13	3	56	688	18868
M004M5.0	482	7.22	7.89	15	1	57	561	7549
F005M5.0	658	11.1	8.48	5	3	57	770	12745
M006M5.0	580	7.53	8.67	23	4	57	792	9015
F007M5.0	494	7.35	8.92	4	6	57	966	24125

* ($\mu\text{Ci } ^{228}\text{Th}/\mu\text{Ci } ^{228}\text{Ra}$) injected = 0.15 for F1M1.0, 2.0, 3.0, 4.0, 5.0.
 = 0.03 for F2M1.0, 1.7, 2.0, 3.0, 4.0, 5.0,
 M3M1.0, 1.7, 2.0, 3.0, 4.0, 5.0.
 = 0.006 for groups 4, 5, 6, 7, 8, 9, 10, 11, 12,
 and dogs F1M0.5, F2M0.5, M3M0.5, F1M1A,
 F1M1.7, and M3M4.0A.

C. RADIUM - 228 (MESOTHORIUM)

DOG NUMBER	COMMENTS ON DEAD DOGS
M010M3.0	OSTEOSARCOMA
F011M3.0	OSTEOSARCOMA
M012M3.0	OSTEOSARCOMA
F001M4.0	OSTEOSARCOMA + CRIPPLING FRACTURE
F002M4.0	OSTEOSARCOMA
M003M4.0	STRANGULATED INGUINAL HERNIA
M003M4.0A	OSTEOSARCOMA, NEPHRITIS, ULCERATIVE GINGIVITIS + PNEUMONIA
M004M4.0	FRACTURED MANDIBLE + ULCERATIVE GINGIVITIS
F005M4.0	OSTEOSARCOMA
M006M4.0	OSTEOSARCOMA
F007M4.0	OSTEOSARCOMA
F001M5.0	NEPHRITIS + SEVERE ANEMIA
F002M5.0	CRIPPLING FRACTURES
M003M5.0	ULCERATIVE GINGIVITIS
M004M5.0	CRIPPLING FRACTURE
F005M5.0	ULCERATIVE GINGIVITIS
M006M5.0	OSTEOSARCOMA + CRIPPLING FRACTURE
F007M5.0	ULCERATIVE GINGIVITIS, MYOCARDIAL INFARCTION + GLAUCOMA

D. THORIUM - 228

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE		DAYS SINCE	DOSE TO SKELETON (RADS)	
	AGE (DAYS)	WEIGHT (KG)		INJECTED	INJECTION	3/31/78 DEATH		
M001T0.0	493	8.24		8	2	54	4895	
M002T0.0	438	7.28		28	9	54	5510	
F003T0.0	797	11.6		6	6	55	2592	
M004T0.0	591	8.10		18	10	55	3072	
M005T0.0	458	10.4		14	10	58	5306	
F006T0.0	489	9.64		10	1	61	171	
F006T0.0A	689	8.61		15	12	60	4549	
M007T0.0	517	10.5		7	2	61	1412	
M008T0.0	533	10.8		24	5	61	4963	
F009T0.0	569	8.28		29	6	61	5061	
F010T0.0	536	10.4		28	7	61	4700	
F011T0.0	530	9.45		4	6	63	4271	
F012T0.0	492	9.09		9	7	63	4137	
M001T0.2	682	11.4	0.00164	27	3	62	4837	20
M002T0.2	682	10.4	0.00166	27	3	62	4822	20
F003T0.2	478	9.86	0.00163	27	3	62	4720	20
M004T0.2	478	10.0	0.00166	27	3	62	4515	20
M005T0.2	625	13.8	0.00162	9	2	60	889	13
M005T0.2A	530	13.4	0.00173	4	6	63	5414	
F006T0.2	489	8.85	0.00176	10	1	61	4767	18
M007T0.2	532	10.5	0.00159	7	2	61	3897	20
M008T0.2	494	13.9	0.00189	24	5	61	4826	23
F009T0.2	569	7.82	0.00171	29	6	61	3897	21
F010T0.2	508	10.5	0.00170	28	7	61	4217	21
F011T0.2	530	9.76	0.00171	4	6	63	4573	21
F012T0.2	492	7.37	0.00190	9	7	63	3350	23
M001T0.5	699	14.3	0.00496	7	9	56	3471	60
M002T0.5	455	10.5	0.00490	28	9	54	1976	55
F003T0.5	659	8.59	0.00485	6	6	55	3032	59
M004T0.5	516	8.58	0.00540	18	10	55	2159	61
M005T0.5	513	8.46	0.00522	14	10	58	4856	67
F006T0.5	489	9.66	0.00510	10	1	61	4518	63
M007T0.5	532	9.11	0.00491	7	2	61	5840	53
M008T0.5	533	9.53	0.00562	24	5	61	4599	69
F009T0.5	569	8.62	0.00529	29	6	61	4149	65
F010T0.5	508	10.2	0.00510	28	7	61	4947	63
F011T0.5	530	7.78	0.00518	4	6	63	3952	63

D. THORIUM - 228

DOG
NUMBER

COMMENTS ON DEAD DOGS

M001T0.0 RETICULUM CELL SARCOMA (SOFT TISSUE)
M002T0.0 NEPHROSIS
F003T0.0 BRAIN HEMORRHAGE
M004T0.0 LYMPHOSARCOMA
M005T0.0 LYMPHOSARCOMA
F006T0.0 TRAUMA
F006T0.0A PERICARDITIS
M007T0.0 BRAIN HEMORRHAGE
M008T0.0 UNDETERMINED
F009T0.0 TRANSITIONAL CELL CARCINOMA
F010T0.0 AORTIC BODY TUMOR
F011T0.0 STATUS EPILEPTICUS
F012T0.0 TRANSITIONAL CELL CARCINOMA

M001T0.2 LUNG CARCINOMA
M002T0.2 MELANOMA (ORAL); GASTRIC CARCINOMA
F003T0.2 STATUS EPILEPTICUS
M004T0.2 TRANSITIONAL CELL CARCINOMA; AORTA THROMBOEMBOLISM
M005T0.2 STRANGULATION ON VOMITUS + GRAND MAL
M005T0.2A
F006T0.2 ISLET CELL TUMOR
M007T0.2 UNDIFFERENTIATED MALIGNANCY (INTESTINE)
M008T0.2 LEIOMYOSARCOMA
F009T0.2 PULMONARY THROMBO EMBOLISM
F010T0.2 BILE DUCT OBSTRUCTION; MAMMARY CARCINOMA
F011T0.2 BILE DUCT OBSTRUCTION; ISLETCELL CARCINOMA
F012T0.2 HEPATIC CELL CARCINOMA

M001T0.5 CEREBRAL INFARCTION HEMORRHAGE
M002T0.5 STRANGULATION ON VOMITUS + GRAND MAL
F003T0.5 PYOMETRITIS + SECONDARY PERITONITIS
M004T0.5 STATUS EPILEPTICUS + PNEUMONIA
M005T0.5 PROSTATITIS
F006T0.5 ISLET CELL TUMOR
M007T0.5 NEPHRITIS; PROSTATE CARCINOMA
M008T0.5 OSTEOSARCOMA
F009T0.5 MAMMARY CARCINOMA
F010T0.5 OSTEOSARCOMA; THYROID CARCINOMA
F011T0.5 PULMONARY THROMBOEMBOLISM

D. THORIUM - 228

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DOSE TO SKELETON (RADS)
F012T0.5	492	9.94	0.00567	9 7 63	1682	60
M001T1.0	493	9.36	0.0146	8 2 54	3172	176
M002T1.0	699	9.27	0.0146	7 9 56	4570	180
F003T1.0	723	8.84	0.0145	7 9 56	4142	177
M004T1.0	699	8.27	0.0146	7 9 56	3217	176
M005T1.0	513	11.9	0.0146	14 10 58	2886	173
F006T1.0	489	8.81	0.0150	10 1 61	3273	181
M007T1.0	532	9.18	0.0147	7 2 61	3538	179
M008T1.0	533	8.69	0.0166	24 5 61	5298	205
F009T1.0	527	10.0	0.0160	29 6 61	2546	187
F010T1.0	508	10.2	0.0150	28 7 61	3420	181
F011T1.0	521	7.55	0.0154	4 6 63	4034	189
F012T1.0	472	9.96	0.0167	9 7 63	1263	157
M001T1.5	699	7.95	0.0289	7 9 56	2894	344
M002T1.5	458	10.0	0.0293	28 9 54	2576	343
F003T1.5	609	10.3	0.0303	6 6 55	1921	332
M004T1.5	591	8.59	0.0299	18 10 55	2309	343
M005T1.5	598	9.65	0.0286	9 2 60	1624	297
F006T1.5	489	8.14	0.0292	10 1 61	2373	336
M007T1.5	517	8.83	0.0292	7 2 61	38	127
M007T1.5A	521	9.08	0.0311	4 6 63	3110	373
M008T1.5	494	11.6	0.0324	24 5 61	2665	381
F009T1.5	527	8.80	0.0306	29 6 61	2983	365
F010T1.5	508	11.6	0.0296	28 7 61	1859	321
F011T1.5	518	11.4	0.0305	4 6 63	2408	375
F012T1.5	465	7.56	0.0329	9 7 63	2120	371
M001T2.0	491	10.2	0.0976	8 2 54	1282	924
M002T2.0	483	9.16	0.0875	28 9 54	1234	815
F003T2.0	474	7.87	0.0908	6 6 55	1541	927
M004T2.0	553	13.0	0.0900	18 10 55	78	93
M004T2.0A	650	10.6	0.0899	7 9 56	1222	833
M005T2.0	598	9.12	0.0848	9 2 60	1085	741
F006T2.0	451	8.65	0.0879	10 1 61	1108	777
M007T2.0	517	8.85	0.0881	7 2 61	1015	744

D. THORIUM - 228

DOG NUMBER	COMMENTS ON DEAD DOGS
F012T0.5	LIVER DEGENERATION, ANESTHETIC REACTION
M001T1.0	OSTEOSARCOMA
M002T1.0	PERIANAL GLAND ADENOMA
F003T1.0	UNDIFFERENTIATED MALIGNANCY (SOFT TISSUE)
M004T1.0	OSTEOSARCOMA THYROID CARCINOMA PERIANAL ADENOCARCINOMA
M005T1.0	STATUS EPILEPTICUS
F006T1.0	STOMACH PERFORATION
M007T1.0	OSTEOSARCOMA
M008T1.0	LUNG CARCINOMA; NEPHRITIS
F009T1.0	LEIOMYOSARCOMA
F010T1.0	OSTEOSARCOMA
F011T1.0	OSTEOSARCOMA
F012T1.0	PNEUMONIA
M001T1.5	OSTEOSARCOMA
M002T1.5	OSTEOSARCOMA
F003T1.5	COMA OF UNKNOWN ETIOLOGY (NO BONE TUMOR)
M004T1.5	OSTEOSARCOMA
M005T1.5	OSTEOSARCOMA
F006T1.5	OSTEOSARCOMA
M007T1.5	LEPTOSPIROSIS
M007T1.5A	OSTEOSARCOMA; (PNEUMONIA)
M008T1.5	OSTEOSARCOMA
F009T1.5	OSTEOSARCOMA
F010T1.5	OSTEOSARCOMA
F011T1.5	OSTEOSARCOMA
F012T1.5	OSTEOSARCOMA
M001T2.0	OSTEOSARCOMA
M002T2.0	OSTEOSARCOMA
F003T2.0	OSTEOSARCOMA
M004T2.0	TRAUMA
M004T2.0A	OSTEOSARCOMA
M005T2.0	OSTEOSARCOMA
F006T2.0	OSTEOSARCOMA
M007T2.0	OSTEOSARCOMA

D. THORIUM - 228

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE INJECTED			DAYS SINCE INJECTION		DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR	3/31/78	DEATH	
M008T2.0	533	10.7	0.0981	24	5	61		1078	855
F009T2.0	527	8.09	0.0979	29	6	61		1209	903
F010T2.0	508	10.7	0.0919	28	7	61		1022	779
F011T2.0	518	10.8	0.0904	4	6	63		1038	772
F012T2.0	464	8.92	0.100	9	7	63		1449	997
M001T3.0	314	9.15	0.301	8	2	54		988	2505
M002T3.0	458	11.9	0.301	28	9	54		859	2315
F003T3.0	471	12.0	0.272	6	6	55		547	1552
M004T3.0	606	9.69	0.285	18	10	55		801	2100
M005T3.0	571	10.7	0.269	9	2	60		890	2112
F006T3.0	451	8.83	0.282	10	1	61		1156	2545
M007T3.0	427	9.90	0.266	7	2	61		861	2048
M008T3.0	494	10.1	0.313	24	5	61		685	2088
F009T3.0	511	11.5	0.298	29	6	61		1062	2577
F010T3.0	508	9.26	0.280	28	7	61		971	2309
F011T3.0	518	10.3	0.290	4	6	63		826	2121
F012T3.0	459	11.5	0.320	9	7	63		804	2364
M001T4.0	480	8.32	0.882	8	2	54		645	5649
M002T4.0	458	8.32	0.916	28	9	54		833	6913
F003T4.0	461	7.25	0.800	6	6	55		763	5720
M004T4.0	606	8.81	0.835	18	10	55		793	6116
M001T5.0	480	9.48	2.76	8	2	54		212	7276
M002T5.0	483	8.22	2.63	28	9	54		97	3380

D. THORIUM - 228

DOG
NUMBER

COMMENTS ON DEAD DOGS

M008T2.0 OSTEOSARCOMA
F009T2.0 OSTEOSARCOMA
F010T2.0 OSTEOSARCOMA
F011T2.0 OSTEOSARCOMA
F012T2.0 OSTEOSARCOMA

M001T3.0 OSTEOSARCOMA + SEVERE ANEMIA
M002T3.0 OSTEOSARCOMA + TRAUMA
F003T3.0 OSTEOSARCOMA
M004T3.0 OSTEOSARCOMA
M005T3.0 OSTEOSARCOMA
F006T3.0 OSTEOSARCOMA
M007T3.0 OSTEOSARCOMA
M008T3.0 OSTEOSARCOMA
F009T3.0 OSTEOSARCOMA
F010T3.0 OSTEOSARCOMA
F011T3.0 OSTEOSARCOMA
F012T3.0 HEMANGIOSARCOMA (HUMERUS)

M001T4.0 OSTEOSARCOMA + CRIPPLING FRACTURE
M002T4.0 OSTEOSARCOMA, CRIPPLING FRACTURE + NEPHRITIS
F003T4.0 ULCERATIVE GINGIVITIS + NEPHRITIS
M004T4.0 ULCERATIVE GINGIVITIS

M001T5.0 NEPHRITIS
M002T5.0 PANCYTOPENIA

E. STRONTIUM - 90

DOG	NUMBER	INJECTION	AGE WEIGHT (KG)	INJECTED (UCI/KG)	DATE	DAYS SINCE INJECTION	DOSE TO SKELETON (RADS)
F00150.0	502	8.48	11.1	14 2 56	18 1 55	5484	5484
M00250.0	600	9.03	11.1	14 2 56	11 9 57	3838	3838
M00350.0	493	8.19	10.6	15 10 57	15 10 57	5755	5755
F00450.0	520	10.6	13.9	19 11 57	19 11 57	4158	4158
M00550.0	542	9.68	12.4	27 5 58	27 5 58	4726	4726
M00650.0	466	9.46	12.4	7 1 59	7 1 59	3303	3303
F00750.0A	483	9.29	12.4	19 5 59	19 5 59	4482	4482
F00850.0	549	11.2	13.9	4 6 63	4 6 63	3425	3425
M01050.0	522	10.3	11.5	29 9 59	29 9 59	4977	4977
F01150.0	541	10.3	11.5	3 11 59	3 11 59	4831	4831
M01250.0	605	13.7	10.3	6 1 60	6 1 60	5374	5374
F00151.0	1525	6.84	0.573	18 1 55	18 1 55	308	308
F00151.0A	521	9.38	0.588	14 2 56	14 2 56	5219	5219
M00251.0	567	8.81	0.606	14 2 56	14 2 56	5077	5077
M00351.0	493	10.9	0.572	11 9 57	11 9 57	5363	5363
F00451.0	525	8.96	0.560	15 10 57	15 10 57	5902	5902
M00551.0	555	10.2	0.532	19 11 57	19 11 57	2705	2705
M00651.0	466	9.56	0.581	27 5 58	27 5 58	5739	5739
F00751.0	524	9.94	0.517	11 11 58	11 11 58	5837	5837
F00851.0	483	10.8	0.697	19 5 59	19 5 59	2783	2783
F00951.0	549	11.6	0.534	11 8 59	11 8 59	3601	3601
M01051.0	522	11.5	0.558	29 9 59	29 9 59	5321	5321
F01151.0	543	10.3	0.550	3 11 59	3 11 59	4944	4944
M01251.0	607	13.7	0.559	6 1 60	6 1 60	4184	4184
F00151.7	526	7.41	1.78	14 2 56	14 2 56	5624	5624
M00251.7	567	11.6	1.84	14 2 56	14 2 56	4297	4297
M00351.7	493	9.19	1.69	11 9 57	11 9 57	4846	4846
F00451.7	522	9.60	1.68	15 10 57	15 10 57	4628	4628
M00551.7	560	9.85	1.60	19 11 57	19 11 57	1715	1715
M00551.7A	493	11.4	1.78	6 3 63	6 3 63	5379	5379
M00651.7	466	10.6	1.72	27 5 58	27 5 58	5581	5581
F00751.7	488	10.2	1.60	11 11 58	11 11 58	3990	3990
F00851.7	472	8.47	2.03	19 5 59	19 5 59	1973	1973
F00951.7	549	10.0	1.62	11 8 59	11 8 59	4803	4803
M01051.7	519	13.6	1.66	29 9 59	29 9 59	2947	2947
F00151.7	627	7.41	1.78	14 2 56	14 2 56	5624	5624
M00251.7	540	11.6	1.84	14 2 56	14 2 56	4297	4297
M00351.7	451	9.19	1.69	11 9 57	11 9 57	4846	4846
F00451.7	372	9.60	1.68	15 10 57	15 10 57	4628	4628
M00551.7	220	9.85	1.60	19 11 57	19 11 57	1715	1715
M00551.7A	765	11.4	1.78	6 3 63	6 3 63	5379	5379
M00651.7	725	10.6	1.72	27 5 58	27 5 58	5581	5581
F00751.7	331	10.2	1.60	11 11 58	11 11 58	3990	3990
F00851.7	285	8.47	2.03	19 5 59	19 5 59	1973	1973
F00951.7	552	10.0	1.62	11 8 59	11 8 59	4803	4803
M01051.7	408	13.6	1.66	29 9 59	29 9 59	2947	2947

E. STRONTIUM - 90

DOG NUMBER	COMMENTS ON DEAD DOGS
F001S0.0	CARCINOMA PANCREAS
M002S0.0	LUNG CARCINOMA
M003S0.0	OBTURATING AORTIC EMBOLISM, NEPHRITIS
F004S0.0	NEPHRITIS; SENILITY
M005S0.0	TRANSITIONAL CELL CARCINOMA
M006S0.0	MELANOMA (ORAL)
F007S0.0A	DIABETES MELLITUS
F008S0.0	DIABETES MELLITUS
F009S0.0	TRAUMA
F009S0.0A	MAMMARY CARCINOMA
M010S0.0	FIBROSARCOMA (NON-SKELETAL)
F011S0.0	MAMMARY CARCINOMA
M012S0.0	INTESTINAL CARCINOMA; SENILITY
F001S1.0	SACRIFICED --IMPROPER INJECTION AGE--
F001S1.0A	PULMONARY THROMBO-EMBOLISM
M002S1.0	AORTIC BODY TUMOR
M003S1.0	SQUAMOUS CELL CARCINOMA (OROPHARYNX)
F004S1.0	NEPHRITIS; MAMMARY CARCINOMA
M005S1.0	STATUS EPILEPTICUS
M006S1.0	LYMPHOSARCOMA
F007S1.0	LYMPHOSARCOMA; MAMMARY CARCINOMA
F008S1.0	PANCREATIC ISLET CELL CARCINOMA
F009S1.0	FOREIGN BODY PNEUMONIA; ENTERITIS
M010S1.0	SEBACEOUS GLAND ADENOCARCINOMA
F011S1.0	TRANSITIONAL CELL CARCINOMA
M012S1.0	BILIARY OBSTRUCTION
F001S1.7	HEMANGIOENDOTHELIAL SARCOMA (LIVER)
M002S1.7	HEMANGIOSARCOMA (SOFT TISSUE ORIGIN)
M003S1.7	OBTURATING THROMBOEMBOLISM, AORTA
F004S1.7	PANCREATIC CARCINOMA
M005S1.7	COMA OF UNKNOWN ETIOLOGY (NO BONE TUMOR)
M005S1.7A	SENILITY
M006S1.7	TRANSITIONAL CELL CARCINOMA; HYDRONEPHROSIS
F007S1.7	ARTHRITIS; MAMMARY CARCINOMA
F008S1.7	STATUS EPILEPTICUS; CHRONIC PANCREATITIS
F009S1.7	LYMPHOSARCOMA; NEPHRITIS
M010S1.7	OBTURATING PULMONARY EMBOLISM, NEPHRITIS

E. STRONTIUM - 90

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DOSE TO SKELETON (RADS)
F011S1.7	543	11.0	1.68	3 11 59	3180	319
M012S1.7	607	11.9	1.68	6 1 60	4717	473
F001S2.0	502	5.59	3.70	18 1 55	3269	636
M002S2.0	567	8.97	3.42	14 2 56	3768	841
M003S2.0	494	7.82	3.39	11 9 57	4295	893
F004S2.0	522	9.68	3.41	15 10 57	4775	981
M005S2.0	560	8.72	3.24	19 11 57	3253	708
M006S2.0	466	9.19	3.50	27 5 58	5193	1131
F007S2.0	488	11.2	3.19	11 11 58	3421	609
F008S2.0	465	9.49	4.14	19 5 59	3955	913
F009S2.0	473	14.1	3.28	11 8 59	2467	755
M010S2.0	508	10.7	3.34	29 9 59	343	791
F011S2.0	543	10.4	3.41	3 11 59	4880	879
M012S2.0	607	11.6	3.49	6 1 60	4584	943
F001S3.0	468	7.36	11.6	18 1 55	5149	4385
M002S3.0	565	9.62	11.6	14 2 56	4263	3473
M003S3.0	494	11.4	10.8	11 9 57	4947	3197
F004S3.0	527	9.17	10.6	15 10 57	3101	1987
M005S3.0	557	8.90	10.1	19 11 57	4640	2849
M006S3.0	466	9.44	10.9	27 5 58	5667	4090
F007S3.0	486	9.80	10.1	11 11 58	4018	2421
F008S3.0	465	12.5	12.9	19 5 59	4832	3749
F009S3.0	468	10.0	10.1	11 8 59	4599	3547
M010S3.0	519	12.5	10.3	29 9 59	2898	2799
F011S3.0	541	9.00	10.8	3 11 59	4831	1273
M012S3.0	605	8.43	10.2	6 1 60	4831	2176
F001S4.0	468	8.74	33.3	18 1 55	3682	8817
M002S4.0	567	11.2	32.6	14 2 56	2093	7584
M003S4.0	593	9.83	32.1	11 9 57	2781	5519
F004S4.0	528	8.24	32.1	15 10 57	4844	10373
M005S4.0	562	9.65	30.6	19 11 57	4427	8369
M006S4.0	504	16.0	32.7	3 9 58	3530	9199
F007S4.0	478	10.9	30.9	11 11 58	4664	10560
F008S4.0	465	10.9	40.6	19 5 59	2206	10355

E. STRONTIUM - 90

DOG NUMBER	COMMENTS ON DEAD DOGS
F011S1.7 M012S1.7	AORTIC THROMBUS; METASTATIC CALCIFICATION OF LUNGS ISLET CELL TUMOR
F001S2.0 M002S2.0 M003S2.0 F004S2.0 M005S2.0 M006S2.0 F007S2.0 F008S2.0 F009S2.0 M010S2.0 F011S2.0 M012S2.0	BACTERIAL PNEUMONIA UNDETERMINED SOFT TISSUE SARCOMA; LUNG CARCINOMA STATUS EPILEPTICUS; THYROID CARCINOMA MAMMARY CARCINOMA ULCERATIVE STOMATITIS UNDIFFERENTIATED SARCOMA (LIVER); NEPHRITIS PANCREATIC ISLET CELL ADENOMA PNEUMONIA UNDETERMINED (NO BONE TUMOR) BACTERIAL VALVULAR ENDOCARDITIS MAMMARY SARCOMA HEPATIC CELL CARCINOMA
F001S3.0 M002S3.0 M003S3.0 F004S3.0 M005S3.0 M006S3.0 F007S3.0 F008S3.0 F009S3.0 M010S3.0 F011S3.0 M012S3.0	UNDETERMINED (NO BONE TUMOR) NEPHRITIS SEMINOMA; HYDROCEPHALUS MAMMARY CARCINOMA SERTOLI CELL TUMOR NEPHRITIS; TESTICULAR MALIGNANCY MAMMARY CARCINOMA; THYROID CARCINOMA UNDETERMINED CHROMAPHOBE ADENOMA FIBROSARCOMA (GINGIVA) PYELONEPHRITIS TRANSITIONAL CELL CARCINOMA
F001S4.0 M002S4.0 M003S4.0 F004S4.0 M005S4.0 M006S4.0 F007S4.0 F008S4.0	NOT DETERMINED (NO OSTEOSARCOMA) SQUAMOUS CELL CARCINOMA -GINGIVA-- OBSTRUCTING PULMONARY EMBOLISM OSTEOSARCOMA; SQUAMOUS CELL CARC. (ORAL); THYROID CARC. HEMANGIOSARCOMA (SPLEEN) SEMINOMA OSTEOSARCOMA UNDETERMINED (NO BONE TUMOR)

E. STRONTIUM - 90

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		INJECTED	D	MO	YR	
F009S4.0	468	9.56	30.6	11	8	59	4942	10132
M010S4.0	517	8.20	31.3	29	9	59	4242	8493
F011S4.0	542	8.86	32.7	3	11	59	2114	4432
M012S4.0	605	10.9	32.3	6	1	60	4226	7053
F001S4.5	530	9.00	64.2	16	3	66	3030	9890
M002S4.5	530	12.20	63.6	16	3	66	2707	9660
M003S4.5	530	11.90	63.8	16	3	66	1493	7932
F004S4.5	530	9.80	64.5	16	3	66	2197	12133
M005S4.5	496	13.30	61.3	16	3	66	993	7232
M006S4.5	496	12.00	63.8	16	3	66	2843	9990
F007S4.5	511	9.90	64.5	16	3	66	2813	13480
F008S4.5	511	9.90	64.5	16	3	66	2325	12725
F009S4.5	511	10.30	64.0	16	3	66	1028	6935
M010S4.5	496	14.00	60.9	16	3	66	2064	14240
F011S4.5	496	11.90	63.8	16	3	66	1758	8579
M012S4.5	485	11.40	63.7	16	3	66	2253	13116
F001S5.0	434	9.38	103.	18	1	55	960	11179
M002S5.0	551	12.2	102.	14	2	56	255	4284
M002S5.0A	545	11.4	96.6	7	1	59	1740	16393
M003S5.0	507	10.3	102.	15	10	57	2256	22079
F004S5.0	528	11.4	105.	15	10	57	1448	12703
M005S5.0	621	8.53	95.2	19	11	57	1285	13657
M006S5.0	504	9.33	98.8	3	9	58	35	869
M006S5.0A	462	11.2	94.2	7	1	59	1021	15384
F007S5.0	478	10.2	92.7	11	11	58	1129	14532
F008S5.0	535	11.2	90.5	7	1	59	1469	14843
F009S5.0	459	8.82	93.5	11	8	59	1982	18143
M010S5.0	517	8.55	95.9	29	9	59	990	10209
F011S5.0	542	8.97	102.	3	11	59	1667	13355
M012S5.0	606	12.5	99.2	6	1	60	1165	10837

E. STRONTIUM - 90

DOG NUMBER	COMMENTS ON DEAD DOGS
F009S4.0	UNDETERMINED
M010S4.0	MENINGIOMA; PERIANAL GLAND CARCINOMA
F011S4.0	BLOOD DYSCRASIA, PYOMETRA
M012S4.0	ADENOCARCINOMA NASAL CAVITY
F001S4.5	PURPURA HEMORRHAGICA
M002S4.5	OSTEOSARCOMA
M003S4.5	SEVERE ANEMIA, INFARCTION, MYELOID METAPLASIA
F004S4.5	HEMANGIOSARCOMA (SPLEEN)
M005S4.5	OSTEOSARCOMA
M006S4.5	OSTEOSARCOMA
F007S4.5	OSTEOSARCOMA; SQUAMOUS CELL CARCINOMA (FRONTAL SINUS)
F008S4.5	HEMANGIOSARCOMA (BONE)
F009S4.5	OSTEOSARCOMA
M010S4.5	SQUAMOUS CELL CARCINOMA (FRONTAL SINUS)
F011S4.5	OSTEOSARCOMA
M012S4.5	OSTEOSARCOMA; HEMANGIOSARCOMA (BONE)
F001S5.0	OSTEOSARCOMA
M002S5.0	STRANGULATED INGUINAL HERNIA
M002S5.0A	OSTEOSARCOMA
M003S5.0	OSTEOSARCOMA
F004S5.0	OSTEOSARCOMA
M005S5.0	SEVERE ANEMIA, AUTOAGGLUTINATION, INFARCTION, SPLENOMEGALY
M006S5.0	INTESTINAL HEMORRHAGE
M006S5.0A	OSTEOSARCOMA, INFARCTION + THROMBOCYTOPENIA
F007S5.0	STATUS EPILEPTICUS
F008S5.0	OSTEOSARCOMA
F009S5.0	SQUAMOUS CELL CARCINOMA ARISING FROM FRONTAL SINUS
M010S5.0	SEVERE ANEMIA + THROMBOCYTOPENIA
F011S5.0	HEMANGIOSARCOMA (LEFT MANDIBLE)
M012S5.0	HEMANGIOSARCOMA (RIB)

F. RADIUM - 224 (QUICKRADIUM)

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DOSE TO SKELETON (RADS)
M001Q0.OH	458	11.6		19 5 77	316	
F002Q0.OH	647	10.7		19 5 77	316	
M003Q0.OH	646	10.4		30 11 77	121	
F004Q0.OH	586	10.3		19 5 77	316	
M005Q0.OH	646	11.3		30 11 77	121	
F006Q0.OH	586	9.58		19 5 77	316	
F046Q0.0	619	11.2		10 8 77	233	
M001Q2.OH	647	11.9		19 5 77	316	
F002Q2.OH	647	10.9		19 5 77	316	
M003Q2.OH	635	9.62		19 5 77	316	
F004Q2.OH	635	8.18		19 5 77	316	
M005Q2.OH	643	10.1		19 5 77	316	
F006Q2.OH	632	9.82		19 5 77	316	
M007Q2.OH	683	10.9		19 5 77	316	
F008Q2.OH	647	11.1		19 5 77	316	
M009Q2.OH	610	11.4		19 5 77	316	
F010Q2.OH	610	8.52		19 5 77	316	
M011Q2.OH	610	10.3		19 5 77	316	
F012Q2.OH	610	8.62		19 5 77	316	
M047Q2.0	636	11.1	0.343	30 11 77	121	
M049Q2.0	646	12.2	0.348	30 11 77	121	
M051Q2.0	636	10.7	0.348	30 11 77	121	
F052Q2.0	619	11.2	.344	10 8 77	233	
M001Q3.OH	647	10.3		19 5 77	316	
F002Q3.OH	647	10.4		19 5 77	316	
M003Q3.OH	642	10.3		19 5 77	316	
F004Q3.OH	643	8.16		19 5 77	316	
M005Q3.OH	632	11.8		19 5 77	316	
F006Q3.OH	647	10.4		19 5 77	316	
M007Q3.OH	642	11.8		19 5 77	316	
F008Q3.OH	632	9.10		19 5 77	316	
M009Q3.OH	666	13.4		19 5 77	316	
F010Q3.OH	666	11.3		19 5 77	316	
M011Q3.OH	610	10.5		19 5 77	316	
F012Q3.OH	610	9.75		19 5 77	316	
M049Q3.0	630	9.58	1.12	30 11 77	121	
M051Q3.0	638	9.85	1.08	30 11 77	121	

F. RADIUM - 224 (QUICKRADIUM)

DOG
NUMBER

COMMENTS ON DEAD DOGS

M001Q0.0H
F002Q0.0H
M003Q0.0H
F004Q0.0H
M005Q0.0H
F006Q0.0H
F046Q0.0

M001Q2.0H
F002Q2.0H
M003Q2.0H
F004Q2.0H
M005Q2.0H
F006Q2.0H
M007Q2.0H
M008Q2.0H
M009Q2.0H
F010Q2.0H
M011Q2.0H
F012Q2.0H
M047Q2.0
M049Q2.0
M051Q2.0
F052Q2.0

M001Q3.0H
F002Q3.0H
M003Q3.0H
F004Q3.0H
M005Q3.0H
F006Q3.0H
M007Q3.0H
F008Q3.0H
M009Q3.0H
F010Q3.0H
M011Q3.0H
F012Q3.0H
M049Q3.0
M051Q3.0

F. RADIUM - 224 (QUICKRADIUM)

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
F052Q3.0	619	9.97	1.10	10 8 77	233	
M001Q4.0H	653	10.2		19 5 77	316	
F002Q4.0H	653	9.44		19 5 77	316	
M003Q4.0H	642	13.5		19 5 77	316	
F004Q4.0H	643	9.10		19 5 77	316	
M005Q4.0H	643	10.5		19 5 77	316	
F006Q4.0H	647	10.8		19 5 77	316	
M041Q4.0	607	10.9	3.04	30 11 77	121	
M045Q4.0	630	10.2	3.28	30 11 77	121	
M001Q5.0H	653	10.6		19 5 77	316	
F002Q5.0H	653	11.4		19 5 77	316	
M003Q5.0H	643	10.6		19 5 77	316	
F004Q5.0H	647	8.35		19 5 77	316	
M005Q5.0H	635	9.88		19 5 77	316	
F006Q5.0H	647	9.12		19 5 77	316	
M045Q5.0	604	9.75	12.	7 12 77	114	

* To date, 46 of the multiple injections have been completed. Cumulative doses ($\mu\text{Ci/kg}$) will appear in the next annual report.

F. RADIUM - 224 (QUICKRADIUM)

DOG
NUMBER

COMMENTS ON DEAD DOGS

F052Q3.0

M001Q4.0H
F002Q4.0H
M003Q4.0H
F004Q4.0H
M005Q4.0H
F006Q4.0H
M041Q4.0
M045Q4.0

M001Q5.0H
F002Q5.0H
M003Q5.0H
F004Q5.0H
M005Q5.0H
F006Q5.0H
M045Q5.0

G. AMERICIUM - 241

DOG	INJECTION	AGE	WEIGHT	INJECTED	INJECTED	DATE	DAYS SINCE	DOSE TO
NUMBER	(DAYS)	(KG)	(UCI/KG)	D MO	YR	3/31/78	DEATH	SKELETON
								(RADS)
F013W0.2	533	10.6	0.00179	13	10	66	3815	7
M014W0.2	533	14.9	0.00178	13	10	66	3185	7
F024W0.2	477	11.3	0.00181	21	3	68	3662	4
F031W0.2	472	10.9	0.00180	8	5	68	1478	
M041W0.2	467	11.9	0.00180	2	7	68		
M048W0.2	484	11.0	0.00174	30	7	68	3531	
M049W0.2	498	10.7	0.00175	25	11	69	3048	
F058W0.2	496	10.4	0.00168	26	1	70	2986	
M062W0.2	486	13.3	0.00175	24	2	70	2957	
F069W0.2	542	10.8	0.00180	22	4	70	2900	
M078W0.2	501	13.5	0.00178	16	7	70	2815	
M079W0.2	501	10.0	0.00179	16	7	70	2815	
F088W0.2	531	8.36	0.00177	25	8	70	2775	
M095W0.2	526	13.1	0.00173	25	8	70	2775	
F011W0.5	533	8.17	0.00532	13	10	66	4187	25
M012W0.5	533	11.9	0.00539	13	10	66	3649	18
M023W0.5	487	12.2	0.00530	21	3	68	3662	
M029W0.5	472	10.4	0.00548	8	5	68	2239	
F030W0.5	472	10.6	0.00538	8	5	68	3614	
F040W0.5	467	9.40	0.00528	2	7	68	3559	
M050W0.5	552	11.8	0.00526	25	11	69	3048	
M059W0.5	496	11.5	0.00503	26	1	70	2986	
M063W0.5	486	11.4	0.00524	24	2	70	2957	
M070W0.5	497	12.8	0.00531	22	4	70	2900	
F080W0.5	501	11.9	0.00545	16	7	70	2815	
F081W0.5	501	12.1	0.00548	16	7	70	2815	
F089W0.5	531	9.66	0.00527	25	8	70	2775	
M096W0.5	490	12.0	0.00533	25	8	70	2775	
F009W1.0	517	8.60	0.016	15	9	66	4206	59
F010W1.0	517	9.90	0.0162	15	9	66	2750	69
M020W1.0	513	10.8	0.0161	21	3	68	3060	6
F021W1.0	513	9.36	0.0166	21	3	68	232	
F021W1.0A	552	11.4	0.0159	25	11	69	3048	
M022W1.0	487	11.6	0.0164	21	3	68	3662	
M028W1.0	472	12.1	0.0158	8	5	68	3606	
F051W1.0	552	8.25	0.0163	25	11	69	3048	
M060W1.0	496	10.0	0.0157	26	1	70	2986	

G. AMERICIUM - 241

DOG
NUMBER

COMMENTS ON DEAD DOGS

F013W0.2	
M014W0.2	HEMANGIOSARCOMA (SPLEEN)
F024W0.2	
F031W0.2	LUNG CARCINOMA
M041W0.2	
M048W0.2	
M049W0.2	
F058W0.2	
M062W0.2	
F069W0.2	
M078W0.2	
M079W0.2	
F088W0.2	
M095W0.2	

F011W0.5	
M012W0.5	PANCREATIC DYSTROPHY
M023W0.5	
M029W0.5	MALIGNANT MELANOMA (ORAL)
F030W0.5	
F040W0.5	
M050W0.5	
M059W0.5	
M063W0.5	
M070W0.5	
F080W0.5	
F081W0.5	
F089W0.5	
M096W0.5	

F009W1.0	
F010W1.0	LUNG CARCINOMA
M020W1.0	MYXOSARCOMA (LIVER)
F021W1.0	ACCIDENTAL STRANGULATION
F021W1.0A	
M022W1.0	
M028W1.0	
F051W1.0	
M060W1.0	

G. AMERICIUM - 241

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DOSE TO SKELETON (RADS)
M064W1.0	486	10.4	0.0158	24 2 70	2957	
F071W1.0	485	12.1	0.0157	22 4 70	2900	
M082W1.0	501	12.4	0.0163	16 7 70	2815	
F090W1.0	526	10.9	0.0160	25 8 70	2775	
M097W1.0	490	10.4	0.0160	25 8 70	2530	63
F122W1.0	504	9.38	0.0150	6 11 75	876	
M123W1.0	516	11.8	0.0156	9 12 75	843	
F124W1.0	516	8.36	0.0157	9 12 75	843	
F127W1.0	494	8.89	0.0152	6 11 75	876	
M128W1.0	493	13.2	0.0153	6 11 75	876	
F130W1.0	491	10.3	0.0153	6 11 75	876	
M132W1.0	482	9.86	0.0153	6 11 75	876	
M134W1.0	490	9.03	0.0150	6 11 75	876	
F137W1.0	515	7.71	0.0154	9 12 75	843	
F138W1.0	514	8.63	0.0152	9 12 75	843	
M139W1.0	513	9.11	0.0157	9 12 75	843	
F141W1.0	504	8.89	0.0154	9 12 75	843	
F042W1.7	495	9.26	0.0484	30 7 68	2960	215
F043W1.7	492	10.4	0.0481	30 7 68	3531	
F044W1.7	492	7.46	0.0473	30 7 68	3306	249
M045W1.7	492	11.9	0.0486	30 7 68	3531	
M046W1.7	484	8.42	0.0479	30 7 68	2848	170
M047W1.7	484	11.1	0.0486	30 7 68	3486	233
F052W1.7	552	9.57	0.0493	25 11 69	3048	
M061W1.7	496	10.7	0.0458	26 1 70	2986	
M065W1.7	486	11.2	0.0471	24 2 70	2957	
F072W1.7	500	11.1	0.0479	22 4 70	2900	
M083W1.7	501	12.6	0.0493	16 7 70	2815	
F091W1.7	490	13.3	0.0480	25 8 70	2193	127
M098W1.7	490	13.3	0.0480	25 8 70	2775	
F115W1.7	502	8.73	0.0468	17 10 74	1261	
F116W1.7	502	8.56	0.0470	17 10 74	1261	
F121W1.7	504	9.36	0.0458	6 11 75	876	
M125W1.7	515	10.0	0.0471	9 12 75	843	
F126W1.7	494	9.63	0.0456	6 11 75	876	
M129W1.7	493	8.26	0.0453	6 11 75	876	
F131W1.7	491	9.16	0.0457	6 11 75	876	
M133W1.7	491	10.8	0.0459	6 11 75	876	
M135W1.7	490	10.0	0.0458	6 11 75	876	
F136W1.7	522	8.91	0.0461	9 12 75	843	

G. AMERICIUM - 241

DOG
NUMBER

COMMENTS ON DEAD DOGS

M064W1.0
F071W1.0
M082W1.0
F090W1.0
M097W1.0
F122W1.0
M123W1.0
F124W1.0
F127W1.0
M128W1.0
F130W1.0
M132W1.0
M134W1.0
F137W1.0
F138W1.0
M139W1.0
F141W1.0

THROMBOSIS RIGHT HEART CHAMBERS

F042W1.7
F043W1.7
F044W1.7
M045W1.7
M046W1.7
M047W1.7
F052W1.7
M061W1.7
M065W1.7
F072W1.7

LYMPHOSARCOMA

UNDIFFERENTIATED MALIGNANCY (SOFT TISSUE)

STATUS EPILEPTICUS
HEPATIC HEMORRHAGE

M083W1.7
F091W1.7
M098W1.7
F115W1.7
F116W1.7
F121W1.7
M125W1.7
F126W1.7
M129W1.7
F131W1.7
M133W1.7
M135W1.7
F136W1.7

BLOOD DYSCRASIA

G. AMERICIUM - 241

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
M140W1.7	513	10.5	0.0469	9 12 75	843	
F007W2.0	561	12.60	0.0952	15 9 66	1847	226
F008W2.0	561	11.70	0.0957	15 9 66	2841	362
M019W2.0	513	13.4	0.0970	21 3 68	2785	368
M027W2.0	473	12.7	0.0961	8 5 68	2887	347
M038W2.0	477	9.88	0.0945	2 7 68	3047	427
F039W2.0	468	9.21	0.0948	2 7 68	3066	473
M053W2.0	498	9.24	0.0960	25 11 69	3048	
F066W2.0	486	9.12	0.0935	24 2 70	2957	
M073W2.0	552	14.3	0.0965	17 6 70	2476	324
F084W2.0	493	10.6	0.0984	16 7 70	2773	398
M085W2.0	493	10.8	0.0987	16 7 70	2815	
F092W2.0	490	10.6	0.0962	25 8 70	2318	345
M005W3.0	561	15.00	0.305	15 9 66	1917	792
F006W3.0	561	11.9	0.310	15 9 66	1510	664
F018W3.0	523	8.60	0.307	21 3 68	1756	823
M026W3.0	473	12.4	0.310	8 5 68	2127	1022
M036W3.0	477	11.0	0.305	2 7 68	1696	749
F037W3.0	468	8.44	0.294	2 7 68	1764	716
M054W3.0	498	10.5	0.306	25 11 69	1876	969
M067W3.0	485	11.8	0.295	24 2 70	1883	904
F074W3.0	542	10.0	0.302	22 4 70	1700	727
F075W3.0	555	9.42	0.308	17 6 70	1533	765
M086W3.0	493	11.3	0.312	16 7 70	1558	761
F093W3.0	490	11.2	0.301	25 8 70	1884	903
M100W3.0	542	11.0	0.304	2 12 70	1198	575
M003W4.0	517	12.60	0.897	28 6 66	1779	2787
F004W4.0	517	9.40	0.911	28 6 66	1533	2393
M017W4.0	523	9.87	0.924	21 3 68	1132	1711
F025W4.0	473	10.5	0.927	8 5 68	1527	2465
M034W4.0	477	10.7	0.893	2 7 68	1566	2011
F035W4.0	477	8.87	0.902	2 7 68	1323	2065
F055W4.0	498	8.37	0.914	25 11 69	1388	2390
M068W4.0	485	11.8	0.890	24 2 70	1415	1980

G. AMERICIUM - 241

DOG
NUMBER

COMMENTS ON DEAD DOGS

M140W1.7

F007W2.0	OSTEOSARCOMA
F008W2.0	OSTEOSARCOMA
M019W2.0	FIBROSARCOMA (LIVER)
M027W2.0	MAST CELL SARCOMA
M038W2.0	OSTEOSARCOMA
F039W2.0	OSTEOSARCOMA; ADENOCARCINOMA (NASAL CAVITY)
M053W2.0	
F066W2.0	
M073W2.0	COLLAPSED VERTEBRA
F084W2.0	OSTEOSARCOMA
M085W2.0	
F092W2.0	OSTEOSARCOMA

M005W3.0	OSTEOSARCOMA
F006W3.0	OSTEOSARCOMA
F018W3.0	OSTEOSARCOMA
M026W3.0	OSTEOSARCOMA; FIBROSARCOMA (BONE); HEPATOMA
M036W3.0	OSTEOSARCOMA
F037W3.0	OSTEOSARCOMA
M054W3.0	OSTEOSARCOMA
M067W3.0	KIDNEY DEGENERATION; THYROID DEGENERATION
F074W3.0	OSTEOSARCOMA
F075W3.0	OSTEOSARCOMA
M086W3.0	OSTEOSARCOMA
F093W3.0	OSTEOSARCOMA
M100W3.0	OSTEOSARCOMA

M003W4.0	OSTEOSARCOMA; NEPHRITIS
F004W4.0	KIDNEY, THYROID AND LIVER DEGENERATION
M017W4.0	OSTEOSARCOMA; THROMBOSIS
F025W4.0	MESOTHELIOMA; KIDNEY DEGENERATION
M034W4.0	OSTEOSARCOMA
F035W4.0	PANCREATIC ADENOCARCINOMA
F055W4.0	OSTEOSARCOMA
M068W4.0	OSTEOSARCOMA

G. AMERICIUM - 241

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE INJECTED			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR		
F076W4.0	485	9.37	0.899	22	4	70	1569	2359
M077W4.0	500	10.5	0.906	22	4	70	633	945
M087W4.0	501	13.1	0.916	16	7	70	1300	1881
F094W4.0	490	11.3	0.912	25	8	70	1381	2159
M001W5.0	517	10.4	2.78	28	6	66	401	1970
M002W5.0	517	12.7	2.83	28	6	66	448	2169

* Measurements made to date indicate the liver dose to be approximately 4 times that to the skeleton.

