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Research in Radiobiology

Annual Report of Work in Progress
in the Internal Irradiation Program

MASTER

RADIOBIOLOGY DIVISION OF THE DEPARTMENT OF ANATOMY,
UNIVERSITY OF UTAH COLLEGE OF MEDICINE

Respectfully Submitted by:
THOMAS F. DOUGHERTY, Director

MARCH 31, 1968

CONTRACT NO. AT (11-1)-119

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RESEARCH IN RADIOBIOLOGY

Annual Report of Work in Progress
in the Internal Irradiation Program

Radiobiology Division of the Department of Anatomy,
University of Utah College of Medicine

Respectfully Submitted by:

Thomas F. Dougherty, Director

March 31, 1968

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TABLE OF CONTENTS

	Page
Group Leaders and Sections	3
Availability of Previous Reports	4
Current Census of the Beagle Colony	6
Preface to Injection Tables	7
Dosimetry	9
Injection Tables	
I. Toxicity Animals	12
A. Radium-226	12
B. Plutonium-239	22
C. Radium-228 (Mesothorium)	32
D. Thorium-228 (Radiothorium)	38
E. Strontium-90	44
II. Test Animals	50
A. Radium-226	50
B. Plutonium-239	56
C. Radium-228 (Mesothorium)	62
D. Thorium-228 (Radiothorium)	64
E. Strontium-90	66
F. Radium-224 (Quickradium)	70
G. Americium-241	74
H. Ancillary	78
Special Topics	
Symposium on Bone-Seeking Radionuclides	84
Hematopoietic Disorders in Beagles Injected with ^{90}Sr	90

TABLE OF CONTENTS (Con't.)	Page
Distribution of ^{90}Sr in the Humerus and Third Lumbar Vertebra of the Beagle Pup After Single and Multiple Injections	101
^{210}Pb Contamination of ^{228}Th : Its Contribution to Dose in Beagles in our ^{228}Th Toxicity Studies	110
Distribution of ^{241}Am in the Beagle	117
Microscopic Distribution of Americium-241 in the Beagle Thyroid Gland	124
Some Observations on the Deposition of ^{241}Am in the Thyroid Gland	133
^{241}Am In the Blood: <u>In Vivo</u> and <u>in Vitro</u> Observations	135
Note on the Exchange of $^{239}\text{PuIV}$ Between Transferrin and Ferritin <u>in Vitro</u>	153
EHPA-Scintillator Method: Analysis of Bone Samples for ^{239}Pu	158
Additions to Bibliography (1 April 1967 through 31 March 1968)	163

GROUP LEADERS AND SECTIONS

Division of Radiobiology, Department of Anatomy,
University of Utah College of Medicine

Section	Group Leader
Director	Prof. Thomas F. Dougherty
Biochemistry	Dr. David L. Berliner
Bone	Dr. Webster S. S. Jee
Chemistry	Dr. Betsy J. Stover
Clinic & Pathology	Dr. Glenn N. Taylor
Hematology	Dr. Jean H. Dougherty
Physics	Dr. Charles W. Mays
Radiology	Dr. William R. Christensen

AVAILABILITY OF PREVIOUS REPORTS

Copies of our reports may be obtained from the Office of Technical Services, U. S. Department of Commerce, Washington 25, D. C.