The original "T" (test) designation for the above animals has been changed to "M or F" (male or female toxicity) designations. For example, the male dog originally injected as T001W5.0 is now redesignated as M001W5.0.

G. AMERICIUM - 241

DOG NUMBER	COMMENTS ON DEAD DOGS
F076W4.0	OSTEOSARCOMA
M077W4.0	LIVER DEGENERATION
M087W4.0	OSTEOSARCOMA
F094W4.0	OSTEOSARCOMA
M001W5.0	LIVER DEGENERATION; KIDNEY DEGENERATION
M002W5.0	LIVER DEGENERATION; KIDNEY DEGENERATION

H. CALIFORNIUM - 252

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE INJECTED			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR		
M001F0.0	562	12.0		1	2	72	2250	
F002F0.0	545	10.6		3	1	73	1913	
F003F0.0	545	9.43		3	1	73	1913	
F004F0.0	492	10.6		27	2	73	1858	
M005F0.0	562	10.4		1	2	72	2250	
M006F0.0	509	10.9		28	11	72	1949	
M001F0.1	498	13.0	0.00060	26	7	72	2074	
F002F0.1	524	9.15	0.00064	2	11	72	1975	
F003F0.1	545	10.1	0.00075	3	1	73	1913	
F004F0.1	492	9.44	0.00060	27	2	73	1858	
M005F0.1	498	10.4	0.00060	26	7	72	2074	
M006F0.1	524	10.3	0.00062	2	11	72	1975	
M001F0.5	498	12.2	0.00525	26	7	72	2074	
F002F0.5	513	11.0	0.00529	2	11	72	1975	
F003F0.5	511	8.89	0.00525	27	2	73	1858	
F004F0.5	485	11.2	0.00518	27	2	73	1858	
M005F0.5	494	9.44	0.00530	26	7	72	2074	
M006F0.5	524	11.0	0.00529	2	11	72	1975	
M001F1.0	586	9.69	0.0163	8	9	71	2396	
F002F1.0	586	8.28	0.0167	8	9	71	2396	
F003F1.0	539	8.89	0.0167	8	9	71	2396	
F004F1.0	539	10.0	0.0165	8	9	71	2396	
M005F1.0	539	12.9	0.0165	8	9	71	2396	
M006F1.0	513	9.67	0.0165	2	11	72	1975	
M001F2.0	498	11.5	0.0922	26	7	72	2074	
F002F2.0	545	9.85	0.0905	3	1	73	1913	
F003F2.0	511	9.16	0.0907	27	2	73	1858	
F004F2.0	473	9.33	0.0910	27	2	73	1858	
M005F2.0	494	10.2	0.0905	26	7	72	2074	
M006F2.0	513	11.4	0.0912	2	11	72	1975	
M001F3.0	583	11.6	0.289	3	3	71	1546	1069

H. CALIFORNIUM - 252

DOG
NUMBER

COMMENTS ON DEAD DOGS

M001F0.0
F002F0.0
F003F0.0
F004F0.0
M005F0.0
M006F0.0

M001F0.1
F002F0.1
F003F0.1
F004F0.1
M005F0.1
M006F0.1

M001F0.5
F002F0.5
F003F0.5
F004F0.5
M005F0.5
M006F0.5

M001F1.0
F002F1.0
F003F1.0
F004F1.0
M005F1.0
M006F1.0

M001F2.0
F002F2.0
F003F2.0
F004F2.0
M005F2.0
M006F2.0

M001F3.0 FIBROSARCOMA (SKELETON)

H. CALIFORNIUM - 252

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		INJECTED	D	MO	YR	
F002F3.0	583	10.6	0.289	3	3	71	1730	1075
F003F3.0	583	8.66	0.292	3	3	71	2030	1104
F004F3.0	583	9.69	0.295	3	3	71	2015	1167
M005F3.0	524	11.1	0.284	28	11	72	1675	1108
M006F3.0	513	10.2	0.293	2	11	72	1610	1120

H. CALIFORNIUM - 252

DOG NUMBER	COMMENTS ON DEAD DOGS
F002F3.0	OSTEOSARCOMA
F003F3.0	OSTEOSARCOMA
F004F3.0	OSTEOSARCOMA
M005F3.0	OSTEOSARCOMA
M006F3.0	

DOE	INJECTION	AGE WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED	DAYS SINCE INJECTION	DOSE TO SKELETON (RADS)
F001G0.0	499	7.77	23 10 73	1620	269	
M002G0.0	509	10.5	28 11 72	1949		
M003G0.0	509	10.1	28 11 72	1949		
F004G0.0	502	11.1	5 3 74	1401		
F005G0.0	514	11.0	30 5 74	1401		
M006G0.0	499	11.4	23 10 73	1620		
F001G0.1	499	9.91	23 10 73	1620		
M002G0.1	486	13.1	5 7 72	2095		
M003G0.1	486	10.1	5 7 72	2095		
F004G0.1	488	11.4	24 4 74	1437		
F005G0.1	488	8.70	24 4 74	1437		
M006G0.1	486	11.6	5 7 72	2095		
F001G0.5	499	9.20	23 10 73	1620		
M002G0.5	514	12.0	29 2 72	2222		
M003G0.5	514	12.6	29 2 72	2222		
F004G0.5	471	10.9	5 3 74	1487		
F005G0.5	504	11.3	30 5 74	1401		
M006G0.5	514	11.8	29 2 72	2037		
F001G1.0	555	8.58	16 12 71	1584		48
M002G1.0	486	11.4	5 7 72	2095		
M003G1.0	486	11.5	5 7 72	2095		
F004G1.0	555	10.5	16 12 71	2297		
F005G1.0	471	9.29	5 3 74	1487		
M006G1.0	524	10.6	28 11 72	1949		
F001G2.0	558	9.32	16 12 71	2029		372
M002G2.0	555	11.0	16 12 71	2297		
M003G2.0	486	10.8	5 7 72	2086		
F004G2.0	558	10.3	16 12 71	2297		
F005G2.0	555	9.44	16 12 71	2297		
M006G2.0	524	10.0	28 11 72	1949		
F001G3.0	584	11.6	24 2 71	1716		960

I. CALIFORNIUM - 249

DOG NUMBER	COMMENTS ON DEAD DOGS
F001G0.0	
M002G0.0	
M003G0.0	
F004G0.0	ACCIDENTAL STRANGULATON
F005G0.0	
M006G0.0	
F001G0.1	
M002G0.1	
M003G0.1	
F004G0.1	
F005G0.1	
M006G0.1	
F001G0.5	
M002G0.5	
M003G0.5	
F004G0.5	
F005G0.5	
M006G0.5	NASAL ADENOCARCINOMA
F001G1.0	STATUS EPILEPTICUS
M002G1.0	
M003G1.0	
F004G1.0	
F005G1.0	
M006G1.0	
F001G2.0	OSTEOSARCOMA
M002G2.0	
M003G2.0	
F004G2.0	
F005G2.0	
M006G2.0	
F001G3.0	OSTEOSARCOMA

I. CALIFORNIUM - 249

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		INJECTED	D	MO YR		
M002G3.0	580	13.2	0.282	24	2	71	1770	977
M003G3.0	580	13.7	0.284	24	2	71	1464	791
F004G3.0	580	8.79	0.283	24	2	71	1551	932
F005G3.0	514	9.12	0.380	30	5	74	1401	
M006G3.0	524	10.1	0.293	28	11	72	1322	807

I. CALIFORNIUM - 249

DOG
NUMBER

COMMENTS ON DEAD DOGS

M002G3.0	OSTEOSARCOMA
M003G3.0	OSTEOSARCOMA
F004G3.0	OSTEOSARCOMA
F005G3.0	
M006G3.0	OSTEOSARCOMA

J. EINSTEINIUM - 253

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
F001E3.0	470	11.2	0.284	5 6 73	1760	
M003E3.0	470	11.3	0.288	5 6 73	1760	
M004E3.0	470	7.93	0.294	5 6 73	1760	
F001E5.0	495	8.70	2.85	5 6 73	1760	
F002E5.0G	483	9.21	2.81	5 6 73	1760	
M003E5.0	470	10.4	2.84	5 6 73	1760	

* F002E5.0G received 0.318 μ Ci/kg of ^{249}Cf on 28 May 1974.

J. EINSTEINIUM - 253

DOG
NUMBER

COMMENTS ON DEAD DOGS

F001E3.0
M003E3.0
M004E3.0

F001E5.0
F002E5.0G
M003E5.0

TABLE II. TEST ANIMALS (MAR. 31, 1978)

A. RADIUM - 226*

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE INJECTED			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR		
T001R5.0	996	11.1	10.3	1	12	52	1074	12625
T002R5.0	920	8.40	4.39	12	1	53	1368	6299
T003R5.0	1467	8.29	4.76	12	1	53	428	1755
T004R5.0	459	10.0	10.6	6	7	53	1	32
T005R5.0	126	6.14	11.7	6	10	53	1	33
T006R5.0	126	6.14	11.4	6	10	53	1	32
T007R5.0	126	6.14	11.8	6	10	53	1	33
T008R5.0	290	5.52	1.92	10	5	55	58	651
T009R5.0	2275	10.4	1.94	10	5	55	58	780
T010R5.0	43	1.02	1.98	10	5	55	49	391
T011R5.0	43	1.58	1.91	10	5	55	49	484
T012R5.0	397	12.3	9.72	9	5	56	22	3609
T013R5.0	397	7.59	9.76	9	5	56	188	3092
T014R4.0	674	8.12	3.17	11	7	56	72	507
T015R4.0	672	9.03	3.11	11	7	56	2127	6823
T016R5.0	604	12.4	9.68	11	7	57	12	244
T017R5.0H	383	12.2	9.87	28	10	58	114	18207
T018R5.0H	383	11.1	10.8	28	10	58	1226	16837
T019R5.0H	383	11.3	10.7	28	10	58	1219	15440
T020R5.0H	383	11.4	10.6	28	10	58	1340	18641
T021R5.0H	381	11.8	10.1	28	10	58	386	4947
T022R5.0H	381	11.9	10.1	28	10	58	587	7881
T023R4.0H	384	9.50	4.05	25	11	58	1471	5787
T024R4.0H	384	11.9	3.24	25	11	58	1505	7457
T025R4.0H	379	11.3	3.42	25	11	58	1309	6229
T026R4.0H	379	11.0	3.48	25	11	58	1780	6292
T027R4.0H	372	11.5	3.34	25	11	58	1414	4509
T028R3.0H	372	11.7	1.11	25	11	58	387	476
T029R5.0	474	13.5	10.4	3	3	59	216	4539

A. RADIUM - 226

DOG NUMBER	COMMENTS ON DEAD DOGS
---------------	-----------------------

T001R5.0	OSTEOSARCOMA
T002R5.0	OSTEOSARCOMA
T003R5.0	SPECIAL STUDY
T004R5.0	SPECIAL STUDY
T005R5.0	SPECIAL STUDY
T006R5.0	SPECIAL STUDY
T007R5.0	SPECIAL STUDY
T008R5.0	SPECIAL STUDY
T009R5.0	SPECIAL STUDY
T010R5.0	SPECIAL STUDY
T011R5.0	SPECIAL STUDY
T012R5.0	SPECIAL STUDY
T013R5.0	SPECIAL STUDY

T014R4.0	SPECIAL STUDY
T015R4.0	OSTEOSARCOMA

T016R5.0	SPECIAL STUDY
T017R5.0H	OSTEOSARCOMA + ULCERATIVE GINGIVITIS
T018R5.0H	OSTEOSARCOMA + ULCERATIVE GINGIVITIS
T019R5.0H	OSTEOSARCOMA + ULCERATIVE GINGIVITIS
T020R5.0H	OSTEOSARCOMA + ULCERATIVE GINGIVITIS
T021R5.0H	NEPHRITIS
T022R5.0H	CRIPPLING FRACTURES

T023R4.0H	OSTEOSARCOMA
T024R4.0H	OSTEOSARCOMA
T025R4.0H	OSTEOSARCOMA
T026R4.0H	OSTEOSARCOMA
T027R4.0H	OSTEOSARCOMA

T028R3.0H	SPECIAL STUDY
-----------	---------------

T029R5.0	NEPHRITIS
----------	-----------

A. RADIUM - 226

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
T030R5.0	474	11.5	10.4	3 3 59	178	3801
T031R5.0	471	10.5	10.4	3 3 59	303	6344
T032R3.0	471	11.4	1.13	3 3 59	2249	2485
T033R3.0	471	10.6	1.15	3 3 59	1822	2561
T034R3.0	470	15.7	1.12	3 3 59	1737	2137
T035R3.0J	670	9.44	0.951	5 5 59	8	19
T036R4.0	695	10.2	2.99	22 12 60	1154	4863
T037R4.0	695	9.53	3.00	22 12 60	1627	4312
T038R4.0	695	10.1	3.02	22 12 60	1503	4876
T040R1.0	899	13.0	0.0483	3 4 62	7	1
T041R1.0	899	12.7	0.0487	3 4 62	63	4
T042R1.7	967	14.0	0.146	4 4 62	7	3
T043R1.7	963	13.2	0.145	4 4 62	64	15
T044R3.0	938	11.1	0.937	4 4 62	68	95
T045R3.0	939	13.6	0.941	5 4 62	7	16
T046R3.0	810	12.5	0.928	5 4 62	69	137
T047R6.0	99	5.27	29.4	11 6 62	4	469
T048R6.0	2842	11.2	25.1	27 12 62	49	2129
T049R5.0	485	10.6	7.54	2 5 63	5	148
T050R5.0	485	13.7	7.46	2 5 63	15	365
T051R5.0	418	13.3	8.48	8 5 63	92	2252
T052R5.0	418	10.7	8.57	8 5 63	15	344

A. RADIUM - 226

DOG
NUMBER

COMMENTS ON DEAD DOGS

T030R5.0 NEPHRITIS
T031R5.0 NEPHRITIS

T032R3.0 OSTEOSARCOMA
T033R3.0 OSTEOSARCOMA, NEPHRITIS
T034R3.0 OSTEOSARCOMA
T035R3.0J SPECIAL STUDY

T036R4.0 OSTEOSARCOMA
T037R4.0 OSTEOSARCOMA
T038R4.0 OSTEOSARCOMA

T040R1.0 SPECIAL STUDY
T041R1.0 SPECIAL STUDY

T042R1.7 SPECIAL STUDY
T043R1.7 SPECIAL STUDY

T044R3.0 SPECIAL STUDY
T045R3.0 SPECIAL STUDY
T046R3.0 SPECIAL STUDY

T047R6.0 SPECIAL STUDY
T048R6.0 LEUKOPENIA, PNEUMONIA + SPECIAL MELANOMA STUDY

T049R5.0 SPECIAL STUDY
T050R5.0 SPECIAL STUDY
T051R5.0 SPECIAL STUDY
T052R5.0 SPECIAL STUDY

A. RADIUM - 226

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DEATH	DOSE TO SKELETON (RADS)
T053R5.0	418	12.0	8.50	8 5 63		33	815
T054R5.0	417	11.4	8.76	22 5 63		5	117
T055R5.0	417	11.6	8.61	22 5 63		33	712
T056R5.0	417	11.6	8.61	22 5 63		90	1948
T057R4.0	501	12.1	2.72	15 8 63		14	72
T058R4.0	496	11.7	2.41	15 8 63		61	381
T059R4.0	496	9.64	2.57	15 8 63		6	363
T060R4.0	490	12.1	2.33	15 8 63		117	553
T061R4.0	490	9.48	2.70	15 8 63		371	2089
T062R4.0	490	8.63	2.68	15 8 63		460	2115
T063R3.0	559	8.72	0.899	29 1 64		36	68
T064R3.0	551	8.42	0.919	29 1 64		63	97
T065R3.0	551	11.6	0.922	29 1 64		70	132
T066R3.0	549	10.1	0.904	29 1 64		132	187
T067R3.0	549	12.7	0.898	29 1 64		134	224
T068R3.0	549	12.1	0.917	29 1 64		1667	1377
T069R3.0	499	8.84	0.919	29 1 64		622	868
T070R3.0	499	14.2	0.922	29 1 64		1996	2819
T071R5.0	4025	13.8	9.23	28 1 69		42	931
T072R5.0	4776	9.45	12.4	17 8 72		54	1593
T073R2.0	487	8.68	0.350	6 5 75		380	225
T074R2.0	488	12.0	0.314	13 5 75		28	21
T075R0.0	488	9.38		13 5 75		134	
T076R2.0	488	11.6	0.318	13 5 75		56	41
T077R2.0	489	12.3	0.313	14 5 75		7	5

A. RADIUM - 226

DOG
NUMBER

COMMENTS ON DEAD DOGS

T053R5.0 SPECIAL STUDY
T054R5.0 SPECIAL STUDY
T055R5.0 SPECIAL STUDY
T056R5.0 SPECIAL STUDY

T057R4.0 SPECIAL STUDY
T058R4.0 SPECIAL STUDY
T059R4.0 SPECIAL STUDY
T060R4.0 SPECIAL STUDY
T061R4.0 SPECIAL STUDY
T062R4.0 SPECIAL STUDY

T063R3.0 SPECIAL STUDY
T064R3.0 SPECIAL STUDY
T065R3.0 SPECIAL STUDY
T066R3.0 SPECIAL STUDY
T067R3.0 SPECIAL STUDY
T068R3.0 OSTEOSARCOMA
T069R3.0 SPECIAL STUDY
T070R3.0 OSTEOSARCOMA

T071R5.0 MELANOMA ORAL CAVITY
T072R5.0 SPECIAL STUDY

T073R2.0 SPECIAL STUDY
T074R2.0 SPECIAL STUDY

T075R0.0 SPECIAL STUDY

T076R2.0 SPECIAL STUDY
T077R2.0 SPECIAL STUDY

A. RADIUM - 226

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DEATH	DOSE TO SKELETON (RADS)
T078R0.0	503	9.77		28 5 75		55	
T079R2.0	503	9.23	0.357	28 5 75		127	94
T080R0.0	500	12.1		28 5 75		208	
T081R2.0	495	11.1	0.365	28 5 75		205	143
T082R2.0	495	10.3	0.359	28 5 75		28	24
T083R0.0	495	8.06		28 5 75		26	
T084R2.0	512	11.0	0.314	6 6 75		132	85
T085R2.0	490	9.24	0.265	10 6 75		210	106
T086R2.0	487	13.8	0.313	24 6 75		15	11
T087R0.0	488	12.2		25 6 75		15	
T088R2.0	490	11.7	0.328	1 7 75		365	204
T089R2.0	491	12.2	0.329	2 7 75		15	12
T090R0.0	502	9.63		9 7 75		7	
T091R2.0	513	10.3	0.253	10 6 75		56	32
T092R2.0	459	11.6	0.327	5 8 75		7	5
T093R3.0	576	7.75	0.969	27 1 76		3	7

A. RADIUM - 226

DOG
NUMBER

COMMENTS ON DEAD DOGS

T078R0.0 SPECIAL STUDY

T079R2.0 SPECIAL STUDY

T080R0.0 SPECIAL STUDY

T081R2.0 SPECIAL STUDY

T082R2.0 SPECIAL STUDY

T083R0.0 SPECIAL STUDY

T084R2.0 SPECIAL STUDY

T085R2.0 SPECIAL STUDY

T086R2.0 SPECIAL STUDY

T087R0.0 SPECIAL STUDY

T088R2.0 SPECIAL STUDY

T089R2.0 SPECIAL STUDY

T090R0.0 SPECIAL STUDY

T091R2.0 SPECIAL STUDY

T092R2.0 SPECIAL STUDY

T093R3.0 SPECIAL STUDY

A. RADIUM - 226

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE INJECTED			DAYS SINCE INJECTION 3/31/78	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR	DEATH	
T094R3.0	571	9.88	0.930	23	1	76	11	25
T095R3.0	580	10.2	1.03	13	2	76	0	35
T096R3.0	584	7.94	0.990	13	2	76	14	33
T097R3.0	583	10.8	0.972	26	2	76	4	10
T098R3.0	549	9.51	0.966	20	2	76	18	42
T099R2.0E	563	55.4	0.335	3	11	77	148	
T100R2.0E	490	48.6	0.341	22	11	77	129	
T101R3.0E	490	45.6	1.05	22	11	77	129	
T102R2.0E	501	47.3	0.342	9	12	77	112	
T103R3.0E	501	45.4	1.10	9	12	77	112	
T104R0.5E	519	47.9	0.0191	27	12	77	94	
T105R1.0E	519	49.5	0.0558	27	12	77	94	
T106R0.1E	535	46.9	0.0021	12	1	78	78	

* The multiple injection dogs were male beagles born in Davis, California, but injected in our laboratory. Each was injected 6 times over a 280 day period with 56 days between each injection. Each ^{226}Ra injection was 20.0 μCi for the dogs T17R5H - T22R5H; 6.41 μCi for T23R4H - T27R4H; and 2.16 μCi for T28R3H. Tabulated for each dog are his age at 1st injection, his average weight during the injection period, total μCi /average weight, the date of 1st injection, the time from 1st injection to death, and sum of the skeletal doses computed from each injection to death.

T35R3J also received 99 μCi ^{85}Sr .

T39R0.0 has been reassigned and is now M12M0.0.

A. RADIUM - 226

DOG
NUMBER

COMMENTS ON DEAD DOGS

T094R3.0	SPECIAL STUDY
T095R3.0	SPECIAL STUDY
T096R3.0	SPECIAL STUDY
T097R3.0	SPECIAL STUDY
T098R3.0	SPECIAL STUDY

T099R2.0E
T100R2.0E

T101R3.0E

T102R2.0E

T103R3.0E

T104R0.5E

T105R1.0E

T106R0.1E

B. PLUTONIUM - 239*

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR		
T000P5.0	647	11.4	3.05	24	6	52	1	5
T001P5.0	1581	12.7	3.04	13	10	52	29	156
T002P5.0	914	11.9	6.85	15	9	52	44	534
T003P5.0	942	9.65	3.22	13	10	52	610	3361
T004P5.0	1016	8.78	3.02	13	10	52	365	1912
T005P5.0	474	10.4	2.69	14	12	54	400	1862
T006P5.0	527	6.16	2.73	14	12	54	406	1918
T007P5.0	475	7.40	2.68	14	12	54	777	3534
T008P5.0	527	8.32	2.67	14	12	54	863	3896
T009P5.0	551	10.3	2.80	22	11	55	15	75
T010P5.0	534	11.9	2.74	23	11	55	15	73
T011P5.0	516	12.1	2.76	22	11	55	28	137
T012P5.0	487	9.23	2.74	23	11	55	28	136
T013P5.0	587	8.27	3.16	24	4	56	3	17
T014P5.0	587	9.38	2.43	24	4	56	7	30
T015P5.0	737	8.32	2.79	15	10	56	1	5
T016P5.0	673	10.7	2.85	10	10	56	92	463
T017P5.0	739	11.1	3.01	12	2	57	210	1107
T018P5.0	739	8.16	2.83	12	2	57	217	1075
T019P5.0	688	8.86	2.91	15	12	60	1400	6752
T020P5.0	688	13.0	2.68	15	12	60	474	2189
T021P5.0	688	10.3	2.72	15	12	60	939	4304
T023P1.0	1485	13.1	0.0172	28	7	61	96	3
T024P1.0	559	13.1	0.0172	28	7	61	97	3
T025P1.0	559	13.8	0.0167	28	7	61	467	12
T026P1.0	556	12.0	0.0160	28	7	61	647	15
T027P3.0	556	11.5	0.332	28	7	61	755	402
T028P1.0	552	10.5	0.0150	9	8	61	559	13
T029P3.0	552	12.1	0.296	9	8	61	560	272
T030P1.0	548	12.4	0.0148	9	8	61	3	<1

R. PLUTONIUM - 239

DOG NUMBER	COMMENTS ON DEAD DOGS
T000P5.0	SPECIAL STUDY
T001P5.0	SPECIAL STUDY
T002P5.0	SPECIAL STUDY
T003P5.0	SPECIAL STUDY
T004P5.0	SPECIAL STUDY
T005P5.0	SPECIAL STUDY
T006P5.0	SPECIAL STUDY
T007P5.0	SPECIAL STUDY
T008P5.0	SPECIAL STUDY
T009P5.0	SPECIAL STUDY
T010P5.0	SPECIAL STUDY
T011P5.0	SPECIAL STUDY
T012P5.0	SPECIAL STUDY
T013P5.0	SPECIAL STUDY
T014P5.0	SPECIAL STUDY
T015P5.0	SPECIAL STUDY
T016P5.0	SPECIAL STUDY
T017P5.0	SPECIAL STUDY
T018P5.0	SPECIAL STUDY
T019P5.0	OSTEOSARCOMA, BLOOD DYSCRASIA, LIVER DEGENERATION
T020P5.0	LIVER DEGENERATION, ASCITES + THROMBOCYTOPENIA
T021P5.0	TOXIC NEPHRITIS + LIVER DEGENERATION
T023P1.0	SPECIAL STUDY
T024P1.0	SPECIAL STUDY
T025P1.0	SPECIAL STUDY
T026P1.0	SPECIAL STUDY
T027P3.0	SPECIAL STUDY
T028P1.0	SPECIAL STUDY
T029P3.0	SPECIAL STUDY
T030P1.0	SPECIAL STUDY

B. PLUTONIUM - 239

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
T031P3.0	520	13.0	0.305	9 8 61	40	21
T032P1.0	520	8.47	0.0162	9 8 61	274	7
T033P1.0	550	10.7	0.0153	15 9 61	375	9
T034P1.0	550	9.68	0.0154	15 9 61	746	17
T035P3.0	550	11.9	0.303	15 9 61	362	184
T036P1.0	544	10.4	0.0158	15 9 61	5	<<1
T037P1.0	542	8.59	0.0148	15 9 61	186	5
T038P3.0	489	7.96	0.304	15 9 61	187	98
T039P1.0	1534	10.7	0.0151	15 9 61	376	9
T040P1.0	1534	9.92	0.0177	15 9 61	769	20
T041P5.0	543	8.50	3.01	30 11 64	1227	6156
T042P5.0	510	11.4	2.40	10 2 65	13	55
T043P5.0H	600	14.0	2.86	15 7 65	40	203
T044P5.0H	517	12.0	2.72	21 9 65	35	169
T045P5.0H	420	12.3	2.98	28 10 65	5/24	1
T046P5.0	420	11.90	3.01	28 10 65	732	3747
T047P5.0	806	12.4	3.02	30 11 65	69	368
T048P5.0	554	8.5	2.61	11 3 66	1327	5754
T049P1.0	103	5.00	0.0162	5 7 66	4287	
T050P3.0	103	5.30	0.296	5 7 66	2835	1175

B. PLUTONIUM - 239

DOG
NUMBER

COMMENTS ON DEAD DOGS

T031P3.0 SPECIAL STUDY

T032P1.0 SPECIAL STUDY

T033P1.0 SPECIAL STUDY

T034P1.0 SPECIAL STUDY

T035P3.0 SPECIAL STUDY

T036P1.0 SPECIAL STUDY

T037P1.0 SPECIAL STUDY

T038P3.0 SPECIAL STUDY

T039P1.0 SPECIAL STUDY

T040P1.0 SPECIAL STUDY

~~T041P5.0 PURPURA-HEMORRHAGICA;AUTOHEMAGGLUTINATION;LIVER-DEGENERATION~~

T042P5.0 SPECIAL STUDY

T043P5.0H SPECIAL STUDY

T044P5.0H SPECIAL STUDY

T045P5.0H SPECIAL STUDY

T046P5.0 LIVER DEGENERATION

T047P5.0 SPECIAL STUDY

T048P5.0 UNDIFFERENTIATED SARCOMA (BONE)

T049P1.0

T050P3.0 OSTEOSARCOMA

B. PLUTONIUM - 239

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
T051P5.0	104	4.80	2.73	6 7 66	1055	4831
T052P4.0	437	11.8	0.949	7 7 67	14	24
T053P5.0	1517	13.9	2.82	11 3 69	1559	7016
T054P5.0	906	11.3	2.77	11 3 69	404	1936
T055P4.0	445	10.6	0.785	3 6 69	14	20
T056P5.5	501	11.2	3.73	29 7 69	7	46
T057P2.0E	618	49.4	0.0961	10 9 69	1506	181
T058P3.0E	573	52.3	0.291	10 9 69	917	421
T059P3.0E	591	44.5	0.290	5 11 69	973	442
T060P3.0E	567	45.2	0.314	6 1 70	784	393
T061P2.0E	581	47.2	0.0983	6 1 70	1639	198
T062P2.0E	583	52.5	0.156	22 1 70	1223	251
T063P5.0	581	9.13	2.77	14 12 70	490	2337
T064P0.0	595	8.60		28 12 70	2650	
T065P4.0P	542	11.5	0.904	30 11 71	14	2

B. PLUTONIUM - 239

DOG NUMBER	COMMENTS ON DEAD DOGS
---------------	-----------------------

T051P5.0	OSTEOSARCOMA
----------	--------------

T052P4.0	SPECIAL STUDY
----------	---------------

T053P5.0	LIVER DEGENERATION; ADRENALECTOMY
T054P5.0	SPECIAL STUDY

T055P4.0	SPECIAL STUDY
----------	---------------

T056P5.5	SPECIAL STUDY
----------	---------------

T057P2.0E	OSTEOSARCOMA
-----------	--------------

T058P3.0E	OSTEOSARCOMA
T059P3.0E	OSTEOSARCOMA
T060P3.0E	OSTEOSARCOMA

T061P2.0E	OSTEOSARCOMA
T062P2.0E	OSTEOSARCOMA

T063P5.0	SPECIAL STUDY
----------	---------------

T064P0.0	REASSIGNED, SEE T124P1.7
----------	--------------------------

T065P4.0P	SPECIAL STUDY
-----------	---------------

B. PLUTONIUM - 239

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DOSE TO SKELETON (RADS)	DEATH
T066P4.0P	542	10.6	0.913	30 11 71		1184	
T067P4.0P	539	10.4	0.907	30 11 71		1148	
T068P1.0E	569	44.2	0.0158	20 4 72	2171		
T069P1.0E	569	32.0	0.0160	20 4 72	2171		
T070P1.0E	588	40.6	0.0152	9 5 72	2152		
T071P0.5E	588	48.9	0.00521	9 5 72	2152		
T072P0.5E	611	44.5	0.00512	1 6 72	2129		
T073P0.5E	611	38.8	0.00507	1 6 72	2129		
T074P4.0	3694	7.73	0.937	28 3 73		705	1096
T075P4.0	3478	8.47	0.897	28 3 73		1451	2058
T076P4.0	3413	10.7	0.894	28 3 73		1357	1928
T077P3.0	3413	9.95	0.310	28 3 73		1623	748
T078P3.0	2488	8.21	0.320	28 3 73		1633	777
T079P0.5	483	11.1	0.00523	5 6 73		134	2
T080P0.2E	569	48.7	0.00153	25 7 73	1710		
T081P0.2E	569	44.3	0.00157	25 7 73	1710		
T082P0.2E	597	47.2	0.00191	22 8 73	1682		
T083P0.1E	575	51.3	0.00061	22 8 73	1682		
T084P0.1E	517	55.7	0.00066	19 2 75	1136		
T085P0.1E	557	52.0	0.00071	1 4 75	1095		
T086P4.0E	525	46.0	0.903	27 2 75		901	1330

B. PLUTONIUM - 239

DOG
NUMBER

COMMENTS ON DEAD DOGS

T066P4.0P FIBROSARCOMA
T067P4.0P OSTEOSARCOMA

T068P1.0E
T069P1.0E
T070P1.0E

T071P0.5E
T072P0.5E
T073P0.5E

T074P4.0 UNDIFFERENTIATED MALIGNANCY (NON-SKELETAL)
T075P4.0 OSTEOSARCOMA
T076P4.0 OSTEOSARCOMA

T077P3.0 OSTEOSARCOMA
T078P3.0 OSTEOSARCOMA

T079P0.5 SPECIAL STUDY

T080P0.2E
T081P0.2E
T082P0.2E

T083P0.1E
T084P0.1E
T085P0.1E

T086P4.0E OSTEOSARCOMA

B. PLUTONIUM - 239

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
T087F5.0	3008	10.1	2.93	24 2 75	182	936
T088F5.0	2194	9.80	3.01	24 2 75	184	972
T089F1.0	490	8.99	0.0176	6 5 75	379	11
T090F0.0	487	7.60		6 5 75	378	
T091F1.0	488	10.6	0.0134	13 5 75	7	<1
T092F1.0	488	10.8	0.0134	13 5 75	29	<1
T093F1.0	488	9.04	0.0144	13 5 75	133	3
T094F1.0	500	11.1	0.0166	28 5 75	27	<1
T095F1.0	511	9.46	0.0178	5 6 75	60	2
T096F1.0	501	10.9	0.0159	8 7 75	7	<1
T097F1.0	490	13.0	0.0164	10 6 75	211	6
T098F1.0	490	11.5	0.0162	10 6 75	209	6
T099F1.0	497	10.9	0.0151	17 6 75	15	<1
T100F1.0	487	13.0	0.0155	24 6 75	363	9
T101F1.0	490	10.0	0.0158	22 8 75	56	2
T102F1.0	494	11.7	0.0152	26 8 75	140	4
T103F1.0	490	8.97	0.0157	5 9 75	14	<1
T104F1.7	565	7.75	0.0477	16 1 76	11	1
T105F0.0	574	11.8		23 2 76	11	
T106F1.7	585	8.84	0.0455	6 2 76	3	<1
T107F1.7	581	9.35	0.0451	6 2 76	7	<1
T108F0.0	582	10.3		6 2 76	14	

B. PLUTONIUM - 239

DOG NUMBER	COMMENTS ON DEAD DOGS
---------------	-----------------------

T087P5.0	SPECIAL STUDY
T088P5.0	SPECIAL STUDY

T089P1.0	SPECIAL STUDY
----------	---------------

T090P0.0	SPECIAL STUDY
----------	---------------

T091P1.0	SPECIAL STUDY
T092P1.0	SPECIAL STUDY
T093P1.0	SPECIAL STUDY
T094P1.0	SPECIAL STUDY
T095P1.0	SPECIAL STUDY
T096P1.0	SPECIAL STUDY
T097P1.0	SPECIAL STUDY
T098P1.0	SPECIAL STUDY
T099P1.0	SPECIAL STUDY
T100P1.0	SPECIAL STUDY
T101P1.0	SPECIAL STUDY
T102P1.0	SPECIAL STUDY
T103P1.0	SPECIAL STUDY

T104P1.7	SPECIAL STUDY
----------	---------------

T105P0.0	SPECIAL STUDY
----------	---------------

T106P1.7	SPECIAL STUDY
T107P1.7	SPECIAL STUDY

T108P0.0	SPECIAL STUDY
----------	---------------

B. PLUTONIUM - 239

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE INJECTED			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR		
T109P0.0	581	8.50		13	2	76	4	
T110P0.0	579	9.31		12	2	76	7	
T111P1.7	578	8.56	0.0433	11	2	76	14	1
T112P1.7	589	8.90	0.0435	23	2	76	4	<1
T113P1.7	548	10.6	0.0438	19	2	76	18	1
T114P0.0	555	9.25		26	2	76	18	
T115P0.0	570	13.2		12	3	76	4	
T116P5.5	533	8.72	4.32	13	1	76	2	15
T117P2.0Y	96	3.79	0.108	15	1	76	7	1
T118P2.0Y	96	3.87	0.105	15	1	76	14	3
T119P2.0Y	84	4.42	0.0922	15	1	76	28	5
T120P2.0Y	96	4.85	0.0840	15	1	76	56	8
T121P2.0Y	84	3.64	0.112	15	1	76	119	2
T122P2.0Y	96	3.69	0.110	15	1	76	89	3
T123P2.0	2366	10.5	0.0882	15	1	76	14	2
T124P1.7	2558	7.68	0.0527	13	5	76	118	8
T125P2.0N	2	0.32	0.127	22	6	76	3	1
T126P2.0N	2	0.29	0.160	22	6	76	3	1
T127P2.0N	2	0.31	0.148	19	7	76	1	1
T128P2.0N	2	0.30	0.153	19	7	76	1	1
T129P2.0N	2	0.28	0.197	19	7	76	1	1
T130P4.0P	609	9.66	0.569	18	11	76	60	7

B. PLUTONIUM - 239

DOG
NUMBER

COMMENTS ON DEAD DOGS

T109P0.0 SPECIAL STUDY
T110P0.0 SPECIAL STUDY

T111P1.7 SPECIAL STUDY
T112P1.7 SPECIAL STUDY
T113P1.7 SPECIAL STUDY

T114P0.0 SPECIAL STUDY
T115P0.0 SPECIAL STUDY

T116P5.5 SPECIAL STUDY

T117P2.0Y SPECIAL STUDY
T118P2.0Y SPECIAL STUDY
T119P2.0Y SPECIAL STUDY
T120P2.0Y SPECIAL STUDY
T121P2.0Y SPECIAL STUDY
T122P2.0Y SPECIAL STUDY
T123P2.0 SPECIAL STUDY

T124P1.7 SPECIAL STUDY

T125P2.0N SPECIAL STUDY
T126P2.0N SPECIAL STUDY
T127P2.0N SPECIAL STUDY
T128P2.0N SPECIAL STUDY
T129P2.0N SPECIAL STUDY

T130P4.0F SPECIAL STUDY

B. PLUTONIUM - 239

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE INJECTED			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR		
T131P4.OP	609	12.6	0.844	18	11	76	498	
T132P4.OP	609	10.1	0.850	18	11	76	132	16
T133P4.OP	609	9.95	0.844	18	11	76	498	
T134P4.OP	609	9.87	0.832	18	11	76	498	
T135P4.OP	609	11.3	0.577	18	11	76	69	8
T136P4.OP	603	10.2	0.842	18	11	76	498	
T137P4.OP	609	11.4	0.572	18	11	76	257	
T138P4.OP	603	9.66	0.831	18	11	76	138	
T139P4.OP	609	12.2	0.576	18	11	76	417	
T140P4.OP	603	9.79	0.574	18	11	76	498	
T141P4.OP	602	10.3	0.834	18	11	76	40	6
T142P4.OP	602	8.28	0.834	18	11	76	33	4
T143P4.OP	603	10.2	0.842	18	11	76	498	
T144P4.OP	602	9.82	0.836	18	11	76	498	
T145P4.OP	603	10.0	0.575	18	11	76	117	23
T146P4.OP	602	9.63	0.570	18	11	76	124	26
T147P4.OP	597	11.0	0.848	18	11	76	498	
T148P4.OP	602	9.67	0.581	18	11	76	250	
T149P4.OP	597	9.86	0.833	18	11	76	498	
T150P4.OP	597	9.84	0.571	18	11	76	424	
T151P4.OP	597	11.4	0.572	18	11	76	498	
T152P4.OP	597	8.90	0.833	18	11	76	498	
T153P5.0	803	12.0	2.55	16	11	76	22	100
T154P2.ON	2	0.20	0.154	9	11	76	7	1
T155P2.ON	2	0.20	0.151	9	11	76	7	1
T156P2.ON	2	0.28	0.0897	9	11	76	7	1
T157P4.OP	609	11.2	0.833	18	11	76	498	
T158P2.0	695	9.68	0.0866	11	1	77	14	1
T159P2.0	700	10.7	0.0783	11	1	77	14	1
T160P2.0	689	8.71	0.0962	11	1	77	14	1
T161P2.0	700	10.4	0.0806	11	1	77	14	1

B. PLUTONIUM - 239

DOG
NUMBER

COMMENTS ON DEAD DOGS

T131P4.0P
T132P4.0P SPECIAL STUDY
T133P4.0P
T134P4.0P
T135P4.0P SPECIAL STUDY
T136P4.0P
T137P4.0P
T138P4.0P
T139P4.0P
T140P4.0P
T141P4.0P SPECIAL STUDY
T142P4.0P SPECIAL STUDY
T143P4.0P
T144P4.0P SPECIAL STUDY
T145P4.0P SPECIAL STUDY
T146P4.0P SPECIAL STUDY
T147P4.0P
T148P4.0P
T149P4.0P
T150P4.0P
T151P4.0P
T152P4.0P

T153P5.0 SPECIAL STUDY

T154P2.0N SPECIAL STUDY
T155P2.0N SPECIAL STUDY
T156P2.0N SPECIAL STUDY

T157P4.0P

T158P2.0 SPECIAL STUDY
T159P2.0 SPECIAL STUDY
T160P2.0 SPECIAL STUDY
T161P2.0 SPECIAL STUDY

B. PLUTONIUM - 239

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE INJECTED			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR		
T162P2.0	686	9.59	0.0874	11	1	77	14	2
T163P2.0	686	10.6	0.0791	11	1	77	14	2
T164P2.0	686	10.0	0.0838	11	1	77	14	1
T165P2.0	695	10.4	0.0806	11	1	77	14	1
T166P2.0	707	9.27	0.0904	1	2	77	14	1
T167P2.0	707	12.6	0.0665	1	2	77	14	1
T168P2.0	707	9.39	0.0893	1	2	77	14	1
T169P2.0	699	10.9	0.0769	1	2	77	14	1
T170P2.0	699	10.8	0.0776	1	2	77	14	2
T171P2.0	710	11.3	0.0742	1	2	77	14	2
T172P2.0	699	9.79	0.0856	1	2	77	14	1
T173P2.0	707	10.4	0.0806	1	2	77	14	1
T174P2.0Y	93	3.52	0.0989	8	2	77	416	
T175P2.0Y	93	3.14	0.0936	8	2	77	416	
T176P2.0Y	93	2.89	0.0953	8	2	77	360	
T177P2.0Y	92	4.01	0.0981	8	2	77	364	
T178P2.0Y	92	4.34	0.0969	8	2	77	416	
T179P2.0Y	92	3.60	0.0967	8	2	77	416	
T180P0.0	502	9.78		24	2	77	27	
T181P1.0	518	8.44	0.0162	24	3	77	33	2
T182P0.0	518	8.52		24	3	77	56	
T183P0.0	516	11.3		14	4	77	28	
T184P1.0	516	9.60	0.0168	14	4	77	56	2
T185P2.0Y	90	3.31	0.0941	9	3	78	22	
T200P5.5	657	10.9	4.34	13	6	77	2	31

B. PLUTONIUM - 239

DOG
NUMBER

COMMENTS ON DEAD DOGS

T162P2.0 SPECIAL STUDY
T163P2.0 SPECIAL STUDY
T164P2.0 SPECIAL STUDY
T165P2.0 SPECIAL STUDY
T166P2.0 SPECIAL STUDY
T167P2.0 SPECIAL STUDY
T168P2.0 SPECIAL STUDY
T169P2.0 SPECIAL STUDY
T170P2.0 SPECIAL STUDY
T171P2.0 SPECIAL STUDY
T172P2.0 SPECIAL STUDY
T173P2.0 SPECIAL STUDY
T174P2.0Y
T175P2.0Y
T176P2.0Y
T177P2.0Y
T178P2.0Y
T179P2.0Y

T180P0.0 SPECIAL STUDY

T181P1.0

T182P0.0

T183P0.0 SPECIAL STUDY

T184P1.0 SPECIAL STUDY

T185P2.0Y

T200P5.5 SPECIAL STUDY

B. PLUTONIUM - 239

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
T201P0.0	576	8.95		4 10 77	29	
T202P1.0	586	7.67	0.0173	12 10 77	27	1

*T22P0.0 has been reassigned and is now F06T0.0A.