<u>Report</u>	<u>Date</u>	<u>Title</u>	<u>Photocopy</u>	<u>Microfilm</u>
C00-119-237*	Mar 1968	Research in Radiobiology	\$16.70	\$ 8.35
C00-119-236*	Mar 1967	Research in Radiobiology	\$26.80	\$13.40
C00-119-235	Sep 1966	Research in Radiobiology	14.20	7.10
C00-119-234*	Mar 1966	Research in Radiobiology	34.80	9.90
C00-119-233*	Sep 1965	Research in Radiobiology	10.90	5.45
C00-119-232*	Mar 1965	Research in Radiobiology	22.20	11.10
C00-119-231*	Sep 1964	Research in Radiobiology	17.20	8.60
C00-119-230*	Jul 1964	Safety Manual	3.10	1.55
C00-119-229	Mar 1964	Research in Radiobiology	13.00	5.84
C00-228*	Sep 1963	Research in Radiobiology	13.00	5.84
C00-227*	Mar 1963	Research in Radiobiology	15.50	7.22
C00-226	Sep 1962	Research in Radiobiology	10.50	4.31
C00-225	Mar 1962	Research in Radiobiology	10.50	4.28
C00-224*	Sep 1961	Research in Radiobiology	9.10	3.32
C00-223	Mar 1961	Research in Radiobiology	6.30	3.00
C00-222	Sep 1960	Research in Radiobiology	22.80	7.20
C00-221	Aug 1960	Interim Report of Sr ⁹⁰	3.30	2.40
C00-220	Mar 1960	Research in Radiobiology	34.80	9.90
C00-219*	Sep 1959	Semi-Annual Report	10.80	3.90
C00-218	Mar 1959	Annual Report	34.80	9.90
AECU-4112	Feb 1959	Radioactive Fallout	3.30	2.40
C00-217	Sep 1958	Semi-Annual Report	28.50	8.40

AVAILABILITY OF PREVIOUS REPORTS (Cont.)

<u>Report</u>	<u>Date</u>	<u>Title</u>	<u>Photocopy</u>	<u>Microfilm</u>
C00-216 *	Mar 1958	Escape of Radon & Thoron	\$ 9.30	6.30
C00-215	Mar 1958	Annual Report	28.80	8.40
AECU-3583	Sep 1957	Semi-Annual Report	19.80	6.30
AECU-3522	Mar 1957	Annual Report	27.30	8.10
TID-16459	Sep 1956	Semi-Annual Report	5.60	2.05
TID-16458	Mar 1956	Annual Report	10.50	4.40
AECU-3109	Sep 1955	Semi-Annual Report	12.30	4.50
AECU-3418	Mar 1955	Annual Report	9.30	3.60
TID-7639	Jun 1954	Consultants Meeting	19.75	9.40

*Also available on request from this laboratory.

CURRENT CENSUS OF THE BEAGLE COLONY

March 31, 1968

²⁴¹ Am (americium)	Test	20
²³⁹ Pu (plutonium)	Toxicity	46
²³⁹ Pu (plutonium)	Test	68
²²⁸ Th (radiothorium)	Toxicity	39
²²⁸ Ra (mesothorium)	Toxicity	39
²²⁶ Ra (radium)	Toxicity	49
²²⁶ Ra (radium)	Test	32
²²⁴ Ra (quickradium)	Test	14
⁹⁰ Sr (strontium)	Toxicity	63
Controls	X-Ray	5
Controls (breeding and others)		47
Unassigned	(male 49) (female 37)	86
	Total	508

INJECTION TABLES

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

Dogs are put into the toxicity study groups of six or seven of the same sex (five or six dose levels plus one control). Litter mates are used whenever possible. Each animal receives the designated dose of one radionuclide in a single I. V. injection. The animals are injected 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 five radionuclides, Ra^{226} , Pu^{239} , Ra^{228} , Th^{228} , and Sr^{90} . The current injection program is limited to Ra^{226} and Pu^{239} at lower dose levels and to a few test run animals receiving various radionuclides of current interest.

The five dose levels designated by integers are those specified at the early meetings of the consultants, and those designated by non-integers have been added by the laboratory staff. Since those dose levels were originally specified as "retained" doses, the actual injected doses are four times the desired "retained" doses of Ra^{226} , Ra^{228} (Mesothorium), and Sr^{90} , and 1.11 times the desired "retained" doses of Pu^{239} and Th^{228} (Radiothorium).*

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

average Ra^{226}	retention = 0.25 after 271 days
average Pu^{239}	retention = 0.90 after 6 days
average Ra^{228}	retention = 0.25 after 214 days
average Th^{228}	retention = 0.90 after 6 days
average Sr^{90}	retention = 0.25 after 135 days

are the same for all the radionuclides except Sr^{90} , in which case they are greater by a factor of 10. Dose level 1 is the basis of the scheme, and is 10 times the maximum permissible Ra^{226} in man. Level 1 = $10 \times \frac{0.1 \mu\text{Ci Ra}^{226}}{70 \text{ kg man}} = 0.0143$ "retained" $\mu\text{Ci/kg}$. All other dose 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 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 = Ra^{226} , P = Pu^{239} , M = Ra^{228} , T = Th^{228} , S = Sr^{90} , Q = Ra^{224} , J = Sr^{85} , W = Am^{241} , 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 assignment to serial sacrifice schedule. Any of the above letters denoting a radionuclide may follow the final number, in which case the letter indicates that two radionuclides were given. The dose level refers to the radionuclide appearing first in the identifying code.

Example: M1R5 is a male animal in the first radium group at the highest dose level.

Although M1R5, M1R4, M1R2, M1R1, and M1R0 constitute a group and were injected at the same time, the tables are arranged according to dose 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; these tumors were the subject of a separate report, Research in Radiobiology, September 30, 1963 (C00-228), pp. 95-108. 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 immanent or when life could no longer be humanely prolonged.

DOSIMETRY

The injection tables include the calculated dose in rads to the skeleton at death. Ra^{226} , Ra^{228} , and Sr^{90} doses are calculated for each dog using his individually observed retention values: Pu^{239} and Th^{228} doses are from our average skeletal retention equations.

For our standard beagle, the following equations were used for the effective* skeletal retention at (t) days after injection:

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

(5-level only)

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

(lower levels)

$$\text{Rn}^{222}/\text{Ra}^{226} = 0.075 \left[1 - e^{-0.181t} \right]^{0.158}$$

(all levels)

$$\text{Pu}^{239} = 0.72 t^{-0.040}$$

$$\text{Ra}^{228} = 0.251e^{-0.982t} + 0.211e^{-0.269t} + 0.210e^{-0.0158t} + 0.177e^{-0.00237t} + 0.151e^{-0.000479t}$$

(pure at t = 0)

84.4% retention of in vivo produced Th^{228} and daughters,

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

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

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

$$\text{Sr}^{90} = 0.402e^{-0.748t} + 0.259e^{-0.102t} + 0.181e^{-0.00469t} + 0.158e^{-0.000302t}$$

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

We hope to present our detailed retention data and dosimetric analysis in a future report.

Ra^{228} doses deserve special comment. The dose from "pure" Ra^{228} and its in vivo produced daughters is based on our best evaluation of 5.77 ± 0.02 yr for the Ra^{228} half-period. The tabulated total doses include the contributions from Th^{228} contamination in the injection solutions. For example, Th^{228} contaminations of 0.6%, 3%, and 15%, respectively, account for 2.8%, 13% and 42% of the total dose in rads at 1000 days. If injected Th^{228} is 4 times more toxic rad-for-rad than is in vivo produced Th^{228} , these injected Th^{228} 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% Th^{228}) dogs in evaluation of Ra^{228} toxicity.

TABLE I. TOXICITY ANIMALS (MAR. 31 1968)