T043P5.0H was also given 1.01 μCi ^{239}Pu /kg one day prior to sacrifice.

T044P5.0H was given 0.833 μCi ^{239}Pu /kg and about 9.17 μCi ^{59}Fe /kg one day prior to sacrifice.

Dogs in the above tabulation having the letter E as the final entry in the "Dog number" column are St. Bernards. Those having the letter P in that position were given plutonium in particulate form.

T117 . . . 122P3Y and T123P2 were given tracer ^{237}Pu in the same solution containing their ^{239}Pu .

B. PLUTONIUM - 239

DOG
NUMBER

COMMENTS ON DEAD DOGS

T201P0.0 SPECIAL STUDY

T202P1.0 SPECIAL STUDY

C. RADIUM - 228 (MESOTHORIUM)*

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE		DAYS SINCE INJECTION	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		INJECTED			
				D	MO	YR	3/31/78 DEATH
T001M4.5	529	9.13	4.23	8	9	54	314
T002M4.5	463	8.93	4.27	8	9	54	755
T003M5.0	579	9.15	10.6	13	3	56	700

* ($\mu\text{Ci } ^{228}\text{Th}/\mu\text{Ci } ^{228}\text{Ra}$) injected = 0.03.

C. RADIUM - 228 (MESOTHORIUM)

DOG
NUMBER

COMMENTS ON DEAD DOGS

T001M4.5 CANINE DISTEMPER
T002M4.5 SPECIAL STUDY

T003M5.0 ULCERATIVE GINGIVITIS, SEVERE ANEMIA + CRIPPLING FRACTURE

D. THORIUM - 228*

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE INJECTED			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR		
T001T5.0	607	9.30	4.88	1	12	53	23	1548
T002T5.0	501	8.48	2.56	8	2	54	77	2639
T003T4.0	429	10.4	0.870	8	2	54	820	6504
T004T5.0	455	8.92	2.59	28	9	54	113	3844
T005T5.0	455	10.1	2.32	28	9	54	65	2032
T006T4.0	591	7.01	0.884	18	10	55	651	5697
T007T3.0	591	9.23	0.298	18	10	55	910	2369
T008T3.0	606	9.23	0.293	14	10	58	1043	2511
T009T3.0	447	11.0	0.285	4	2	59	1	4
T010T3.0	447	14.2	0.289	4	2	59	8	32
T011T3.0	500	8.62	0.335	16	6	59	22	101
T012T3.0	514	10.6	0.302	7	7	59	22	92
T013T3.0	754	13.1	0.298	28	7	59	22	91

*T11, 12, 13T3 received 40, 4, and 0.4 mg ²³²Th, respectively.

D. THORIUM - 228

DOG NUMBER	COMMENTS ON DEAD DOGS
T001T5.0	DIED, SPECIAL STUDY
T002T5.0	SPECIAL STUDY
T003T4.0	CRIPPLING FRACTURES + NEPHRITIS
T004T5.0	THROMBOCYTOPENIA + PURPURA
T005T5.0	NEPHRITIS, THROMBOCYTOPENIA + PURPURA
T006T4.0	CRIPPLING FRACTURES
T007T3.0	SPECIAL STUDY
T008T3.0	OSTEOSARCOMA
T009T3.0	SPECIAL STUDY
T010T3.0	SPECIAL STUDY
T011T3.0	SPECIAL STUDY
T012T3.0	SPECIAL STUDY
T013T3.0	SPECIAL STUDY

E. STRONTIUM - 90*

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DEATH	DOSE TO SKELETON (RADS)
T001S0.0	151	7.71		5 3 54		112	
T002S5.0	149	6.85	148.	5 3 54		18	835
T003S5.0	144	6.19	148.	5 3 54		28	1276
T004S5.0	151	7.05	148.	5 3 54		41	2593
T005S5.0	144	5.25	148.	5 3 54		116	6484
T006S5.0	155	7.01	87.0	16 3 54		1/24	3
T007S5.0	155	6.74	87.0	16 3 54		2	112
T008S0.0	243	7.00					
T008S2.0H	67	3.69	2.74	27 9 55		66	41
T009S2.0H	67	2.79	3.62	27 9 55		66	53
T010S2.0H	67	3.11	3.25	27 9 55		132	124
T011S2.0H	67	3.85	2.62	27 9 55		132	100
T012S3.0	593	10.6	10.5	11 9 57		5	20
T013S4.0	324	10.5	19.1	8 7 60		8	67
T014S5.0	542	10.0	96.1	7 11 61		9	233
T015S5.0	595	9.43	98.4	7 11 61		30	564
T016S2.0	604	9.71	3.27	8 11 61		9	8
T017S6.0	670	7.18	295.	19 1 62		14	919
T018S6.0	670	5.94	302.	19 1 62		1369	25217

E. STRONTIUM - 90

DOG NUMBER	COMMENTS ON DEAD DOGS
T001S0.0	SPECIAL STUDY
T002S5.0	SPECIAL STUDY
T003S5.0	SPECIAL STUDY
T004S5.0	SPECIAL STUDY
T005S5.0	SPECIAL STUDY
T006S5.0	SPECIAL STUDY
T007S5.0	SPECIAL STUDY
T008S0.0	SPECIAL STUDY
T008S2.0H	SPECIAL STUDY
T009S2.0H	SPECIAL STUDY
T010S2.0H	SPECIAL STUDY
T011S2.0H	SPECIAL STUDY
T012S3.0	BREMSSTRAHLUNG PHANTOM
T013S4.0	BREMSSTRAHLUNG PHANTOM SAM MCGEE
T014S5.0	SPECIAL STUDY
T015S5.0	SPECIAL STUDY
T016S2.0	SPECIAL STUDY
T017S6.0	LEUKOPENIA, THROMBOCYTOPENIA + PURPURA
T018S6.0	HEMANGIOSARCOMA (ISCHIUM)

E. STRONTIUM - 90

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE INJECTED			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RAIS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR		
T019S6.0	670	5.43	284.	19	1	62	23	849
T020S4.0J	440	8.54	28.9	2	10	63	13	104
T021S2.5J	363	7.20	8.3	2	10	63	13	191
T022S5.0	545	9.01	99.0	1	4	69	1525	11690
T023S5.0	545	11.6	100.	1	4	69	1379	14121

*T08 . . . 11S2.0H were given 10 injections, 1 μ Ci each at weekly intervals. Age at first injection, wt. is average during the injection period, μ Ci/kg is total ^{90}Sr /average weight, date is at first injection, days are from first injection to death, and dose is computed from mid-injection to death.

T20S4J received 0.5 μ Ci ^{85}Sr in addition to the 246.8 μ Ci ^{90}Sr .

T21S2.5J received 0.5 μ Ci ^{85}Sr and 600 μ Ci ^{89}Sr in addition to the 59.8 μ Ci ^{90}Sr .

E. STRONTIUM - 90

DOG NUMBER	COMMENTS ON DEAD DOGS
T019S6.0	LEUKOPENIA, THROMBOCYTOPENIA + PURPURA
T020S4.0J	SPECIAL STUDY
T021S2.5J	SPECIAL STUDY
T022S5.0	HEMANGIOSARCOMA (BONE)
T023S5.0	OSTEOSARCOMA

F. RADIUM - 224 (QUICKRADIUM)*

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DEATH	DOSE TO SKELETON (RADS)
T001Q3.0J	460	9.55	0.875	26 3 63		4/24	
T002Q4.0	466	12.0	2.91	27 3 63		2317	937
T003Q4.0	466	13.1	2.91	27 3 63		2708	1017
T004Q5.0	480	9.55	9.71	24 4 63		1462	4951
T005Q5.0	455	9.67	9.59	24 4 63		1638	5236
T006Q6.0	455	8.29	21.4	17 10 63		13	1137
T007Q5.0	465	11.8	8.56	6 11 63		2053	604
T008Q5.0	475	9.77	8.62	6 11 63		16	450
T009Q4.0	503	9.80	2.57	4 12 63		1451	156
T010Q4.0	503	10.3	2.57	4 12 63		262	144
T011Q3.0	495	9.10	0.885	4 12 63		3668	56
T012Q3.0	495	13.5	0.889	4 12 63		4087	56
T013Q3.0	495	11.3	0.912	4 12 63		4605	58
T014Q3.0	438	10.3	0.870	4 12 63		4785	55
T015Q4.0	515	12.7	2.73	1 2 68		1692	3881
T016Q2.0	515	9.36	0.310	1 2 68		3711	
T017Q2.0	515	10.2	0.311	1 2 68		3711	
T018Q2.0	502	9.68	0.306	1 2 68		3711	
T019Q1.0	515	11.8	0.0475	1 2 68		3711	

F. RADIUM - 224 (QUICKRADIUM)

DOG
NUMBER

COMMENTS ON DEAD DOGS

T001Q3.0J SPECIAL STUDY

T002Q4.0 OSTEOSARCOMA
T003Q4.0 HEMANGIOSARCOMA (ILIUM)

T004Q5.0 OSTEOSARCOMA, EPIDERMOID CARCINOMA (FRONTAL SINUS)
T005Q5.0 OSTEOSARCOMA

T006Q6.0 PURPURA HEMORRHAGICA

T007Q5.0 OSTEOSARCOMA
T008Q5.0 PURPURA HEMORRHAGICA

T009Q4.0 STRANGULATION ON VOMITUS AND GRAND MAL
T010Q4.0 STATUS EPILEPTICUS

T011Q3.0 AORTIC BODY TUMOR
T012Q3.0 AORTA THROMBO-EMBOLISM
T013Q3.0 CIRCULATORY FAILURE
T014Q3.0 NEPHRITIS

T015Q4.0 OSTEOSARCOMA

T016Q2.0
T017Q2.0
T018Q2.0

T019Q1.0

F. RADIUM - 224 (QUICKRADIUM)

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		INJECTED	D	MO	YR	
T020Q1.0	515	10.4	0.0472	1	2	68	3711	
T021Q1.0	502	9.08	0.0447	1	2	68	3711	
T022Q5.0	643	8.39		13	12	77	3/24	7
T023Q5.0	619	10.9	8.37	3	1	78	1/24	1
T024Q5.0	649	9.14	10.1	19	12	77	1	72
T025Q5.0	638	8.78	10.1	10	1	78	8/24	17
T026Q5.0	685	8.81	9.98	24	1	78	7	332
T027Q5.0	642	10.6	10.1	14	1	78	3	148

*The skeletal doses in rads are from ^{224}Ra (and daughters) plus contamination from ^{210}Pb and ^{228}Th . In some cases the ^{210}Pb and ^{228}Th contamination was appreciable. Please see the article, " ^{224}Ra toxicity from a pilot study in beagles" in C00-119-252, March 1977, pp. 272-287, particularly see p. 278.

T001Q3.0J also received 18.0 μCi ^{85}Sr .

**Skeletal doses in rads for T22Q5 to T27Q5 are from ^{224}Ra (and daughters). Contamination of the injection solution with other emitters was negligible. Dosimetric details are to be found in C00-119-253, March 1978.

F. RADIUM - 224 (QUICKRADIUM)

DOG
NUMBER

COMMENTS ON DEAD DOGS

T020Q1.0
T021Q1.0

T022Q5.0	SPECIAL STUDY
T023Q5.0	SPECIAL STUDY
T024Q5.0	SPECIAL STUDY
T025Q5.0	SPECIAL STUDY
T026Q5.0	SPECIAL STUDY
T027Q5.0	SPECIAL STUDY

G. AMERICIUM - 241*

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DEATH	DOSE TO SKELETON (RADS)
T015W5.5	858	11.5	4.53	23 10 67		1	6
T016W5.0	461	10.7	2.78	29 1 68		2	66
T032W5.5	553	11.0	4.46	30 4 68		7	36
T033W5.5	393	10.5	4.47	30 4 68		8	44
T056W5.0	552	11.3	2.90	25 11 69		15	65
T057W5.0	496	7.01	2.77	26 1 70		15	56
T099W5.0	547	11.3	2.67	10 11 70		252	966
T101W5.0	399	10.4	2.98	17 8 72		1	4
T102W3.0	515	11.6	0.280	10 10 72		17	7
T103W3.0	501	10.6	0.283	10 10 72	1998		
T104W3.0	2658	7.67	0.305	28 11 72		1864	701
T105W3.0	2224	7.78	0.301	28 11 72		1100	647
T106W3.0	2224	13.8	0.308	28 11 72		1909	791
T107W5.0	3543	9.24	2.34	2 4 73		36	110
T108W3.0	507	12.6	0.304	8 8 73	1696		
T109W3.0	506	9.90	0.306	8 8 73	1696		
T110W3.0	506	9.30	0.306	8 8 73		1506	341
T111W3.0	506	9.81	0.303	8 8 73	1696		
T112W3.0	506	6.92	0.333	23 10 73		44	19
T113W3.0	499	9.35	0.333	23 10 73	1620		
T114W3.0	531	12.9	0.300	2 7 74	1368		
T117W4.0	385	9.98	1.20	19 11 74	1228		

G. AMERICIUM - 241

DOG NUMBER	COMMENTS ON DEAD DOGS
T015W5.5	SPECIAL STUDY
T016W5.0	SPECIAL STUDY
T032W5.5	SPECIAL STUDY
T033W5.5	SPECIAL STUDY
T056W5.0	SPECIAL STUDY
T057W5.0	SPECIAL STUDY
T099W5.0	SPECIAL STUDY
T101W5.0	SPECIAL STUDY
T102W3.0	SPECIAL STUDY
T103W3.0	
T104W3.0	EMPHYEMA
T105W3.0	FIBROSARCOMA (ORAL); KIDNEY DEGENERATION
T106W3.0	TRAUMA
T107W5.0	MELANOMA (MOUTH)
T108W3.0	
T109W3.0	
T110W3.0	ANESTHETIC ACCIDENT; ADRENO-CORTICAL HYPOPLASIA
T111W3.0	
T112W3.0	INTUSSUSCEPTION
T113W3.0	
T114W3.0	
T117W4.0	

G. AMERICIUM - 241

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78	DOSE TO SKELETON (RADS)
T118W4.0	385	8.96	1.34	19 11 74	1228	
T119W4.0	385	8.36	1.44	19 11 74	1228	
T120W5.0	2894	8.77	3.17	24 2 75	283	1376
T142W3.0	586	9.76	0.299	28 1 76	793	
T143W3.0	533	9.21	0.317	4 2 76	786	
T144W4.0	397	11.8	0.804	19 5 76	545	697
T145W4.0	397	11.6	0.983	19 5 76	545	852
T146W3.0	593	7.07	0.301	13 2 76	777	
T147W5.0N	1	0.25	3.11	1 2 76	1	6
T148W5.0N	1	0.26	2.97	1 2 76	3	21
T149W5.0N	1	0.27	2.88	1 2 76	5	33
T150W5.0N	1	0.28	2.79	1 2 76	5	32
T151W5.0N	1	0.24	3.20	1 2 76	1	6
T152W5.0N	1	0.25	3.11	1 2 76	1	7
T153W5.0N	1	0.27	2.84	1 2 76	3	18
T154W3.0	535	9.96	0.287	4 8 76	21	11
T155W3.0	532	10.2	0.280	4 8 76	604	
T156W3.0	528	10.0	0.286	4 8 76	604	
T157W3.0	526	9.99	0.286	4 8 76	23	10
T158W0.0	553	12.9		30 12 76	456	
T159W0.0	546	10.6		30 12 76	456	
T160W1.0	577	11.4	0.0159	30 12 76	456	

G. AMERICIUM - 241

DOG NUMBER	COMMENTS ON DEAD DOGS
T118W4.0	
T119W4.0	
T120W5.0	KIDNEY DEGENERATION; LIVER DEGENERATION
T142W3.0	
T143W3.0	
T144W4.0	SPECIAL STUDY
T145W4.0	SPECIAL STUDY
T146W3.0	
T147W5.0N	SPECIAL STUDY
T148W5.0N	SPECIAL STUDY
T149W5.0N	SPECIAL STUDY
T150W5.0N	SPECIAL STUDY
T151W5.0N	SPECIAL STUDY
T152W5.0N	SPECIAL STUDY
T153W5.0N	SPECIAL STUDY
T154W3.0	SPECIAL STUDY
T155W3.0	
T156W3.0	
T157W3.0	SPECIAL STUDY
T158W0.0	
T159W0.0	
T160W1.0	

G. AMERICIUM - 241

DOG NUMBER	INJECTION			DATE			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	INJECTED	D	MO	YR	
T161W1.0	546	11.9	0.0159	30	12	76	456	
T162W1.0	546	9.64	0.0164	30	12	76	456	
T163W1.0	544	9.32	0.0162	30	12	76	456	
T164W1.7	553	11.3	0.0481	30	12	76	456	
T165W1.7	546	8.73	0.0488	30	12	76	456	
T166W1.7	544	9.28	0.0480	30	12	76	456	
T167W1.7	544	9.04	0.0482	30	12	76	456	

*²⁴¹Am dogs missing from the sequence for "test" animals have been redesignated as "Toxicity" animals and appear earlier in Table 1.

G. AMERICIUM - 241

DOG
NUMBER

COMMENTS ON DEAD DOGS

T161W1.0
T162W1.0
T163W1.0

T164W1.7
T165W1.7
T166W1.7
T167W1.7

H. LEAD - 210

DOG NUMBER	INJECTION			DATE		DAYS SINCE		DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	INJECTED D MO YR		INJECTION 3/31/78	DEATH	
T001L5.0	522	9.78	107.	24	6	69	1497	8160
T002L5.0	522	9.16	10.7	24	6	69	28	30
T003L5.0	522	9.78	107.	24	6	69	1100	6950

H. LEAD - 210

DOG NUMBER	COMMENTS ON DEAD DOGS
T001L5.0	OSTEOSARCOMA
T002L5.0	SPECIAL STUDY
T003L5.0	OSTEOSARCOMA

I. CALIFORNIUM - 252

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE		DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		INJECTED			
				D	MO	YR	
T001F5.0	586	11.4	2.81	8	9	71	36 382
T002F5.0	540	10.7	2.87	17	11	71	13 138

I. CALIFORNIUM - 252

DOG
NUMBER

COMMENTS ON DEAD DOGS

T001F5.0	SPECIAL STUDY
T002F5.0	SPECIAL STUDY

J. CALIFORNIUM - 249

DOG NUMBER	INJECTION			DATE		DAYS SINCE		DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	INJECTED D MO YR	3/31/78	INJECTION DEATH		
T001G5.0	597	12.2	2.84	24	2	71	500	2728
T002G5.0	584	10.7	2.77	24	2	71	7	39
T003G5.0	584	9.89	2.80	24	2	71	21	111

J. CALIFORNIUM - 249

DOG
NUMBER

COMMENTS ON DEAD DOGS

T001G5.0	NEPHRITIS; MYOCARDIAL INFARCTION
T002G5.0	SPECIAL STUDY
T003G5.0	SPECIAL STUDY

K. CURIUM - 243/244

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR		
T001C5.0	511	10.4	2.60	27	2	73	1142	7346
T002C5.0	485	12.2	2.64	27	2	73	6	32
T003C5.0	485	11.4	2.64	27	2	73	13	69
T004C5.0	485	12.5	2.64	27	2	73	20	107
T005C5.0	485	12.8	2.63	27	2	73	384	2613
T006C5.0	498	10.7	2.90	22	10	73	87	463

K. CURIUM - 243/244

DOG NUMBER	COMMENTS ON DEAD DOGS
T001C5.0	KIDNEY DEGENERATION; LIVER DEGENERATION
T002C5.0	SPECIAL STUDY
T003C5.0	SPECIAL STUDY
T004C5.0	SPECIAL STUDY
T005C5.0	LIVER DEGENERATION
T006C5.0	SPECIAL STUDY

L. EINSTEINIUM - 253

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE		DAYS SINCE INJECTION	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		INJECTED			
				D	MO	YR	3/31/78 DEATH
T001E5.0	470	9.82	2.87	5	6	73	7 33
T002E5.0	483	12.2	2.89	5	6	73	21 171
T003E5.0	483	11.0	2.84	5	6	73	55 201
T004E5.0	484	12.3	2.97	6	6	73	1759
T005E5.0	484	11.2	2.93	10	9	73	7 57

L. EINSTIENIUM - 253

DOG
NUMBER

COMMENTS ON DEAD DOGS

T001E5.0	SPECIAL STUDY
T002E5.0	SPECIAL STUDY
T003E5.0	SPECIAL STUDY
T004E5.0	
T005E5.0	SPECIAL STUDY

M. PLUTONIUM - 237

DOG NUMBER	INJECTION			DATE		DAYS SINCE		DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	INJECTED D MO YR		INJECTION 3/31/78	DEATH	
T001K1.0	520	9.53	0.0286	10	12	74	13	1
T002K1.0	517	10.3	0.0266	10	12	74	20	1
T003K1.0	517	9.72	0.0281	10	12	74	27	1

M. PLUTONIUM - 237

DOG
NUMBER

COMMENTS ON DEAD DOGS

T001K1.0	SPECIAL STUDY
T002K1.0	SPECIAL STUDY
T003K1.0	SPECIAL STUDY

N. URANIUM - 233

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE			DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR		
T001U5.0	539	10.4	2.91	23	2	76	94	45
T002U5.0	524	12.0	2.91	11	3	76	726	196
T003U5.0	541	11.4	2.42	25	2	76	7	4
T004U5.0	541	9.01	2.91	25	2	76	14	9
T005U5.0	541	9.08	2.96	25	2	76	21	7
T006U5.0	509	12.2	2.92	25	2	76	364	192
T007U5.0	667	10.4	2.77	10	5	76	1	1

N. URANIUM - 233

DOG. NUMBER	COMMENTS ON DEAD DOGS
T001U5.0	SPECIAL STUDY
T002U5.0	
T003U5.0	SPECIAL STUDY
T004U5.0	SPECIAL STUDY
T005U5.0	SPECIAL STUDY
T006U5.0	SPECIAL STUDY
T007U5.0	SPECIAL STUDY

O. URANIUM - 238

DOG NUMBER	INJECTION AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 3/31/78 DEATH	DOSE TO SKELETON (RADS)
T001V0.1	568	11.3	0.0001	16 11 76	500	

-147 -

O. URANIUM - 238

DOG
NUMBER

COMMENTS ON DEAD DOGS

T001V0.1

P. ANICILLARY '

DOG NUMBER	INJECTION		DATE			AGE (DAYS)	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)	INJECTED (UCI/KG)	INJECTED D MO YR	AS OF 3/31/78	DEATH	
F001A0.0						1383	
F002A0.0						2492	
M003A0.0						1451	
M004A0.0						3346	
M005A0.0						3747	
M006A0.0						5266	
M007A0.0						3896	
M008A0.0						3746	
F009A0.0						3719	
F010A0.0						2605	
F011A0.0						4198	
F012A0.0						4219	
F013A0.0						4527	
F014A0.0						3777	
F015A0.0						4874	
F016A0.0						4410	
F017A0.0						2145	
F018A0.0						5921	
F019A0.0						4166	
F020A0.0						2464	
F021A0.0						5508	
F022A0.0						4350	
M023A0.0						1741	
M024A0.0						3074	
F025A0.0						5646	
M026A0.0						4133	
M027A0.0						2130	
M028A0.0						3114	
M029A0.0						5017	
F031A0.0						5266	
F032A0.0						1990	
F033A0.0						3282	
F034A0.0						2584	
M035A0.0						529	
M036A0.0						1971	
M037A0.0						4091	
F038A0.0						3802	
M039A0.0						4406	
M040A0.0						4666	
F041A0.0						4704	
M042A0.0						1265	
F043A0.0						3883	
F044A0.0						5016	

F. ANICILLARY

DOG NUMBER	COMMENTS ON DEAD DOGS
F001A0.0	SPECIAL STUDY
F002A0.0	SPECIAL STUDY
M003A0.0	SPECIAL STUDY
M004A0.0	NOT DETERMINED
M005A0.0	TRANSITIONAL CELL CARCINOMA; NEPHRITIS; PNEUMONIA
M006A0.0	BRAIN HEMORRHAGE
M007A0.0	LYMPHOSARCOMA
M008A0.0	PROGRESSIVE PARALYSIS; CAUSE UNKNOWN
F009A0.0	VAGINAL FIBROMA
F010A0.0	SPECIAL STUDY
F011A0.0	MAMMARY CARCINOMA
F012A0.0	SEVERE OSTEOARTHRITIS
F013A0.0	SPECIAL STUDY
F014A0.0	OBTURATING EMBOLISM OF PORTAL VEIN
F015A0.0	TRANSITIONAL CELL CARCINOMA URINARY BLADDER
F016A0.0	SPECIAL STUDY
F017A0.0	TRAUMA
F018A0.0	NEPHRITIS
F019A0.0	MAMMARY GLAND CARCINOMA
F020A0.0	SPECIAL STUDY
F021A0.0	MAMMARY CARCINOMA; THYROID CARCINOMA
F022A0.0	LYMPHOSARCOMA
M023A0.0	OBTURATING PULMONARY EMBOLISM
M024A0.0	SPECIAL STUDY
F025A0.0	ISLET CELL TUMOR; PNEUMONIA
M026A0.0	SEMINOMA
M027A0.0	SPECIAL STUDY
M028A0.0	SPECIAL STUDY
M029A0.0	MELANOMA ORAL CAVITY
F031A0.0	UNDETERMINED
F032A0.0	LYMPHOSARCOMA
F033A0.0	OBTURATING PULMONARY EMBOLISM
F034A0.0	SPECIAL STUDY
M035A0.0	SPECIAL STUDY
M036A0.0	SPECIAL STUDY
M037A0.0	SPECIAL STUDY
F038A0.0	MAMMARY CARCINOMA
M039A0.0	OBTURATING PULMONARY THROMBO EMBOLISM
M040A0.0	EPIDERMOID CARCINOMA (GINGIVA); PNEUMONIA
F041A0.0	LEIOMYOSARCOMA (SPLEEN)
M042A0.0	STATUS EPILEPTICUS
F043A0.0	SPECIAL STUDY
F044A0.0	ADRENAL CORTICAL CARCINOMA

P. ANICILLARY

DOG NUMBER	INJECTION AGE WEIGHT (DAYS) (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	AGE (DAYS) AS OF 3/31/78	DOSE TO SKELETON (RADS)
F045A0.0				6182	
F047A0.0				1732	
F048A0.0				5075	
F049A0.0				4773	
M050A0.0				2264	
F051A0.0				1089	
F052A0.0				509	
F053A0.0				5520	
F054A0.0				3190	
F055A0.0				4563	
M056A0.0				701	
F057A0.0				4322	
M058A0.0				767	
M059A0.0				567	
M061A0.0				5511	
F062A0.0				5348	
F063A0.0				4530	
F068A0.0				4521	
F070A0.0				5914	
M071A0.0				1472	
M073A0.0				5695	
F074A0.0				5553	
M075A0.0				5284	
F076A0.0				5813	
F077A0.0				6046	
F078A0.0				5110	
F079A0.0				4359	
F080A0.0				5419	
F081A0.0				5921	
M082A0.0				3627	
F083A0.0				4988	
M084A0.0				5859	
M085A0.0				5499	
M086A0.0				499	
F087A0.0				4862	
F088A0.0				5367	
F089A0.0					
F090A0.0					
F091A0.0					
F092A0.0				4799	
M093A0.0					
F094A0.0					
F095A0.0				4719	

P. ANICILLARY

-151 -

DOG	NUMBER	COMMENTS ON DEAD DOGS
F045A0.0		PNEUMONIA; SENILITY
F047A0.0		SPECIAL STUDY
F048A0.0		CHRONIC PANCREATITIS
F049A0.0		ISLET CELL TUMOR; BRAIN HEMORRHAGE
F050A0.0		SPECIAL STUDY
F051A0.0		SPECIAL STUDY
F052A0.0		SPECIAL STUDY
F053A0.0		THYROID CARCINOMA
F054A0.0		SPECIAL STUDY
F055A0.0		NEPHRITIS; METASTATIC CALCIFICATION
F056A0.0		VOLVULUS + PERITONITIS
F057A0.0		UNDIFFERENTIATED MALIGNANCY
F058A0.0		SPECIAL STUDY
F059A0.0		SPECIAL STUDY
F061A0.0		FIBROSARCOMA (ABDOMEN)
F062A0.0		AORTA THROMBO-EMBOLISM
F063A0.0		MAMMARY CARCINOMA; TRANSITIONAL CELL CARCINOMA
F068A0.0		UNDIFFERENTIATED CARCINOMA
F070A0.0		FIBROSARCOMA (ORAL); NEPHRITIS
F071A0.0		SPECIAL STUDY
F073A0.0		DEGENERATION OF ADRENAL GLAND + DIABETES MELLITUS
F074A0.0		LYMPHO SARCOMA
F075A0.0		AORTIC THROMBUS
F076A0.0		EPIDERMOID CARCINOMA (ORAL); THYROID CARCINOMA
F077A0.0		
F078A0.0		MAMMARY CARCINOMA
F079A0.0		PNEUMONIA
F080A0.0		LUNG CARCINOMA
F081A0.0		FIBROSARCOMA (ORAL); NEPHRITIS
F082A0.0		LUNG CARCINOMA
F083A0.0		SARCOMA (INTESTINE)
F084A0.0		
F085A0.0		SENILITY
F086A0.0		SPECIAL STUDY
F087A0.0		
F088A0.0		
F089A0.0		REASSIGNED; SEE 1074P40
F090A0.0		REASSIGNED; SEE 1075P40
F091A0.0		REASSIGNED; SEE 1076P40
F092A0.0		
F093A0.0		REASSIGNED; SEE 1076P40
F094A0.0		
F095A0.0		REASSIGNED; SEE 1077P30

P. ANICILLARY

DOG NUMBER	INJECTION AGE WEIGHT (DAYS) (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	AGE (DAYS) AS OF 3/31/78 DEATH	DOSE TO SKELETON (RADS)
F096A0.0				4373	
F097A0.0				4117	
F098A0.0				3752	
F099A0.0				479	
M100A0.0				407	
M101A0.0				290	
F102A0.0				243	
M103A0.0				217	
M104A0.0				188	
F105A0.0				157	
F106A0.0				4320	
F107A0.0				4131	
F108A0.0				1969	
F109A0.0				2253	
F110A0.0					
F111A0.0				2923	
F112A0.0				2942	
F113A0.0					
F114A0.0				2591	
F115A0.0				2057	
F116A0.0					
F117A0.0					
F118A0.0					
F119A0.0					
F120A0.0					
F121A0.0					
F122A0.0					
F123A0.0				375	
F124A0.0					
F125A0.0					
F126A0.0				2518	
F127A0.0					
F128A0.0					
F129A0.0					
F130A0.0				2099	
F131A0.0				2098	
F132A0.0				2054	
F133A0.0				1958	
F134A0.0				1958	
F135A0.0				1934	
M136A0.0				2054	
F137A0.0				1815	
F138A0.0				1763	

P. ANICILLARY

DOG NUMBER	COMMENTS ON DEAD DOGS
F096A0.0	
F097A0.0	SPECIAL STUDY
F098A0.0	MAMMARY CELL CARCINOMA
F099A0.0	SPECIAL STUDY
M100A0.0	SPECIAL STUDY
M101A0.0	SPECIAL STUDY
F102A0.0	SPECIAL STUDY
M103A0.0	SPECIAL STUDY
M104A0.0	SPECIAL STUDY
F105A0.0	SPECIAL STUDY
F106A0.0	
F107A0.0	
F108A0.0	ENCEPHALOMALACIA (BACTERIAL)
F109A0.0	METRITIS
F110A0.0	REASSIGNED; SEE T078P30
F111A0.0	PNEUMONIA
F112A0.0	SPECIAL STUDY
F113A0.0	REASSIGNED; SEE T123P2.0
F114A0.0	
F115A0.0	GASTRIC CARCINOMA
F116A0.0	REASSIGNED; SEE F501P20+
F117A0.0	REASSIGNED; SEE F501R40+
F118A0.0	REASSIGNED; SEE F501P10+
F119A0.0	REASSIGNED; SEE F501P17+
F120A0.0	REASSIGNED; SEE F501P30+
F121A0.0	REASSIGNED; SEE F501R30+
F122A0.0	REASSIGNED; SEE F502P3.0+
F123A0.0	ACCIDENTAL STRANGULATION
F124A0.0	REASSIGNED; SEE F502P1.7+
F125A0.0	REASSIGNED; SEE F502P2.0+
F126A0.0	REASSIGNED; SEE F503P1.7
F127A0.0	REASSIGNED; SEE F503P2.0+
F128A0.0	REASSIGNED; SEE F502R40+
F129A0.0	REASSIGNED; SEE F503R30+
F130A0.0	
F131A0.0	
F132A0.0	
F133A0.0	
F134A0.0	
F135A0.0	
M136A0.0	
F137A0.0	
F138A0.0	

P. ANICILLARY

DOG NUMBER	INJECTION AGE WEIGHT (DAYS) (KG)	INJECTED (UCI/KG)	DATE INJECTED D MO YR	AGE (DAYS) AS OF 3/31/78 DEATH	DOSE TO SKELETON (RADS)
F139A0.0				1744	
F140A0.0				1807	
F141A0.0				1763	
F142A0.0				1816	
F143A0.0				1727	
F144A0.0				1899	
F145A0.0				1915	
F146A0.0				1693	
F147A0.0				1784	
F148A0.0				1693	
F149A0.0				1541	
F150A0.0				1428	
F151A0.0				1428	
F152A0.0					568
F153A0.0				1505	
F154A0.0				1367	
F155A0.0				1365	
F156A0.0				1380	
F157A0.0				1367	
F158A0.0				1356	
F159A0.0				1150	
F160A0.0				1150	
F161A0.0				1150	
F162A0.0				1150	
F163A0.0				1149	
F164A0.0				1136	
M165A0.0				365	
M166A0.0					388
M167A0.0					369
M168A0.0					517
M169A0.0					513
M170A0.0					510
M171A0.0					95
F172A0.0					518
F173A0.0					89
F174A0.0					94
F175A0.0					520
F176A0.0					521
M177A0.0					3420
M178A0.0					1168
M179A0.0					4125
F180A0.0					3658
M181A0.0					1211

P. ANICILLARY

DOG
NUMBER

COMMENTS ON DEAD DOGS

F139A0.0

F140A0.0

F141A0.0

F142A0.0

F143A0.0

F144A0.0

F145A0.0

F146A0.0

F147A0.0

F148A0.0

F149A0.0

F150A0.0

F151A0.0

F152A0.0 SPECIAL STUDY

F153A0.0

F154A0.0

F155A0.0

F156A0.0

F157A0.0

F158A0.0

F159A0.0

F160A0.0

F161A0.0

F162A0.0

F163A0.0

F164A0.0

M165A0.0 SPECIAL STUDY

M166A0.0 SPECIAL STUDY

M167A0.0 SPECIAL STUDY

M168A0.0 SPECIAL STUDY

M169A0.0 SPECIAL STUDY

M170A0.0 SPECIAL STUDY

M171A0.0 SPECIAL STUDY

F172A0.0 SPECIAL STUDY

F173A0.0 SPECIAL STUDY

F174A0.0 SPECIAL STUDY

F175A0.0 SPECIAL STUDY

F176A0.0 SPECIAL STUDY

M177A0.0 SPECIAL STUDY

M178A0.0 SPECIAL STUDY

M179A0.0 SPECIAL STUDY

F180A0.0 SPECIAL STUDY

M181A0.0 SPECIAL STUDY

P. ANICILLARY

DOG NUMBER	INJECTION		INJECTED (UCI/KG)	DATE INJECTED		AGE (DAYS)	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIGHT (KG)		D	MO	YR	
M182A0.0							196
M183A0.0							3064
F184A0.0							184
M185A0.0							524
M186A0.0							189
F187A0.0							93
F188A0.0							193
F189A0.0							262
F190A0.0							372
F191A0.0							176
M192A0.0							91
M193A0.0							369
F194A0.0							371
M195A0.0							362
M196A0.0							1168
M197A0.0							275
F198A0.0							274
M199A0.0							279
M200A0.0							263
F201A0.0							267
M202A0.0							4150
F203A0.0							3546
M204A0.0							182
F205A0.0							
F206A0.0						982	
F207A0.0						951	
M208A0.0							797
M209A0.0							782
M210A0.0						1024	
F211A0.0						852	
F212A0.0						796	
F213A0.0						796	
F214A0.0						794	
F215A0.0						751	
F216A0.0						1550	
F217A0.0						1150	
F218A0.0						1132	
F219A0.0						1108	
F220A0.0						1060	
F221A0.0						668	
F222A0.0						569	

P. ANICILLARY

DOG
NUMBER

COMMENTS ON DEAD DOGS

M182A0.0	SPECIAL STUDY
M183A0.0	SPECIAL STUDY
F184A0.0	SPECIAL STUDY
M185A0.0	SPECIAL STUDY
M186A0.0	SPECIAL STUDY
F187A0.0	SPECIAL STUDY
F188A0.0	SPECIAL STUDY
F189A0.0	SPECIAL STUDY
F190A0.0	SPECIAL STUDY
F191A0.0	SPECIAL STUDY
M192A0.0	SPECIAL STUDY
M193A0.0	SPECIAL STUDY
F194A0.0	SPECIAL STUDY
M195A0.0	SPECIAL STUDY
M196A0.0	SPECIAL STUDY
M197A0.0	SPECIAL STUDY
F198A0.0	SPECIAL STUDY
M199A0.0	SPECIAL STUDY
M200A0.0	SPECIAL STUDY
F201A0.0	SPECIAL STUDY
M202A0.0	SPECIAL STUDY
F203A0.0	SPECIAL STUDY
M204A0.0	SPECIAL STUDY
F205A0.0	SPECIAL STUDY
F206A0.0	
F207A0.0	
M208A0.0	SPECIAL STUDY
M209A0.0	SPECIAL STUDY
M210A0.0	
F211A0.0	
F212A0.0	
F213A0.0	
F214A0.0	
F215A0.0	
F216A0.0	
F217A0.0	
F218A0.0	
F219A0.0	
F220A0.0	
F221A0.0	
F222A0.0	

BONE SARCOMA INDUCTION IN BEAGLES BY LOW DOSES
FROM ^{239}Pu AND ^{226}Ra

Charles W. Mays, Webster S. S. Jee, Glenn N. Taylor,
and Walter Stevens

ABSTRACT: In our on-going low-level studies in beagles, ^{239}Pu has induced 3 bone sarcomas at average skeletal doses of about 22 rad and 1 bone sarcoma (and 1 head sinus carcinoma) at 2 rad; ^{226}Ra has caused 1 bone sarcoma at 275 rad. More α -induced cancers are expected because most of the dogs in the low-level study are still alive. Results within the next several years should indicate whether the dose-response from low doses of ^{239}Pu is linear, concave upward or concave downward, with respect to bone sarcoma induction in beagles.

From our original and completed lifespan study of dogs injected with 0.016-0.048 $\mu\text{Ci } ^{239}\text{Pu}/\text{kg}$ or 0.058-1.07 $\mu\text{Ci } ^{226}\text{Ra}/\text{kg}$ we have derived linear risk coefficients, in terms of average skeletal dose of: ⁽¹⁾

5200 bone sarcomas/ 10^6 beagle $\cdot$ rad from ^{239}Pu

320 bone sarcomas/ 10^6 beagle $\cdot$ rad from ^{226}Ra

It is now appropriate to ask, "What is the shape of the dose-response in beagles at lower doses of these α -emitters: Is it approximately linear, or is it concave upward, or is it concave downward?" We cannot answer this question at the present time, but we draw attention to an important low dose study we started in 1964 that is now in progress (Table 1). Results within several more years should indicate the dose-response that is best supported experimentally.

Based on the linear risk coefficients previously derived, 18.4 cases of induced bone sarcoma would eventually be expected when all the 200 dogs in the low-level ^{239}Pu study have died, and 1.7 cases among the 84 dogs ^{226}Ra -injected dogs when they die.

Table 1. BONE SARCOMAS IN LOW-LEVEL BEAGLES (INJECTED 1964-1974)

Nuclide	Dose Level	Injected $\mu\text{Ci/kg}$	Av. Skel. Rad	Total	Eventual	Dead Dogs (1 Dec. 1977)	
			at 10 Years Post-Injection	Injected Dogs	Predicted* Bone Sar.	Total Dead	Observed Bone sar.
Pu-239	1	0.015	55	12	3.7	1	0
	0.7	0.010	37	38	7.9	1	0
	0.5	0.0053	22	38	4.7	8	3
	0.2	0.0018	7	46	1.8	15	0
	0.1	0.00070	2	28	0.3	11	1**
	0	0	0	38	0	11	0
	Sum			200	18.4	47	4
Ra-226	1	0.066	275	10	0.9	6	1
	0.5	0.021	70	32	0.7	16	0
	0.2	0.0074	25	10	0.1	8	0
	0	0	0	32	0	7	0
	Sum			84	1.7	37	1

* Predicted cases of bone sarcoma among the dogs at a given dose level:

for ^{239}Pu = (5200 bone sarcomas/ 10^6 beagle·rad) (No. of beagles) (dose in rad)

for ^{226}Ra = (320 bone sarcomas/ 10^6 beagle·rad) (No. of beagles) (dose in rad)

** One carcinoma of the frontal sinus has also occurred in a beagle at this dose (2 rad from ^{239}Pu).

As of 1 December 1977, 4 cases of bone sarcoma have appeared among the 47 dead ^{239}Pu dogs, and for ^{226}Ra , 1 bone sarcoma has appeared among the 37 dead ^{226}Ra dogs. But the results to date should be viewed with extreme caution, not only because of the small number of tumors but, more importantly, because most of the low-level dogs are still alive. At low doses from long-lived emitters, the induced bone sarcomas tend to have very long appearance times.

The one conclusion we can state at this time, in view of the bone sarcoma at 2 rad from ^{239}Pu (and a head sinus carcinoma in another dog at the same dose), is that if a threshold exists in the beagle for ^{239}Pu -induced cancer, it is below an average skeletal dose of 2 rad.

Both of these tumors at 2 rad appear to be radiation-induced, since bone sarcomas and head sinus carcinomas are extremely rare in non-irradiated beagles⁽²⁾ and have never appeared in any of our controls. Both of these types of cancer have been induced by higher doses of Pu-239 and Ra-226 in beagles, and by ^{226}Ra in humans.⁽³⁾

It must be remembered that the bone cancer risk per rad is about 25 times greater in beagles than in humans.⁽¹⁾ Thus, the effect from an average skeletal dose of 2 rad in the beagle may correspond to that from about 50 rad in man.

REFERENCES

1. C.W. Mays, H. Spiess, G.N. Taylor, R.D. Lloyd, W.S.S. Jee, S.S. McFarland, D.H. Taysum, T.W. Brammer, D. Brammer, and T.A. Pollard, Estimated risk to human bone from ^{239}Pu , in The Health Effects of Plutonium and Radium, W.S.S. Jee (Ed.), J.W. Press, University of Utah, Salt Lake City, pp. 343-362 (1976).
2. C.W. Mays and G.N. Taylor, Low natural incidence of osteosarcomas in beagles, in Research in Radiobiology, University of Utah Report C00-119-231, pp. 70-75 (1964).
3. R.D. Evans, The effect of skeletally deposited alpha-ray emitters in man, Brit. J. Radiol. 39: 881-895 (1966).

DIFFERENCES IN THE INITIAL DEPOSITION OF Pu AND Ra IN THE SKELETON

D. R. Atherton, F. W. Bruenger and W. Stevens

The ratio (still unknown) relating the experimentally determined effects of Pu and Ra in some animal species to observed effects of various isotopes of Ra in man presently provides the most reasonable basis for an assessment of the risk resulting to man from Pu. Extensive studies with the beagle have shown that an evaluation of this ratio on the basis of average skeletal radiation dose is complicated by several factors, one of which is the difference in the initial (gross) distribution of Pu and Ra between the various skeletal parts.

The initial deposition of Pu and Ra in the whole skeleton and in individual parts of the skeleton as seen after injection of the two nuclides as their citrates is shown in the following table. This table compares the initial deposition (% injected dose/part) of Pu in 11 beagles injected with 0.016 μCi Pu/kg and the deposition in 5 beagles injected with 9 μCi Ra/kg. The ratio $\frac{\text{Pu}}{\text{Ra}}$ is a measure of the variation in the initial deposition of the two nuclides. Confidence limits for the observed dissimilarities are given. The table demonstrates that significant differences in the distribution within the various skeletal parts exist although the total deposition of the two nuclides in the whole skeleton is practically the same. It is assumed that the observed diversity is the result of different mechanisms by which the nuclides interact with the elements of skeletal tissue.

INITIAL DEPOSITION OF Pu AND Ra IN INDIVIDUAL BONES
% of Injected Dose/Part

	Pu	Ra	$\frac{\text{Pu}}{\text{Ra}}$	p*
Skull	3.53	5.57	0.634	< 0.001
Mandibles	1.08	2.02	0.535	< 0.001
Cervical Vertebrae	2.43	2.82	0.862	0.2 - 0.3
Thoracic Vertebrae	7.00	5.49	1.28	0.01
Lumbar Vertebrae + Sacrum	6.07	5.83	1.04	~ 0.60
Caudal Vertebrae	0.263	0.77	0.342	< 0.001
Paws	1.78	2.67	0.667	< 0.001
Radii	0.396	0.78	0.508	< 0.001
Ulnae	0.462	0.86	0.537	<< 0.001
Humeri	5.89	3.70	1.59	< 0.001
Scapulae	2.46	2.35	1.05	~ 0.50
Tibiae-Fibulae	1.90	2.06	0.922	~ 0.30
Femora	4.20	3.46	1.21	~ 0.02
Pelvis	3.17	3.56	0.890	0.1 - 0.2
Ribs	6.57	6.14	1.07	0.4 - 0.5
Sternum	0.708	1.78	0.398	~ 0.5
TOTAL	48.9	49.9	0.980	0.7 - 0.8

* Probability of samples coming from the same population

REVISION OF SKELETAL DOSE CALCULATION IN BEAGLES INJECTED
WITH 2.8 $\mu\text{Ci}/\text{KG}$ AT 3 MONTH OF AGE

W. Stevens, D. R. Atherton and F. W. Bruenger

In an earlier report (C00-119-252) the average skeletal radiation dose had been reported for 12 beagles which had been injected with 2.82 μCi ^{239}Pu at three month of age. These animals died from osteosarcoma at an average time after injection of 1306 ± 163 days. In calculating the average skeletal dose, a tentative equation for the retention had been used and the growth of the skeleton during the time from injection to death had not been considered. This led to abnormally high values of the average skeletal dose.

Based on data obtained from a serial sacrifice study in juveniles the following skeletal retention equation was calculated which adequately describes the Pu retention in those twelve animals.

$$R = 19.5e^{-0.0011t} + 51.8$$

where R is in % of injected dose and t is in days.

Also, the serial sacrifice program provided accurate data from which the following equation describing the growth of the skeletal mass (w_{Sk}) at time t after birth was calculated.

$$w_{\text{Sk}} = [1 - (0.35e^{-0.01t} + 0.60e^{-0.005t})] \times \bar{w}_{\text{Sk}}$$

In this equation, $\bar{w}_{\text{Sk}}$ is the average skeletal wet weight at time of maturity. For the twelve animals in this study the average of four measured skeletal weights was taken. Its numerical value was 0.988 kg. However for dose calculations of individual dogs, each respective measured skeletal weight should

be used.

The average skeletal doses were then reevaluated using the concentration of Pu [B] in these animals as given by:

$$[B] = \frac{19.5e^{-0.0011t} + 51.8}{\bar{W}_{Sk} [1 - (0.35e^{-0.01t} + 0.60e^{-0.005t})]}$$

From this, the skeletal dose (D) is calculated by:

$$D = \frac{0.00268 \times A}{\bar{W}_{Sk}} \times \int_0^t \frac{19.5e^{-0.0011t} + 51.8}{[1 - (0.35e^{-0.01t} + 0.60e^{-0.005t})]} dt$$

in which A is the total μCi Pu injected. This leads to an average skeletal dose of 2785 rads for the above twelve beagles. Individual data for the skeletal dose to each animal as shown in the injection tables will be corrected for the 1979 progress report.

SERIAL STUDY OF ^{239}Pu RETENTION AND DISTRIBUTION IN THE JUVENILE BEAGLE

D. R. Atherton, F. W. Bruenger and W. Stevens

A program designed to evaluate the initial deposition and changes in the retention and distribution of ^{239}Pu as a function of time following its administration to the juvenile (3 month old) beagle is in its second year. Presently, data have been obtained by serial sacrifice at 7, 14, 28, 56, 89, 119, 360, and 364 days following injection of 0.096 $\mu\text{Ci Pu/kg}$ (2-level).

Concentrations of Pu (% of injected Pu/gm of tissue) measured in some of the soft tissues are shown in Table 1. Although characterized by considerable scatter the values shown seem to indicate that concentrations in the liver, kidney and muscle changed very little during that period. Loss from

TABLE 1
% OF INJECTED Pu/GRAM OF TISSUE

	Liver	Kidney	Spleen	Lung	Gonad	Adrenal	Muscle
σ							
7	0.0692	0.00745	0.0211	0.00706	0.0028	0.0093	0.0030
28	0.0663	0.00876	0.0117	0.00204	0.0030	0.0061	0.0004
119	0.0762	0.00903	0.00989	0.00056	0.0004	0.0048	0.0004
364	0.0765	0.00665	0.00734	0.00070	0.0003	0.0031	0.0003
ϕ							
19	0.0928	0.00850	0.0232	0.00376	0.0039	0.0120	0.0009
56	0.0709	0.00999	0.0164	0.00284	0.0033	0.0087	0.0009
89	0.0862	0.00935	0.0163	0.00359	0.0054	0.0100	-----
360	0.0795	0.00717	0.00646	0.00082	0.0087	0.0040	0.0046

the spleen, lung, testicle and adrenal seemed to be occurring. Changes in Pu concentration of the ovary are not very remarkable but, if a trend is indicated, it appears to suggest some translocation of nuclide to the organ.

The skeleton, of course, retains the major fraction of the injected Pu. Initial deposition is about 72% of that injected, considerably more than the 50% skeletal deposition associated with the injection of Pu in the young adult beagle.

Skeletal retention of Pu by the young adult can be described by an equation of the form

$$B = ae^{-bt} + C$$

where B is % of the injected dose retained by the skeleton; a is that fraction (% of injected Pu) in the skeleton which changes with time; b is its rate of change per unit of time t (days); and c is that fraction (%) of Pu deposited in bone for which a change with time is too small to be measured.

The equation describing the retention for 2-level young adult beagles is:

$$B = 28.6e^{-0.0011t} + 21.0 \quad (\text{Eq. 1})$$

Inspection of presently available values for skeletal retention by the 2-level juvenile shows that not enough time has passed to justify any speculation about the shape this retention curve will take.

Presently accrued data were used to derive the following equation which has a correlation coefficient of 0.95.

$$B = 71.7e^{-0.0012t} \quad (\text{Eq. 2})$$

Using equations 1 and 2 one can calculate that 1 year after injection the juvenile and young adult beagle will retain 64% and 81% respectively of their initial skeletal deposits of Pu.

In Table 2 the skeletal distribution and retention is shown for short times and extended times following injection of juvenile, young adult and mature beagles.

Inspection of the table shows that there are differences in the magnitude of skeletal retention associated with age at injection and that the distribution of retained Pu among the skeletal parts may also change with that parameter.

TABLE 2
PERCENT OF INJECTED Pu/SKELETAL PART IN VARIOUS AGE GROUPS

Age	Short Times Post-Injection			Long Times Post-Injection		
	Juvenile	Young Adult	Mature	Juvenile	Young Adult	Mature
Dose Level*	2	1	1.7 & 2	5	0.5	3
n	6	11	2	4	2	2
Skull	5.37	3.73	1.54	4.36	3.03	2.08
Mandible	1.83	1.25	0.87	1.60	1.20	0.72
Humeri	6.37	4.40	3.64	5.00	1.66	2.59
Pelves	4.29	2.79	3.52	4.07	1.59	1.72
Thoracic V.	6.40	5.68	5.07	5.34	2.68	3.27
Lumbar V. + Sacrum	6.81	4.67	5.22	5.29	2.73	3.38
Scapulae	2.82	2.03	2.52	2.60	1.12	1.40
Ribs-Sternum	5.77	5.29	5.90	4.36	2.29	5.79
Cervical V.	5.04	2.09	1.89	4.30	1.44	1.43
Caudal V.	0.91	0.28	0.27	0.84	0.29	0.31
Paws	7.02	1.78	0.94	6.94	1.28	1.48
Radii	1.97	0.45	0.23	1.58	0.38	0.28
Ulnae	2.00	0.46	0.18	1.61	0.40	0.22
Tib-Fib	4.44	1.53	0.66	3.18	0.76	0.78
Femora	6.33	3.30	2.57	4.83	1.42	1.82

* A definition of the dose level may be found in the preface to the Injection Tables of this volume.

COMPARISON OF SOME SKELETAL EFFECTS OF ^{239}Pu ADMINISTERED AT
3 MONTHS VS. 17 MONTHS OF AGE IN BEAGLES

J. W. Hitchman, G. N. Taylor, J. A. Eaton,
L. R. Shabestari, and W. Angus

ABSTRACT: Fracture incidence and healing rates have been intercompared in beagles injected with ^{239}Pu at 17 months and 3 months of age. At the same injected dose (^{239}Pu 2.86 $\mu\text{Ci/kg}$), beagles injected at 3 months of age developed significantly fewer fractures, and the incidence of healed fractures was higher.

Growth retardation, which has been reported in humans receiving I.V. Ra therapy in their youth, was not observed in beagles injected I.V. with 2.86 $\mu\text{Ci } ^{239}\text{Pu/kg}$ at 3 months of age.

Changes, however, radiographically apparent in the trabecular and cortical structure of the metaphaseal area was seen in dogs injected at 3 months of age, but not in those injected at 17 months of age.

INTRODUCTION

Skeletal injury, resulting in a significant number of pathological fractures, is common in beagles with relatively high retained skeletal burdens of ^{239}Pu .⁽¹⁻¹⁰⁾ A high incidence of fractures in the axial skeleton and pelvis, with many non-healing fractures, resulted when beagles were injected at about 17 months of age with 2.86 $\mu\text{Ci/kg } ^{239}\text{Pu}$.^(1,8)

Spiess⁽¹¹⁾ and Mays, Spiess, and Gerspach⁽¹²⁾ summarized the effects of ^{224}Ra therapy given German patients. Growth retardation was noted in 42% of patients who had been treated in their youth. Polednak did not observe impaired growth in female radium dial painters exposed between ages 14-29 years to ^{226}Ra and ^{228}Ra .⁽¹⁴⁾

Long bone measurements were recorded from beagles injected at three months of age with ^{239}Pu and are compared to similar measurements from an uninjected control group. It is the purpose of this report to intercompare the growth data

and fracture incidence, distribution, and healing rate in beagles injected with 2.86 $\mu\text{Ci } ^{239}\text{Pu/kg}$ at approximately three months of age and 17 months of age.

METHODS

The animals summarized were purebred beagles, progeny from a moderately inbred colony.⁽⁴⁾ Environmental, dietary, and general animal care factors were comparable for each animal throughout its lifespan. A complete physical and radiographic examination was performed at approximately six-month intervals on all animals. At death or sacrifice a detailed postmortem examination was performed, and a complete set of radiographs was taken of the defleshed skeleton. Radiographs of the defleshed bones were examined for evidence of fractures, healed or unhealed. The individual sequential lifetime x-ray series was then examined backward to determine when fractures occurred and when they healed (Table 1). Data from beagles injected at 17 months of age (young adults) are from Taylor et al.⁽¹⁾ and are so labeled where presented for comparison.

The percentages illustrated in Fig. 1 were calculated by dividing the total number of fractures occurring in a specific bone by the total number of these bones present and multiplying by 100. For example, if 12 dogs were evaluated, the total number of bones used in computing the percentage of mandibular fractures would be 24. Twenty-six ribs per dog were used in computing the percentage of rib fractures.⁽¹⁾

Long bone measurements were made from radiographs of defleshed, disarticulated bones. Dogs injected at three months of age with 2.86 $\mu\text{Ci } ^{239}\text{Pu/kg}$ were compared with uninjected controls (Table 2) and evaluated by the "T" test (Table 3).

RESULTS

Table 1 and Figure 1 summarize the frequency and distribution of fractures in beagles injected at 3 months of age compared to those reported by Taylor et al.⁽¹⁾ injected at 17 months of age. These data indicate the following trends:

1. The fracture incidence was lower when injection was given at three-months of age as compared to 17-months of age. There was a total of 31 fractures in 12 dogs (2.6/dog) for the three-month group compared to 121 fractures in eight dogs (15.1/dog) for the 17-month group (Table 1).
2. In the three-month group, relatively fewer rib and thoracic vertebral fractures occurred, and no pelvic fractures were observed.
3. Rib fractures tended to be near the distal epiphysis in the three-month group, as in the 17-month group.⁽¹⁾ All three-month group rib fractures healed rapidly, being completely healed at postmortem, with the exception of one recent fracture in the process of healing. This is compared to a 39% unhealed rib fracture rate reported in beagles injected at 17-months of age.⁽¹⁾
4. Rib fractures occurred later and were not observed until 22-months of age in the three-month injection group.
5. Although the most common location of rib fractures was similar in both groups, the "hot line"^(1,7,10) noted in the 17-month group was not so prominent in the group injected at three-months of age (Fig. 2A,B,C).
6. Of the 15 rib fractures observed in the juvenile (three-month) group, 12 were at the 4/5 and 3 were at the 3/5 locations (if the rib is divided into 5 equal segments beginning at the spinal articulation); 12 of the 15 fractures involved the right rib cage.

DISCUSSION

Retention and concentration of ^{239}Pu in the beagle skeleton is a function of age at the time of injection, ^(15,16) resulting in greater deposition in juvenile skeletons than in those of young adults (17 months of age at injection) or adults (≥ 60 months of age at injection). It might, therefore, be assumed that greater damage would occur to the juvenile bone resulting in more fractures and possibly retardation of growth. Stevens et al., point out that at the same injected dose level ($\mu\text{Ci/kg}$), the early concentration of ^{239}Pu in the juvenile skeleton will be higher than that in the young adult since the initial juvenile retention is higher. However, even though the terminal fractional skeletal retention in the juvenile is also higher, the concentration becomes progressively lower in the juveniles ⁽¹⁶⁾ since the skeletal growth continues during the early part of the exposure period. This may explain the fewer fractures observed in the juvenile group. Obviously, the highest injected dose studied, $2.86 \mu\text{Ci } ^{239}\text{Pu/kg}$, was too low to retard growth.

Rib fractures were by far the most common fractures in both groups. The retained ^{239}Pu is not uniformly distributed throughout the skeleton. In the young adult, the rad dose to the rib for ^{239}Pu is about 1.6 the average skeletal dose. ⁽⁸⁾ Therefore, greater radiation toxicity might be expected in the ribs because of this high retention plus the relatively late closure of the rib epiphyses.

Another consideration with regard to rib fractures is that those dogs injected at 17 months of age had a higher dose at the rib epiphysis just prior to its closure resulting in "hot line" ^(1,7,10) lesions and predisposition to fracture at that site. The juvenile dogs tended to dilute their dose through continued growth and the dose was distributed over a wider portion of the distal rib as growth continued in that area. Also, it has been shown that in beagles

injected with Pu as juveniles there is significantly lower relative deposition in the rib cage as compared to dogs injected as young adults.⁽¹³⁾ This may explain the absence of a well defined "hot line" in the younger injection group and may have contributed to fewer observed rib fractures. The reason for, or significance of, the predominance of right side fractures was not determined.

Juvenile beagles averaged less than 1/2 the weight of young adults. Because of growth, distribution, and retention factors, beagles injected at three-months of age with 2.86 $\mu\text{Ci/kg}$ ^{239}Pu are similar to beagles injected at 17-months of age with 0.9 $\mu\text{Ci/kg}$, with regard to cumulative rads to skeleton and time of injection to death.⁽¹⁶⁾ However, considering fracture incidence, Taylor et al., found only eight unhealed and two healed fractures in eight beagles given 0.9 $\mu\text{Ci/kg}$ at 17-months of age. Only one rib fracture was reported.⁽¹⁾

Long bone measurements are tabulated in Table 2 for dogs injected at three-months of age for uninjected controls. "T" test values are shown in Table 3. Long bone growth retardation in humans, resulting from ^{224}Ra therapy during youth,^(11,12) led us to look for similar changes in beagles given ^{239}Pu during their youth. Growth retardation was not observed in these animals (Table 3). However, a definite change was noted radiographically in long bone structure following ^{239}Pu injection. The changes were seen consistently and were most pronounced in the humeri, consisting of a transverse line across the shaft with thinning of the cortices and alteration to the trabecular pattern proximal to the line (Fig. 3C). The transverse sclerotic line is considered to represent the location of the proximal humeral epiphysis at the time of injection (Fig. 3D). The radiographically apparent injury occurred in bone laid down (new bone growth) after injection. These changes were not seen in uninjected controls (Fig. 3A) nor in dogs injected at about 17-months of age (Fig. 3B).

The humeral epiphysis has closed seven-months prior to injection in young adults, but is still open in the juvenile injection group (Fig. 3D). In spite of this radiographically apparent change in the humeri, fractures did not occur in the humeri of beagles injected at three-months of age. Growth retardation in humans has been reported only in individuals receiving multiple injections of ^{224}Ra during youth.^(11,12) Chronic ingestion of ^{226}Ra and ^{228}Ra did not cause growth retardation in young dial painters.⁽¹⁴⁾ Beagles at this laboratory have been injected with ^{226}Ra at three-months of age and are presently being maintained on lifespan studies. At postmortem, bone length measurements will be taken to determine the effect of ^{226}Ra on growth.

ACKNOWLEDGMENTS

Because of the time period covered, it is impossible to list all who have contributed to the collection of material reported herein. Special assistance was provided by D. R. Atherton (rad dose calculations) and is gratefully acknowledged.

REFERENCES

1. Taylor G.N., Christensen W.R., Jee W.S.S., Rehfeld C.E., and Petermann P. Intercomparison of pathological fractures in beagles injected with ^{226}Ra , ^{228}Ra , ^{239}Pu or ^{90}Sr . *Health Physics* 12: 361 (1966).
2. Aub J.C., Evans R.D., Hempelmann L.H., and Mertland H.S. The late effects of internally-deposited radioactive materials in man. *Medicine* 31: 221 (1952).
3. Christensen W.R., Smith C.C., Rehfeld C.E., and Taylor G.N. Radiographic changes in internally irradiated dogs. in Proc. of the Symposium of Some Aspects of Internal Irradiation (Dougherty, Jee, Mays, and Stover, Eds.), Pergamon Press, Oxford, p. 63 (1962).

5. Finkel M.P., Flynn R.J., and Beskis B.O. Pathological consequences of Sr^{90} in growing beagles: Interina observations. *Radiation Research* 11: 443 (1959).
6. Jee W.S.S. and Arnold J.S. Effect of internally deposited radioisotopes upon blood vessels of cortical bones. *Proc. Soc. Biol. and Med.* 105: 351 (1960).
7. Jee W.S.S. and Arnold J.S. The toxicity of plutonium deposited in skeletal tissues of beagles. *Lab. Invest.* 10: 797 (1961).
8. Rehfeld C.E., Stover B.J., Taylor G.N., and Mays C.W. Fracture incidence in beagles receiving single injections of radium and plutonium. in Proc. of the Symposium on Some Respects of Internal Irradiation (Dougherty, Jee, Mays, and Stover, Eds.), Pergamon Press, Oxford, p. 131 (1962).
9. Taylor G.N., Christensen W.R., Jee W.S.S., Rehfeld C.E., and Fisher W. Anatomical distribution of radiation-induced fractures in beagles. in *University of Utah Radiobiology Laboratory Annual Report C00-119-225*, p. 31 (1962).
10. Taylor G.N., Christensen W.R., Jee W.S.S., Rehfeld C.E., and Fisher W. Anatomical distribution of fractures in beagles injected with Pu^{239} . *Health Physics* 8: 609 (1962).
11. Spiess H. ^{224}Ra -induced tumors in children and adults. in Delayed Effects of Bone-Seeking Radionuclides (Mays C.W., Jee W.S.S., Lloyd R.D., Eds.), Univ. of Utah Press, pp. 227 (1969).
12. Mays C.W., Spiess H., Gerspach A. *Proc. of International Symposium at Alta, Utah, on Biological Effects of ^{224}Ra and thorotrast.* *Health Phys.* (in press).
13. Lloyd R.D. and McFarland S.S. Plutonium retention, excretion and distribution in juvenile beagles soon after injection. *Radiat. Res.* 67: 577 (1976).
14. Polednak A.P. Adult height and weight of female radium dial painters, with analysis of radiation effect on growth. *Human Biology* 49: 1 (1977).

15. Stevens W., Atherton D.R., Bates D., and Bruenger F. The deposition of ^{239}Pu in the skeleton and soft tissues of beagles: Effect of age at time of injection. University of Utah Radiobiology Laboratory Annual Report C00-119-225, p. 172 (1976).
16. Stevens W., Atherton D., Bruenger F., Stover B., Gleason M., and Buster D. Retention and distribution of ^{239}Pu in beagles injected at three months of age. University of Utah Radiobiology Lab. Annual Report C00-119-225, p. 210 (1977).
17. Miller M. Guide to the Dissection of the Dog. 3rd Edition (1958), Edwards Brothers, Inc., Ann Arbor, Mich.

TABLE 1

FRACTURE SITES-HEALED & UNHEALED

		3 MONTH INJ. GROUP		17 MONTH INJ. GROUP*	
		U	H	U	H
AXIAL SKELETON					
MANDIBULAE		2	-	1	-
HEAD (EXCEPT MAND.)		-	-	-	-
CERVICAL VERTEBRAE		-	-	-	-
THORACIC VERTEBRAE					
	1	4	-	1	-
	2	3	1	4	-
	3	-	-	6	-
	4	-	-	5	-
	5	-	-	3	1
	6	-	-	2	-
	7	-	-	-	-
	8	-	-	-	-
	9	-	-	-	-
	10	-	-	-	-
	11	-	-	-	-
	12	-	-	-	-
	13	-	-	-	-
RIBS					
	1	-	7	4	5
	2	-	-	-	1
	3	-	2	1	1
	4	-	-	-	2
	5	-	-	-	7
	6	-	1	2	4
	7	-	2	1	10
	8	-	1	4	8
	9	-	2	4	11

* From Taylor, et al

U = Unhealed Fractures

H = Healed Fractures

TABLE 1 (CONTINUED)

	3 MONTH INJ. GROUP		17 MONTH INJ. GROUP *	
	U	H	U	H
RIBS				
10	-	-	6	6
11	-	-	1	6
12	-	-	2	1
13	-	-	1	2
LUMBAR VERTEBRAE				
1	-	-	-	-
2	-	-	-	-
3	-	-	-	-
4	-	-	-	-
5	-	-	-	-
6	-	-	-	-
7	3	-	-	-
SACRAL VERTEBRAE	-	-	-	-
COCCYGEAL VERTEBRAE	-	-	-	-
<u>APPENDICULAR SKELETON</u>				
SCAPULAE	-	-	-	-
HUMERI	-	-	1	-
RADII	-	-	-	-
ULNAE	-	1	1	-
CARPI	-	-	-	-
METACARPI	1	1	1	1
ILIA	-	-	1	2
PUBES	-	-	1	-
ISCHIA	-	-	-	-
FEMORA	1	-	-	-
TIBIAE	-	-	-	-
FIBULAE	-	-	-	-
METATARSI	-	-	-	-
	<u>14</u>	<u>17</u>	<u>53</u>	<u>68</u>

* From Taylor, et al

U = Unhealed Fractures

H = Healed Fractures

TABLE 2

AVERAGE LONG BONE LENGTH (mm)

	<u>EXPERIMENTALS-P5Y GROUP</u>			<u>CONTROLS-PO GROUP</u>		
	<u>TOTAL</u>	<u>FEMALES</u>	<u>MALES</u>	<u>TOTAL</u>	<u>FEMALES</u>	<u>MALES</u>
HUMERI	113	110	117	110	105	114
RADII	102	98	107	100	94	104
ULNAE	125	120	130	121	117	124
METACARPI	48	45	50	46	43	48
FEMORI	121	117	125	118	112	123
TIBIAE	120	116	125	117	111	122
METATARSI	52	50	55	50	48	52
	<u>12 DOGS</u>			<u>11 DOGS</u>		

TABLE 3

"T" VALUES FOR LENGTH VARIATIONS
OF LONG BONES IN PLUTONIUM vs
CONTROL BEAGLE

<u>BONE</u>	<u>"T" VALUE*</u>
HUMERI	1.5
RADI I	1.0
ULNAE	1.5
METACARPI	1.8
FEMORI	1.1
TIBIAE	0.9
METATARSI	1.0

* SIGNIFICANT AT 2.2 (95%
CONFIDENCE INTERVAL).

Fig. I Fracture distribution as a percent of total bones.

Fig. 2a 3 MONTHS INJECTION GROUP

NOTE: HEALED FRACTURES AT MID RIBS 8 AND 9 OF RIGHT RIBS, AND ABSENCE OF "HOT LINES".

Fig. 2b 17 MONTH INJECTION GROUP

NOTE: FRACTURES PRIMARILY AT "HOT LINE". THESE ARE UNHEALED FRACTURES FORMING FALSE JOINTS (1).

"HOT LINES" IN UNFRACTURED RIBS INDICATED BY ARROWS (2).

Fig. 2c CONTROL

RIBS FROM UNINJECTED CONTROLS DO NOT SHOW "HOT LINE"
AND DO NOT TEND TO FRACTURE.

Fig. 3a

3b

3c

3d

3a - UNINJECTED CONTROL

3b - INJECTED AT 17 MONTHS AGE

{ SHOWING NORMAL CORTICAL
AND TRABECULAR PATTERN.
NO TRANSVERSE SCLEROTIC
ZONE IS NOTED.

3c - INJECTED AT 3 MONTHS AGE

1. TRANSVERSE SCLEROTIC ZONE CORRESPONDING TO LOCATION OF PROXIMAL EPIPHYSIS AT TIME OF INJECTION. (SEE 3d)
2. CORTICES ARE THICKENED NEAR TRANSVERSE LINE AND THINNED PROXIMAL TO LINE.
3. TRABECULAR PATTERN IS DISRUPTED WITH LOSS OF NORMAL CONTINUITY.

d - HUMERUS AT 3 MONTHS AGE (TIME OF INJECTION).

NOTE THAT PROXIMAL EPIPHYSEAL PLATE APPROXIMATES THE SCLEROTIC LINE IN (3c). THE PROXIMAL EPIPHYSIS WILL CLOSE AT ABOUT 10 MONTHS OF AGE (17).

USE OF RIB BIOPSY SPECIMENS IN UNDERSTANDING SKELETAL KINETICS OF Pu-239

D.B. Kimmel, D.R. Atherton, W. Stevens, F.W. Bruenger and W.S.S. Jee

ABSTRACT: Rib biopsy specimens from Pu-239 injected beagles were analyzed radiochemically, autoradiographically, and by quantitative histology. Results were compared to earlier data obtained from a few serial sacrifice animals. Data compare favorably with those seen in studies of whole animal skeletons, leading to the conclusion that study of a large number of biopsy specimens will yield reliable information on retention of Pu, bone surface concentration of Pu, and bone turnover.

In order to understand the effect of Pu-239 on the skeletal turnover of juvenile and mature beagles during the post-injection period, interim data on skeletal retention are needed. This need can be met most thoroughly by a serial sacrifice program, but also may be adequately served by the analysis of rib biopsy specimens from lifespan dogs. Information can easily be gained on three aspects: 1) Pu-239 retention by radiochemical analysis, 2) trabecular surface concentration of Pu-239 by quantitative neutron-induced autoradiography, and 3) bone turnover by histologic measurement.

At the dose level used, no radiation effects on skeletal metabolism were discernable. The retention of Pu is presented as % of injected dose per gram tissue or as per cm^2 of trabecular bone surface.

In Figure 1, the concentration of Pu-239 in individual biopsy specimens of mature beagles is compared to a curve that describes the Pu concentration in the whole rib cage of young adult beagles injected with Pu-239. The biopsy data are distributed about that curve in a manner consistent with the fact that mature beagles have somewhat lower skeletal uptake when compared to young adult beagles (1).

In Figure 2, the concentration of Pu in biopsy specimens of juvenile beagles is compared to the average concentration in the whole rib cage of juvenile beagles which had been sacrificed sequentially. The early biopsy values are generally consistent with that curve. At times later than 90 days after injection, considerable elongation of the rib has occurred, which may result in the analysis of some regions of bone formed completely after the time of injection. Thus, it seems less likely that individual animals may be studied sequentially by the biopsy technique.

In Table 1, the concentration of Pu-239 at trabecular surfaces in rib biopsy specimens of both mature and juvenile beagles is compared to that found on trabecular surfaces of the lumbar vertebral body or ulna of young adult beagles. The initial uptake and rate of loss of Pu-239 from trabecular surfaces in ribs of mature beagles is similar to that seen in the ulna of young adult beagles and much less than that seen in trabecular bone of the

TABLE 1
RETENTION OF Pu-239 AT TRABECULAR BONE SURFACES
IN YOUNG ADULT AND MATURE BEAGLES

Bone	$t_{1/2}$ (days)	Initial Concentration (% Inj. Dose/cm ²)
<u>Young Adult</u>		
Lumbar vertebral body	187	0.00462
Ulna	280	0.00199
<u>Mature Beagle</u>		
Rib	252	0.00245

lumbar vertebral body of young adult beagles. At this time, the juvenile biopsy program has produced too few data for the formulation of precise descriptions of retention, redistribution, surface concentration and turnover rates, but it is interesting to note that the surface concentrations in these dogs seem to be about one order of magnitude lower than those from more mature animals.

In Table 2, the rate of bone turnover in ribs of juvenile and mature beagles as measured in biopsy specimens or after sacrifice is compared. The biopsies taken at seven days post-injection in juveniles and 30 days post-injection in mature beagles show lower turnover than those taken at all later time periods. It is felt that the lower turnover seen at the shorter times

TABLE 2
COMPARISON OF BONE TURNOVER IN RIB BIOPSY SPECIMENS TO THAT IN RIBS
FROM SERIAL SACRIFICE BEAGLES OF ALL AGES

Origin	No.	Age (months)	Time Post-Injection	Turnover (rate (%/yr))
Serial sacrifice	7	3		684
Biopsy	8	3	1 week	194
Biopsy	13	3-4	2-4 weeks	314
Biopsy	5	6	3 months	257
Serial sacrifice	19	6-12		158
Serial sacrifice	7	17		147
Serial sacrifice	3	38-40		76
Biopsy	3	61	1 month	24
Biopsy	16	63-72	3-12 months	102
Serial sacrifice	5	80-120		106
Serial sacrifice	8	136-158		96

after injection is a reflection of the inactivity of the beagles during their four week cage confinement surrounding the time of injection. The biopsy values are consistent with turnover values reported in studies of the rib in the aging beagle.

The measurement of radionuclide retention, both in whole bones and at bone surfaces, and measurement of bone turnover, is reliably done in rib biopsy specimens. Serial comparison of these parameters in individual animals is difficult, but comparisons of groups of animals seem feasible.

REFERENCES

1. W. Stevens, D. R. Atherton, D. Bates and F. W. Bruenger: 1976. The deposition of Pu-239 in the skeleton and soft tissues of beagles: Effect of age at the time of injection. In Research in Radiobiology, University of Utah C00-119-251, pp. 172-180.

FIGURE 1

FIGURE 2

MEASUREMENTS OF TRABECULAR BONE CHARACTERISTICS OF LUMBAR VERTEBRAE
AND PROXIMAL FEMORA OF JUVENILE (3 MONTH OLD) BEAGLES

W. Srisukonth, J.M. Smith, R. Dell, L.A. Woodbury and W.S.S. Jee

ABSTRACT: The structural morphometry of trabecular bone from the lumbar vertebra and proximal femur of 3 month old beagles was measured with the Quantimet 720 Image Analyzer. The trabecular width, percent bone, surface to bone volume and surface to tissue volume ratios were determined for both primary and secondary trabeculae. The average primary trabeculae values varied by a factor of 2 to those for secondary trabeculae. Average trabeculae bone values were estimated by assuming a growing bone is composed of $1/3$ primary bone and $2/3$ secondary bone. A comparison of morphometric values of these two sites in 3 month old and young adult beagles showed that in the 3 month old the trabecular width is 2-3 times thinner, the percent bone is slightly less, the surface to bone and tissue volume is 2-3 times less than that of the young adult.

This report summarizes a preliminary effort to characterize the structural morphometry of trabecular bone from lumbar vertebrae and proximal femora of 3 month old beagles. This study is part of an attempt to develop a program to characterize all trabecular bone in the 3 month old beagle.

The growing bone creates numerous hurdles to those who attempt to characterize the structural morphometry of the trabeculae. A typical long bone possesses epiphyseal plates with its accompanying primary and secondary spongiosae. The primary spongiosa contains trabeculae varying from those with traces of mineral deposits to trabeculae with a significant fraction of their mature stature. This wide variation in trabecular sizes of growing bones makes it difficult to derive meaningful average trabecular morphometric values.

In this study, the trabeculae from the primary and secondary spongiosa were measured separately; we then assume the primary bone made up $1/3$ and the secondary bone $2/3$ of the trabecular population to derive average morphometric

values. These values for the lumbar vertebra and proximal femur were compared to those observed in the adult beagle.

The cross sections of the first lumbar vertebra from male and female and the proximal femur from one female (all 3 months of age) were prepared for analysis as described in an accompanying report (1). The protocol differed only in that the primary (smaller) bone trabeculae were analyzed separately from secondary (larger) trabeculae with the use of the image editing capability of the quantitative television microscope (QTM 720 Image Analyzer, Cambridge-Imanco, Monsey, N.Y.) (Fig. 1).

Fig. 1. The primary and secondary spongiosa in populations are analyzed separately with the use of the image editing capability of the QTM 720 Image Analyzer.

SUBDIVISION OF LUMBAR VERTEBRA

Representative cross sections of the first lumbar vertebra from a 3 month old beagle are shown in Fig. 2.

In cross sections where the spinal canal is complete, a horizontal line was drawn across the canal and surrounding bone at the level of about 1/3 of the

diameter of the canal in the dorso-ventral direction to separate into dorsal and ventral regions (Fig. 3b). The dorsal regions contained mainly the spinous and associated processes and a part of the neural arch. The ventral region contained the anterior, posterior epiphyses, a part of the neural arch, and the centrum with its transverse processes. Measurements were obtained from the dorsal region and the primary and secondary trabecular populations in the ventral region (Fig. 3b).

Fig. 2. Representative microradiographs from a cross section of a lumbar vertebra of a 3 month old beagle. The figures under the sections are distances from the anterior end. EP - epiphysis; NA - neural arch; C - centrum (X2).

Fig. 3. Longitudinal (a) and cross sections (b) of lumbar vertebrae showing the division into dorsal and ventral regions. The dorsal part contains part of the neural arch (NA) and articular and accessory spines while the ventral part contains the anterior and posterior epiphyses (EP), the centrum (C), neural arch portion of the body and its transverse processes (X2).

ANALYSIS OF LUMBAR VERTEBRA

Table 1 summarizes the values obtained for trabecular width (W_b), percent bone (A_{ab}), surface area per bone volume (S_{vb}), and surface area per tissue volume (S_{vt}) from the lumbar vertebrae in two 3 month old beagles. The trabecular characteristics of the dorsal region did not differ greatly from the "secondary" trabeculae of the epiphyses. It possessed a single population of trabeculae, while both the centrum and the epiphyseal fraction of the ventral region contained primary and secondary trabeculae. On the average, the primary trabeculae are 2-3 times thinner, and possess a factor of 2 more bone surface areas to bone and tissue volume.

SUBDIVISION OF PROXIMAL FEMUR

Representative cross sections of the proximal femur from a 3 month old beagle are shown in Fig. 4. In cross section, it can be divided into head and non-head portions. The non-head portion contained both middle and lateral components.

Fig. 4. Representative microradiographs from cross sections of the proximal femur of a 3 month old beagle. Three portions (head, middle and lateral) are clearly separated. The middle portion is the inter-trochanteric region and the lateral belongs to the greater trochanter. The figures under the sections are distances from the proximal end (X2.8).

TABLE 1. TRABECULAR MORPHOMETRIC MEASUREMENTS OF THE FIRST LUMBAR VERTEBRA OF 3 MONTH OLD BEAGLES

Sites	Trabecular size	Parameters			
		$W_b (\mu m)$	$A_{ab} (\%)$	$S_{vb} (mm^2/mm^3)$	$S_{vt} (mm^2/mm^3)$
Dorsal		80	28	32	9.0
Ventral-centrum					
	primary	32	20	79	15.6
	secondary	72	19	36	6.7
Ventral-epiphyses					
	primary	47	40	55	21.8
	secondary	78	28	33	9.1

ANALYSIS OF PROXIMAL FEMUR

Table 2 summarizes the trabecular morphometric values in one proximal femur from a 3 month old female beagle. The morphology of the trabeculae in the head and non-head varied slightly.

TABLE 2. TRABECULAR MORPHOMETRIC MEASUREMENTS OF THE PROXIMAL FEMUR OF A 3 MONTH OLD BEAGLE

Sites	Trabecular size	Parameters			
		$W_b (\mu m)$	$A_{ab} (\%)$	$S_{vb} (mm^2/mm^3)$	$S_{vt} (mm^2/mm^3)$
Head					
	primary	39	34	67	22
	secondary	79	30	33	9.8
Non-head					
	primary	35	34	74	23
	secondary	70	40	37	15

COMPARISON OF TRABECULAR CHARACTERISTICS OF LUMBAR VERTEBRA
AND PROXIMAL FEMUR OF 3 MONTH OLD AND ADULT BEAGLES

Table 3 compares these values in these two different age groups. The differences are expressed as a ratio of 3 month old to adult values. If one assumes that the primary trabeculae occupied 1/3 and the secondary trabeculae 2/3 of the total trabecular area of a given bone, average trabecular morphometric values can be derived for a given region of the trabecular bone.

TABLE 3. COMPARISON OF TRABECULAR MORPHOMETRY OF
3 MONTH OLD AND ADULT BEAGLES*

Site	Parameter (Ratio: $\frac{(3 \text{ mo old})}{(\text{adult})}$)			
	W_b	A_{ab}	S_{vb}	S_{vt}
Lumbar vertebra				
dorsal	0.63	0.77	1.67	1.3
ventral-centrum	0.49	0.59	2.5	1.7
ventral-epiphysis	0.43	0.77	2.5	2.5
Proximal femur				
head	0.29	0.63	3.3	2.5
non-head	0.37	1.00	3.3	2.5

*Assume primary bone is 1/3 and secondary bone is 2/3 of total.

REFERENCE

1. W. Srisukonth, J.M. Smith, R. Dell, L.A. Woodbury and W.S.S. Jee, Measurement of lumbar vertebral and proximal femoral trabecular bone structures of adult beagles (this report).

MEASUREMENTS OF LUMBAR VERTEBRAL AND PROXIMAL FEMORAL
TRABECULAR BONE STRUCTURES IN ADULT BEAGLES

W. Srisukonth, J.M. Smith, R. Dell, L.A. Woodbury and W.S.S. Jee

ABSTRACT: The heterogeneity of trabecular bone structure in the lumbar vertebra and the proximal femur and the changes as a function of age were studied using the Quantimet 720 Image Analyzer. Microradiographs of bone sections from beagles 17 months to 11.6 years of age were measured. In the lumbar vertebra, the trabecular bone of the spinous, accessory, and articular processes and the ends of the centrum contained thicker trabeculae, more bone and a smaller surface to bone and tissue volume ratios than the major part of the centrum. In the proximal femur, the head of the femur contained thicker trabeculae, more bone, and a smaller surface to bone volume ratio than the remainder of the proximal femur (greater trochanter, intertrochanteric region and lesser trochanter). The surface to tissue volume ratio was the same for all areas. No statistically significant difference in trabecular bone characteristics were found for these parts of bones between age 17 months and 11.6 years.

The present study was undertaken to provide the structural information needed to determine the average endosteal dose to those tissues in bone which are at risk with respect to the induction of bone tumors from internally deposited radionuclides.

It is well known the structure of trabecular bone varies from bone to bone, and from site to site within a bone, as well as with age; however, these variations are poorly described except for a few bones. It is the purpose of this preliminary report to characterize the heterogeneity of trabecular bone structure in the lumbar vertebra and the proximal femur and the changes in these two bones as a function of age and sex.

In this study only the trabecular bone parameters were measured. Cross sections of the lumbar vertebra and proximal femur were chosen for analysis

because their trabeculae showed isotropic orientation while in the longitudinal sections anisotropic trabeculae were detected in all parts of the vertebra and the non-head portion of the proximal femur. The isotropic structures were preferred since the three dimensional measurements could be calculated from a universal k value of $4/\pi$ (1,2), whereas in anisotropic structures the k value could not be given directly, since the anisotropy varied from section to section and within different regions of the same section.

The first lumbar vertebrae and proximal femurs from 10 beagles were selected for analysis (Table 1). Two female beagles, aged 17 months (F175A) and 11 years (F107A) were chosen to study serially the first lumbar vertebra and proximal femur in order to ascertain the variation of morphometric parameters throughout the bone and to determine the number of sections needed for proper sampling. All the animals listed in Table 1 were included in the aging study.

TABLE 1. EXPERIMENTAL DOGS

Animal Code	Sex	Age (mo.)	Weight (Kg)
M169A	M	17.1	12.6
M168A	M	17.2	13.2
F172A	F	17.3	11.2
F175A	F	17.3	10.9
M178A	M	38.9	11.5
M181A	M	40.4	12.5
M177A	M	114.0	8.5
F180A	F	121.9	8.8
F107A	F	137.7	8.9
M179A	M	138.6	10.8

At autopsy, the first lumbar vertebra and right femur were disarticulated and trimmed of muscle. The lumbar vertebra was sawed transversely into two

halves (Fig. 1a). The 3 cm of the proximal femur was sawed at a right angle to the shaft (Fig. 1b). The two halves of the lumbar vertebra and the 3 cm segments of proximal femur were fixed and defatted in 6 changes of acetone followed by 12 changes of ether for at least 3 hr in each solution. Bones were dried at room temperature overnight and embedded in bioplastic casting resin. Embedded bones were sawed serially in cross sections to a thickness of approximately 0.5 mm each. Selected sections were ground equally on both sides to 100 μ m thickness in preparation for microradiography.

Fig. 1a,b. Diagrams of lumbar vertebra (a) and proximal femur (b). The lumbar vertebra was sawed (dotted line) transversely into two halves. The proximal femur was sawed (dotted lines) into two zones. Zone I contains head (left knob), neck and greater trochanter (right elevation). Zone II contains superior part of the lesser trochanter.

Contact microradiographs of 100 μ m bone sections with sufficient contrast for analysis were produced by using a low voltage x-ray source (Machlett C-529A Type A-2 diffraction tube) for 5 min at 12 Kv and 25 ma on 3 1/4 in. by 4 1/2 in. Kodak spectroscopic plates (Type 649-0, Eastman Kodak Co., Rochester, N.Y.).

The microradiographs were standardized by a step wedge made from layers of 100 μ m thick aluminum foil. The standard was three layers of aluminum foil giving a microradiograph with an optical density of 0.80 ± 0.1 (3).

The bone area, bone marrow area, tissue area and bone perimeter of the trabecular bone in each micrograph were determined using a Quantimet 720 Image Analyzer (Cambridge-Imanco, Monsey, N.Y.). The general protocol for the use of the QTM-720 for the measurement of radiographs of bone section was reported previously (4). Cortical bone was carefully excluded from this analysis by the use of an image editing pen, which allows interaction of the operator with the image (Fig. 2).

Fig. 2. Exclusion of cortical bone using image editing. (A) Microradiograph of a portion of the lumbar vertebra containing an outlined area for analysis. (B) The first box shows an enlargement of the outlined area. It contains both trabecular (thin) and cortical (thick) bone. (C) The next box shows the exclusion of cortical bone, a result from the use of image editing pen.

Derived parameters were calculated from direct measurements as follows: (3)

Mean trabecular width (w_b) is estimated by the equation

$$w_b = \frac{2 A_b}{P} \quad (1)$$

where A_b is bone area and P is bone perimeter.