A. RADIUM-226

DOG NUMBER	AT INJECTION AGE WEIG HT (DAYS) (KG)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
M001R0.0	558 8.03		20 4 53	3116	
M002R0.0	487 14.60		16 11 53	3675	
F003R0.0	601 11.40		10 3 54	2139	
M004R0.0	461 11.00		7 4 54	5107	
M005R0.0	460 6.57		22 6 54	4018	
F006R0.0	483 8.43		27 7 54	3182	
M007R0.0	511 11.00		24 8 54	3360	
F008R0.0	638 8.21		21 12 54	3361	
F009R0.0	700 11.70		11 4 55	1550	
M010R0.0	522 10.90		27 7 55	4631	
F011R0.0	544 10.20		20 12 55	4485	
F012R0.0	501 8.68		17 1 56	4283	
M013R0.0	515 12.30		4 3 64	1488	
F014R0.0	536 10.80		23 10 64	1255	
M015R0.0	564 12.80		4 2 65	1151	
F016R0.0	469 10.00		7 4 65	1089	
M017R0.0	469 12.50		27 4 66	704	
F018R0.0	497 12.00		25 5 66	676	
F019R0.0	526 8.42		13 10 66	535	
M020R0.0	536 9.70		29 12 66	458	
F021R0.0	549 9.90		26 1 67	430	
M022R0.0	533 12.10		22 3 67	375	
F031R0.0B	536 10.60		23 10 64	1255	
F031R0.0C	536 9.88		23 10 64	1255	
F031R0.0D	542 9.90		21 9 65	922	
F032R0.0B	542 7.80		21 9 65	922	
F032R0.0C	532 11.70		21 9 65	922	
F032R0.0D	532 9.70		21 9 65	922	
F033R0.0B	532 9.80		21 9 65	922	
F033R0.0C	496 9.50		25 5 66	676	
F033R0.0D	496 11.80		25 5 66	676	
F034R0.0B	525 8.20		26 1 67	430	
F034R0.0C	520 8.90		22 3 67	375	
F034R0.0D	484 9.90		22 3 67	375	
F035R0.0B	502 9.41		1 2 68	59	
F035R0.0C	502 9.38		1 2 68	59	
M013R0.2	529 9.77	0.00577	4 3 64	1488	
F014R0.2	460 8.10	0.00836	23 10 64	1255	
M015R0.2	504 10.80	0.00873	4 2 65	1151	
F016R0.2	485 8.90	0.00665	7 4 65	1089	
M017R0.2	494 11.80	0.00711	27 4 66	704	

DOG
NUMBER

COMMENTS ON DEAD DOGS

M001R0.0	SEMINOMA, LYMPHOSARCOMA
M002R0.0	TRANSITIONAL CELL CARCINOMA
F003R0.0	STATUS EPILEPTICUS
M004R0.0	
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	
F011R0.0	
F012R0.0	UNDETERMINED
M013R0.0	
F014R0.0	
M015R0.0	
F016R0.0	
M017R0.0	
F018R0.0	
F019R0.0	
M020R0.0	
F021R0.0	
M022R0.0	
F031R0.0B	
F031R0.0C	
F031R0.0D	
F032R0.0B	
F032R0.0C	
F032R0.0D	
F033R0.0B	
F033R0.0C	
F033R0.0D	
F034R0.0B	
F034R0.0C	
F034R0.0D	
F035R0.0B	
F035R0.0C	

M013R0.2
F014R0.2
M015R0.2
F016R0.2
M017R0.2

DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (CM)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
F018R0.2	497	9.30		0.00652	25 5 66	676	
F019R0.2	526	10.60		0.00785	13 10 66	535	
M020R0.2	546	11.40		0.00676	29 12 66	458	
F021R0.2	549	11.50		0.00687	26 1 67	430	
M022R0.2	533	12.90		0.00961	22 3 67	375	
M013R0.5	529	11.00		0.0171	4 3 64	1488	
F014R0.5	510	9.75		0.022	23 10 64	1255	
M015R0.5	490	10.40		0.0263	4 2 65	1151	
F016R0.5	500	11.40		0.0205	7 4 65	1089	
M017R0.5	494	9.20		0.0215	27 4 66	704	
F018R0.5	496	9.10		0.0197	25 5 66	676	
F019R0.5	526	10.00		0.023	13 10 66	535	
M020R0.5	536	13.20		0.0206	29 12 66	458	
F021R0.5	538	8.80		0.0208	26 1 67	430	
M022R0.5	520	12.30		0.029	22 3 67	375	
M031R0.5B	508	11.40		0.021	27 4 66	704	
F031R0.5C	537	9.40		0.0235	22 12 65	830	
F031R0.5D	537	11.70		0.0238	22 12 65	830	
M032R0.5B	496	13.40		0.0196	25 5 66	676	
F032R0.5C	519	10.10		0.0239	22 12 65	830	
F032R0.5D	509	10.10		0.024	22 12 65	830	
M033R0.5B	497	12.90		0.0194	25 5 66	676	
F033R0.5C	527	10.60		0.0212	27 4 66	704	
F033R0.5D	527	8.70		0.0217	27 4 66	704	
M034R0.5B	496	10.50		0.0196	25 5 66	676	
F034R0.5C	524	9.90		0.0215	27 4 66	704	
F034R0.5D	508	9.70		0.0212	27 4 66	704	
M035R0.5B	536	10.40		0.0205	29 12 66	458	
F035R0.5C	532	9.00		0.0201	29 12 66	458	
F035R0.5D	532	10.20		0.0202	29 12 66	458	
M001R1.0	471	8.48		0.0618	20 4 53	5459	
M002R1.0	627	10.00		0.0876	16 11 53	4054	237
F003R1.0	706	8.68		0.0576	10 3 54	3850	151
M004R1.0	414	8.60		0.0642	7 4 54	2038	108
M005R1.0	490	11.70		0.0436	22 6 54	3780	112
F006R1.0	483	7.23		0.0584	27 7 54	4996	
M007R1.0	511	11.40		0.0651	24 8 54	3544	167
F008R1.0	861	8.98		0.0559	21 12 54	2988	93