Percent bone (A_{ab}) is the ratio of bone area to tissue area (A_b/A_t). (2)

Surface area of bone per bone volume ratio (S_{vb}) is estimated by the equation

$$S_{vb} = \frac{Pk}{A_b} \quad (3)$$

k is $4/\pi$ or 1.273 for isotropic structures.

Surface area of bone per volume of tissue (bone and marrow) is calculated by the equation

$$S_{vt} = \frac{Pk}{A_t} \quad (4)$$

ANALYSIS OF SERIAL CROSS SECTIONS OF LUMBAR VERTEBRAL TRABECULAR CHARACTERISTICS

Representative cross sections of the first lumbar vertebra from the 17 mo. old beagle (F175A) is shown in Fig. 3.

In the typical cross section, there was an abrupt change in the characteristics of the trabeculae at approximately the level of the ventral 1/3 of the neural canal. In order to separate the two populations of trabeculae, a horizontal line was drawn across the canal and surrounding bone about 1/3 of the canal to separate it into dorsal and ventral regions (Fig. 4). The dorsal region contained the spinous, articular, accessory, and mamillary processes, while the ventral portion contained part of the neural arch, the centrum and transverse processes.

The appearance of the trabeculae in the dorsal region was consistent from section to section, while the trabeculae residing in the ventral region varied greatly (Table 2, Figs. 5,6). Furthermore, the analysis of the ventral region showed there is one population of trabeculae located at the "ends" of the body and another population in the remainder of the body. The "end" population can

Fig. 3. Representative microradiographs from cross sections of the first lumbar vertebra (F175A) (X1.6).

TABLE 2. COMPARISON OF THE SERIAL CROSS SECTIONS WITHIN THE VENTRAL PORTION OF THE FIRST LUMBAR VERTEBRA IN 17 MONTH (F175A) AND 11 YEAR (F107A) OLD FEMALE BEAGLES.

DISTANCE STARTS AT THE ANTERIOR END OF THE VERTEBRA

Distance (mm)	A_b (mm ²)		W_b (microns)		A_{ab} (percent)		S_{vb} (mm ² /mm ³)		S_{vt} (mm ² /mm ³)	
	17 mos.	11 yrs.	17 mos.	11 yrs.	17 mos.	11 yrs.	17 mos.	11 yrs.	17 mos.	11 yrs.
0-0.99	7		88		41		29		11.9	
1-1.99	--	12	--	122	--	55	--	21	----	11.5
2-2.99	53	34	122	138	42	47	21	18	8.8	8.7
3-3.99	40	41	79	111	32	36	32	23	10.3	8.2
4-4.99	35	35	76	99	28	29	34	26	9.4	7.5
5-5.99	35	31	81	94	27	25	32	27	8.5	6.9
6-6.99	32	28	81	95	25	24	31	27	7.9	6.4
7-7.99	--	25	--	93	--	23	--	27	----	6.2
8-8.99	24	23	83	98	22	23	31	26	6.9	5.9
9-9.99	24	--	88	--	23	--	29	--	6.7	----
10-10.99	17	19	84	97	21	24	30	26	6.3	6.2
11-11.99	--	--	--	--	--	--	--	--	----	----
12-12.99	21	19	79	98	23	23	32	26	7.3	6.1
13-13.99	23	24	78	97	25	27	33	26	8.1	7.1
14-14.99	27	31	84	99	28	30	30	26	8.6	7.8
15-15.99	29	39	79	103	29	35	32	25	9.2	8.6
16-16.99	35	48	79	124	31	43	32	21	10.0	8.7
17-17.99	45	25	93	168	38	58	27	15	10.3	8.7
18-18.99	43		119		46		21		9.8	
19-20.99	8		107		46		24		11.0

Fig. 4. Cross section of lumbar vertebra divided into dorsal (D) and ventral (V) regions.

Figs. 5 and 6. Percent bone, surface to bone volume and tissue volume ratios in the ventral vertebra as a function of the distances from the anterior end of the vertebra (F175A).

be characterized as possessing thicker trabeculae ($\sim 130 \mu\text{m}$), higher percent bone ($\sim 45\%$), and smaller surface to bone volume ratio ($\sim 20\text{mm}^2/\text{mm}^3$) than the rest of the body (Figs. 5,6, Table 2)

The ventral portion of the lumbar vertebra varied in percent bone and surface area to bone volume and tissue volume from site to site (Table 2, Figs. 5,6). Percent bone varied from 21 to 38% (Fig. 5) while surface to bone and tissue volume ratios varied from 21-34% and 6.3 to 10.3%, respectively (Fig. 6).

Because of the large variation in many morphometric parameters as a function of distance from the anterior end of the ventral portion of the vertebra, it was decided that the values would be presented for two parts of ventral vertebra: the ends and main portions. Six to seven sections were measured in all subsequent analyses of this bone.

EFFECTS OF AGE AND SEX UPON LUMBAR VERTEBRAL TRABECULAR CHARACTERISTICS

No statistically significant differences in trabecular morphometric values were found as a function of age or sex. Table 3 summarizes the trabecular morphometry values for the three regions of the first lumbar vertebra.

TABLE 3. TRABECULAR MORPHOMETRIC MEASUREMENTS OF THE FIRST LUMBAR VERTEBRA OF 1.5 to 11 YEAR OLD BEAGLES

Sites	Parameters			
	$W_b (\mu\text{m})$	$A_{ab} (\%)$	$S_{vb} (\text{mm}^2/\text{mm}^3)$	$S_{vt} (\text{mm}^2/\text{mm}^3)$
Dorsal	127	35	21	7.6
Ventral/middle	105	32	25	7.6
Ventral/ends	130	45	21	9.1

W_b - mean trabecular width; A_{ab} - percent bone; S_{vb} - surface to bone volume; S_{vt} - surface to tissue volume.

ANALYSIS OF SERIAL CROSS SECTIONS OF PROXIMAL FEMUR

Representative cross sections of the proximal femur from F175A, a 17 mo. old beagle, is shown in Fig. 7. The sections are taken in a plane oriented at right angles to the shaft. The proximal femur contains two populations of trabeculae: head and non-head. The non-head consists of neck, intertrochanteric region and lesser and greater trochanters.

These preliminary observations were restricted to sampling the proximal femoral cross section to the inferior level of the head (Fig. 1b). In the case of dog F175A, this would include 14 sections involving 15 mm of the proximal femur. Five equally spaced sections of the 14 sections were analyzed.

No statistically significant differences in trabecular morphometric values were found as a function of age or sex. Table 4 summarizes the trabecular morphometric values for the head and non-head regions of the proximal half of the proximal femur.

TABLE 4. TRABECULAR MORPHOMETRIC MEASUREMENTS OF THE PROXIMAL PORTION OF THE PROXIMAL FEMUR OF 1.5 TO 11 YEAR OLD BEAGLES

Site	Parameters			
	W_b (μ m)	A_{ab} (%)	S_{vb} (mm^2/mm^3)	S_{vt} (mm^2/mm^3)
Head	175	54	15	8.0
Non-head	128	37	20	7.5

The trabecular bone in the head portion contained wider trabeculae and therefore more trabeculae with lower surface to bone volume ratios than the non-head portion (Figs. 8,9). The trabecular width decreased and the surface area to bone volume ratio increased in the more distal sections (Fig. 8).

Fig. 7. Representative microradiographs from cross sections of the proximal end of the femur from a 17 mo. old beagle. Most proximal part is 7A consisting of the head (upper) and greater trochanter (non-head - lower). (X2.8)

The non-head portion exhibited a gradual decrease in percent bone (Fig. 8) and surface area to tissue volume ratio values as one progresses distally toward the shaft. Surprisingly, the surface area to bone volume values exhibited no significant change (Fig. 9).

Fig. 8. Variation of percent bone in head and non-head portions on different sections (cross section of proximal femur, F175A). Arrow indicates the end of the head portion.

Fig. 9. Variation of surface area per bone volume (S_{vb}) and surface area per tissue volume (S_{vt}) in head and non-head portions on different sections of proximal femur (F175A). Arrows indicate the end of head portion.

ESTIMATING AVERAGE TRABECULAR BONE CHARACTERISTICS FOR A GIVEN BONE

It is obvious that it would be too tedious and costly to characterize the trabeculae in all bones of the skeleton as was performed for the lumbar vertebra and proximal femur in this study. Thus, tentatively, we have decided to derive average trabecular morphometric information of beagle bones by 1) identifying different populations of trabeculae within a bone; 2) determining the fraction

of the total population for each type of trabeculae, and 3) analyzing the relevant morphometric parameters of a few sections of each population. This should enable us to estimate the average value for a given bone.

The above observations confirm the findings of Whitehouse (5-8) that the trabecular populations in a given bone are varied. This makes it most difficult to assign average morphometric values for any bone. More discouraging is that proper characterization of trabecular morphometry of the skeleton will involve several years of several full time investigators.

REFERENCES

1. W.J. Whitehouse, The quantitative morphology of anisotropic trabecular bone. *J. Microscopy* 101: 153-168 (1974).
2. W.J. Whitehouse, A stereological method for calculating internal surface areas in structures which become anisotropic as the result of linear expansions or contractions. *J. Microscopy* 101: 169-176 (1974).
3. W. Srisukonth, Quantitative morphometry of the vertebrae and femur of the beagle as a function of age and sex. Univ. of Utah, Ph.D. Thesis (1978).
4. L.A. Woodbury, N.A. Woodbury, T. Wronski and W.S.S. Jee, Preliminary studies on the use of the Quantimet-720 for the measurement of radiographs of bone sections. In *Research in Radiobiology, U. of Utah C00-119-251*, pp. 285-304 (1976).
5. W.J. Whitehouse, Scanning electron micrographs of cancellous bone from the human sternum. *J. Path.* 116: 213-223 (1975).
6. W.J. Whitehouse and E.D. Dyson. Scanning electron microscope studies of trabecular bone in the proximal end of the human femur, *J. Anat.* 118: 417-444 (1974).
7. W.J. Whitehouse, E.D. Dyson and C.K. Jackson, The scanning electron microscope in studies of trabecular bone from a human vertebral body. *J. Anat.* 108: 481-496 (1971).
8. W.J. Whitehouse, Cancellous bone in the anterior part of the iliac crest. *Calc. Tiss. Res.* 23: 67-76 (1977).

A CORRELATION BETWEEN INITIAL DEPOSITION OF Pu, TRABECULAR BONE
CONTENT AND TUMOR FREQUENCY

F. W. Bruenger, W. Stevens, D. R. Atherton and W. S. S. Jee

The distribution of osteosarcoma within the skeleton which results from the exposure of beagles to Pu or Ra is nonuniform. In addition, there are anatomical sites in individual bones which have a high or low tumor incidence and these sites vary with the respective nuclide (Fig. 1). A major effort of this laboratory is to study if there is a correlation between initial nuclide deposition, bone composition, retention of nuclide and tumor incidence. If there is a correlation, conclusions may be drawn regarding the mechanisms which are responsible for tumor formation.

Of particular interest is the humerus because it combines sites of high and low tumor incidence in one bone. It has been known for many years that the pattern of initial deposition of Pu in the humerus is nonuniform and that the relative gross distribution within the bone changes as a function of time after injection. Experiments have been initiated to: a) determine the distribution of Pu (and Ra) at short times after injection and the change of that distribution as a function of time, and b) determine the ratio of trabecular bone to cortical bone in each of eight sections of a humerus. Other bones with high and/or low tumor incidence will be added to this study at a later time.

Preliminary data for the fraction of trabecular bone in each of eight sections of humeri from six beagles were obtained by physical separation of ashed trabecular from cortical bone. No correction has been made at this

time for the presence of marrow which adds substantially to the total mass of the wet bone but makes only a small contribution to the ashed bone. These data indicated that about 1/3 of the bone ash is associated with trabecular bone, most of which is concentrated in the proximal epiphysis and metaphysis. Little trabecular bone is found in the shaft. The amount of trabecular bone increases again in the distal metaphysis and epiphysis but, by inspection, it appears that the trabeculae have a less delicate structure and probably a lower surface/volume ratio.

The distribution of Pu in eight sections of the humerus was measured in 3 beagles at ~ 5 month after injection and in 4 beagles at 3-5 years after injection. Concentrations of Pu (% of Pu/g wet bone) in the sectioned humeri and the average concentrations in the whole humerus are shown in Fig. 2. The change in Pu-concentration in these sections is expressed numerically in the following table. Also given in this table is the fraction of total bone ash in each section which was associated with trabecular bone.

These data show that the proximal humerus which is a site of high tumor incidence for Pu-irradiation is characterized by high initial deposition, a relatively high rate of loss of Pu and high trabecular bone content. The distal humerus, which is a site of low tumor incidence is characterized by a much lower initial deposition, a smaller rate of loss and a relatively low trabecular bone content. No tumors have been induced by Pu in the shaft of the humerus in which little Pu is present and which is poor in trabecular bone.

Further studies will be necessary to improve the measurement of trabecular bone content, to determine the rates of loss in individual sections as a function of time and to relate these two parameters and other morphometric

and dosimetric information with tumor incidence. This study also will include other bones and will be carried out with Ra as well as Pu.

CHANGE IN Pu-CONCENTRATION DURING FIRST FOUR YEARS AFTER INJECTION
AND % OF TRABECULAR BONE ASH IN SECTIONS OF HUMERUS.

	Initial Deposition (% D/Part)	Concentration (% D/g Wet Bone)			% of Ash Contributed by Trabecular Bone
		Initial	After 4 Years	% Change	
H-1	0.206	0.117	0.076	-35	85
H-2	0.804	0.155	0.115	-26	90
H-3	0.469	0.092	0.064	-31	22
H-4	0.098	0.028	0.028	--	3
H-5	0.065	0.023	0.020	-11	2
H-6	0.091	0.031	0.024	-22	7
H-7	0.214	0.051	0.049	- 6	37
H-8	0.046	0.047	0.053	+12	70
Σ-H	1.99	0.076	0.058	-23	33

Figure 1 Distribution of osteosarcoma in beagles injected with low doses of Pu or Ra ($^{239}\text{Pu} \leq 0.048 \mu\text{Ci/kg}$ or $^{226}\text{Ra} 1.08 \mu\text{Ci/kg}$).

Figure 2 . Percent of injected Pu/gram of wet bone in sectioned humerus at short times after injection and after 4 years.

THE MICRODISTRIBUTION AND RETENTION OF ^{239}Pu ON
TRABECULAR SURFACES IN THE BEAGLE

T.J. Wronski, J.M. Smith and W.S.S. Jee

ABSTRACT: An attempt was made to characterize the initial uptake and retention of ^{239}Pu on trabecular surfaces at times up to one year post-injection at five skeletal sites of the beagle. The first lumbar vertebra, pelvis, and proximal humerus exhibited a high initial uptake of ^{239}Pu and tended to lose ^{239}Pu from their trabecular surfaces with time. The proximal ulna and distal humerus had a low initial concentration of ^{239}Pu on trabecular surfaces, which remained approximately constant with time. These differences in the retention of ^{239}Pu are attributed to differences in the rate of trabecular bone turnover at these skeletal sites.

Young adult beagles of approximately 17 months of age were injected intravenously with $\sim 0.016 \mu\text{Ci/kg}$ of monomeric ^{239}Pu citrate. Two animals were sacrificed at each of the following time periods post injection: 7, 15, 28, 56, 133, 210 and 365 days. The skeletal sites selected for this study were the first lumbar vertebra, pelvis, proximal humerus, distal humerus, and proximal ulna. These bones were embedded in a bioplastic resin and sawed into cross sections of approximately $300 \mu\text{m}$ thickness. Neutron-induced autoradiographs of selected sections were produced at a thermal neutron fluence of 10^{16} n/cm^2 (1). Details of technical procedures and the calculation of ^{239}Pu concentration on trabecular surfaces from microscopic counts of fission fragment tracks have been previously described (2).

^{239}Pu concentration on trabecular surfaces at the five skeletal sites at times up to one year post injection is plotted in Figure 1. Individual data points are listed in Table 1.

The profile for the retention of ^{239}Pu on trabecular surfaces in the first lumbar vertebra, pelvis, and proximal humerus is quite different from that of

the proximal ulna and distal humerus. There is a greater initial deposition of ^{239}Pu on trabecular surfaces ($\sim 7-8$ pCi/cm²) in the former three skeletal sites, followed by a decrease in ^{239}Pu concentration to ~ 2.0 pCi/cm² by one year post injection. The greatest rate of loss of ^{239}Pu occurs between 28 and 56 days post injection. On the other hand, ^{239}Pu concentration on trabecular surfaces in the proximal ulna and distal humerus remains relatively constant at $\sim 1.0-1.5$ pCi/cm² for the one year period.

These trends are consistent with trabecular bone turnover data previously reported (2) in which the first lumbar vertebra, pelvis, and proximal humerus were found to have a rate of trabecular bone turnover which was at least a factor of 3 greater than that of the proximal ulna and distal humerus. This study therefore emphasizes the role of bone turnover processes in removing ^{239}Pu from trabecular surfaces at a given skeletal site.

REFERENCES

1. M.H. Fellows, L. Clark, J.J. O'Toole, D.B. Kimmel and W.S.S. Jee, An improved technique for neutron-induced autoradiography of bone containing plutonium. *Health Phys.* 29: 97-101 (1975).
2. T.J. Wronski, J.M. Smith and W.S.S. Jee, A preliminary report on the correlation of the rate of trabecular bone turnover and ^{239}Pu concentration on trabecular surfaces with the incidence of osteosarcoma at selected skeletal sites. In *Research in Radiobiology*, University of Utah Report C00-119-252, pp. 172-187 (1977).

TABLE 1*

Days Post Inj.	²³⁹ Pu Conc. in pCi/cm ² of trabecular surface area @0.016 µCi/kg				
	Lumbar Vertebra	Proximal Humerus	Pelvis	Proximal Ulna	Distal Humerus
7	7.2 ± 3.2	7.2 ± 3.0	7.6 ± 3.0	2.3 ± 1.4	1.3 ± 1.1
15	8.5 ± 2.9	8.0 ± 3.0	7.8 ± 3.1	1.4 ± 1.0	1.4 ± 1.4
28	7.5 ± 2.7	7.7 ± 2.5	7.7 ± 2.5	1.6 ± 0.9	0.9 ± 0.8
56	3.5 ± 1.6	4.0 ± 1.7	3.1 ± 1.5	1.0 ± 0.8	1.0 ± 0.8
133	4.1 ± 1.9	4.0 ± 1.9	2.9 ± 1.8	1.4 ± 0.9	1.5 ± 1.2
210	3.8 ± 1.7	3.9 ± 1.7	2.5 ± 1.5	1.0 ± 0.9	1.2 ± 1.0
365	1.6 ± 1.2	2.5 ± 1.3	1.6 ± 1.2	0.8 ± 0.8	1.2 ± 0.9

*This table lists ²³⁹Pu concentration on trabecular surfaces (pCi/cm²) at five skeletal sites at various times up to one year post injection. At a given skeletal site, the ²³⁹Pu concentration on trabecular surfaces has a wide, asymmetric distribution. The values listed above are the mean of this distribution ± the standard deviation. These values have been corrected for "background", which was found to be equivalent to 0.9 ± 0.2 pCi/cm² in control animals. Two animals were sampled at each of the above time periods.

Fig. 1. ^{239}Pu concentration on trabecular surfaces is plotted vs. time post injection. The first lumbar vertebra, pelvis, and proximal humerus have a greater initial uptake of ^{239}Pu and tend to lose ^{239}Pu from their trabecular surfaces due to their relatively high rate of trabecular bone turnover. ^{239}Pu concentration on trabecular surfaces in the proximal ulna and distal humerus, which have a low rate of trabecular bone turnover, remains approximately constant for the first year post injection.

THE RELATIONSHIP OF TRABECULAR BONE SURFACE AREAS, BONE TURNOVER
RATES, AND INITIAL UPTAKE OF PU AND RA TO SITES OF
OCCURRENCE OF OSTEOSARCOMA IN BEAGLES

W.S.S. Jee

Recently Spiers and colleagues (1) demonstrated a strong correlation between tumor frequency and trabecular area of five long bones from radium-case data of Rowland and Keane (33 cases), from naturally-occurring cases from a series of Sissons (139 cases), and one of Dahlin (473 cases). Furthermore, their analysis of the available dose data for radium cases shows that, in this instance, dose does not contribute to the observed correlations. This led them to support the thesis that tumor occurrence depends on surface area, i.e., on the number of cells at risk. This report summarizes our attempt to do a similar type of analysis with ^{239}Pu and ^{226}Ra beagle data.

Since the concentration of radionuclide and bone turnover rates have been postulated to influence the site of bone tumor induction, these factors were compared to the site of bone tumor occurrence to detect whether they contribute to the observed correlations.

RELATIONSHIP OF TRABECULAR BONE SURFACE AREAS TO OCCURRENCE OF BONE TUMORS

When trabecular bone surface area for a specific part of a long bone is scored against the site frequency of bone tumor occurrence, the correlation coefficients shown in Table 1 were determined for ^{239}Pu and ^{226}Ra induced bone tumors in beagles. These values are compared to those reported by Spiers et al. (6) for man.

TABLE 1. CORRELATION COEFFICIENTS

Data	Correlation Coefficients
1. ^{239}Pu beagle tumor incidence vs. trabecular area	0.63
2. ^{226}Ra beagle tumor incidence vs. trabecular area	0.68
3. Natural dog tumor incidence vs. trabecular area	0.14
4. Human radium case tumor incidence vs. trabecular area	0.96*

*From Spiers et al. (1)

There is a reasonable correlation of this parameter in dog, but they were significantly lower than the near ideal correlation obtained by Spiers and colleagues in man. It is apparent that there is no correlation of trabecular bone surface area to naturally occurring dog bone tumors. This is due to a large number of bone tumors occurring at the distal radius, a site containing very little trabecular bone surface area. If one were to assign a zero incidence or eliminate the distal radii site, the correlation coefficient improved to 0.77 and 0.74, respectively.

RELATIONSHIP OF OTHER MODIFYING FACTORS TO SITE OF BONE TUMOR OCCURRENCE

Other factors such as bone turnover rates and initial concentration of ^{239}Pu and ^{226}Ra were compared to the frequency of bone sarcomas at the same site to detect whether they contribute to the observed correlation. Also various products were considered, e.g., (trabecular bone area) * (bone tumors) vs. ^{239}Pu tumor distribution, to determine whether they improved the correlation (Table 2).

Bone turnover rate measurements were obtained from two 17 month young adult beagles. Details of these measurements are given in an accompanying progress report. The initial distribution of ^{239}Pu and ^{226}Ra in these selected long bone sites were estimated from these data by Stover et al. (2) and Lloyd et al. (3).

TABLE 2

Factor	Site and Number of Tumors ^{239}Pu	Tumors ^{226}Ra
Trabecular area	0.63	0.68
(Trabecular area)·(bone turnover	0.81	0.45
(Trabecular area)·(initial nucl. distribution)	0.53	0.60
(Trabecular area)·(initial nucl. distribution)· (bone turnover)	0.80	0.38
Bone turnover	0.84	0.25
Initial nuclide distribution	0.69	0.60
(Initial nucl. distribution)·(bone turnover)	0.98	0.37

It is apparent in the ^{239}Pu bone tumor comparisons that the best correlation occurred when one related the site and number of bone tumors to bone turnover rates. An improved correlation is obtained when initial ^{239}Pu distribution is multiplied by bone turnover. On the contrary, the correlation coefficient for trabecular bone and initial ^{226}Ra distribution deteriorated when the bone turnover rates were introduced. For example, the correlation coefficient for initial ^{226}Ra distribution to tumor is 0.60 and combining initial ^{226}Ra distribution and bone turnover rate to tumor decreased the value to 0.37.

It should be emphasized that one should not attribute significance to minor differences in correlation coefficients. The important finding is the lack of correlation between bone turnover and the distribution of ^{226}Ra induced tumors, which may imply complex differences between ^{239}Pu and ^{226}Ra in their relative effectiveness in inducing osteosarcoma.

It is obvious there is a need for better information for specific bone sites in the following parameters:

1. Trabecular bone ash.
2. Trabecular bone surface area.
3. Surface to volume ratios.
4. Bone turnover rate data.
5. Initial surface distribution of radionuclide.
6. Cumulative surface distribution of radionuclide.

REFERENCES

1. F.W. Spiers, S.D. King and A.H. Beddoe, Measurements of endosteal surface areas in human long bones: Relationship to sites of occurrence of osteosarcoma, *Brit. J. Radiol.* 50: 769-776 (1977).
2. B.J. Stover, D.R. Atherton, and D.S. Buster, Retention of $^{239}\text{Pu}(\text{IV})$ in the beagle. In Radiobiology of Plutonium, B.J. Stover and W.S.S. Jee (Eds.), J.W. Press, University of Utah, Salt Lake City, pp. 149-169 (1972).
3. R.D. Lloyd, C.W. Mays and D.R. Atherton, Distribution of injected ^{226}Ra and ^{90}Sr in the beagle skeleton, *Health Phys.* 30: 183-189 (1976).

PRELIMINARY SURFACE/VOLUME RATIOS AND BONE TURNOVER RATES
OF TRABECULAR BONE IN YOUNG ADULT BEAGLES

W.S.S. Jee, J.M. Smith, D.B. Kimmel, S.C. Miller,
C. Van Dura, C. Smith and R. Dell

ABSTRACT: Using morphometric and tetracycline bone labeling techniques, the surface to volume ratios and the bone turnover rates have been determined for trabecular bone sites of two young adult beagles. The surface to volume ratios varied from 153 to 419 cm^2/cm^3 . A preliminary value for average trabecular bone surface/volume ratio is 268 cm^2/cm^3 . Bone turnover rates varied between 60 to 300%/year. They may vary as much as a factor of 5 within a bone.

This is an interim report on our studies to provide structural and dynamic information needed to determine the absorbed dose to the cells at risk in bone from bone seeking radionuclides, particularly ^{239}Pu and ^{226}Ra . Currently an average bone surface to volume ratio for the beagle skeleton is needed so the average endosteal bone dose can be calculated. Furthermore, the bone turnover rates for regions of bones, i.e., proximal vs. distal, are needed in determining the relative sensitivity to tumor induction and the rate of burial and removal of radionuclides.

This report gives preliminary values of surface to volume ratios (structural) and bone turnover rates (dynamic morphometry) for selected trabecular sites.

MATERIALS AND METHODS

Two young adult beagles, M168 at 517 days and F175A at 520 days of age were selected for the measurement of the trabecular bone surface/volume ratio and turnover rate.

Bone formation rates can be measured if one uses tetracycline labeling techniques (1,2). Prior to sacrifice, the dogs were injected with Terramycin, a

tetracycline derivative (Pfizer, Inc Laboratories Division, New York, N.Y.) according to the following daily regimen: 2 daily injections of 30 mg/kg Terramycin, 10 days without injections, another 2 daily injections of Terramycin, 3 to 5 days without injections, followed by sacrifice.

During autopsy, the bones were defleshed, sawed into 2 cm cross sections (Table 1) and placed in acetone. Table 1 does not list bony parts of the skull, fore and hind paws, sternbrae and coccygeal vertebrae. Future reports will list these parts. Only ribs Nos. 6 and 10 were studied. They were divided into portions representing the proximal, mid-proximal, mid-distal and distal parts. The 2 cm chunks of bone were then dehydrated with a series of five acetone, and ten ether changes and embedded in polyester resin with a styrene monomer (Plastic Fabricating and Supply, Salt Lake City, Utah). Following embedding and curing, these blocks were sawed serially into cross sections of approximately 400 μ m thickness. The number of sections analyzed to date are listed in Table 1.

MEASUREMENT OF TRABECULAR BONE TO SURFACE/VOLUME RATIO

The cross sections were ground to 100 μ m and x-rayed (Machlett C-529A, Type A-2 diffraction tube) for 6 min at 12 Kv and 25 ma on 3 1/4" x 4 1/4" in Kodak spectroscopic plates (Type 649-0, Eastman Kodak Co., Rochester, N.Y.). The total perimeter and total area of trabecular bone in each microradiograph were measured with a Quantimet 720 Image Analyzer (Cambridge-Imanco, Monsey, N.Y.). Procedures used in these measurements have been reported in previous progress reports (3). The surface/volume ratio (S_{vb}) of trabecular bone was calculated using the measured perimeter and area values with the following equation:

$$S_{vb} = \frac{Pk}{A}$$

where k is the proportionality constant which is equal to $4/\pi$ for isotropic trabeculae, P is the trabecular perimeter and A is the area of trabecular bone.

CALCULATED TRABECULAR BONE TURNOVER

The same bone sections which were microradiographed were ground to 50 μm and mounted with Permount on microscopic slides for UV analysis at a magnification of 60X. Linear intercepts of trabecular bone surfaces labeled with and without tetracycline were counted using a Merz gird (4) to determine the fraction of trabecular surface labeled with tetracycline ($S_{\text{Fract. (lab)}}$).

At a magnification of 240X, the distance between double label was measured at an average of 3 equally-spaced sites per label by means of a calibrated eyepiece micrometer. The value for the distance between the two labels divided by the inter-tetracycline labeling interval will give a bone apposition rate number.

The trabecular bone turnover values can be computed if one assumes bone formation is equal to bone resorption and the values for surface to volume, fraction of tetracycline labeled surface and the bone apposition rate are known. It can be calculated from the equation listed below:

$$\text{Trabecular bone turnover} = S_{\text{Fract. (lab)}} \cdot S_{\text{vb}} \cdot A \cdot 100$$

(%/year)

where $S_{\text{Fract. (lab)}}$ represents the fraction of actively forming (tetracycline labeled) trabecular bone surface, S_{vb} is the surface/volume ratio and A is the bone apposition rate.

TRABECULAR BONE SURFACE/VOLUME RATIOS

Table 1 lists the trabecular bone surface/volume ratios determined to date. The trabecular bone of the mandible exhibited the smallest value (153 ± 24), while the rib near the costochondral junction showed the highest value

TABLE 1. SURFACE TO VOLUME RATIOS OF SELECT TRABECULAR BONE SITES

Bones	No. Sections	S/V $\pm$ S.E. cm ² /cm ³
Calvarium	12	183 $\pm$ 10
Mandible	9	153 $\pm$ 8
CV Body	16	224 $\pm$ 5
TV Body	6	296 $\pm$ 20
LV Body	13	275 $\pm$ 8
Scapula	22	212 $\pm$ 0.6
Prox. Hum.	10	299 $\pm$ 10
Dist. Hum.	7	221 $\pm$ 14
Prox. Ulna	13	201 $\pm$ 16
Dist. Ulna	18	246 $\pm$ 6
Prox. Radius	11	250 $\pm$ 8
Dist. Radius	12	239 $\pm$ 10
Metacarpal	12	207 $\pm$ 7
Pelvis	17	216 $\pm$ 13
Prox. Fem.	47	214 $\pm$ 3
Dist. Fem.	23	271 $\pm$ 0.4
Prox. Tibia	11	258 $\pm$ 1.5
Dist. Tibia	10	239 $\pm$ 4
Metatarsal	10	220 $\pm$ 6
R6A	9	243 $\pm$ 4
R6B	3	325 $\pm$ 21
R6C	4	367 $\pm$ 4
R6D	3	384 $\pm$ 46
R10A	4	236 $\pm$ 13
R10B	2	351 $\pm$ 33
R10C	2	371 $\pm$ 12
R10D	5	419 $\pm$ 2

(419 ± 4). Applying the values reported by Gong et al. (5) for the distribution of trabecular bone in beagles, we calculated the average trabecular bone surface/volume ratio to be $268 \text{ cm}^2/\text{cm}^3$. This was compared to values reported for man, Rhesus monkey, beagle and miniature pig by Beddoe (6, Table 2). The average surface/volume value reported by Beddoe was approximately 30% less than that reported in the current study. This discrepancy in value may be due to the procedure used to determine the average trabecular bone values in the current studies. Beddoe reported surface to volume values for rib and pelvis which were identical to those cited in this study, while his values for the vertebra and other long bones were considerably lower.

TABLE 2. COMPARISON OF TRABECULAR BONE SURFACE/VOLUME RATIO IN FOUR SPECIES

Species	$S_{vb} \text{ cm}^2/\text{cm}^3$	Source
Man	190	Beddoe (6)
Rhesus monkey	190	Beddoe (6)
Beagle	268	Jee et al.*
Beagle	185	Beddoe (6)
Miniature pig	130	Beddoe (6)

*Present study

A more extensive automated measurement of these trabecular bone characteristics will be initiated in the near future; therefore, these values should be used with caution.

BONE TURNOVER RATES

Bone turnover rates are reported for some selected sites in Table 3. Again, these are preliminary values and will change when more readings are added. The values varied from bone to bone as well as sites within a bone. It varied from

the lowest value of 60%/year for the distal ulna compared to the highest of over 300%/year in the proximal humeral and distal femoral metaphyses. It was two times greater in the proximal than distal humerus. Neighboring sites like the epiphysis and metaphysis of the distal femur varied by a factor of 3.

Again the reader should be cautioned that these are preliminary values. At times the value reported was the result of reading 1 or 2 sections. A minimum of 6 sections per site should be read before a representative value for a given region can be obtained.

We will soon initiate a program to determine the surface/volume ratios and bone turnover rates for cortical bone sites. The surface to volume values will allow us to obtain an average bone surface to volume ratio value for the Utah beagle skeleton. This in turn will allow us to calculate reliable average bone surface (endosteal) doses.

REFERENCES

1. H.M. Frost, Tetracycline-based histological analysis of bone remodeling. *Calc. Tiss. Res.* 3: 211-237 (1969).
2. G. Marotti, Map of bone formation rate values recorded throughout the skeleton of the dog. In *Proc. of the First Workshop on Bone Morphometry*, Z.F.G. Jaworski (Ed.), U. of Ottawa Press, pp. 202-207 (1976).
3. L.A. Woodbury, N.A. Woodbury, T. Wronski and W.S.S. Jee, Preliminary studies on the use of the Quantimet-720 for the measurement of radiographs of bone sections. *Research in Radiobiology*, University of Utah Report C00-119-248, pp. 285-328 (1976).
4. W.A. Merz and R.K. Schenk, Quantitative structural analysis of human cancellous bone. *Acta Anat.* 76: -15 (1970).
5. J.K. Gong, J.S. Arnold and S.H. Cohn, Composition of trabecular and cortical bone. *Anat. Rec.* 149: 325-332 (1964).
6. A.H. Beddoe, A quantitative study of the structure of trabecular bone in man, Rhesus monkey, beagle and miniature pig. *Calc. Tiss. Res.* (in press).

TABLE 3. TURNOVER RATES IN SELECT TRABECULAR BONE SITES

Bone Sites	No. of Sections	Turnover rate $\pm$ S.E. (%/yr)
Calvarium	9	112 $\pm$ 15
Cervical vertebra	8	165 $\pm$ 18
Thoracic vertebra	8	245 $\pm$ 11
Lumbar vertebra	4	208 $\pm$ 13
Proximal tibial epiphysis	2	94 $\pm$ 3
Proximal tibial metaphysis	2	221 $\pm$ 1
Distal tibial metaphysis	2	116 $\pm$ 23
Proximal femur	2	240 $\pm$ 41
Distal femoral epiphysis	2	115 $\pm$ 42
Distal femoral metaphysis	1	360 $\pm$
Proximal radius	8	235 $\pm$ 21
Distal radius	8	121 $\pm$ 15
Proximal ulna	8	99 $\pm$ 10
Distal ulna	6	61 $\pm$ 13
Scapula	12	127 $\pm$ 14
Proximal humerus	8	328 $\pm$ 33
Distal humerus	5	123 $\pm$ 17
Metacarpal	8	111 $\pm$ 9
Metatarsal	2	106 $\pm$ 16

QUANTITATIVE STUDIES OF BONE CELLS IN BEAGLES

D.B. Kimmel and W.S.S. Jee

ABSTRACT: The nuclei of bone surface cells of the iliac crest of nine young adult beagles were examined. Bone marrow cells were excluded from the study because they do not make bone in the absence of inducing agents. Only two trabecular bone surface cell types are active in DNA synthesis: 1) endosteal bone lining cell nuclei are discs of 11 μm diameter and about 1 μm thickness, found on 92% of the iliac crest trabecular bone surface at a density of about 80/mm², 2) nuclei of osteoprogenitor cells, those associated with areas of bone turnover and likely to divide and give rise to osteoblasts and/or osteoclasts, are ellipsoids of revolution (11 μm X 7 μm X 7 μm), found at only 2% of the surfaces at a density of 5600/mm². Both cell types must be considered as ones which may absorb significant radiation damage from skeletally-deposited alpha emitters, then give rise to an osteosarcoma following cell division.

OBJECTIVE AND METHODS

The purpose of this study is to complete quantitative characterization of the cells at risk from alpha irradiation from ²³⁹Pu, in an animal model where the complete spectrum of effects of internally deposited ²³⁹Pu has been explored. This project will increase the meaning of internal emitter microdosimetry studies now underway.

The study is made in the iliac crest trabecular bone of young adult beagles because 1) the iliac crest is a common site of ²³⁹Pu-induced bone tumors (9 of 75), and 2) the iliac crest is the most common site of bone biopsy in humans, from which the best normal human data on trabecular bone is expected to become available.

The methodology for this project involves formalin fixation, methyl methacrylate embedding, preparation of 7 μm sections, and Goldner (1938) staining for both cellular and hard tissue details. The sections, studied at about 1000X on the light microscope, contain minimal shrinkage or preparation artefact

(Figs. 1 and 2). The proliferative bone cells of the trabecular surface are identified, then studied for frequency, size, orientation, and distance from the bone surface.

RESULTS

This study concentrates on bone cells as a first priority, since bone marrow cells, though found in great numbers near the trabecular surface, have no native capacity to form bone. The four principal types of bone cells found at trabecular surfaces are 1) bone lining cells, 2) osteoprogenitor cells, 3) osteoblasts, and 4) osteoclasts (Table 1). It was noted in a companion study of DNA-synthesizing cells at bone surfaces, that only bone lining cells and osteoprogenitor cells were labeled with $^3\text{HTdR}$ in significant frequency at 1.5 hrs after injection. Labeling at this time period is the hallmark of DNA-synthesizing/dividing cells. Detailed quantitative studies were limited to these two cell types.

Bone lining cells have a disc-shaped nucleus of $11.0 \pm 1.2 \mu\text{m}$ diameter and about one micron thickness, which is found at an average distance of one micron from the bone surface (nuclear center to bone surface). A more exact measurement of nuclear thickness and cytoplasmic characteristics awaits ultrastructural examination. They are found at a density of $80.6 \pm 28.0/\text{mm}^2$, randomly distributed on $91.4 \pm 2.6\%$ of the trabecular surface.

Osteoprogenitor cells have a nucleus which is an ellipsoid of revolution with major axis of about $11 \mu\text{m}$ and minor axis about $7 \mu\text{m}$. A more exact measurement of the cytoplasmic characteristics must be done ultrastructurally. They are found at a density of $5643 \pm 3140/\text{mm}^2$ covering only $2.3 \pm 0.8\%$ of the trabecular surface. The nuclear center is found at $5.5 \pm 2.8 \mu\text{m}$ from the bone surface.

On a typical 100 mm² of young adult beagle iliac crest trabecular bone surface, then, one would expect to find 7367 ± 2210 bone lining cell nuclei randomly distributed and 12979 ± 7138 osteoprogenitor cells in clusters.

These cell counts apply only to the iliac crest of the beagle as a representative area for osteosarcoma occurrence, and provide a minimal rational basis for biologically meaningful microdosimetry to bone tissue at endosteal surfaces in beagle. There is good reason to believe that these numbers for bone lining cells may be accurate for most bones, but that the numbers for osteoprogenitor cells are likely a function of the level of bone remodeling activity found in the region of trabecular bone under analysis.

TABLE 1. CRITERIA FOR BONE CELL IDENTIFICATION ON TISSUE SECTIONS

Name	Physical Appearance
Bone Lining Cells	Nucleus only visible; tightly adherent to trabecular surface, but randomly distributed; nucleus five to ten times as long as thick; long dimension parallel to bone surface.
Osteoprogenitor Cells (OPC)	Nucleus only visible; found in vicinity of bone surface in discrete groups; nucleus elliptical in shape; no orientation; generally near osteoclasts and osteoblasts.
Osteoblasts	Nucleus plus basophilic cytoplasm and Golgi apparatus usually visible; tightly adherent to bone surface in clusters; nuclei quite round, similar to OPC in shape; grouped with OPC and osteoclasts.
Osteoclasts	Multinucleated with abundant cytoplasm; often found near osteoblasts and OPC.

STUDY OF SKELETAL CELL KINETICS OF YOUNG ADULT BEAGLES

D. B. Kimmel and W. S. S. Jee

ABSTRACT: An autoradiographic study of thoracic vertebral bodies of six young adult beagles injected with $^3\text{HTdR}$, then sacrificed at times up to 11 days later was completed. The principal labeled cells were endosteal bone lining cells and osteoprogenitor cells; less than 1% of all labeled cells were osteoblasts. The labeling index (1.5 hrs post-injection) of bone lining cells was about 1.3%, while that for osteoprogenitor cells was about 1.6%. It is certain that all bone lining cells divide within 16 hrs of injection. It is uncertain for osteoprogenitor cells because they are more difficult to study since their overall numbers are proportional to the rate of bone remodeling.

OBJECTIVES AND METHODS

The purpose of studying bone cell kinetics is 1) to identify the principal DNA-synthesizing cells in young adult beagle trabecular bone, 2) to determine the rate at which they divide and differentiate, 3) to measure the fraction of the population which divides, and 4) to study their movements relative to the trabecular bone surface. This report is rather preliminary in nature, and addresses only two of the above questions.

To accomplish these objectives, many young adult beagles have been sacrificed at 1.5 hrs after injection of 0.5 $\mu\text{Ci/g}$ tritiated thymidine ($^3\text{HTdR}$). In addition, single beagles have been killed at 16, 24, 40, 64 hours, and 4, 8, 11 and 14 days after $^3\text{HTdR}$ injection. The thoracic vertebral body has been chosen for detailed study at this time, because 1) it has a high turnover rate, 2) it has a relatively high incidence of osteosarcoma in beagles injected with ^{239}Pu , and 3) it has a relatively large amount of trabecular surface in a small region.

The bone is fixed in formalin, decalcified in neutral 14% EDTA, trimmed into 1.5 mm thick longitudinal slabs, and embedded in methyl methacrylate (1).

Three μm thick sections are prepared on the Jung microtome and affixed to slides coated with 0.5% calfskin gelatin. Autoradiographs of about 9 months exposure are prepared, using Kodak NTB emulsion

Autoradiographs of sections separated by at least 60 μm are scanned at 1000X. The amount of trabecular bone surface and $^3\text{HTdR}$ -labeled bone cells encountered is recorded. About 500 to 800 mm of linear surface per dog is scanned to record this preliminary data.

RESULTS

Bone lining cells, osteoprogenitor cells, and occasional osteoblasts are seen labeled at 1.5 hrs after $^3\text{HTdR}$ injection. The total number of labeled and unlabeled osteoprogenitor cells seems to be proportional to the bone turnover activity as measured by tetracycline labeling in adjacent thoracic vertebral bodies, while the total number of bone lining cells labeled is constant (Table 1). Examination of more control animals and examination of more bones of relatively different turnover rates within these animals is now underway. The first labeled osteoclast nuclei appear by 16 hrs post- $^3\text{HTdR}$. A steady state for osteoclast labeling may have been reached by four days post injection.

In Table 1, quantitative data are presented. The labeling index for osteoprogenitor cells and bone lining cells for one dog (T_{78}R_0) is 1.59% and 1.26%, respectively. From these data (Table 1), it is reasonable to infer that most bone lining cells have divided by 16 hrs. No such conclusion is possible for osteoprogenitor cells as their numbers, as well as labeled numbers, are likely proportional to the bone remodeling activity measured by tetracycline.

The quantitative results presented herein are accurate at least to the order of magnitude, but await study of more animals for better resolution.

TABLE 1. LABELED CELLS/mm ENDOSTEAL SURFACE (LABELING INDEX)

Post- ³ HTdR Intervals	Bone Lining Cells	Osteoprogenitor Cells	Obl	OCN
1.5h(a) (low bone turnover)	0.098	0.027	-	none
1.5h(b) (high bone turnover)	0.113(1.26)	0.084(1.59)	-	none
16h	0.242	0.089	-	0.00146
1.67 d	-	-	-	0.00620
4 d	0.140	0.200	-	0.01663
11 d	-	-	-	0.01366

COMPARISON OF BIOLOGIC ACTIVITY OF YOUNG ADULT
HUMAN AND BEAGLE TRABECULAR BONE

D.B. Kimmel and W.S.S. Jee

ABSTRACT: Bone specimens from the iliac crest of nine young adult beagles and up to 164 humans in the third decade of life are compared histologically. Except for two parameters, no significant differences were observed: 1) the appositional rate of bone formation was about three times greater in the beagle, and 2) the turnover rate was four to five times faster in the beagle.

The incidence of osteosarcoma arising from trabecular bone regions in beagles injected with ^{239}Pu is known. One approach in attempting to predict the incidence of osteosarcoma in humans from this beagle data is to be familiar with the structural and biologic aspects of trabecular bone of beagles and humans. This study is a comparison of the biologic activity parameters of trabecular bone from young adult beagle and human trabecular bone.

During the past several years, the iliac crest has become the accepted site for human bone biopsies. Technical problems of section preparation and staining of bone have been minimized. There remains disagreement over what bone histological activity parameters are most appropriate as well as a paucity of normal human data with which to compare to beagle data. The purpose of this report is to provide direct comparison of human and beagle iliac crest trabecular bone for the following bone characteristics: bone mass, bone formation, bone resorption, and bone turnover. Data from ten quantitative histologic studies of normal young adult humans are presented along with the current findings for the young adult beagle.

METHODS

The methodology of obtaining and processing an iliac crest biopsy specimen for humans was duplicated in nine young adult beagles, as a post-mortem procedure. It included: 1) specimen removal with an 8 mm trephine about 2 cm below the anterior iliac crest, 2) formalin fixation, 3) methyl methacrylate embedding, 4) preparation of 5 μ m and 10 μ m thick sections, 5) Goldner staining for cellular detail, 6) analysis of in vivo tetracycline labeling. The data collection was identical to that used in a large quantitative histologic study of human bone biopsies. The human data reported is for humans of age 17-30 years, except as noted.

RESULTS

Bone mass in the young adult beagle was essentially identical to that in the young adult human (Table 1). Indications are that bone turnover in the young adult beagle is four to five times that in a human in the third decade of life (Table 2). This is due mainly to a bone apposition rate of about 1.3 μ m/day in beagles vs. about 0.4-0.5 μ m/day in young adult humans. The static data also seem to indicate that there is somewhat more trabecular surface involved in bone turnover activity (surface bearing osteoblasts or osteoclasts) in the beagle when compared to the human (Tables 2 and 3).

TABLE 1. BONE MASS IN YOUNG ADULT HUMANS

Sampling Site (reference)	(n)	Per Cent Bone (percentage of space occupied by trabecular osteoid and mineralized tissue)
Iliac crest (1)	6	21-22
Iliac crest (15)	15*	20.0 ± 7.3
Iliac crest (5)	23	22.8 ± 3.2
Iliac crest (6)	10	17.9 ± 3.1
Iliac crest (12)	59	22.9 ± 5.3
Iliac crest (2)	28	21.7 ± 4.4
Iliac crest (14)	7	20.4 ± 4.0
Iliac crest (9)	16	22.8 ± 4.3
Lumbar vertebral body (4)	19	25.1 ± 3.3
Iliac crest (16)	3	19.4 ± 3.1

BONE MASS IN YOUNG ADULT BEAGLES

Iliac crest	9	23.0 ± 2.8
Lumbar vertebral body (7)	13	22.5 ± 5.0

*Average age of group was 41 years.

The data presented is from humans aged 17-30 years and beagles aged 400-800 days.

There is no significant difference between males and females at this age for this parameter, so the data are presented together.

TABLE 2. BONE FORMATION IN YOUNG ADULT HUMANS

Sampling Site (reference)	(n)	Percentage of Peri- meter with Osteoid	Percentage of Perimeter with Osteoblasts	Percentage of Surface Labeled with Tetracycline	Bone Appo- sition Rate (mm/yr)	Turnover# (%/yr)
Iliac crest (15)	15*	17.7 ± 8.5	-	-	0.113	34
Iliac crest (10)	16	13.8 ± 6.2	5.0 ± 2.9	-	-	-
Iliac crest (14)	7	17.5 ± 7.2	4.8 ± 2.0	-	-	-
Iliac crest (2)	11*	12 ± 10	4.5 ± 4.0	-	-	-
Iliac crest (8)	12 males	21.9 ± 7.3	-	18 ± 8	0.180	56
Iliac crest (8)	29 females	16.2 ± 5.9	-	12 ± 5	0.170	35
Iliac crest	Group Estimate (age 45 years)	-	-	-	-	32

BONE FORMATION IN YOUNG ADULT BEAGLES

Iliac crest	9	14.4 ± 4.9	7.1 ± 2.7	19 ± 7	0.460	194
-------------	---	------------	-----------	--------	-------	-----

*Average age of group is 41 years.

**Average age of group is 40 years.

#Turnover is defined as the percentage of bone volume renewed during one year. It is calculated only in the cases where apposition rate is measured, using the surface to volume ratio (SV_b) of 17.3(10) for humans and 22.2 for beagles. The formula is $\text{App. Rate} \times SV_b \times \% \text{-Osteoid Surfaces or \% -Tetracycline Labeled Surface}$.

TABLE 3. BONE RESORPTION IN YOUNG ADULT HUMANS

Sampling Site (reference)	(n)	Percentage of Surface with Howship's Lacunae	Percentage of Surface with Osteoclasts
Iliac crest (14)	7	6.1 ± 1.9	2.5 ± 1.5
Iliac crest (2)	11*	15.3 ± 7.6	0.6 ± 1.0
Iliac crest (13)	16	5.3 ± 1.7	0.5 ± 0.4
Iliac crest (15)	15**	4.4 ± 2.1	-
Iliac crest (16)	3	10.2 ± 2.2	-

BONE RESORPTION IN YOUNG ADULT BEAGLES

Iliac crest	9	-#	1.0 ± 0.5
-------------	---	----	---------------

*Average age of group was 40 years.

**Average age of group was 41 years.

#Howship's lacunae in beagles were not well identified in this work.

REFERENCES

1. J.S. Beck and B.E.C. Nordin, Histological assessment of osteoporosis by iliac crest biopsy, J. Path. Bact. 80: 391-399 (1960).
2. Ph. J. Bordier, L. Miravet and D. Hioco. Young adult osteoporosis, Clinics in Endo. and Metab. 2: 277-286 (1973).
3. R.G. Bromley, N.L. Dockum, J.S. Arnold and W.S.S. Jee, Quantitative histologic study of human lumbar vertebrae. J. Geront. 21: 537-543 (1966).
4. M.S. Dunnill, J.A. Andersen and R. Whitehead, Quantitative histological studies on age changes in bone. J. Path. Bact. 94: 275-291 (1967).
5. H.A. Ellis and K.M. Peart, Quantitative observations on mineralized and non-mineralized bone in the iliac crest. J. Clin. Path. 25: 272-286 (1972).
6. A. Garner and J. Ball, Quantitative observations of mineralized and unmineralized bone in chronic renal azotemia. J. Path. Bact. 91: 545-561 (1966).
7. W.S.S. Jee, D. Kimmel, E.G. Hashimoto, R.B. Dell and L.A. Woodbury, Quantitative studies of beagle lumbar vertebral bodies. In Proc. of the First Workshop on Bone Morphometry, Z.F.G. Jaworski (Ed.), U. of Ottawa Press, pp. 110-117 (1976).

8. F. Melsen (data to be published in Calc. Tiss. Res.).
9. W.A. Merz and R.K. Schenk, Quantitative structural analysis of human cancellous bone. *Acta Anat.* 74: 149-164 (1969).
10. W.A. Merz and R.K. Schenk, Quantitative histological study on bone formation in human cancellous bone. *Acta Anat.* 76: 1-15 (1970).
11. P. Meunier, P. Courpron, C. Eduoard, J. Bernard, J. Bringuier and G. Vignon, Physiological senile involution and pathological rarefaction of bone, *Clinics Endo. and Metab.* 2: 239-256 (1973).
12. P. Meunier, P. Courpron, J.M. Giroux, C. Eduoard, J. Bernard and G. Vignon, Osteoporosis: newer methods for quantitation. *Calc. Tiss. Res.* 21 (Suppl.) 354-360 (1976)
13. R.K. Schenk, W.A. Merz and J. Muller. A quantitative histological study on bone resorption in human cancellous bone. *Acta Anat.* 74: 44-53 (1969).
14. A. Schulz and G. Delling, Histomorphometric studies of age related changes in iliac crest trabecular bone. In *Proc. of the First Workshop on Bone Morphometry*, Z.F.G. Jaworski (Ed.), U. of Ottawa Press, pp. 106-107, 161-162, 189-190 (1976).
15. D.J. Sherrard, D.J. Baylink, J.E. Wergedahl and N.A. Maloney, Quantitative histological studies on the pathogenesis of uremic bone disease, *J. Clin. Endo. and Metab.* 39: 119-135 (1974).
16. Ph. Bordier, H. Matrajt, L. Miravet and D. Hioco, Mesure histologique de la masse et de la resorption des fravees osseuses, *Path. Biol.* 12: 1238-1243 (1964).

HISTOLOGIC STUDY OF TRABECULAR BONE OF BEAGLE RIB

S.C. Miller, D.B. Kimmel and W.S.S. Jee

In order to characterize the beagle rib as a function of age and to obtain baseline data for the analysis of biopsies of ribs from mature and juvenile beagles, a study of the right sixth rib from 49 beagles of various ages was made. The ribs were prepared for study and analyzed as in previous studies (1,2), except that all tetracycline-labeled surfaces, both single and double-labeled, were included in the calculation of bone turnover rate. The results are listed in Table 1.

The appositional rate of bone formation in the rib is greatest at three months of age, but decreases to a lifetime-steady rate by six months of age. Turnover of the rib is greatest at age three months, has decreased about four-fold by age six months, then reaches a lifetime-steady rate of about 100%/yr by age three-four years.

TABLE 1
SURFACE TO VOLUME RATIO (SV_b), BONE APPPOSITION RATE, AND BONE
TURNOVER RATE IN BEAGLES FROM SIX AGE GROUPS

Age Group	n	SV_b	App. Rate ($\mu\text{m}/\text{day}$)	Turnover/yr
3 months	7	28.2	2.0	684
6-12 months	19	25.3	1.0	158
17 months	7	24.7	1.0	147
38-40 months	3	23.0	1.0	76
85-120 months	5	25.5	1.0	106
136-158 months	8	25.5	1.0	96

REFERENCES

1. W.S.S. Jee, D.B. Kimmel, T.J. Wronski, J.E. Gotcher, and R.B. Dell, Preliminary evaluation of bone formation in sixth rib of beagles, in Research in Radiobiology, U. of Utah C00-119-251, pp. 253-258 (1976).
2. T.J. Wronski, J.M. Smith, and W.S.S. Jee, A preliminary report on the correlation of the rate of trabecular bone turnover and Pu-239 concentration on trabecular surfaces with the incidence of osteosarcoma at selected skeletal sites, in Research in Radiobiology, U. of Utah C00-119-252, pp. 172-187 (1977).

PLUTONIUM-INDUCED OSTEOSARCOMAS IN THE ST. BERNARD

G. N. Taylor, G. B. Thurman,* C. W. Mays, L. Shabestari,
W. Angus, J. Eaton, and J. Hitchman

ABSTRACT: Thirteen osteosarcomas have been observed among the 7 St. Bernards that have died following the injection of ^{239}Pu . Preliminary data indicate that the St. Bernard is about 6 times more sensitive than the Beagle, and about 150 times more sensitive than the average person is to ^{239}Pu -induced bone sarcomas. Thus, the St. Bernard may be an excellent model to study the pathogenesis of bone cancer induction, to evaluate the relationship between spontaneous susceptibility and radiosensitivity, and to determine whether or not radiosensitivity significantly affects the toxicity ratio.

INTRODUCTION

A direct relation between body size and susceptibility to naturally-occurring bone cancer is well established in dogs.⁽¹⁻⁴⁾ Animals with adult weights of 80 pounds or higher are up to 185 times more sensitive than dogs under 40 pounds. In 1969 we began the study of bone-seeking radionuclides in St. Bernards. The objectives of this study were: (a) to intercompare the $^{239}\text{Pu}/^{226}\text{Ra}$ toxicity ratio in Beagles and in St. Bernards, so that the toxicity ratio for man could be predicted with greater confidence; (b) to examine the dose-response relationships of Pu and Ra at very low dose levels in an extraordinarily susceptible breed; and (c) to investigate the fundamental nature of the relationship between natural sensitivity and susceptibility to radiation-induced bone diseases.

Although the experiments encompass both ^{226}Ra and ^{239}Pu toxicity, the radium phase was begun relatively recently and radium-induced endpoints have not yet appeared. Thus, this report will discuss only those data derived from the plutonium-treated animals.

* Now at Department of Biochemistry, University of Texas Medical Center at Galveston.

METHODS

Pure-bred St. Bernards were obtained from several suppliers. However, each dog had been registered with the American Kennel Club. They averaged about 106 pounds at the time of injection.

The radionuclides were administered in a citric acid, sodium citrate buffer (pH 3.5), via a single intravenous injection.⁽⁵⁾ The average age at injection was about 19 months.

The dietary and husbandry factors were similar to those employed in our beagle studies.⁽⁵⁾

RESULTS AND DISCUSSION

Thus far, 13 plutonium-induced bone tumors have developed in 7 of our St. Bernards (Table 1). All were histologically-confirmed osteosarcomas. Their anatomical sites are shown in Fig. 1.

Only 1 of these 13 osteosarcomas arose in the axial skeleton (a tumor in the lumbar vertebrae). By comparison, the axial skeleton contains about 10% of the naturally-occurring osteosarcomas in dogs of the giant breeds,⁽¹⁻³⁾ but a much larger 45% of the ^{239}Pu -induced osteosarcomas in beagles.^(6,7) Thus, in this respect, the distribution of ^{239}Pu -induced osteosarcomas in the St. Bernard is more similar to the distribution of naturally-occurring osteosarcomas in the giant breeds than to the distribution of ^{239}Pu -induced osteosarcomas in the beagle (a small breed).

The appearance times for ^{239}Pu -induced bone sarcomas are compared in Fig. 2. For similar injected dosages (in $\mu\text{Ci/kg}$) the osteosarcomas appeared sooner in St. Bernards than in beagles. For the same appearance time less dosage was required for St. Bernards than for beagles. For example, the injection of $0.117 \mu\text{Ci/kg}$ in St. Bernards resulted in an average tumor appearance time of 4 years, whereas,

for the same appearance time in beagles the corresponding interpolated dosage was 0.68 $\mu\text{Ci/kg}$. Thus, present data indicate that St. Bernards are about 6 times more sensitive to osteosarcoma induction than beagles:

$$\text{Relative sensitivity} = \frac{0.68 \text{ } \mu\text{Ci/kg (beagle, interpolated)}}{0.117 \text{ } \mu\text{Ci/kg (St. Bernard, observed)}} = 6$$

While St. Bernards are more sensitive than beagles to both radiation-induced and naturally-occurring osteosarcomas, the relative sensitivity factors are not the same, being 6 for ^{239}Pu -induction, and about 185 for natural occurrence. (1-3) At least, for bone sarcomas, this argues against the "relative risk hypothesis" which assumes that radiation-induction is exactly proportional to natural incidence. (8)

However, the increased risk from radiation-induced osteosarcomas in animals with high natural incidence suggests that conditions, such as Paget's disease, that elevate the "natural" incidence of bone cancer, may also make these persons more susceptible to radiation-induced bone cancer, but probably not in direct proportion to their enhanced natural sensitivity. Roughly, 0.1% of the deaths in the USA are due to osteosarcoma. But Dahlin states that the incidence is about 1% for all patients with Paget's disease and, perhaps, 10% for those with severe Paget's disease. (9)

Since the St. Bernard is about 6 times more sensitive to ^{239}Pu -induced bone sarcomas than the beagle, and the beagle appears to be about 25 times more sensitive to ^{239}Pu than man, (10) the St. Bernard seems to be about 150 times more sensitive than the average person. Therefore, the St. Bernard may be an excellent experimental model, corresponding to the most susceptible members of the human population.

The growth rate of our St. Bernards, based on body weight, was much greater than that of our Beagles (Fig. 3). Also, the plasma concentration of somatotropin (growth hormone) in our St. Bernards was about twice that in our Beagles of comparable age. In view of these factors, it was somewhat surprising that the osteosarcoma volume doubling times in the 11 St. Bernard tumors in which growth rates could be evaluated radiographically (19 days average, range 9 to 32 days, see Table 1) were similar to those measured in 249 beagle osteosarcomas (14 days average, range 5 to 60 days).⁽⁷⁾ The shorter tumor appearance times in the St. Bernard are due to its greater radiosensitivity to bone tumor induction, and not to a faster growth rate of the tumor after it has been induced.

The marked sensitivity of the St. Bernard makes it a useful animal model with which to investigate some of the factors in radiation toxicity. For example, it is likely that its high sensitivity will make some of the mechanisms of bone carcinogenesis much more visible. Comparison of bone kinetic features and serological parameters with those of less sensitive experimental animals may possibly aid in defining some of the measurable parameters in bone carcinogenesis. For example, children with bone cancer tend to be taller than age-matched controls.⁽¹¹⁾ And patients with Paget's disease are unusually susceptible to bone cancer.^(9,12)

If the $^{239}\text{Pu}/^{226}\text{Ra}$ toxicity ratio in an animal of high radiosensitivity, such as the St. Bernard, is similar to the toxicity ratios in animals of lower radiosensitivity, such as the Beagle and mouse, then such ratios can be applied to man with much greater confidence. The St. Bernard will permit the testing of the following relationship:

$$\frac{\text{Pu}}{\text{Ra}}_{\text{mouse}} \approx \frac{\text{Pu}}{\text{Ra}}_{\text{Beagle}} \approx \frac{\text{Pu}}{\text{Ra}}_{\text{St. Bernard}} \approx \frac{\text{Pu}}{\text{Ra}}_{\text{man}}$$

REFERENCES

1. Tjalma R.A.: Canine bone sarcoma; estimation of relative risk as a function of body size. J. Nat. Cancer Inst. 36: 1137-1150 (1966).
2. Brodey R.S. and Riser W.H.: Canine osteosarcoma, a clinicopathologic study of 194 cases. Clin. Orthopaedics Related Res. 62: 54-64 (1969).
3. Ling G.V., Morgan J.P., and Pool R.R.: Primary bone tumors in the dog: a combined clinical, radiographic, and histologic approach to early diagnosis. J. Am. Vet. Med. Assoc. 165: 55-67 (1974).
4. Misdorp W. and Van der Heul R.O.: XXI. Tumors of bones and joints: Bull. World Health Organ. 53: 265-282 (1976).
5. Dougherty T.F., Stover B.J., Dougherty J.H., Jee W.S.S., Mays C.W., Rehfeld C.E., Christensen W.R., and Goldthorpe H.C.: Studies of the biological effects of ^{226}Ra , ^{239}Pu , ^{228}Ra (MsTh), ^{228}Th (RdTh), and ^{90}Sr in adult beagles. Radiat. Res. 17: 625-681 (1962).
6. Thurman G.B., Mays C.W., Taylor G.N., Keane A.T., and Sissons H.A.: Skeletal location of radiation-induced and naturally occurring osteosarcomas in man and dog. Cancer Res. 33: 1604-1607 (1973).
7. Thurman G.B.: Growth dynamics of osteosarcomas in beagles. University of Utah Report C00-119-243 (1971).
8. BEIR Report: The effects on populations of exposure to low levels of ionizing radiation. National Academy of Sciences, Washington D.C., 217 pages (1972).
9. Dahlin D.C.: Bone Tumors. Second Edition, C.C. Thomas, Publisher, see p. 172 (1967).
10. Mays C.W., Spiess H., Taylor G.N., Lloyd R.D., Jee W.S.S., McFarland S.S., Taysum D.H., Brammer T.W., Brammer D., and Pollard T.A.: Estimated risk to human bone from ^{239}Pu . Pages 343-362 in The Health Effects of Plutonium and Radium (W.S.S. Jee, Ed.), J.W. Press, Salt Lake City (1976).

11. Fraumeni J.F.: Stature and malignant tumors of bone in childhood and adolescence. Cancer 20: 967-973 (1967).
12. Price C.H.G.: Osteogenic sarcoma; an analysis of the age and sex incidence. British J. Cancer 9: 558-574 (1955).

Table 1. OSTEOSARCOMAS IN ^{239}Pu -INJECTED ST. BERNARDS (31 MARCH 1978)

Dog	Injected $\mu\text{Ci/kg}$	Tumor Location	Volume Doubling Time (Days)	Days from Injection to: Est. Start of Tumor	Death
T86P4E	0.903	R. Ilium	----	---	901
T58P3E	0.291	Mid. R. Humerus	15.5	179	917
T58P3E	0.291	Prox. L. Humerus	14.2	416	917
T59P3E	0.290	Prox. L. Femur	9.4	603	973
T59P3E	0.290	L. Ilium	----	---	973
T60P3E	0.314	6th Lumbar Vert.	19.2	150	784
T57P2E	0.096	Prox. L. Humerus	19.3	759	1506
T57P2E	0.096	Prox. R. Humerus	26.2	523	1506
T57P2E	0.096	Dist. R. Femur	13.0	1064	1506
T57P2E	0.096	Dist. L. Tibia	23.4	700	1506
T61P2E	0.098	Dist. L. Humerus	18.7	880	1639
T61P2E	0.098	Prox. L. Humerus	32.1	348	1639
T62P2E	0.156	Prox. R. Humerus	19.7	351	1223

Av. All

19.2

Fig. 1. Anatomical distribution of ^{239}Pu -induced osteosarcomas in the St. Bernard.

FIG2. OSTEOSARCOMA LATENT PERIODS IN ST. BERNARDS & BEAGLES

Fig 3. ST. BERNARD AND BEAGLE GROWTH CURVES

EFFECT OF GONADECTOMY ON THE INCIDENCE OF PLUTONIUM-INDUCED BONE CANCER IN MICE

G. N. Taylor, P. Gardner, C. W. Mays, L. Talbot, and D. Van Moorhem

ABSTRACT: The incidence of ^{239}Pu -induced bone cancer, after a single intraperitoneal injection of the monomeric (PuIV) form, is significantly higher in female than in male mice. To evaluate the role of the gonads in this sex-related difference, BALB/c mice, male and female, were castrated 40 days prior to plutonium injection and their plutonium-induced tumor incidence was determined. After castration, the bone sarcoma incidence in the two sexes was approximately equal. This resulted from an increased incidence in the castrated males and a decreased incidence in the ovariectomized females, as compared to the intact plutonium-treated group.

INTRODUCTION

Male and female mice often differ considerably with respect to morphological features, functional factors, and reactions to toxic agents. For example, morphological differences are prominent in the terminal duct of the submaxillary gland⁽¹⁾ and in the parietal lining of Bowman's membrane in the glomerulus.⁽²⁾ Metabolic differences are suggested by sex related differences in the distribution of alkaline phosphatase within the tubular epithelium of the kidney,⁽³⁾ the composition of the urine,⁽⁴⁾ the fat content of the adrenal gland,⁽⁵⁾ and in the metabolism of plutonium.⁽⁶⁾ Sex related differences have also been noted in the response of mice to some toxic agents, especially chloroform.⁽⁴⁾

Another very obvious sexual difference in mice is seen in their sensitivity to radiation-induced bone cancer. It is well established that the female mouse is several times more susceptible than the male to osteosarcoma induction by internal emitters.⁽⁷⁻⁹⁾ This is in contrast to beagles⁽¹⁰⁾ and to humans,⁽¹¹⁾ where the distribution of radiation-induced bone cancer is approximately equal for the two sexes.

The reason for the much higher incidence of radiation-induced osteosarcomas in female mice has not been established. It is the purpose of this study to present some interim results of an experiment that has been designed to evaluate the effect of gonadectomy on this sex-related difference.

METHODS

All of the animals used in this study were BALB/c mice. They were maintained in a controlled temperature environment (72 °F). Lighting was regulated at 12 hours on and 12 hours darkness.

Neutering was performed at approximately 40 days of age, using methoxyflurane^{*} anesthesia and an abdominal surgical approach in both males and females. The seminal vesicles, coagulating glands, and the uterus were excised with the gonads.

The radionuclide was administered in a citric acid-sodium citrate buffer (pH 3.5),⁽¹²⁾ via a single intraperitoneal injection, at 90 ± 5 days age.

For statistical purposes, only those animals that survived beyond 250 days post-injection were considered to be at risk. The earliest tumor death in any of the irradiated groups was 318 days post-injection.

Tumor diagnosis was based on both radiography and histological evaluation.

RESULTS

Gonadectomy produced a marked change in the incidence of plutonium-induced bone cancer in BALB/c mice (Table 1). Compared to the intact animals, the incidence rose appreciably in the castrated males, and a prominent decrease occurred in the ovariectomized females. After castration the bone tumor incidence in the sexes was approximately equal. These data tentatively indicated that in BALB/c

^{*}Penthrane, Abbott Laboratories, North Chicago, Illinois.

mice the sex related difference in the incidence of plutonium-induced bone cancer is gonad dependent. Gonadectomy in the control groups did not alter the expected zero incidence.

Table 1. INCIDENCE OF ^{239}Pu -INDUCED OSTEOSARCOMAS IN NEUTERED VS. INTACT BALB/c MICE.

Injected Dose ($\mu\text{Ci } ^{239}\text{Pu/kg}$)	Intact		Neutered	
	Female	Male	Female	Male
2.9	19/20=95%(404)	2/12=17%(522)	10/19=53%(452)*	9/15=60%(485)**
0	0/15=0% (603)	0/14=0% (698)	0/8=0% (603)	0/10=0% (625)

(The average days from injection to death are shown in parentheses.)

*Six mice still living.

**Nine mice still living.

DISCUSSION

The influence of the gonads on the incidence of spontaneously occurring bone sarcomas is uncertain. This is largely because of the very low natural incidence of this type of neoplasia in mice.⁽¹³⁾ However, there is an indication that a sex related difference, at least in the C57Bl strain, does exist. For example, in one survey, involving 4381 autopsies, the seven observed bone cancers all occurred in female mice.⁽¹⁴⁾ The only bone tumor that has arisen in a control animal in the mouse colony of this laboratory, involved a female (C57Bl/Do strain).⁽⁹⁾ This is in contrast to the sex distribution of spontaneous bone cancer in humans, where the incidence in men is slightly higher than in women.⁽¹⁵⁾

Smith et al., have demonstrated a higher retention of monomeric plutonium in male, as compared to female mice.⁽¹⁶⁾ This sex related difference was eliminate when the males were castrated prior to injection.⁽⁶⁾ Ovariectomy did not change

the retention of plutonium. Since the tumor incidence in the two sexes tended to run counter to the retention differences, it appeared reasonably certain that this was not a factor in the higher bone tumor incidence in female mice in our study.

A feature of mice that may possibly be involved in the significantly higher osteosarcoma incidence in females is their unusual skeletal response to estrogens. In mice, large amounts of endosteal bone are produced by estrogen administration, in both females and males, and prolonged treatment will eventually fill the marrow cavities of some of the long bones.⁽¹⁷⁾ This effect occurs physiologically, during the preovulatory phase of the egg laying cycle in birds,⁽¹⁸⁾ but only after estrogen administration in mice. It is perhaps more than coincidental that estrogen administration does not induce endosteal bone growth in rats,⁽¹⁹⁾ a species that, also, does not show a sex related difference in the incidence of bone cancer.⁽²⁰⁾

ACKNOWLEDGMENTS

Appreciation is extended to David Atherton, Tony Fallis, and Terry Pollard for assistance in this study.

REFERENCES

1. Lacassagne A.: Dimorphisme sexuel de la glande sous - maxillaire chez la souris. *Compt. Rend. Soc. Biol.* 133: 180-181 (1940).
2. Crabtree E.E.: The structure of Bowman's capsule as an index of age and sex - variation in normal mice. *Anat. Rec.* 79: 395-413 (1941).
3. Dunn T.B.: Some observation on the normal and pathologic anatomy of the kidney of the mouse. *J. Nat. Cancer Inst.* 9: 285-301 (1949).
4. Deringer M.M., Dunn T.B., and Heston W.E.: Results of exposure of strain C3H mice to chloroform. *Proc. Soc. Exp. Biol. Med.* 183: 474-479 (1953).

5. Deanesley R.: Adrenal cortex difference in male and female mice. *Nature* 141: 79 (1938).
6. Smith J.M., Taylor G.N., Mays C.W., and Atherton D.R.: The early retention of monomeric $^{239}\text{Pu}(\text{IV})$ -citrate in C57Bl/Do and BALB/cj mice. *Radiation Res.* 73: 502-509 (1978).
7. Finkel M. and Biskis B.O.: Experimental induction of osteosarcomas. *Progr. Exp. Tumor Res.* 10: 72-111 (1968).
8. Loutit J.F., Sansom Janet, and Carr T.E.F.: The pathology of tumors induced in Harwell mice by ^{239}Pu and ^{226}Ra . Pages 505-519 in The Health Effects of Plutonium and Radium (W.S.S. Jee, Ed.), J.W. Press, Salt Lake City (1976).
9. Mays C.W., Spiess H., Taylor G.N., Lloyd R.D., Jee W.S.S., McFarland S.S., Taysum D.H., Brammer T.W., Brammer D., and Pollard T.A.: Estimated risk to human bone from ^{239}Pu . Pages 343-362 in The Health Effects of Plutonium and Radium (W.S.S. Jee, Ed.), J.W. Press, Salt Lake City (1976).
10. Mays C.W. and Lloyd R.D.: Bone sarcoma incidence vs. alpha particle dose. Pages 409-430 in Radiobiology of Plutonium (B.J. Stover and W.S.S. Jee, Eds.), J.W. Press, Salt Lake City (1972).
11. Spiess H. and Mays C.W.: Bone cancers induced by $^{224}\text{Ra}(\text{Th X})$ in children and adults. *Health Physics* 19: 713-729 (1970).
12. Dougherty T.F., Stover B.J., Dougherty J.H., Jee W.S.S., Mays C.W., Rehfeld C.E., Christensen W.R., and Goldthorpe H.C.: Studies of the biological effects of ^{226}Ra , ^{239}Pu , $^{228}\text{Th}(\text{RdTh})$, and ^{90}Sr in adult beagles. *Radiation Res.* 17: 625-681 (1962).
13. Pubus F.C. and Miller E.W.: Spontaneous bone tumors of mice. *Am. J. Cancer* 33: 98-111 (1938).

14. Franks L.M., Rowlatt C., and Chesterman F.C.: Naturally occurring bone tumors in C57BL/1crf mice. *J. Nat'l. Cancer Inst.* 50: 431-438 (1973).
15. McKenna, R.J., Schwinn C.P., Soong K.Y., and Higinbotham N.L.: Sarcomata of the osteogenic series (osteosarcoma, fibrosarcoma, chondrosarcoma, parosteal osteogenic sarcoma, and sarcomata arising in abnormal bone). *J. Bone and Joint Surg.* 48-A, 1-26 (1966).
16. Smith J.M., Lloyd R.D., Atherton D.R., and Mays C.W.: The early retention and distribution of monomeric $^{237}\text{Pu}(\text{IV})$ and $^{239}\text{Pu}(\text{IV})$ in C57BL/Do mice. Pages 7-20 in The Health Effects of Plutonium and Radium (W.S.S. Jee, Ed.), J.W. Press, Salt Lake City (1976).
17. Urist M.R., Budy A.M., and McLean F.C.: Endosteal bone formation in estrogen treated mice. *J. Bone Jt. Surg.* 32-A: 143-162 (1950).
18. Kyes P. and Potter T.S.: Physiological marrow ossification in female pigeons. *Anat. Rec.* 60: 377-379 (1934).
19. Lindquist B., Budy A.M., McLean F.C., and Howard J.L.: Skeletal metabolism in estrogen-treated rats studied by means of Ca^{45} . *Endocrinol.* 66: 100-111 (1960).
20. Bensted J.P.M., Taylor D.M., and Sowby F.D.: The carcinogenic effects of Americium-241 and Plutonium-239 in the rat. *Brit. J. Radiol.* 38: 920-925 (1965).

SEPARATION OF ^{224}Ra FROM ^{228}Th

F. W. Bruenger, D. R. Atherton, E. R. Neilson, and W. Stevens

ABSTRACT: A simple method was devised to separate ^{224}Ra from a source of ^{228}Th . The procedure involves coprecipitation of ^{228}Th and Zirconium as the hypophosphate in HCl . ^{224}Ra was soluble in the acidic medium and was separated from ^{228}Th by 3 successive centrifugations at 40,000 xg. Initial yield was $\sim 40\%$ and the separation factor was 10^5 or better.

In order to secure a back-up supply which, for extended periods of time would provide an excess of more than 100 μCi of ^{224}Ra weekly, a source was developed which provided the necessary quantity of ^{224}Ra free of long half-life contaminants.

The chemical separation of ^{224}Ra and ^{228}Th by several ion exchange procedures has been described by König et al. Excellent separation of the daughter products from the parent ^{228}Th was accomplished when the Th was adsorbed onto an inorganic ion exchanger consisting of zirconiumhypophosphate which had been incorporated into an inactive matrix of SiO_2 . A separation of $^{228}\text{Th} : ^{224}\text{Ra}$ of "1 part per 5×10^5 " has been reported after elution with HCl at a concentration ranging from 0.1 - 6 N HCl . At an acid concentration of 0.1 N, the yield of ^{224}Ra was $\sim 60\%$. However, in our hands, elution of ^{224}Ra from such a column proved to be somewhat cumbersome and did not provide the Ra in a form which met stringent specifications for radiochemical purity. Therefore, a slightly different method of ^{224}Ra preparation was developed and the following procedure was adopted:

Fifteen mg of Zr ($50 \text{ mg } \text{ZrOCl}_2 \times 8 \text{ H}_2\text{O}$) or 0.16 m mole and a twofold excess of $\text{Na}_2\text{H}_2\text{P}_2\text{O}_6 \times 6 \text{ H}_2\text{O}$ (100 mg) each were dissolved in 3 ml of 0.1 N

HCl. The ZrOCl_2 was combined with 0.5 mCi of ^{228}Th and precipitated by addition of the acidic hypophosphate solution. After 3 hours, the precipitate was sedimented by centrifugation at 40,000 xg using a centrifuge which was equipped with a charcoal trap in its exhaust system for the adsorption of radon. The precipitate was then suspended in 0.5 N HCl and the supernatant was separated by centrifugation. The last step was repeated at one-day intervals 3 more times in order to eliminate long half-life contaminants (^{210}Pb , ^{226}Ra , ^{228}Ra). The final precipitate was stored in 0.5 N HCl.

For repetitive preparation of ^{224}Ra , the following centrifugation scheme was used:

1. Original separation from carrier: 30' at 40,000 xg
2. Supernatant for 30' at 40,000 xg
3. Supernatant for 60' at 40,000 xg

The initial yield of ^{224}Ra was $\sim 215 \mu\text{Ci}$. The decay was followed over a span of 40 ^{224}Ra half-lives and corresponded to the known half-life of ^{224}Ra (3.64 d). In three such preparations no ^{210}Pb was detected either subjectively (by spectral analysis) or objectively by 3 $\sqrt{\text{Bkg}}$ criteria. There was no detectable ^{226}Ra in two specimens, but a small amount of ^{226}Ra (exceeding the 3 $\sqrt{\text{Bkg}}$) was found in another specimen ($< 2 \times 10^{-6} \text{ }^{226}\text{Ra}/^{224}\text{Ra}$). No ^{228}Th was detected in 2 specimens, but in 1 specimen the $^{228}\text{Th}/^{224}\text{Ra}$ ratio (adjusted to $t = 0$) was 6×10^{-6} .

The purity of the ^{224}Ra satisfied the imposed criteria. The method described offers an easy way to produce ^{224}Ra of high purity. The only disadvantage is that probably, because of crystal growth in the precipitate, yields

decrease with a half-time of about 6 months. However, stirring the suspension for 24 hours before separation will lead to substantially higher yields of ^{224}Ra . If yields decrease below reasonable limits, dissolution of the Zr-Th hypophosphate and reprecipitation can provide an easy way of regeneration of the source.

REFERENCES

1. König, K. H. and F. Hoyer: 1965. Trägerfreies ^{224}Ra (ThX) aus ^{228}Th (RdTh) durch Ionenaustausch an Zirkonhypophosphat. Atompraxis 11(5): 275-277.

EARLY RETENTION AND DISTRIBUTION OF INJECTED ^{224}Ra IN BEAGLES

R. D. Lloyd, C. W. Mays, G. N. Taylor, D. R. Atherton,
F. W. Bruenger, and C. W. Jones

ABSTRACT: The retention, distribution, and skeletal dosimetry of injected ^{224}Ra in beagles has been studied in six young adult dogs sacrificed 0.04 to 7 days after ^{224}Ra administration. Biological retention of ^{224}Ra in the skeleton averaged 48% (37 to 60%); and soft tissue retention decreased from 61% at 0.04 days to 6% at 7 days. At death there was an excess of ^{212}Pb over ^{224}Ra in red cells and liver, an excess of ^{212}Bi over ^{224}Ra in kidneys and plasma, and a deficiency of both ^{212}Pb and ^{212}Bi relative to ^{224}Ra in eyes and bone. These data indicate that the escape of ^{220}Rn produced in bone by ^{224}Ra decay is roughly 8%. From the retention in the skeleton of ^{224}Ra , ^{212}Pb , and ^{212}Bi , it was calculated that the injection of 1 μCi ^{224}Ra /kg results in an average skeletal dose of about 40 rad in a beagle having 75 g skeleton/kg body.

INTRODUCTION

Biological effects have been observed in the skeleton, kidneys, eyes, and livers among persons injected with ^{224}Ra (Spiess et al., 1978, Mays et al., 1978). Because of its relatively short 3.62 day physical half-time, most of the alpha disintegrations of ^{224}Ra and its retained daughters (Fig. 1) within the skeleton occur on bone surfaces, in a fashion somewhat analogous to that of ^{239}Pu . A number of beagles in our laboratory are being injected with ^{224}Ra , and resulting biological effects will be compared with those in beagles given ^{239}Pu , to enable the prediction of effects in bone from ^{239}Pu in the human using the model:

$$\frac{{}^{239}\text{Pu effects}}{{}^{224}\text{Ra effects}} \quad \sim \quad \frac{{}^{239}\text{Pu effects}}{{}^{224}\text{Ra effects}}$$

in man in dog

This information will supplement data of a companion experiment conducted within our laboratory involving ^{239}Pu and ^{226}Ra in beagles utilizing the experience with humans containing long-lived ^{226}Ra ($T_{1/2} = 1620$ yr), as reported in the literature. This can be represented by the expression:

$$\frac{{}^{239}\text{Pu effects}}{{}^{226}\text{Ra effects}} \sim \frac{{}^{239}\text{Pu effects}}{{}^{226}\text{Ra effects}}$$

in man in dog

Although most of the alpha disintegrations within the skeleton of ${}^{226}\text{Ra}$ and its retained daughters occur within bone volume, the irradiation continues over the remaining lifespan in a fashion similar to that of alpha-emitting ${}^{239}\text{Pu}$, which has a long physical half-time of about 24,000 years. Even after the initial deposit of ${}^{226}\text{Ra}$ in the skeleton has shifted mainly from bone surfaces to bone volume, some irradiation of bone surface continues throughout the lifetime. It is believed that a better prediction of ${}^{239}\text{Pu}$ toxicity in humans can be made if both of these experiments are considered rather than either one alone.

METHODS

Calculation of radiation doses resulting from ${}^{224}\text{Ra}$ administration is essential to a meaningful comparison of biological effects which will be observed among the lifespan animals. In order to accomplish this goal, six young adult beagles were each given an intravenous injection of ${}^{224}\text{Ra}$ chloride, as shown in Table 1. Injected daughter activities were about 0.98 (${}^{212}\text{Pb}$) and 0.95 (${}^{212}\text{Bi}$) of the Pb/Ra and Bi/Ra ratios at transient equilibrium. Ages and weights of these animals were similar to those of the lifespan dogs at injection, and dogs of both sexes were utilized. The animals were sacrificed by exsanguination under sodium pentothal anesthesia at various times after injection. Serial gamma-ray counting of selected bones and soft tissues was begun a few minutes after death and continued for several days to determine the initial content of ${}^{212}\text{Pb}$ and ${}^{212}\text{Bi}$. All bones and soft tissues were assayed for their ${}^{224}\text{Ra}$ content after storage at below freezing temperatures for 6 days.

RESULTS AND DISCUSSION

Retention. At death there was an excess of ^{212}Pb over ^{224}Ra in red cells and liver, an excess of ^{212}Bi over ^{224}Ra in kidney (Fig. 2) and plasma, and a deficiency of both daughters relative to the parent radium in eyes and in bone (Fig. 3). Initial deposition of injected ^{212}Pb and ^{212}Bi in bone appeared to be about 0.3 and 0.2, respectively, of their equilibrium values (Fig. 4), and the retention of these two nuclides in bones of the dogs dying at 3 and 7 days after injection indicated an escape of ^{220}Rn (Fig. 1) from the skeleton of roughly 8%.

Biological retention of ^{224}Ra in the skeleton ranged from about 37% to 60% (Fig. 5), and the relative distribution of retained ^{224}Ra among the various bones was similar to that found for beagles injected with ^{226}Ra (Lloyd et al., 1976a). Soft tissue retention (Fig. 5) decreased from 61% at 0.04 days to 6% at 7 days after injection. Total-body retention of injected ^{224}Ra (Fig. 6) in these six dogs was similar to that of ^{226}Ra (Lloyd et al., 1976b).

Skeletal Dosimetry. Empirically-derived equations of the form

$$R = Ae^{-\alpha t} - Be^{-\beta t} \quad (1)$$

were fitted to the effective retention values in bone for ^{224}Ra , ^{212}Pb , and ^{212}Bi (Fig. 7), with the constraint of having the reduction constant " α " associated with the longest-lived term for ^{212}Pb and for ^{212}Bi match that derived by the method of least squares for ^{224}Ra , and the retention of $\text{Ra} > \text{Pb} > \text{Bi}$. A similar equation for the effective retention of short-lived ^{220}Rn (and ^{216}Po) (Fig. 1) was chosen so as to be intermediate between the expressions derived from the data for ^{224}Ra and ^{212}Pb using geometric means of corresponding parameters and was:

$$R_{(\text{Rn and Po})} = 0.486 e^{-0.214t} - 0.276 e^{-4.65t}$$

Decay energies for use in the dosimetry calculations were obtained from Lederer et al. (1967), and are given in Table 2. Recoil energies were included. Fractional absorption of β -energy in the beagle skeleton was taken to be 0.94 for ^{212}Pb and 0.81 for $^{212}\text{Bi} + ^{208}\text{Tl}$, based on the studies of Parmley et al. (1962).

Average skeletal dose-rates at "t" days after injection can be calculated from the formula (Evans, 1955)

$$\text{dose rate} = \left(\frac{51.2 \text{ g dis rad}}{\mu\text{Ci MeV day}} \right) \left(\frac{\text{EMeV}}{\text{dis.}} \right) \left(\frac{\text{I } \mu\text{Ci/kg}}{\text{G g/kg}} \right) R_t \quad (2)$$

where " R_t " is the instantaneous skeletal retention at "t" days after injection and "G" represents the g skel/kg body at injection. For a given nuclide, the product of the first 3 factors in parentheses represent a constant = "C," so that the cumulative average skeletal dose, from injection to "t" days later is the constant "C" multiplied by the integral of the retention function, or

$$\text{Dose} = C \int_0^t R \, dt .$$

For ^{224}Ra , $C = \frac{(51.2)(5.77)\text{I}}{\text{G}} \frac{\text{rad}}{\text{day}}$, or $295 \frac{\text{I}}{\text{G}} \text{ rad/day}$.

Corresponding values of "C" for the other nuclides in the decay chain are:

NUCLIDE	C
$^{220}\text{Rn} + ^{216}\text{Po}$	682 I/G rad/day
^{212}Pb	10 I/G rad/day
$^{212}\text{Bi} + ^{212}\text{Po} + ^{208}\text{Tl}$	439 I/G rad/day

Integration of a retention function of the form of Eq. 1 yields

$$\int_0^t R \, dt = \frac{A}{x} (1 - e^{-xt}) - \frac{B}{y} (1 - e^{-yt}) . \quad (3)$$

Therefore, the cumulative average skeletal dose to "t" days after injection becomes for ^{224}Ra :

$$D = [295 \text{ I/G}] [2.467(1-e^{-0.214t}) - 0.025(1-e^{-9.01t})] \text{ rad} \quad (4)$$

for $^{220}\text{Rn} + ^{216}\text{Po}$:

$$D = [682 \text{ I/G}] [2.271(1-e^{-0.214t}) - 0.059(1-e^{-4.65t})] \text{ rad} \quad (5)$$

for ^{212}Pb :

$$D = [10 \text{ I/G}] [2.089(1-e^{-0.214t}) - 0.140(1-e^{-2.40t})] \text{ rad} \quad (6)$$

for $^{212}\text{Bi} + ^{212}\text{Po}, + ^{208}\text{Tl}$:

$$D = [439 \text{ I/G}] [1.827(1-e^{-0.214t}) - 0.147(1-e^{-2.38t})] \text{ rad} \quad (7)$$

The total dose from retained ^{224}Ra and its retained daughters is just the sum of equations 4, 5, 6, and 7. Since the dose equations are based upon measured values, the fact that 98% of the equilibrium ^{212}Pb and 95% of the equilibrium ^{212}Bi are injected in the ^{224}Ra solution is already taken into account.