DOG
NUMBER COMMENTS ON DEAD DOGS

F018R0.2
F019R0.2
M020R0.2
F021R0.2
M022R0.2

M013R0.5
F014R0.5
M015R0.5
F016R0.5
M017R0.5
F018R0.5
F019R0.5
M020R0.5
F021R0.5
M022R0.5

M031R0.5B
F031R0.5C
F031R0.5D
M032R0.5B
F032R0.5C
F032R0.5D
M033R0.5B
F033R0.5C
F033R0.5D
M034R0.5B
F034R0.5C
F034R0.5D
M035R0.5B
F035R0.5C
F035R0.5D

M001R1.0
M002R1.0 SEMINOMA
F003R1.0 MAMMARY GLAND CARCINOMA
M004R1.0 TRAUMA
M005R1.0 TRANSITIONAL CELL CARCINOMA, HYDRONEPHROSIS
F006R1.0
M007R1.0 STATUS EPILEPTICUS
F008R1.0 LYMPHOSARCOMA

DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (CM)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
F009R1.0	781	9.88		0.0521	11 4 55	4399	99
M010R1.0	523	11.50		0.0573	27 7 55	4003	157
F011R1.0	511	11.20		0.0522	20 12 55	4485	
F012R1.0	501	9.71		0.0444	17 1 56	3978	124
M013R1.0	529	11.70		0.0527	4 3 64	1488	
F014R1.0	510	10.50		0.0701	23 10 64	1255	
M015R1.0	490	8.88		0.0797	4 2 65	893	82
F016R1.0	501	8.99		0.0611	7 4 65	1089	
M017R1.0	494	11.40		0.0639	27 4 66	704	
F018R1.0	496	10.00		0.0589	25 5 66	676	
F019R1.0	526	11.60		0.0682	13 10 66	535	
M020R1.0	536	10.00		0.061	29 12 66	458	
F021R1.0	525	8.10		0.0633	26 1 67	430	
M022R1.0	484	10.90		0.0861	22 3 67	375	
F031R1.0B	509	10.40		0.0712	22 12 65	830	
M001R1.7	523	9.98		0.137	17 1 56	4438	341
M002R1.7	598	7.85		0.163	30 11 56	1273	116
M002R1.7A	493	12.00		0.222	6 3 63	1852	
F003R1.7	473	13.10		0.165	20 12 55	3267	385
M004R1.7	514	6.20		0.163	20 12 55	4485	
M005R1.7	511	10.10		0.151	20 12 55	4108	488
F006R1.7	491	7.90		0.152	20 12 55	3432	417
M007R1.7	598	7.17		0.163	30 11 56	3142	309
F008R1.7	491	9.50		0.154	20 12 55	2577	378
F009R1.7	598	7.55		0.168	30 11 56	3914	262
M010R1.7	590	9.57		0.167	30 11 56	557	109
M010R1.7A	545	10.60		0.183	7 1 59	3371	
F011R1.7	598	8.17		0.165	30 11 56	4139	
F012R1.7	590	8.95		0.167	30 11 56	2399	210
M001R2.0	471	8.74		0.382	20 4 53	3440	860
M002R2.0	592	8.21		0.387	16 11 53	3775	625
F003R2.0	541	8.53		0.347	10 3 54	4459	872
M004R2.0	414	10.50		0.361	7 4 54	325	189
M004R2.0A	420	10.60		0.306	11 4 55	4368	1142
M005R2.0	461	11.50		0.267	22 6 54	4703	994
F006R2.0	486	10.60		0.36	27 7 54	4615	1264
M007R2.0	514	11.10		0.413	24 8 54	3425	922
F008R2.0	572	6.95		0.331	21 12 54	4781	996