For times which are long compared to the 3.62 day half-time of ^{224}Ra , $t \rightarrow \infty$ and the cumulative dose equation reduces to:

$$D = \text{I/G} [720 + 1509 + 19 + 737] = 2985 \text{ I/G rad} .$$

In beagles having 75 g skeleton/kg body and injected with 1 μCi $^{224}\text{Ra/kg}$,

$$D = 39.8 \text{ rad} ,$$

with the alpha dose contributing about 96% of the total.

REFERENCES

- Evans R.D., 1955, The Atomic Nucleus, McGraw Hill, New York, p. 742.
- Lederer C.M., Hollander J.M., and Perlman I., 1967, Table of Isotopes Sixth Edition; Wiley, New York.
- Lloyd R.D., Mays C.W., and Atherton D.R., 1976a, Distribution of injected ^{226}Ra and ^{90}Sr in the beagle skeleton, Health Physics **30**: 183-189.
- Lloyd R.D., Mays C.W., Atherton D.R., Taylor G.N., and VanDilla M.A., 1976b, Retention and skeletal dosimetry of injected ^{226}Ra , ^{228}Ra , and ^{90}Sr in beagles, Radiation Research **66**: 274-287.
- Mays C.W., Spiess H., and Gerspach A., 1978, Skeletal effects following ^{224}Ra injections into humans, Health Physics **35**: (July 1978).
- Parmley W.W., Jensen J.B., and Mays C.W., 1962, Skeletal self-absorption of beta-particle energy, pages 437-453 in Some Aspects of Internal Irradiation, Dougherty T.F., editor, Pergamon Press, Oxford.
- Spiess H., Gerspach A., and Mays C.W., 1978, Soft-tissue effects following ^{224}Ra injections into humans, Health Physics **35**: (July 1978).

Table 1. BEAGLES INJECTED WITH ^{224}Ra FOR STUDIES OF EARLY RETENTION AND DISTRIBUTION.

DOG →	T23Q5	T22Q5	T25Q5	T24Q5	T27Q5	T26Q5
SEX →	M	F	M	F	M	F
Age at Injection, Months	20	21	21	21	21	22
Weight at Injection, kg	10.9	8.39	8.78	9.14	10.6	8.81
Injected $\mu\text{Ci } ^{224}\text{Ra/kg}$	8.37	10.1	10.1	10.1	10.1	9.98
Days from Injection to Sacrifice	0.04	0.14	0.34	1	3	7

Table 2. DECAY ENERGIES, (LEDERER ET AL., 1967) USED IN THE CALCULATION OF AVERAGE SKELETAL DOSE FROM INJECTED ^{224}Ra IN BEAGLES.

NUCLIDE	α -ENERGY/DIS.	α + RECOIL ENERGY	AVERAGE β -ENERGY ABSORBED IN SKELETON
^{224}Ra	(94%) (5.68 MeV) + (6%) (5.45 MeV) = 5.67 MeV	5.77 MeV	
$^{220}\text{Rn} + ^{216}\text{Po}$	6.29 MeV + 6.78 MeV = 13.07 MeV	13.32 MeV	
^{212}Pb			0.19 MeV
$^{212}\text{Bi} + ^{212}\text{Po} + ^{208}\text{Tl}$	(34%) (6.06 MeV) + (66%) (8.78 MeV) = 7.86 MeV	8.01 MeV	0.57 MeV

Figure 1. Decay scheme of ^{224}Ra and its daughters.

Figure 2. Decrease of ^{212}Pb and ^{212}Bi in the kidneys of dog T26Q5 as a function of time after death, which occurred 7 days following ^{224}Ra injection. These data show that the $^{212}\text{Bi}/^{224}\text{Ra}$ content in the kidney at death was about 9 times the value determined at transient equilibrium.

Figure 3. Ingrowth of ^{212}Pb and ^{212}Bi in the humerus of dog T23Q5 as a function of time after death, which occurred about 1 hour following ^{224}Ra injection. These data indicate that the $^{212}\text{Pb}/^{224}\text{Ra}$ and $^{212}\text{Bi}/^{224}\text{Ra}$ content in bone at death were about 0.3 and 0.2 of their respective values at transient equilibrium.

Figure 4. Initial $^{212}\text{Pb}/^{224}\text{Ra}$ or $^{212}\text{Bi}/^{224}\text{Ra}$ content in bone (humerus and lumbar vertebrae) at death as a function of time after injection.

Figure 5. Biological retention of injected ^{224}Ra in skeleton and soft-tissue as a function of time after injection.

Figure 6. Total-body biological retention of injected ^{224}Ra . Circles represent values for the six dogs in this study, while the curve shown for comparison is the retention equation derived previously for the total-body biological retention of injected ^{226}Ra in young adult beagles (Lloyd et al., 1976b).

Figure 7. Effective skeletal retention of ^{224}Ra , ^{212}Pb , and ^{212}Bi as a function of time after injection. Effective retention includes the effect of radioactive decay and the effect of biological uptake and loss.

RETENTION EQUATIONS AND REVISED SKELETAL DOSIMETRY FOR ^{241}Am IN BEAGLES

R. D. Lloyd and C. W. Mays

ABSTRACT: Equations have been derived which describe the retention of injected ^{241}Am into 17-month old beagles in the liver, the non-liver tissue, and in the skeleton. Retention was found to be dose-level dependent, and different sets of equations were obtained for dogs given about (a) 3 $\mu\text{Ci/kg}$ and higher; (b) 0.9 $\mu\text{Ci/kg}$; (c) 0.3 $\mu\text{Ci/kg}$; and (d) 0.1 $\mu\text{Ci/kg}$ and lower. Average skeletal doses for all dead animals in our ^{241}Am experiment have been recalculated, based on these equations.

The injection of $^{241}\text{Am}(\text{III})$ citrate into young adult beagles at dose-levels ranging from 0.0018 to 4.53 $\mu\text{Ci/kg}$ was begun in our colony in 1966. Gamma-ray spectroscopy of the living dogs has been done periodically using techniques described previously (Lloyd et al., 1970; Lloyd and Mays, 1975) to yield an estimate of the ^{241}Am retention in the liver and in non-liver tissue (mainly skeleton) as a function of time after injection. These measurements were fitted by a series of retention equations of the form:

$$\text{Liver retention} = (0.492 \pm 0.039) e^{-bt} \quad (1)$$

and

$$\text{Non-liver retention} = (0.406 \pm 0.037) + J(1 - e^{-mt}) \quad (2)$$

at t days after injection. Values of parameters b , J , and m are given for the various dose-levels in Table 1.

The retention equations for liver reflect the observed decrease of ^{241}Am content in liver, which is more pronounced at the higher levels due to the release of ^{241}Am from damaged liver cells. Also modeled by the equations is the observed increase in ^{241}Am content of non-liver tissue as some of the ^{241}Am which is lost from the liver then redeposits in the skeleton and other tissue. This effect is more extreme at the higher injection levels.

Each bone and soft tissue of 37 beagles injected with ^{241}Am was assayed for its ^{241}Am content by gamma-ray spectroscopy immediately following death. It was found that the ratio of skeletal ^{241}Am to total non-liver ^{241}Am in these animals averaged 0.885 ± 0.037 (S.D.), with no significant dependence upon either dose-level or time after injection ($P > 0.05$). Therefore, the retention equations for non-liver ^{241}Am were multiplied by 0.885 to obtain a set of equations to describe the retention of ^{241}Am in the skeleton $\underline{S}$ as a function of time after injection. The resulting expressions are exhibited in Fig. 1. The exponential rate constants are the same as those shown for the non-liver in Table 1. Skeletal retention $\underline{S}$ could be expressed as:

$$S = A + H (1 - e^{-mt}) \quad (3)$$

Where $\underline{A}$ represents the initial deposition in the skeleton, while $\underline{H(1 - e^{-mt})}$ is due to translocation of ^{241}Am from the liver into the skeleton. The skeletal retention $\underline{S}$ at each dose level was:*

$$\text{5-level } (\sim 3 \text{ } \mu\text{Ci/kg}) \quad S_5 = 0.359 + 0.157 (1 - e^{-0.0065t})$$

$$\text{4-level } (\sim 0.9 \text{ } \mu\text{Ci/kg}) \quad S_4 = 0.359 + 0.141 (1 - e^{-0.0029t})$$

$$\text{3-level } (0.3 \text{ } \mu\text{Ci/kg}) \quad S_3 = 0.359 + 0.076 (1 - e^{-0.0021t})$$

$$\text{2-level \& lower} \quad S_2 = 0.359 + 0.015 (1 - e^{-0.0014t})$$

Average skeletal dose rates were calculated from the expression (Evans, 1955):

** Values of "A" = 0.359 were chosen such that they were equal for all dose-levels, indicating that the initial deposition of injected ^{241}Am in the skeleton is independent of dose-level. Subsequent dynamics (parameters "H" and "m") depend upon dose-level as a consequence of radiation damage, especially in the liver.

$$\text{Dose rate} = \left[51.2 \frac{\text{g dis rad}}{\mu\text{Ci MeV day}} \right] \left[\frac{(I \mu\text{Ci/kg}) (S)}{G \text{ g/kg}} \right] \left[E \frac{\text{MeV}}{\text{dis}} \right] \quad (4)$$

where injected activity = $I \mu\text{Ci/kg}$

skeletal retention $S = A + H (1 - e^{-mt})$

α + recoil energy $E = 5.57 \text{ MeV/disintegration}$

skeletal mass $G = 75 \text{ g of skel/kg of body}$

Substituting these values into equation 4:

$$\text{Dose rate} = 3.802 (I) [A + H (1 - e^{-mt})] \frac{\text{rad}}{\text{day}} \quad (5)$$

The cumulative average skeletal dose is the integral of the dose rate (equation 5) from time zero up to time t .

$$\text{Dose} = 3.802 (I) \left[(A + H) t - \frac{H}{m} (1 - e^{-mt}) \right] \text{ rad} \quad (6)$$

The numerical values of dose are:

$$\text{Dose (5 \& higher)} = (I) [1.96t - 92 (1 - e^{-0.0065t})] \text{ rad}$$

$$\text{Dose (4-level)} = (I) [1.90t - 185 (1 - e^{-0.0029t})] \text{ rad}$$

$$\text{Dose (3-level)} = (I) [1.65t - 138 (1 - e^{-0.0021t})] \text{ rad}$$

$$\text{Dose (2 \& below)} = (I) [1.42t - 41 (1 - e^{-0.0014t})] \text{ rad}$$

The dose to each dog was then adjusted to its individual retention by multiplying the calculated dose (Eq. 6) by the average ratio of the dog's measured non-liver retention/calculated non-liver retention (Eq. 2).

REFERENCES

Evans R.D., 1955, The Atomic Nucleus, McGraw-Hill, New York, page 742.

Lloyd R.D., Mays C.W., Atherton D.R., and Taylor G.N., 1970, ^{241}Am studies in beagles, Health Physics 18: 149-156.

Lloyd R.D. and Mays C.W., 1975, Determining liver retention of transuranium elements in living beagles, Radiation and Environmental Biophysics 12: 139-145.

Table 1. RETENTION PARAMETERS OF ^{241}Am IN BEAGLES (FOR EQUATIONS 1 & 2).

Dose Level*	Liver	Non-Liver	
	b $\pm$ S.D.	J $\pm$ S.D.	m $\pm$ S.D.
5 and higher	0.002393 $\pm$ 0.000146	0.177 $\pm$ 0.035	0.0065 $\pm$ 0.0007
4	0.000643 $\pm$ 0.000150	0.159 $\pm$ 0.032	0.0029 $\pm$ 0.0003
3	0.000367 $\pm$ 0.000116	0.086 $\pm$ 0.017	0.0021 $\pm$ 0.0002
2 and lower	0.000216 $\pm$ 0.000057	0.017 $\pm$ 0.005	0.0014 $\pm$ 0.0001

*Dose levels: "5" $\approx$ 3 $\mu\text{Ci/kg}$; "4" $\approx$ 0.9 $\mu\text{Ci/kg}$; "3" $\approx$ 0.3 $\mu\text{Ci/kg}$; "2" $\approx$ 0.1 $\mu\text{Ci/kg}$.

Figure 1. Skeletal retention of injected ^{241}Am in young adult beagles. Open circles represent values obtained from non-liver measurements made in vivo multiplied by 0.885, while solid circles show values derived from mea-

REVISED SKELETAL DOSIMETRY FOR BEAGLES INJECTED WITH ^{249}Cf OR ^{252}Cf

R. D. Lloyd and C. W. Mays

ABSTRACT: When 17-month beagles are injected intravenously with californium citrate, 50% deposits in the skeleton and is retained with a biological half-time of about 26 years. Revised average skeletal doses were calculated for the beagles injected with ^{249}Cf or ^{252}Cf that have died.

In a previous publication (Lloyd et al., 1976) equations were given for the biological retention of injected californium in beagles at t days after injection:

$$\text{Total-body biol. ret.} = 0.24 e^{-0.445t} + 0.76 e^{-0.000222t} \quad (1)$$

$$\text{Liver biol. ret.} = 0.096 e^{-0.282t} + 0.183 e^{-0.000454t} \quad (2)$$

Results of NaI(Tl) spectroscopy of all bones and soft tissues immediately following the death of four beagles given ^{249}Cf and four beagles given ^{252}Cf at 7 to 1546 days earlier, indicated that the ratio of skeletal Cf to total non-liver Cf was about 0.8 from 7 to 20 days after injection, and about 0.9 from 21 to 1546 days after injection.

Most beagles, given either ^{249}Cf or ^{252}Cf , have been assayed 3 to 20 times while living for the retention in the total-body, liver, and non-liver tissue. Dogs injected with $0.005 \mu\text{Ci } ^{249}\text{Cf/kg}$ or $0.016 \mu\text{Ci } ^{252}\text{Cf/kg}$ had only their total-body content determined. For those injected with less than $0.005 \mu\text{Ci } ^{249}\text{Cf/kg}$ or $0.016 \mu\text{Ci } ^{252}\text{Cf/kg}$, the counting rates were too low to make reliable measurements. Skeletal retention values were computed by multiplying the measured non-liver retention by 0.8 (for times up to 20 days after injection) or 0.9 (for times of 21 days or more). The plotted retention values were described well by single exponential curve

(Fig. 1). Least squares analysis yielded the following equation for the net biological retention of injected californium in the skeleton at t days after injection:

$$\text{Skeletal biol. ret.} = 0.498 e^{-0.0000741t} \quad (3)$$

For dogs given ^{249}Cf , the effective retention in the skeleton S(^{249}Cf) is a combination of the biological retention and physical decay of 360 year ^{249}Cf :

$$S(^{249}\text{Cf}) = 0.498 [e^{-0.0000741t}] [e^{-0.0000053t}] = 0.498 e^{-0.0000794t} \quad (4)$$

For 2.65 year ^{252}Cf , the effective retention in the skeleton S(^{252}Cf) is:

$$S(^{252}\text{Cf}) = 0.498 [e^{-0.0000741t}] [e^{-0.000717t}] = 0.498 e^{-0.000791t} \quad (5)$$

Average skeletal dose-rates were calculated for an injection of I $\mu\text{Ci/kg}$ and an effective skeletal retention S from the expression (Evans, 1955):

$$\text{dose rate} = \left[\frac{51.2 \text{ g dis rad}}{\mu\text{Ci MeV day}} \right] \left[\frac{(I \mu\text{Ci/kg}) (S)}{G \text{ g/kg}} \right] \left[\frac{E \text{ MeV}}{\text{dis}} \right] \quad (6)$$

For the injection of 1 $\mu\text{Ci/kg}$ into a dog having G = 75 g skeleton/kg body,

$$\text{dose rate} = \left(\frac{51.2}{75} \right) (E) (S) \frac{\text{rad}}{\text{day}} \quad (7)$$

The alpha plus recoil energy for ^{249}Cf is $E = 5.93 \text{ MeV/disintegration}$ and the average alpha plus fission plus recoil energy for ^{252}Cf is $E = 11.76 \text{ MeV/dis}$ (Lederer et al., 1967, Prince, 1969). Therefore, the dose rate equations for the injection of 1 $\mu\text{Ci/kg}$ become:

$$\text{dose rate } (^{249}\text{Cf}) = 2.02 e^{-0.0000794t} \text{ rad/day} \quad (8)$$

$$\text{dose rate } (^{252}\text{Cf}) = 4.00 e^{-0.000791t} \text{ rad/day} \quad (9)$$

Cumulative average skeletal doses for the injection of 1 $\mu\text{Ci/kg}$ are found by integrating the dose rate (equations 8 or 9) from time zero to time "t":

$$\text{Dose } (^{249}\text{Cf}) = 25,390 (1 - e^{-0.0000794t}) \text{ rad} \quad (10)$$

$$\text{Dose } (^{252}\text{Cf}) = 5,054 (1 - e^{-0.000791t}) \text{ rad} \quad (11)$$

The dose to each dog was adjusted for its individual retention by multiplying the calculated dose (equations 10 or 11) by the average ratio of the dog's measured total-body retention/calculated total-body retention from equation 1. Results were normalized by means of total-body retention rather than non-liver retention because (a) most of the retained Cf is in the skeleton, not the liver, (b) total-body retention values are more accurate than non-liver values, and (c) for some lower level animals, only the total-body retention is measured.

REFERENCES

- Evans R.D., 1955, The Atomic Nucleus, McGraw-Hill, New York, page 742.
- Lederer C.M., Hollander J.M., and Perlman I., 1967, Table of Isotopes, Sixth Edition, Wiley, New York.
- Lloyd R.D., Mays C.W., McFarland S.S., Atherton D.R., and Williams J.L., 1976, Californium studies in beagles, Radiation Research 65: 462-473.
- Prince A., 1969, Nuclear and physical properties of Cf-252, pp. 23-130 in Californium-252 USAEC Report CONF-681032, see p. 37.

Figure 1. Biological retention of injected ^{249}Cf or ^{252}Cf in the skeleton. Non-liver retention values measured in vivo were multiplied by 0.8 (0 to 20 days post injection) or 0.9 (21 days or more after injection) to obtain the data herein displayed. Dogs injected with ^{249}Cf are shown as open circles and dogs given ^{252}Cf are indicated by solid circles.

THE EARLY DISTRIBUTION AND EXCRETION OF ^{233}U IN THE BEAGLE

F. W. Bruenger, D. R. Atherton, W. Stevens,
D. S. Buster and G. N. Taylor

Abstract: The distribution, excretion and retention of ^{233}U after its injection as U VI citrate was studied between 1 day and 2 years post injection (P.I.). The nuclide was removed rapidly from the circulation and up to 60% of the injected dose was excreted during the first day in the urine. Whole body retention was 17% at 1 week, 11% at 3 weeks and < 5% at 2 years P.I.. The main target organs are skeleton and kidney. High concentrations of U in the kidney caused irreparable damage. The concentration of the nuclide in plasma, selected soft tissue organs and in the skeleton was described by either biphasic or single exponential equations.

The study of the distribution, retention and excretion of ^{233}U in young adult beagles has been completed. Seven animals were given a single intravenous injection of $2.8 \mu\text{Ci } ^{233}\text{U VI/kg}$ in citrate buffer ($\sim 3 \text{ mg}$ of uranium per dog). In addition, one beagle received 3 mg of natural uranium. Animals were sacrificed sequentially at times ranging from 1 day to 726 days post injection (P.I.).

Uranium was removed from the circulation at a rapid rate. For the first 24 hours P.I., its concentration in plasma could be described by the following equation:

$$[P] = 0.04069e^{-0.01523t} + 0.004629e^{-0.00218t}$$

where $[P]$ is % of injected dose per gram of plasma and t is time in minutes.

Whole body retention was 17% at 1 week, 11% at 3 weeks and < 5% at 2 years P.I.. Initially, uranium was divided about equally between skeleton and soft tissue. However, the loss from the skeleton was less rapid than from soft tissues.

Excretion of the nuclide was very rapid and occurred mainly via urine. Variation between animals was large but as much as 60% of the injected dose was excreted during the first day. As a result, the concentration of U in the kidney at 1 day exceeded that in the liver by 2 orders of magnitude. The temporarily high concentration of U in the kidney caused irreparable damage which resulted in extreme diuresis and an abnormally high blood urea nitrogen (BUN) during the first 10 days P.I.. Urine output returned to normal by ~ 6 weeks P.I. but the BUN was still elevated at 2 years P.I.. A comparison of the kidney function between the animal injected with ^{233}U and the one injected with natural uranium showed that kidney damage was due primarily to chemical toxicity. However the symptoms were more severe in the animals injected with ^{233}U , indicating that the chemical damage was aggravated by α -irradiation.

The liver, a critical target organ for all transuranium elements contained only 1.1% of the injected dose at 1 day P.I. and the concentration in this organ decreased to 1/10 of the initial concentration by 1 year P.I. The concentration in the liver can be described by the following equation:

$$[L] = 0.00155e^{-0.0294t} + 0.00106e^{-0.00210t}$$

where $[L]$ is % of injected dose per gram and t is time in days.

The subcellular distribution of U as seen after differential centrifugation of liver homogenates from which nuclei and debris had been removed, is listed in Table 1.

The concentration of U as a function of time P.I. in selected soft tissue organs was determined and retention equations of the form $R = ae^{-bt}$

TABLE 1
SUBCELLULAR DISTRIBUTION OF ^{233}U IN BEAGLE LIVERS
% of ^{233}U in Each Fraction Relative to that in
the Homogenate

	1 H	1 D	2 D	7 D	14 D	21 D	264 D	726 D
Liver Homog.	100.	100.	100.	100.	100.	100.	100.	100.
Mitochondria	15.	41.1	56.9	56.1	70.5	67.7	84.	76.1
Lysosomes	15.7	14.	22.1	15.7	8.2	9.3	6.7	12.3
Microsomes	10.3	15.8	6.6	10.	4.8	3.7	2.1	2.
Cytosol	55.8	26.5	14.2	16.1	12.2	9.1	N.D.*	4.5
RECOVERY	96.8	97.4	99.8	97.9	95.7	89.8		94.9

* Not Determined

were fitted to the data. The corresponding parameters together with the respective correlation coefficients are listed in Table 2.

A significant fraction of the injected U.VI was deposited initially in the skeleton and retained with a biological halftime of about 880 days. The skeletal retention can be described by the following equation:

$$R_{Sk} = (7.67 \pm 0.31)e^{-(0.000795 \pm 0.00012)t}$$

where R_{Sk} = % of injected dose and t is time in days.

The correlation coefficient for this equation is 0.96 and the confidence limit for the slope to be different from 0 is greater than 99% ($p < 0.01$).

In summary, when ^{233}U is injected as the uranyl citrate, most of the nuclide is excreted rapidly. Only a small fraction of it is retained in soft tissue organs, but ~8% is deposited in the skeleton and retained with a

TABLE 2
CONCENTRATION ($[R] = ae^{-bt}$)* OF ^{233}U IN SELECTED SOFT TISSUE ORGANS

Organ	a ($\times 10^3$)	σ_a ($\times 10^3$)	b ($\times 10^3$)	σ_b ($\times 10^3$)	$t_{1/2}$ (D)	Correlation Coefficient
Kidney	150.2	± 77.5	8.72 ± 1.54		79.5	0.94
Spleen	0.873	± 0.105	3.81 ± 0.366		181.9	0.98
Lung	0.206	± 0.0404	3.64 ± 0.387		190.4	0.95
Gonad	0.254	± 0.0748	4.00 ± 0.886		173.3	0.92
Salivary	0.138	± 0.0364	2.55 ± 0.793		271.8	0.85
Muscle	0.0402	± 0.00127	3.92 ± 0.967		176.8	0.92

* $[R]$ is % of injected dose per gram, b is days $^{-1}$.

biological halftime of 880 days. As a result of this skeletal deposition, formation of osteosarcoma can be expected from an exposure to either ^{233}U or ^{232}U . Acute lesions were seen in the kidneys and these are due to the chemical toxicity of U although simultaneous α -irradiation did aggravate the symptoms. The distribution of U in the body may be different after exposure to U IV rather than U VI.

DISTRIBUTION AND TRANSLOCATION OF PARTICULATE PLUTONIUM
(HOT PARTICLE - SERIAL SACRIFICE STUDY)

W. Stevens, F. W. Bruenger, D. R. Atherton,
and D. S. Buster

Abstract: The dissolution and elimination of particulate ^{239}Pu (Pu-P) from its initial sites of deposition, its translocation, and redeposition in other soft tissue organs and the skeleton are being investigated. At the present time, beagles have been sacrificed sequentially at times ranging from 30 to 420 days post-injection (P.I.). During this time, the deposit in the liver, spleen, and lung decreased with half times of ~ 410 , 240, and 285 days, respectively. Approximately 56% of the Pu lost from these organs was redeposited in the skeleton, while the remaining 44% was either excreted via feces or redeposited in soft tissue organs. While initial deposition of Pu-P in the skeleton was largely in macrophages of the marrow, secondary deposition resulting from translocation was on bone surfaces. This continuous deposition resulted in a diffuse distribution in areas of growing bone and in a dense accumulation of Pu on non-growing surfaces. Such a distribution has the potential for exposing to α -irradiation all cells involved in osteogenesis and, therefore, thought to be critical in formation of osteosarcoma.

In an earlier report (C00-119-252), the distribution of ^{239}Pu given intravenously to the beagle as particulate (hydrolyzed) Pu was described for dogs sacrificed at 33, 40, 60, and 69 days P.I.. As of March 31st, 1978, six more beagles have been sacrificed, extending the time of observation to 425 days P.I.. One-half of the symmetrical and a known fraction of the asymmetrical skeleton, liver, spleen, kidney, lung and other selected soft tissue organs were analyzed for their Pu content. The measured retentions of Pu in each of the main target organs are given in Table I. Values shown are the average of the data provided by the analysis of 2 dogs.

Since most of the Pu-P was deposited in the liver, and since this organ served as the largest pool for the translocation of the nuclide to the skeleton,

a more detailed analysis of liver tissue was performed. The organ was perfused immediately after sacrifice and a separation of hepatocytes and sinusoidal lining cells was carried out. The distribution of Pu between these two cell types was determined by radiochemical analysis and by autoradiography. The concentration of Pu in sinusoidal lining cells was always much higher than in parenchymal cells. Consistent with the view that after dissolution and reentry into the bloodstream part of the nuclide is redeposited in monomeric form, its concentration in hepatocytes increased as a function of time after injection. This is demonstrated in Fig. 1 which shows autoradiographs of isolated sinusoidal lining cells and hepatocytes at 33 and 424 days P.I..

The whole liver tissue was homogenized, following which cytosol and subcellular organelles were separated. The concentration of Pu in each of these compartments was then determined. Results are shown in Table 2. As in an earlier pilot experiment, the concentration of Pu in the cytosol increased slightly during the early time after injection and stayed relatively high thereafter. This is consistent with the view that Pu particles undergo continuous dissolution over a long period of time and may enter the circulation. This observation is supported by the fact that concurrently the concentration of Pu in plasma was about 3 times as high as observed after I.V. injection of Pu-citrate. The retention in the phagocytic target organs decreased and about one-half of the Pu released by these organs was deposited in the skeleton. The retention in bone increased from 7.6% of the injected dose at 36 days P.I. to 31% at 420 days P.I..

The initial deposit of Pu in the skeleton was primarily in macrophages of the marrow. Deposition of nuclide after dissolution and translocation

was mostly on bone surfaces or a dense deposit accumulated on surfaces on which no bone growth was apparent. Growing surfaces produced layers of bone which were uniformly labeled while intermittent resorption eroded some of the dense deposit on inactive surfaces. As bone resorption ceased, Pu again deposited leading to surface deposits with a reduced track density. Neutron induced autoradiographs taken from bone specimen at 40 days and 420 days P.I., as shown in Fig. 2, demonstrate this dynamic pattern of nuclide distribution.

Empirically derived retention equations which describe the decreasing quantities of Pu found in liver, lung and spleen are given in Table 3. The maximum amount of Pu which the skeleton can acquire through translocation is limited by the size of the phagocytic pool. In order to describe the increasing skeletal deposition, an equation of the form $R = A(1 - ae^{bt})$ was fitted to the observed retention data. The parameter A in this equation was first estimated graphically and then refined by an iterative procedure. Extrapolated to $t = 0$, the initial deposition of Pu-P in the skeleton was 2.6% of the injected dose, which is in good agreement with results obtained in the earlier experiment with Pu-P (1). The original data and the curves corresponding to the respective equations are shown in Fig. 3.

A model which describes the translocation of Pu from the initial site of deposition to the skeleton was developed. The model and a preliminary calculation of the rates of transfer to bone are described in this report under the title "A Kinetic Model for Translocation of Pu-P from Phagocytic Organs to Bone".

The retentions of Pu as calculated by the equations shown in Table 3 and the accumulation of Pu in bone as predicted by the model are listed in Table

4. Also listed in this table is the estimated cumulative fecal excretion of Pu-P. A comparison of observed and predicted data shows very good agreement. Further refinements will be made after completion of the experiment.

REFERENCES

1. Stover, Betsy J., D. R. Atherton, W. Stevens, D. S. Buster and F. W. Bruenger: 1977. Effect of dose level on skeletal retention of $^{239}\text{Pu(IV)}$ in the beagle. Radiation Research 69(3): 442-458.

TABLE 1
PERCENT OF INJECTED Pu FOUND IN VARIOUS ORGANS
FOLLOWING INJECTION OF Pu-P*

	Days After Injection				
	36	68	120	254	420
Liver	74.4	68.8	73.1	50.5	40.1
Kidney	0.078	0.141	0.186	0.260	0.170
Spleen	9.08	13.1	6.33	6.54	3.16
Lung	1.53	1.92	1.88	0.96	0.78
Skeleton	7.6	10.2	12.0	22.4	31.0

* Average of two dogs

TABLE 2
PERCENT OF THE Pu FOUND IN WHOLE LIVER HOMOGENATE
FREE OF NUCLEI AND DEBRIS (600 x g)

	Days After Injection				
	37	64	120	250	420
600 x g	100.	100.	100.	100.	100.
Mitochondria	65.6	69.6	62.7	62.8	65.6
Lysosomes	16.1	15.2	12.8	12.7	13.0
Microsomes	5.8	5.9	10.9	9.7	8.7
Cytosol	6.6	8.0	10.3	9.7	10.1
Recovery	94.1	98.7	96.7	94.9	97.4

TABLE 3
EMPIRICALLY DERIVED EQUATIONS FOR THE RETENTION
AND TRANSLOCATION OF Pu-P

	Correlation Coefficient
$R_{\text{Liver}} = 80.6e^{-0.001698t}$	0.88
$R_{\text{Spleen}} = 11.5e^{-0.002884t}$	0.84
$R_{\text{Lung}} = 2.0e^{-0.00244t}$	0.78
$R_{\text{Skeleton}} = 45(1 - 0.943e^{-0.002594t})$	0.98

TABLE 4
PREDICTED RETENTION (ACCUMULATION) OF Pu IN VARIOUS
ORGANS AFTER INJECTION OF Pu-P*

	Days After Injection					
	0	30	60	120	240	420
Liver	80.4	76.4	72.6	65.6	53.5	39.4
Spleen	11.5	10.6	9.71	8.16	5.78	3.44
Lung	2.0	1.85	1.73	1.49	1.11	0.72
Skeleton	2.6	5.74	8.68	13.9	22.2	30.7
Feces (Estimated)	---	1.92	3.76	7.34	13.9	22.2

* % of injected dose

Figure 1 Autoradiographs of isolated hepatocytes (A) and sinusoidal lining cells (B) at 33 days P.I. and of isolated hepatocytes at 424 days P.I. (C). A higher magnification (D) clearly shows that α -tracks emanate from the cells. Few α -tracks are seen in hepatocytes at early times P.I. but their number increases as a result of translocation and redeposition in the liver.

Figure 2 Neutron induced autoradiographs of a bone specimen from a lumbar vertebrae (left) and a proximal femur (right) of beagles sacrificed at 40 (top) and 420 days (bottom) P.I.. Autoradiographs demonstrate the increasing deposition of Pu on inactive surfaces and the diffuse deposition resulting from bone growth. M = Marrow with Pu-P in macrophages, B = Bone Mineral, G = Deposition in growing bone.

Figure 3 Loss of Pu-P from phagocytic organs and translocation of Pu to the skeleton.

A KINETIC MODEL FOR TRANSLOCATION OF Pu-P FROM PHAGOCYtic ORGANS TO BONE

F. W. Bruenger, W. Stevens, D. R. Atherton and J. M. Smith

Following initial deposition after injection of particulate Pu (Pu-P), the nuclide is lost gradually from the primary deposit in phagocytic organs but the deposit in bone increases. Each of the decreasing retentions observed in liver, spleen and lung can be described by an equation of the following form:

$$R_{(\text{organ})} = ae^{-bt}$$

The coefficients a and b together with their standard deviations and the correlation coefficients for the retention equations are listed in the table below.

Organ	Organ at t = 0 a ± σ _a (% of Injected Pu)	b ± σ _b (days ⁻¹)	Correlation Coefficient
Liver (L)	80.36 ± 6.06	0.001698 ± 0.00033	0.88
Spleen (S)	11.59 ± 1.75	0.002884 ± 0.000665	0.84
Lung (P)	2.0 ± 0.32	0.00244 ± 0.00069	0.78

The increase of Pu in skeleton can be described empirically by an equation of the form

$$R_{Sk} = A(1 - ae^{-Bt}) \quad (\text{Eq. 1})$$

In this equation A is the upper boundary for skeletal burden. The values

of the parameters of this equation were determined by an iterative procedure such that the correlation coefficient for R_{Sk} was maximized. The following parameters gave the "best" fit.

$$A = 45$$

$$\alpha = 0.943 \pm 0.034$$

$$\beta = 0.002594 \pm 0.00016$$

$$cc = 0.985 \text{ (n = 10)}$$

$$R_{Sk} = 45(1 - 0.943e^{-0.002594t}).$$

Thus the maximal skeletal burden would be 45% of the injected dose. The initial skeletal (i.e., marrow) deposition as calculated by this equation would be 2.6% of the injected Pu. This is in good agreement with earlier data.

A preliminary model for the translocation of Pu from the above soft tissue organs to the skeleton is described in Fig. 1. The following assumptions are made:

1. Pu is released from the phagocytic pool of liver, spleen and lung at a rate proportional to the amount present in that organ at any time, t , following injection.
2. Released from these organs, Pu enters the blood stream from which it is redistributed in about the same way as if it were injected as nonparticulate Pu or in a form which does not give rise to substantial hydrolysis.
 - a. Pu is translocated to the skeleton and deposited on available bone surfaces. Since this translocation is a continuous process, the resulting deposition pattern gives a high probability for

bone cells to be exposed to α -irradiation. The rate of increase in skeletal burden ($\frac{dB}{dt}$) is proportional to the concentration of Pu in the blood.

- b. Pu will also be redeposited in the liver and from earlier experience it is anticipated that the partition of redistribution is about 30% to the liver and $\sim 50\%$ to the skeleton, assuming that damage resulting from irradiation of the liver by the phagocytic deposit does not decrease that organ's ability to deposit Pu. Redeposited Pu probably will not be eliminated at the same rate of Pu deposited in phagocytic organs. Thus the observed retention of Pu is dominated by a biphasic deposition (phagocytic and diffuse-hepatic).

3. A substantial part of the liver-Pu is excreted via bile without entering the blood pool.

The transfer to bone can be approximated as follows:

$$\frac{dB}{dt} = K [R_L(t) + R_S(t) + R_P(t)] \quad (\text{Eq. 2})$$

$$\frac{dB}{dt} = K [L_0 e^{-K_L t} + S_0 e^{-K_S t} + P_0 e^{-K_P t}]$$

$$B(t) = B_0 + K \left[-\frac{L_0}{K_L} e^{-K_L t} - \frac{S_0}{K_S} e^{-K_S t} - \frac{P_0}{K_P} e^{-K_P t} \right]_0^t$$

$$B(t) = B_0 + K \left[\left(\frac{L_0}{K_L} + \frac{S_0}{K_S} + \frac{P_0}{K_P} \right) - \left(\frac{L_0}{K_L} e^{-K_L t} + \frac{S_0}{K_S} e^{-K_S t} + \frac{P_0}{K_P} e^{-K_P t} \right) \right] \quad (\text{Eq. 3})$$

from (Eq. 1), $B_{\infty} \equiv \lim_{t \rightarrow \infty} B(t) = 45$ and K can be estimated from

$$B_{\infty} = 45 = B_0 + K \left(\frac{L_0}{K_L} + \frac{S_0}{K_S} + \frac{P_0}{K_P} \right)$$

where $B_0 = 2.6$ (from Eq. 1), and therefore

$$K = 0.000814 \text{ d}^{-1}$$

Thus:

$$B(t) = 2.6 + 0.000814 [52147 - (47326e^{-0.001698t} + 4001e^{-0.002884t} + 820e^{-0.00244t})]$$

This equation leads to a value of B which is lower than predicted by the empirical R_{Sk} . The reason for this is that K_L is not the true rate constant for the loss of Pu from the phagocytic pool but the rate constant for the observed change of liver retention, i.e., the loss from the phagocytic pool plus the gain due to redeposition from the blood pool. Thus the true value is somewhat higher. Again an iterative method (change in K_L) is used to provide the best fit with the observed skeletal data. A corrected value for $K_L = 0.00259$ satisfies that condition and gives the following equation.

$$B(t) = B_0 + 0.00119 [35848 - (31027e^{-0.00259t} + 4001e^{-0.002884t} + 820e^{-0.00244t})].$$

It can be calculated that about 35% of the loss of $Pu-P$ from the liver into the blood stream is redeposited in the liver. This value is in good agreement with data obtained after injection of Pu -citrate in which case ~ 32% is redeposited in the liver.

Figure 1 - Model of principal pathways of deposition and translocation after contamination with particulate Pu.

FURTHER STUDIES ON THE REMOVAL OF SYSTEMICALLY ABSORBED ^{109}Cd IN MICE USING A COMBINATION OF CHELATING AGENTS

J. J. Boseman, R. D. Lloyd, C. W. Jones, and C. W. Mays

ABSTRACT: A pilot study showed that certain combinations of chelating agents significantly reduced the total-body burden of systemically absorbed ^{109}Cd in mice. Further investigation was necessary to determine if the observed effect was directly attributable to a combination of the chelating agents or to any one agent alone. The agents were ZnNa_3 diethylenetriaminepentaacetate (ZnDTPA) and 2,3-dimercaptopropanol (British Anti Lewisite, or BAL). C57BL/Do male mice were each injected intraperitoneally (i.p.) at 191 to 195 days of age with approximately 2 μCi of carrier-free ^{109}Cd . Mice were caged in groups of six animals per cage, with two cages of males being assigned to each treatment. The treatment regimens were as follows: (a) physiological saline, (b) ZnDTPA, (c) BAL, and (d) ZnDTPA + BAL. All mice were treated Monday through Thursday each week. Total-body ^{109}Cd retention was determined periodically by counting the 88 keV γ -ray emitted by ^{109}Cd , using a NaI(Tl) detector. After six weeks on the treatment schedule, the mice fell into two statistically different groups. Mice with the lowest mean biological retention of ^{109}Cd (approximately 38%) were treated with BAL or BAL + ZnDTPA. Mice with the highest mean biological retention (approximately 72%) were treated with physiological saline or ZnDTPA. The fraction of total-body ^{109}Cd content was determined in the kidneys, livers, femurs, and gonads. Chelation therapy with BAL indicated that a larger fraction of ^{109}Cd was removed from the kidneys than from the liver. Retention in femurs and gonads in mice given BAL was indistinguishable from that of control animals.

INTRODUCTION

It was previously reported by this laboratory⁽¹⁾ that treatment with certain combinations of chelating agents (BAL + ZnDTPA, and BAL + PA + ZnDTPA)* significantly reduced the total-body burden of systemically absorbed ^{109}Cd in mice. It was found that ^{109}Cd was preferentially removed in the following order: kidneys > liver > femurs. In order to determine if the observed effect was directly

*The chelating agents were 2,3-dimercaptopropanol (British Anti Lewisite, or BAL), penicillamine (PA), and ZnNa_3 diethylenetriaminepentaacetate (ZnDTPA).

attributable to a combination of the chelating agents or to any one individual chelating agent alone, further investigation was necessary. The present study attempts to resolve this question.

MATERIALS AND METHODS

Forty-eight C57BL/Do mice (28 g avg. wt., and 191-195 days old) were injected intraperitoneally (i.p.) with approximately 2 μ Ci of carrier-free ^{109}Cd (New England Nuclear) in citrate buffer. Total-body retention in each mouse was determined immediately following injection and, again, three days later just prior to starting treatment. All measurements of radioactivity were made by counting the 88 keV γ -ray emitted by ^{109}Cd using dual 20 x 10 cm NaI(Tl) detectors.⁽²⁾ Animals that showed a drastic reduction in ^{109}Cd activity at the 3-day counting were assumed to have been misinjected into the gastrointestinal tract and were discarded before beginning treatment.

Mice were caged initially in groups of six animals per cage, with two cages of males being assigned to each treatment. Five of the mice were discarded due to misinjection of the ^{109}Cd , so that when treatment was started some cages had fewer than six mice. The various treatments were as follows:

1. Saline control
2. ZnDTPA
3. BAL
4. ZnDTPA + BAL.

Commercial H_5DTPA (Aldrich Chemical Co.) was converted to its trisodium zinc form in this laboratory. BAL was obtained from Sigma Chemical Company. Peanut oil (Matheson, Coleman, and Bell) was used as the liquid medium in the BAL injection solutions to minimize tissue irritation due to the BAL. The ZnDTPA injection solution was prepared using aqueous medium buffered at pH 7.0.

A 0.9% NaCl solution (0.154 moles NaCl/liter), Cutter Laboratories, was used for the physiological saline controls. The following daily dosages were used:

1. Saline (NaCl): .64 mg/kg/day
2. ZnDTPA: 303 mg/kg/day
3. BAL: 120 mg/kg/day

The saline and ZnDTPA injections each consisted of 0.2 ml of injection solution. The BAL injections each consisted of 0.04 ml total volume and were administered using a 500 μ l syringe (Hamilton Co.). All treatments were administered by subcutaneous injection. The animals receiving the BAL + ZnDTPA treatment received two separate injections. All mice receiving BAL as part of their treatment gradually developed small pockets of BAL and peanut oil with accompanying deep ulcerations and hair loss in the vicinity of the injection site. For this reason, all mice were treated only four days a week (Monday through Thursday). This allowed the BAL mice to resorb most of the built-up BAL and peanut oil and allowed the ulcerations to heal for three days/week.

At the conclusion of the experiment, 44 days (average) after the start of therapy, each mouse was sacrificed by penthrane anesthetic overdose. The liver, both kidneys, both femurs, and both gonads were removed and placed in separate 3 dram glass vials with 95% ethanol as preservative, and the ^{109}Cd activity was determined by counting in a well-type scintillation crystal.⁽³⁾ Heart, lungs, and brain were removed from one mouse in each of the four treatment groups and assayed for ^{109}Cd activity as described above.

RESULTS

Total-Body Retention

Using the group Comparison ("t") Test,⁽⁴⁾ analysis of the total-body retention data for treatment days zero through forty-two indicated that the mice fell into two distinct statistically different groups ($P < 0.001$) (see Fig. 1 and Table 1).

1. Highest retention = animals given saline or ZnDTPA alone;
2. Lowest retention = animals given BAL or BAL + ZnDTPA.

Treatment groups within these two categories did not differ significantly from each other ($P > 0.20$).

Organ Retention

Statistical treatment of the data obtained from γ -ray counting of livers and kidneys showed that ^{109}Cd retention in each of these organs differed significantly between the two groups ($P < 0.005$) (see Table 2). Retention of ^{109}Cd in femurs did not differ significantly between the saline and the BAL treatments ($P > 0.10$). The retention of ^{109}Cd in gonads was not significantly different between treatments with BAL vs. treatments without BAL ($P > 0.10$). Analysis of these four tissues within each group showed that there was no significant difference in organ retentions ($P > 0.10$) between the different treatment types. Heart, lung, and brain retentions were determined in one mouse from each treatment group. Although slight differences existed in the individual retentions, it could not be determined if the differences were significant due to the small sample size.

DISCUSSION

The data presented here indicate that BAL and BAL + ZnDTPA effectively remove ^{109}Cd from mice. It is apparent, due to the fact that total-body retentions in the ZnDTPA treatment group were not significantly different from the retentions in the saline control group, and retentions in the ZnDTPA + BAL group were not significantly different from the retentions in the BAL group, that the ZnDTPA alone is not very effective at removing ^{109}Cd , and it does not enhance the efficacy of BAL in removing ^{109}Cd . Likewise, ZnDTPA apparently does not affect the distribution of ^{109}Cd in the mouse tissues studied. It was found that BAL,

contrary to former reports (see 1), does not translocate ^{109}Cd from the tissues and concentrate it in the kidneys. In fact, it was found that the BAL removes ^{109}Cd selectively from the kidneys and liver. Although it was not found that ^{109}Cd was concentrated in the kidneys, that is not to say that this will or will not occur with larger body burdens of ^{109}Cd , or that histological damage to the kidney or any other organ for that matter does not occur due to the translocation of ^{109}Cd by BAL therapy.

ACKNOWLEDGMENTS

We thank David R. Atherton for preparing the injection solutions, Thomas Brammer for assisting with the husbandry of mice, and Nancy Peixhot for typing the manuscript.

REFERENCES

1. Boseman J.J., Lloyd R.D., and Mays C.W. Removal of systemically absorbed ^{109}Cd in mice using a combination of chelating agents. Research in Radiobiology, University of Utah Report C00-119-252, p. 288-305, 1977.
2. Lloyd R.D., Aamodt R.L., Wagner W.W., and Pendleton R.C. Calibration of a gamma-ray spectrometer for soils counting. Int. J. Appl. Radiat. Isotopes 19: 773-775, 1968.
3. Lloyd R.D., Mays C.W., and Atherton D.R. Knothole, a new sidewall gamma-ray detector. Nucl. Instr. Methods 49: 109-113, 1967.
4. Woolf C.M. Principles of Biometry. D. Van Nostrand Co., Inc., pp. 62-69 and 329, Princeton, N.J., 1968.

Figure 1. ^{109}Cd retention in male mice as measured by total-body counting. The ^{109}Cd had been injected three days before the start of chelation treatment.

TABLE 1. Biological Retention of ^{109}Cd in Male C57BL/Do Mice As Measured By Total-Body Counting At Various Times During Progress Of Decorporation Treatment. Retention Normalized To 100% At Start Of Treatment (3 Days After ^{109}Cd Injection).

Days on Treatment	% Biological Retention (mean $\pm$ S.D.)			
	Saline	ZnDTPA	BAL	BAL + ZnDTPA
(-) 3	105.8 $\pm$ 2.1	111.0 $\pm$ 6.9	113.5 $\pm$ 10.8	111.1 $\pm$ 7.1
0	100.0	100.0	100.0	100.0
3	96.8 $\pm$ 2.5	97.4 $\pm$ 1.9	79.3 $\pm$ 5.1	76.2 $\pm$ 4.2
7	93.7 $\pm$ 2.0	93.6 $\pm$ 2.3	75.6 $\pm$ 4.0	71.8 $\pm$ 4.5
14	87.4 $\pm$ 3.5	87.1 $\pm$ 2.2	58.2 $\pm$ 3.7	57.8 $\pm$ 4.8
21	84.7 $\pm$ 3.3	84.9 $\pm$ 3.7	49.0 $\pm$ 4.4	48.8 $\pm$ 3.9
28	79.2 $\pm$ 3.1	80.1 $\pm$ 4.3	43.2 $\pm$ 3.9	43.4 $\pm$ 2.5
35	74.6 $\pm$ 3.7	76.1 $\pm$ 4.4	39.4 $\pm$ 4.0	39.8 $\pm$ 2.6
42	72.2 $\pm$ 2.3	74.0 $\pm$ 4.3	37.9 $\pm$ 3.8	38.0 $\pm$ 3.0

TABLE 2. Differences in the Tissue Distribution of ^{109}Cd at Autopsy Among Male Mice Receiving BAL and Those Not Receiving BAL as Part of Their Daily Treatment.

<u>Tissue</u>	<u>% Biological Retention* (mean $\pm$ S.D.)</u>	
	<u>Receiving BAL</u>	<u>Receiving no BAL</u>
Liver	6.0 $\pm$ 0.8	17.8 $\pm$ 3.1
Kidneys	1.9 $\pm$ 0.27	14.7 $\pm$ 1.9
Femurs	0.16 $\pm$ 0.05	0.23 $\pm$ 0.07
Gonads	0.20 $\pm$ 0.07	0.34 $\pm$ 0.31

* $\frac{^{109}\text{Cd in tissue at autopsy on treatment day } t}{[^{109}\text{Cd in total body on treatment day } 0] [e^{-\lambda t}]}$

TABLE 3. Differences in the Tissue Distribution of ^{109}Cd at Autopsy Among Male Mice Receiving Saline, ZnDTPA, BAL, and BAL + ZnDTPA as Their Daily Treatment.

Tissue	% Biological Retention* (mean $\pm$ S.D.)			
	Saline	ZnDTPA	BAL	BAL + ZnDTPA
Liver	17.3 $\pm$ 2.6	18.4 $\pm$ 3.5	6.1 $\pm$ 1.0	5.8 $\pm$ 0.5
Kidneys	14.5 $\pm$ 1.1	14.9 $\pm$ 2.4	2.0 $\pm$ 0.2	1.8 $\pm$ 0.3
Femurs	0.20 $\pm$ 0.05	0.25 $\pm$ 0.03	0.17 $\pm$ 0.06	0.13 $\pm$ 0.03
Gonads	0.25 $\pm$ 0.11	0.42 $\pm$ 0.40	0.20 $\pm$ 0.06	0.20 $\pm$ 0.10
Heart**	0.25 $\pm$ --	0.09 $\pm$ --	0.10 $\pm$ --	0.11 $\pm$ --
Lungs**	0.58 $\pm$ --	0.25 $\pm$ --	0.20 $\pm$ --	0.32 $\pm$ --
Brain**	0.05 $\pm$ --	0.03 $\pm$ --	0.03 $\pm$ --	0.03 $\pm$ --

* $\frac{^{109}\text{Cd in tissue at autopsy on treatment day } t}{[^{109}\text{Cd in total body on treatment day } 0][e^{-\lambda t}]}$

** Only counted one sample in each group.

CHELATION OF SYSTEMICALLY ABSORBED CADMIUM IN MICE WITH 2,3-DIMERCAPTOPROPANOL

C. W. Jones, R. D. Lloyd, and C. W. Mays

ABSTRACT: The cadmium chelating efficacy of 2,3-dimercaptopropanol (BAL), at two dose levels in two oil media was evaluated. C57BL/Do mice, aged 9 to 11 months, were injected intraperitoneally (ip) with 0.052 mg. of stable cadmium as CdCl_2 labeled with approximately 2 μCi of carrier-free ^{109}Cd . Six males and six females, in separate cages, were each assigned to one of the following treatments: (a) Physiological saline (69 mg/kg/day), (b) BAL (84 mg/kg/day) in peanut oil, (c) BAL (84 mg/kg/day) in cottonseed oil, and (d) BAL (28 mg/kg/day) in peanut oil. Mice were treated four days a week (Monday through Thursday). Using a NaI(Tl) detector system, the total-body retention of ^{109}Cd was determined periodically by measuring the 88 keV γ -ray emitted by ^{109}Cd . After 42 days on this regimen, the mean total-body retention of ^{109}Cd in the saline controls was approximately 86% in males and 91% in females. Mice treated with BAL at 28 mg/kg/day did not have total-body retentions significantly different from the saline controls. After 42 days, the mice at 84 mg BAL/kg/day in either peanut oil or cottonseed oil showed a significant reduction in total-body retention, with 71% in males and 70% in females for the groups given BAL in peanut oil, and 62% in males and 72% in females for those given BAL in cottonseed oil. Measurement of ^{109}Cd content in kidneys, livers, femora, and gonads indicated that BAL removed a larger fraction of ^{109}Cd from the kidneys than from the liver. Relatively little ^{109}Cd was removed from the femora, and ^{109}Cd was strongly retained by gonadal tissue.

INTRODUCTION

In a previous study,⁽¹⁾ combinations of chelating agents (ZnDTPA, PA + ZnDTPA, BAL + ZnDTPA, and BAL + PA + ZnDTPA)^{*} were administered to reduce the total-body burden of systemically absorbed ^{109}Cd in mice. Significant amounts of ^{109}Cd were preferentially removed from mice receiving BAL + ZnDTPA or BAL + PA + ZnDTPA, but not by treatments without BAL. A second study⁽²⁾ was undertaken to determine if the observed effect was directly attributable to the combination of chelating

^{*}The chelating agents were 2,3-dimercaptopropanol (British Anti Lewisite or BAL penacillamine (PA), and ZnNa_3 diethylenetriaminepentaacetate (ZnDTPA).

agents administered or to any one chelating agent alone. ZnDTPA alone was not effective at removing ^{109}Cd , and ZnDTPA did not enhance the efficacy of BAL in removing ^{109}Cd . BAL removed fractions of ^{109}Cd from the organs studied in the following order: kidneys > liver > femora > gonads.

In the previous studies, mice were injected with carrier-free ^{109}Cd . The present investigation evaluated the effectiveness of BAL at two dose levels in two oil media in chelating chemical amounts of cadmium.

MATERIALS AND METHODS

Seventy-two C57BL/Do mice (26 g avg. wt., and 9 to 11 months old) were each injected intraperitoneally (i.p.) with 0.052 mg of cadmium (CdCl_2) labeled with approximately 2 μCi of carrier-free ^{109}Cd (New England Nuclear) in citrate buffer. Total-body retention in each mouse was determined immediately following injection and three days later, just prior to starting treatment. All radioactivity measurements were made by counting the 88 keV γ -ray emitted from ^{109}Cd using dual 20 x 10 cm NaI(Tl) crystals in conjunction with a 1024 channel pulse-height analyzer.⁽³⁾ Animals that showed a drastic reduction in ^{109}Cd retention at the 3-day counting were assumed to have been injected into the gastrointestinal tract and were replaced before starting treatment.

Mice were caged in groups of six animals per cage, with a cage of males and a cage of females assigned to each treatment. The various regimens follow:

1. Saline control
2. BAL high dose in peanut oil
3. BAL high dose in cottonseed oil
4. BAL low dose in peanut oil

BAL was obtained from Sigma Chemical Company. Peanut oil (Matheson, Coleman, and Bell of Norwood, Ohio) and cottonseed oil (ICN Pharmaceuticals,

Cleveland, Ohio) were used as the liquid media in the BAL injection solutions. The controls were injected with a 0.9% NaCl solution (0.154 moles NaCl/liter) from Cutter Laboratories. The following daily dosages were used:

1. Saline (NaCl): 69 mg/kg/day
2. BAL (high dose): 168 mg/kg/day
3. BAL (low dose): 56 mg/kg/day

The saline injections were each 0.2 ml. The BAL injections initially consisted of 0.04 ml total volume and were administered using a 500 μ l syringe (Hamilton Co., Reno, Nevada). After five days of treatment, all BAL injections were decreased from 0.04 to 0.02 ml because of toxicity. At the high dose level of BAL (168 mg/kg/day) in peanut oil, all of the female mice and one-half of the male mice were dead by treatment day five. BAL toxicity was the suspected cause of death. Animals receiving the high dose of BAL were replaced, and mice were each given one injection of BAL at 168 mg/kg/day before the injection volume was decreased from 0.04 to 0.02 ml. In order to minimize the toxic effects of BAL, the following daily dosages were used for the duration of the experiment:

1. BAL (high dose): 84 mg/kg/day
2. BAL (low dose): 28 mg/kg/day

Mice were treated four days a week (Monday through Thursday). The injection site, at the high dose of BAL (84 mg/kg/day), gradually developed small pockets of unresorbed BAL and oil with accompanying hair loss and ulcerations. The 4 day/wk treatment schedule allowed the ulcerations to heal for 3 days/week while the BAL and oil was resorbed.

When the experiment was concluded, after 43 days of treatment, mice were sacrificed using penthrane anesthetic overdose. The liver, kidneys, gonads,

and femora were excised and placed in separate 3-dram glass vials with 95% ethanol as preservative. The ^{109}Cd activity in each sample was determined by gamma-ray spectroscopy in a well-type scintillation crystal.⁽⁴⁾

RESULTS

Total-Body Retention

Gamma-ray spectroscopy of mice indicated that for treatment days zero through forty-two, the cadmium total-body retention was influenced by the high treatment dose of BAL (see Figs. 1 and 2).

Statistical analysis, using the group comparison ("t") test,⁽⁵⁾ of all total-body retention data (see Tables 1 and 2) indicated that for each sex there was no significant difference ($P > 0.05$, but usually $P > 0.1$) between the means in the BAL low dose (28 mg/kg/day) vs. saline control groups. For both males and females, there was a significant difference ($P < 0.01$) in total-body retention between mice treated with BAL in cottonseed oil at 84 mg/kg/day vs. saline control mice. Male and female mice treated with BAL in peanut oil at 84 mg/kg/day also showed a significant difference ($P < 0.05$) in total-body retention when compared to the saline controls. Female mice receiving BAL in either peanut oil or cottonseed oil showed no significant difference in retention ($P > 0.2$), while their male counterparts had retentions which were significantly higher ($P < 0.05$) than that of males treated with BAL in cottonseed oil.

Organ Retention

Table 3 exhibits the ^{109}Cd content of the liver, kidneys, femora, and gonads. Statistical results of group comparison ("t") tests for all treatment groups of both males and females are presented in Tables 4 and 5.

The kidneys of both male and female mice, at the high dose of BAL in either

cottonseed oil or peanut oil, showed a significant difference in relative retention ($P < 0.001$) from the saline control group. Those receiving the high dose of BAL in peanut oil did not have significantly lower liver retentions ($P > 0.05$ males, $P > 0.2$ females) than the saline controls, while mice given the high BAL dose in cottonseed oil showed a significantly lower liver retention ($P < 0.001$ males, $P < 0.01$ females).

None of the organs removed from animals at the low BAL dose had significantly lower retentions ($P > 0.05$, but commonly $P > 0.2$) than the corresponding organs in the saline controls.

DISCUSSION

The efficacy of BAL as a chelating agent for chemical amounts of cadmium was influenced by dose. It is apparent from the data presented here that the high dose of BAL removed significantly more cadmium than the BAL low dose, since the biological retention of cadmium for the low BAL dose was not significantly different from the saline control mice.

Studies have shown that cadmium levels in the kidneys increase with time.^(6,7) Results presented here show that protracted BAL therapy removed a larger fraction of cadmium from the kidneys than from the liver. Relatively little cadmium was removed from the femora with BAL treatment. Cadmium was strongly retained by gonadal tissue and BAL treatment was ineffective.

The efficacy of BAL as a cadmium chelating agent was not enhanced or inhibited by either a peanut oil or a cottonseed oil injection medium. It does appear, though, that the toxicity of BAL was reduced when administered in cottonseed oil, since only the male and female mice at the high dose level of BAL in peanut oil died of suspected BAL toxicity.

ACKNOWLEDGMENTS

Thanks are expressed to David R. Atherton for preparing the BAL injection solutions, Thomas Brammer for his help with the injections and mouse husbandry, and Nancy Peixhot for typing the manuscript.

REFERENCES

1. Boseman J.J., Lloyd R.D., and Mays C.W. Removal of systemically absorbed ^{109}Cd in mice using a combination of chelating agents. in Research in Radiobiology, University of Utah Report C00-119-252, pp. 288-305, 1977.
2. Boseman J.J., Lloyd R.D., Jones C.W., and Mays C.W. Further studies on the removal of systemically absorbed ^{109}Cd in mice using a combination of chelating agents. in Research in Radiobiology, University of Utah Report C00-119-253.
3. Lloyd R.D., Aamodt R.L., Wagner W.W., and Pendleton R.C. Calibration of a gamma-ray spectrometer for soils counting. Int. J. Appl. Radiat. Isotopes 19: 773-775, 1968.
4. Lloyd R.D., Mays C.W., and Atherton D.R. Knothole, a new sidewall gamma-ray detector. Nucl. Instr. Methods 49: 109-113, 1967.
5. Woolf C.M. Principles of Biometry. D. Van Nostrand Co., Inc., pp. 62-69 and 329. Princeton, N.J., 1968.
6. Friberg L., Piscator M., Nordberg G.F., and Kjellström T. Cadmium in the Environment, 2nd Edition, p. 248, CRC Press, Cleveland, Ohio, 1974.
7. Thomas R.G., Wilson J.S., London J.E., and Drake G.A. Retention of ^{109}Cd in mice, rats, monkeys, and dogs. in Biomedical and Environmental Research Program of the LASL Health Division. Los Alamos - 6898-PR, p. 4-5, 1977.

FIGURE 1. Biological retention of ^{109}Cd in male C57BL/Do mice as measured by total-body counting during chelation treatment. The stable cadmium labeled with ^{109}Cd had been injected 3 days prior to the start of treatment.

FIGURE 2. Biological retention of ^{109}Cd in female C57BL/Do mice as measured by total-body counting during chelation treatment. The stable cadmium labeled with ^{109}Cd had been injected 3 days prior to the start of treatment.

TABLE 1. BIOLOGICAL RETENTION OF ^{109}Cd IN MALE C57BL/Do MICE AS MEASURED BY TOTAL-BODY COUNTING AT VARIOUS TIMES DURING PROGRESS OF DE-CORPORATION TREATMENT. THE RETENTION AT DAY ZERO OF TREATMENT WAS TAKEN AS 100%.

Days on Treatment	% Biological Retention (Mean $\pm$ S.D.)			
	Saline	BAL 28 mg/kg/day (Peanut Oil)	BAL 84 mg/kg/day (Peanut Oil)	BAL 84 mg/kg/day (Cottonseed Oil)
(-) 3	160.81 $\pm$ 8.81	139.30 $\pm$ 23.93	134.24 $\pm$ 4.79	140.71 $\pm$ 11.46
0	100.0	100.0	100.0	100.0
3	94.59 $\pm$ 4.0	88.47 $\pm$ 8.47	89.80 $\pm$ 2.95	84.83 $\pm$ 5.68
7	93.85 $\pm$ 4.27	88.00 $\pm$ 9.17	88.77 $\pm$ 2.83	80.84 $\pm$ 3.30
14	93.82 $\pm$ 4.56	86.42 $\pm$ 8.34	84.47 $\pm$ 4.30	75.96 $\pm$ 4.89
21	90.95 $\pm$ 3.61	84.88 $\pm$ 8.50	79.84 $\pm$ 3.70	73.44 $\pm$ 4.89
28	89.20 $\pm$ 3.92	82.95 $\pm$ 9.68	76.74 $\pm$ 3.75	68.05 $\pm$ 4.61
35	88.32 $\pm$ 3.58	82.16 $\pm$ 9.93	73.37 $\pm$ 4.83	64.21 $\pm$ 5.13
42	86.51 $\pm$ 4.30	80.17 $\pm$ 9.63	71.22 $\pm$ 4.36	61.85 $\pm$ 5.21

TABLE 2. BIOLOGICAL RETENTION OF ^{109}Cd IN FEMALE C57BL/Do MICE AS MEASURED BY TOTAL-BODY COUNTING AT VARIOUS TIMES DURING PROGRESS OF DECORPORATION TREATMENT. THE RETENTION AT DAY ZERO OF TREATMENT WAS TAKEN AS 100%.

Days on Treatment	% Biological Retention (Mean $\pm$ S.D.)			
	Saline	BAL 28 mg/kg/day (Peanut Oil)	BAL 84 mg/kg/day (Peanut Oil)	BAL 84 mg/kg/day (Cottonseed Oil)
(-) 3	139.11 $\pm$ 8.28	145.94 $\pm$ 11.13	126.39 $\pm$ 8.31	146.34 $\pm$ 9.26
0	100.0	100.0	100.0	100.0
3	94.77 $\pm$ 4.09	92.88 $\pm$ 3.15	88.31 $\pm$ 2.50	85.99 $\pm$ 6.58
7	95.38 $\pm$ 4.63	92.19 $\pm$ 4.24	88.14 $\pm$ 2.30	83.68 $\pm$ 5.92
14	93.64 $\pm$ 5.28	90.69 $\pm$ 4.25	83.71 $\pm$ 2.94	81.26 $\pm$ 4.96
21	94.12 $\pm$ 4.15	88.71 $\pm$ 4.22	79.89 $\pm$ 4.16	78.74 $\pm$ 5.65
28	92.65 $\pm$ 4.09	87.62 $\pm$ 3.78	76.65 $\pm$ 2.76	76.58 $\pm$ 5.80
35	90.99 $\pm$ 3.87	86.68 $\pm$ 3.29	73.87 $\pm$ 3.89	73.50 $\pm$ 5.36
42	91.13 $\pm$ 4.86	86.37 $\pm$ 4.04	70.32 $\pm$ 4.24	71.53 $\pm$ 4.96

TABLE 3. DIFFERENCES IN THE ORGAN RETENTION OF ^{109}Cd AT AUTOPSY (43 DAYS AVERAGE) AMONG THE VARIOUS TREATMENT GROUPS.

% Biological Retention* (Mean $\pm$ S.D.)					
Tissue	Sex	Saline	BAL 28 mg/kg/day (Peanut Oil)	BAL 84 mg/kg/day (Peanut Oil)	BAL 84 mg/kg/day (Cottonseed Oil)
Liver	♂	47.16 $\pm$ 3.27	45.70 $\pm$ 6.62	43.15 $\pm$ 4.22	32.80 $\pm$ 3.87
Liver	♀	50.04 $\pm$ 5.09	48.31 $\pm$ 5.41	45.90 $\pm$ 4.95	41.41 $\pm$ 2.14
Kidneys	♂	11.82 $\pm$ 1.39	10.58 $\pm$ 5.18	4.09 $\pm$ 0.75	4.05 $\pm$ 0.59
Kidneys	♀	12.20 $\pm$ 1.81	10.26 $\pm$ 1.00	4.02 $\pm$ 0.96	4.12 $\pm$ 1.11
Femora	♂	0.18 $\pm$ 0.03	0.16 $\pm$ 0.05	0.13 $\pm$ 0.01	0.14 $\pm$ 0.01
Femora	♀	0.14 $\pm$ 0.02	0.17 $\pm$ 0.04	0.12 $\pm$ 0.03	0.12 $\pm$ 0.02
Gonads	♂	0.12 $\pm$ 0.03	0.10 $\pm$ 0.03	0.11 $\pm$ 0.02	0.13 $\pm$ 0.05
Gonads	♀	0.07 $\pm$ 0.03	0.07 $\pm$ 0.04	0.06 $\pm$ 0.03	0.07 $\pm$ 0.03

* ^{109}Cd in organ at autopsy on treatment day t
 $[\text{^{109}Cd in total body on treatment day 0}] [e^{-\lambda t}]$

Table 4. STATISTICAL RESULTS OF GROUP COMPARISON ("t") TESTS FOR ALL TREATMENT GROUPS OF MALE MICE.

<u>Pairs</u> [*]	<u>Liver</u>	<u>Kidneys</u>	<u>Femora</u>	<u>Gonads</u>
A. vs. B.	P<0.001	P<0.001	P<0.02	P>0.7
C.	>0.05	<0.001	<0.005	>0.3
D.	>0.6	>0.5	>0.5	>0.2
B. vs. C.	<0.001	>0.9	>0.95	>0.3
D.	>0.1	<0.005	>0.05	>0.99
C. vs. D.	>0.4	<0.005	>0.1	>0.7

- *A. Saline controls.
 B. BAL high dose in cottonseed oil.
 C. BAL high dose in peanut oil.
 D. BAL low dose.

Table 5. STATISTICAL RESULTS OF GROUP COMPARISON ("t") TESTS FOR ALL TREATMENT GROUPS OF FEMALE MICE.

<u>Pairs</u> [*]	<u>Liver</u>	<u>Kidneys</u>	<u>Femora</u>	<u>Gonads</u>
A. vs. B.	P<0.01	P<0.001	P>0.1	P>0.95
C.	>0.2	<0.001	>0.2	>0.9
D.	>0.5	>0.05	>0.2	>0.8
B. vs. C.	>0.1	>0.8	>0.99	>0.8
D.	<0.05	<0.001	<0.05	>0.9
C. vs. D.	>0.5	<0.001	>0.05	>0.8

- ^{*}
- A. Saline controls.
 - B. BAL high dose in cottonseed oil.
 - C. BAL high dose in peanut oil.
 - D. BAL low dose

Zn-DTPA SAFETY IN THE MOUSE FETUS

Scott E. Calder, Charles W. Mays, Glenn N. Taylor, and Thomas Brammer

ABSTRACT: An experiment was conducted to determine the effect of very high doses of subcutaneously injected Zn-DTPA on pregnant mice and their fetuses. Seventy-nine female C57/B1 mice were divided into four groups and caged with males for 11 consecutive days. Starting on day 4, the females were subcutaneously injected daily with one of the following: (a) Zn-DTPA made from ZnO and DTPA by the Sigma Chemical Co.; (b) a preparation of Zn-DTPA made from ZnCl_2 and DTPA which contained an additional 2 moles of NaCl per mole of DTPA; (c) hypertonic saline with an osmolarity equal to the Zn-DTPA + 2 NaCl preparation; or (d) isotonic saline (controls). The two preparations of Zn-DTPA were injected in daily doses of 11.5, 5.75 or 2.88 m mole DTPA/kg. Hypertonic saline was injected in daily doses of 46 or 23 m mole NaCl/kg. Control mice received daily injections of 5 or 1.25 m mole NaCl/kg in isotonic solution. The injections were concluded when the pups were born or on day 33.

Zn-DTPA (Sigma Chemical Co.): Among the mice injected with 11.5 m mole Zn-DTPA/kg/day, no statistically significant variations from the controls were noted in number of parturient dams, number of pups per litter, or total number of pups surviving at 7 days of age. Only birth weights in this group deviated from the controls, the average weight being 1.09 compared to 1.30 g for the controls ($P < 0.001$). At the 5.75 and 2.88 m mole Zn-DTPA/kg/day level, all results were indistinguishable from those of the controls.

Zn-DTPA (+ 2 NaCl): The 11.5 m mole Zn-DTPA/kg/day injections also resulted in depressed birth weights (1.11 g vs. 1.30 g for controls). However, three dams in this group died on days 19, 30, and 32 of the experiment with acute kidney damage (degeneration and/or necrosis of the proximal and distal tubules). Evidence of one abortion was also found in this group. At 5.75 and 2.88 m mole Zn-DTPA/kg/day, no deleterious effects were noted.

Hypertonic NaCl: The group of mice injected with hypertonic saline solutions proved in all respects to be statistically identical to the control group.

Teratogenic effects were not observed in any of the pups used in this study. Subsequent studies showed no evidence for impaired fertility in mature pups or reduced viability of their offspring.

INTRODUCTION

The chelating agent, Zn-DTPA (zinc trisodium diethylenetriaminepentaacetate), is much safer than Ca-DTPA (calcium trisodium diethylenetriaminepentaacetate), both to the adult animal (Ca65, Ga74, Ta74, P175) and to the developing fetus (Bö71, Fi75, Si75, Br77). Therefore, Zn-DTPA may become the drug-of-choice for the safe removal of Pu and other actinide elements from pregnant women.

Fisher, et al. (Fi75), reported that in pregnant C57/B1 mice, Zn-DTPA given at 12 and 100 times the prescribed human dose (30 μ mole DTPA/kg/day, or about 1 gram of Zn-DTPA per day to an adult) caused no untoward effects on the offspring, whereas Ca-DTPA given at 100 times the human dose resulted in no living pups. In a subsequent study (Fi76), Ca-DTPA, given at intermediate doses (25 and 50 times the prescribed human dose) from 2 through 6 days after mating, caused the following fetal deformities: exencephaly, ablepharia, spina bifida aperta, and cleft palate. These malformations were attributed to the consequences of trace metal depletion (particularly zinc and manganese depletion) in the growing fetus (Ga74, Co75). Because Zn-DTPA has a higher stability constant than either Ca-DTPA or Mn-DTPA (Ca68), the administration of Zn-DTPA does not deplete the developing fetus of either zinc or manganese and, as a result, the probability of teratogenic effects is dramatically reduced.

The purposes of the present study were to: (1) Evaluate in C57/B1 mice the fetal toxicity of very high doses of Zn-DTPA when given from early after conception until the end of pregnancy; (2) identify any differences in toxicity between Zn-DTPA produced commercially (containing no NaCl), and Zn-DTPA produced in our lab (containing two moles of NaCl for every mole of Zn-DTPA); (3) compare the toxicity of the two types of Zn-DTPA with the toxicity of

hypertonic saline; and (4) begin a lifetime study to determine if any delayed damage to the dams or their offspring may result from very high doses of Zn-DTPA during pregnancy.

METHODS

Seventy-nine virgin female C57/B1 mice of the Dougherty strain, 130-149 days of age, were divided into test groups and housed two per cage. One male mouse of the same strain and age was placed in each cage and allowed to remain with the two females for eleven days. Starting at four days after placement with males, the females only were subcutaneously injected daily with one of the four following solutions: pure Zn-DTPA procured commercially (containing no NaCl^{*}), Zn-DTPA made in our lab (containing NaCl), hypertonic saline (81 g NaCl/liter), or bacteriostatic isotonic saline (9 g NaCl/liter). Injections were continued for each female mouse until either it bore pups or had received 29 injections. The two types of Zn-DTPA were injected in volumes of 0.2 ml, 0.4 ml or 0.8 ml, according to whether the daily dose level was 2880, 5750, or 11500 μ mole Zn-DTPA/kg, respectively (100, 200, or 400 times the prescribed human dose). Hypertonic saline was injected in volumes of 0.4 ml or 0.8 ml, equivalent to 23000 or 46000 μ mole NaCl/kg/day, having roughly the same osmolarity as injections of 200 or 400 times the human dose of laboratory Zn-DTPA. Controls were injected with 0.2 ml or 0.8 ml of isotonic saline in order to factor out any possible effect of differing injection volumes. Purina Lab Chow and tap water were available ad libitum.

The mice were examined daily to determine if any adverse effects resulted

*The pure Zn-DTPA was made from ZnO and DTPA by the Sigma Chemical Company of St. Louis, Missouri. Our sample was from the same batch manufactured for use in human therapy, pending FDA approval.

from the injections. When the females bore young, the date, number of pups, their status (living or dead), and weight were determined and recorded. In addition, all pups were externally examined for any evidence of gross malformation, and subsequently returned to the dam and allowed to suckle normally.

RESULTS

Viable offspring were produced by dams in every injection group. The number of births per litter for all injection groups was similar to that of the isotonic saline controls, except the highest level of laboratory Zn-DTPA which contained NaCl. Among dams in this group (injected daily with 11500 μ mole Zn-DTPA/kg + 23000 μ mole NaCl/kg) only 2 of 7 dams bore live young (see Table 1). This compared with at least 5 dams bearing young per injection group among those given various other doses of Zn-DTPA or saline. Fifteen of 16 control group dams gave birth to live young.

Acute effects of the chelate administration were noted only among dams at the highest daily dosage of laboratory Zn-DTPA (11500 μ mole Zn-DTPA/kg + 23000 μ mole NaCl/kg). In this group, three dams died on days 19, 30, and 32 of the experiment as a result of severe damage to the proximal and distal tubules of the kidney. In addition, pups from the highest level of the laboratory Zn-DTPA and the pure Zn-DTPA groups showed a significant weight deficiency at birth. No congenital malformation was noted among pups in any of the groups.

DISCUSSION

In agreement with previous studies (Fi75, Br77), pregnant mice injected daily from early after conception until birth with massive amounts of Zn-DTPA bore no pups which were grossly malformed. There is no evidence that pure Zn-DTPA, even when given at 11500 μ moles/kg/day, is toxic to mice or their offspring.

Laboratory-produced Zn-DTPA accompanied by NaCl, however, proved toxic both to dams and pups at this level. At lower levels of either kind of Zn-DTPA, fecundities and pup weights for the treated animals were not statistically different from the isotonic saline controls. The highest level of laboratory Zn-DTPA + NaCl was also the only treatment group where evidence of abortion was found. Mice given this form of DTPA at high levels showed local irritation and scabs at injection sites, which abated only after treatment had been discontinued.

Interestingly, the injection of dams with hypertonic saline of the same total osmolarity as the laboratory Zn-DTPA (containing NaCl), though causing the same local irritation and injection-site scabs, was not toxic to the animals or their pups. Thus, the deleterious effects of high-dosage laboratory Zn-DTPA (with NaCl) administration cannot be solely attributed to the high osmolarity of the injections.

Except for the mice receiving the highest daily dosages of Zn-DTPA, pup weights were within the range to be expected. Newborn pups whose mothers received 11500 μ mole Zn-DTPA/kg/day or 11500 μ mole Zn-DTPA + 23000 μ mole NaCl/kg/day had average weights of 1.1 g and 1.1 g, respectively, whereas the average weight for controls was 1.3 g.

The results of this experiment indicate that Zn-DTPA exhibits very low toxicity. Although Zn-DTPA accompanied by NaCl resulted in toxic effects when administered in massive doses, pure Zn-DTPA was shown to be non-toxic to adult mice and non-teratogenic to offspring at the highest injection dosages used in this experiment. The only treatment-associated effect of administering pure Zn-DTPA to pregnant mice was the lowering of pup birth weights, and this occurred only at 400 times the prescribed dose for humans. Zn-DTPA is much less toxic than Ca-DTPA to fetal mice.

The fact that no effects of any kind were seen in mice at 5750 μ mole Zn-DTPA/kg/day, does not imply that daily doses of this magnitude could be used with impunity in humans. If body surface area is used rather than body weight as the parameter in scaling the amount of drug to be given (Pi58), the predicted "no effect" dose in humans would be about 1/14 of the μ mole/kg/day "no effect" dose in mice. Thus, for humans, based on present evidence, the daily dose of Zn-DTPA should not exceed $5750/14 \approx 400$ μ mole Zn-DTPA/kg/day, which is about 13 times the prescribed human dose.

A lifespan-follow up is now in progress on the dams and pups from this experiment to evaluate the possibility of delayed effects from the Zn-DTPA treatment. Already, we have found no evidence for any impaired fertility in the mature pups or reduced viability in their offspring. In 1980, when all of the mice have been autopsied and examined histologically, we hope to recommend with confidence an appropriate treatment schedule for the pregnant woman who accidentally becomes contaminated with significant actinide radioactivity.

ACKNOWLEDGMENTS

We are grateful to Fred Bruenger and Dave Atherton for their preparation of the injection solutions used in this study.

REFERENCES

- B871 Bömer H., 1971, "Metabolismus und Toxizität Therapeutischer Chelatbildner," *Strahlentherapie* 142, 349.
- Br77 Brummet E.S., and Mays C.W., 1977, "Teratological Studies of Zn-DTPA in Mice," *Health. Phys.* 33, 624.
- Ca68 Catsch A., 1968, "Dekorporierung Radioaktiver und Stabiler Metallionen," Thieme, Munich, p. 25.
- Ca65 Catsch A. and von Wedelstaedt E., 1965, "Vergleichende Untersuchungen über die Toxizität der Ca- und Zn- (II) - Chelate der Diäthylentriaminpentaessigsäure," *Experientia* 21, 210.
- Co75 Cohen N. and Guilmette R., 1975, "Biological Effects of the Enhanced Excretion of Zinc after Ca-DTPA Chelation Therapy," *Bioinorg. Chem.* 5, 203.
- Fi75 Fisher D.R., Mays C.W., and Taylor G.N., 1975, "Ca-DTPA Toxicity in the Mouse Fetus," *Health. Phys.* 29, 780.
- Fi76 Fisher D.R., Calder S.E., Mays C.W., and Taylor G.N., 1976, "Ca-DTPA-Induced Fetal Death and Malformation in Mice," *Teratology* 14, 123.
- Ga74 Gabard B., 1974, "The Influence of DTPA on the Synthesis of DNA, RNA, and Proteins in the Regenerating Rat Liver," *Biochem. Pharmacol.*, 23, 901.
- Pi58 Pinkel D., "The Use of Body Surface Area as a Criterion on Drug Dosage in Cancer Chemotherapy," *Cancer Res.* 18, 853.
- Pi75 Planas-Bohne F., and Ebel H., 1975, "Dependence of DTPA Toxicity on the Treatment Schedule," *Health. Phys.* 30, 249.

- Si75 Sikov M.R., Smith V.H., and Mahlum D.D., 1975, "Teratological Effectiveness and Fetal Toxicity of DTPA in the Rat," Pacific Northwest Laboratory Annual Report BNWL-1950 PT1, p. 138.
- Ta74 Taylor G.N., Williams J.L., Roberts L., Atherton D.R., and Shabestari L., 1974, "Increased Toxicity of Na_3Ca DTP when Given by Protracted Administration," Hlth. Phys. 27, 285.

Table 1. INJECTION SCHEDULE AND BIRTH DATA

<u>Treatment</u>	<u>Dosage</u> (μ mole/kg/day)	<u>Dams</u>	<u>Litters</u>	<u>Pups/Litter</u> (av. $\pm$ S.D.)	<u>Pup Weight(g)</u> (av. $\pm$ S.D.)
Zn-DTPA	11500	8	6	6.0 $\pm$ 2.8	1.09 $\pm$ 0.15 [†]
	5750	8	8	7.5 $\pm$ 1.6	1.31 $\pm$ 0.13
	2880	8	8	7.1 $\pm$ 1.2	1.30 $\pm$ 0.15
Zn-DTPA*	11500	7 ^{**}	2	5.5 $\pm$ 6.4	1.11 $\pm$ 0.13 [†]
	5750	8	6	7.8 $\pm$ 2.6	1.23 $\pm$ 0.13
	2880	8	5	8.6 $\pm$ 2.1	1.24 $\pm$ 0.13
NaCl	46000	8	6	8.0 $\pm$ 1.3	1.27 $\pm$ 0.14
(hypertonic)	23000	8	5	9.0 $\pm$ 2.4	1.21 $\pm$ 0.11
NaCl	5000	8	7	8.6 $\pm$ 2.2	1.30 $\pm$ 0.13
(isotonic)	1250	8	8	7.5 $\pm$ 2.8	

*This Na₃ Zn-DTPA was accompanied by 2 NaCl; the other Na₃ Zn-DTPA was pure.

**Evidence of one abortion was found in this group.

†P<0.001 when compared to isotonic saline controls.

ADDITIONS TO BIBLIOGRAPHY

(1 April 1977 to 31 March 1978)

PUBLISHED PAPERS

1. Bugher, J.C., Snyder, W.S., Abrahamson, S., Andrews, H.L., Comar, C.L., Forbes, G.B., Gustafson, P.F., Marshall, J.H., Mays, C.W., and Rivera, J., 1977. Cesium-137 from the environment to man: Metabolism and dose. National Council on Radiation Protection and Measurements, NCRP Report 52, 48 pages.
2. Brummett, E.S. and Mays, C.W., 1977. Teratological studies of Zn-DTPA in mice. *Health Phys.* 33: 624-626.
3. Clayton, C.J., Grosser, B.I., and Stevens, W., 1976. The ontogeny of corticosterone and dexamethasone receptors in rat brain. *Brain Research* 134: 443-453.
4. Grube, B.J., Stevens, W., and Atherton, D.R., 1977. The retention of plutonium in hepatocytes and sinusoidal lining cells isolated from rat liver. *Radiation Research* 73: 168-179.
5. Hofer, K.G., Keough, G., and Smith, J.M., 1977. Biological toxicity of Auger emitters: Molecular fragmentation vs. electron irradiation. *Curr. Topics Radiat. Res. Quart.* 12: 335-354.
6. Jee, W.S.S., and Kimmel, D.B., 1977. Bone cell origin at the endosteal surface. *Bone Histomorphometry, Second International Workshop*, P. Meunier (Ed.), Armour Montagu, Paris, pp. 113-132.
7. Kimmel, D.B., and Jee, W.S.S., 1977. Morphometric measurements in tissue bands isometric to an irregular reference line. *Bone Histomorphometry, Second International Workshop*, P. Meunier (Ed.), Armour Montagu, Paris, pp. 97-102.

8. Lloyd, R.D., Taylor, G.N., Boseman, J.J., Mays, C.W., and Atherton, D.R., 1977. Further comparison of Ca-DTPA and Zn-DTPA for removal of ^{241}Am from beagles. *Health Physics* 33: 92-94.
9. Mays, C.W., 1978. On the scientific work of Fritz Schales. in Biological Effects of ^{224}Ra : Benefit and Risk of Therapeutic Application, W.A. Müller and H.G. Ebert, Eds., Martinus Nijhoff Medical Division, The Hague/Boston, pp. 5-6.
10. Mays, C.W., 1978. Risk to bone from present ^{224}Ra therapy. in Biological Effects of ^{224}Ra : Benefit and Risk of Therapeutic Application, W.A. Müller and H.G. Ebert, Eds., Martinus Nijhoff Medical Division, The Hague/Boston, pp. 37-43.
11. Mays, C.W., and Spiess, H., 1978. Bone sarcoma risk to man from ^{224}Ra , ^{226}Ra , and ^{239}Pu . in Biological Effects of ^{224}Ra : Benefit and Risk of Therapeutic Application, W.A. Müller and H.G. Ebert, Eds., Martinus Nijhoff Medical Division, The Hague/Boston, pp. 168-181.
12. Miller, S.C., and Jee, W.S.S., 1977. The comparative effects of dichloromethylene diphosphonate (Cl_2MDP) and ethane-1-hydroxy-1, 1-diphosphonate (EHDP) on growth and modeling of the rat tibia. *Calc. Tissue Res.* 23: 207-214.
13. Miller, S.C., 1977. Osteoclast cell surface changes during the egg-laying cycle in Japanese Quail. *J. Cell Biol.* 75: 104-118.
14. Miller, S.C., 1978. Rapid activation of the medullary bone osteoclast cell surface by parathyroid hormone. *J. Cell Biol.* 76: 615-618.
15. Rossi, H.H. and Mays, C.W., 1978. Leukemia risk from neutrons. *Health Physics* 34: 353-360.

16. Smith, J.M., Lloyd, R.D., Mays, C.W., and Lloyd, A.T., 1977. On the determination of the half-life of ^{237}Pu . J. Inorg. Med. Chem. 39: 1850-1852.
17. Smith, J.M., Taylor, G.N., Mays, C.W., and Atherton, D.R., 1978. The early retention of monomeric $^{237,239}\text{Pu(IV)}$ -citrate in C57BL/Do and BALB/cJ mice. Radiat. Res. 73: 502-509.
18. Stevens, W., Atherton, D.R., Bates, D.S., Lloyd, R.D., Buster, D.S., and Bruenger, F.W., 1977. Retention and distribution of $^{241}\text{AmIII}$ in neonatal beagles. Health Phys. 33: 553-559.
19. Taylor, G.N., Shabestari, Lorraine, Williams, J., Mays, C.W., Angus, W., and McFarland, Susan, 1976. Mammary neoplasia in a closed beagle colony. Cancer Research 36: 2740-2743.
20. Warters, R.L., Hofer, K.G., Harris, C.R., and Smith, J.M., 1977. Radionuclide toxicity in cultured mammalian cells: elucidation of the primary site of radiation damage. Curr. Topics Radiat. Res. Quart. 12: 389-407.

PUBLISHED ABSTRACTS

1. Bruenger, F.W., Neilson, E.S., Atherton, D.R., and Stevens, W., 1978. Development of chelating agents for enhanced excretion of actinide elements. Abstracts of the 26th Annual Meeting Radiation Research Society, Toronto.
2. Kimmel, D.B., and Jee, W.S.S., 14-18 May, 1978. Quantitative studies of endosteal cells at risk. Abstract Fd-5 (26th Annual Meeting of Radiation Research Society), Toronto, Ontario, Canada.

3. Lloyd, R.D., Boseman, J.J., Taylor, G.N., Bruenger, F.W., Atherton, D.R., Stevens, W., and Mays, C.W., 1977. Plutonium decorporation in beagles with Ca-DTPA or Zn-DTPA. *Health Physics* 33: 680.
4. Smith, J.M., Kimmel, D.B., Wronski, T.J., and Jee, W.S.S., 1978. Alpha particle flux and local dose rates to endosteal cells at risk in beagles. Twenty-Sixth Annual Meeting of the Radiation Research Society, Toronto.
5. Stevens, W., Atherton, D.R., Bruenger, F.W., and Stover, Betsy J., 1978. Retention, distribution, and toxicity of ^{239}Pu in beagles injected at 3-months of age. Abstracts of the 26th Annual Meeting Radiation Research Society, Toronto.
6. Wronski, T.J., Smith, J.M., and Jee, W.S.S., 14-18 May, 1978. The microdistribution and retention of Pu-239 on trabecular surfaces at five skeletal sites of the beagle. Abstract Fd-9. (26th Annual Meeting of Radiation Research Society), Toronto, Ontario, Canada.