DOG NUMBER	COMMENTS ON DEAD DOGS
F009R1.0	PNEUMONIA
M010R1.0	FIBROSARCOMA (GINGIVA)
F011R1.0	
F012R1.0	MELANOMA (GINGIVA)
M013R1.0	
F014R1.0	
M015R1.0	UNDETERMINED (NO NEOPLASIA)
F016R1.0	
M017R1.0	
F018R1.0	
F019R1.0	
M020R1.0	
F021R1.0	
M022R1.0	
F031R1.0B	
M001R1.7	OBTURATING ABDOMINAL AORTA AND PULMONARY EMBOLISM
M002R1.7	LYMPHOSARCOMA
M002R1.7A	
F003R1.7	MAMMARY GLAND CARCINOMA
M004R1.7	
M005R1.7	OSTEOSARCOMA
F006R1.7	
M007R1.7	BACTERIAL TOXEMIA, INTERSTITIAL CELL ADENOMA
F008R1.7	DRUG ALLERGY
F009R1.7	PYOMETRA
M010R1.7	TRAUMA
M010R1.7A	
F011R1.7	
F012R1.7	UNDETERMINED (NO BONE TUMOR)
M001R2.0	HEMANGIOSARCOMA (SPLEEN)
M002R2.0	OSTEOSARCOMA
F003R2.0	RETICULUM CELL SARCOMA (NON-SKELETAL)
M004R2.0	PERFORATED ILEUM
M004R2.0A	VALVULAR ENDOCARDITIS
M005R2.0	OSTEOSARCOMA, ADRENAL CORTICAL CARCINOMA
F006R2.0	EPIDERMOID CARCINOMA (TYMPANIC BULLA)
M007R2.0	OSTEOSARCOMA, CUSHING SYNDROME
F008R2.0	

DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (CM)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68	DEATH	DOSE TO SKELETON (RADS)
F009R2.0	592	9.38		0.317	11 4 55		3998	1016
M010R2.0	523	9.95		0.345	27 7 55		3569	1220
F011R2.0	495	9.30		0.31	20 12 55		3297	728
F012R2.0	497	10.30		0.281	17 1 56		2948	742
M001R3.0	473	8.91		1.2	20 4 53		2850	2395
M002R3.0	470	9.02		1.21	16 11 53		2226	1727
F003R3.0	386	7.74		1.11	10 3 54		2497	2323
M004R3.0	412	11.70		1.16	7 4 54		1917	2361
M005R3.0	461	13.00		0.846	22 6 54		2955	2317
F006R3.0	486	9.75		1.14	27 7 54		1932	2246
M007R3.0	514	12.30		1.29	24 8 54		2099	3029
F008R3.0	542	7.76		1.03	21 12 54		2612	1916
F009R3.0	551	8.02		0.987	11 4 55		2487	1839
M010R3.0	525	10.10		1.06	27 7 55		1737	2336
F011R3.0	495	12.90		0.938	20 12 55		1610	1333
F012R3.0	497	11.40		0.883	17 1 56		1897	1639
M001R4.0	471	9.08		3.51	20 4 53		1606	6575
M002R4.0	470	9.53		3.55	16 11 53		1884	6150
F003R4.0	384	8.65		3.33	10 3 54		490	2208
F003R4.0A	598	7.20		3.1	30 11 56		1614	3855
M004R4.0	408	8.83		3.47	7 4 54		1518	6063
M005R4.0	461	13.20		2.42	22 6 54		1659	4505
F006R4.0	486	8.55		3.44	27 7 54		1939	7133
M007R4.0	453	9.55		3.88	24 8 54		1647	5844
F008R4.0	474	8.94		3.14	21 12 54		1324	4615
F009R4.0	542	8.53		3.02	11 4 55		1471	4095
M010R4.0	527	10.80		3.28	27 7 55		1553	7582
F011R4.0	491	10.40		2.84	20 12 55		1469	5273
F012R4.0	496	9.61		2.81	17 1 56		1435	3877
M001R5.0	473	9.87		10.5	20 4 53		908	14943
M002R5.0	470	8.85		10.8	16 11 53		1380	18071
F003R5.0	380	7.82		10.1	10 3 54		481	7147
M004R5.0	408	8.90		10.6	7 4 54		1091	16417
M005R5.0	458	10.90		10.1	22 6 54		1220	15433
F006R5.0	486	9.66		10.2	27 7 54		1015	15414

DOG
NUMBER COMMENTS ON DEAD DOGS

F009R2.0 MAMMARY CARCINOMA
M010R2.0 OSTEOSARCOMA
F011R2.0 OSTEOSARCOMA
F012R2.0 MAMMARY ADENOCARCINOMA

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

M001R4.0 OSTEOSARCOMA
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

M001R5.0 OSTEOSARCOMA
M002R5.0 OSTEOSARCOMA
F003R5.0 CANINE DISTEMPER
M004R5.0 OSTEOSARCOMA
M005R5.0 OSTEOSARCOMA
F006R5.0 OSTEOSARCOMA

DOG NUMBER	AT INJECTION			DATE			DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIG (KG)	HT (μ C/KG)	INJECTED	D	MO YR		
M007R5.0	453	8.85	11.9	24	8	54	1288	16708
F008R5.0	474	7.76	9.68	21	12	54	968	11564
F009R5.0	420	9.16	9.48	11	4	55	1288	15941
M010R5.0	527	10.70	10.2	27	7	55	825	11179

DOG NUMBER	COMMENTS ON DEAD DOGS
M007R5.0	OSTEOSARCOMA
F008R5.0	OSTEOSARCOMA
F009R5.0	OSTEOSARCOMA + ANEMIA
M010R5.0	OSTEOSARCOMA + FRACTURED MANDIBLE

B. PLUTONIUM-239

DOG NUMBER	AT INJECTION AGE WEIG HT (DAYS) (KG)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
M001P0.0	443	9.70	1 12 52		4003
F002P0.0	424	6.36	2 3 53		2755
M003P0.0	515	10.80	1 6 53		5362
M004P0.0	426	10.70	16 9 53		5138
F005P0.0	620	9.75	14 10 53		4088
F006P0.0	410	5.59	12 5 54		4499
F007P0.0	515	6.90	25 10 54	4906	
M008P0.0	585	10.90	15 3 55		4072
F009P0.0	658	11.00	22 11 55		3032
F010P0.0	658	11.00	22 11 55		3971
M011P0.0	602	10.30	24 4 56		3821
M012P0.0	630	10.90	29 5 56		4143
F013P0.0	517	9.47	4 3 64	1488	
F014P0.0	452	9.89	12 5 64	1419	
M015P0.0	527	12.10	23 10 64	1255	
M016P0.0	485	13.90	7 4 65	1089	
M017P0.0	551	12.20	18 11 66	509	
F018P0.0	536	11.40	29 11 66	488	
M019P0.0	536	13.10	29 11 66	488	
F020P0.0	546	8.50	29 12 66	458	
M021P0.0	549	13.30	26 1 67	430	
F022P0.0	489	10.60	25 5 67	311	
M031P0.0B	452	11.80	12 5 64	1419	
M031P0.0C	452	12.60	12 5 64	1419	
M032P0.0B	452	11.20	12 5 64	1419	
M032P0.0C	542	10.30	21 9 65	922	
M033P0.0B	517	12.10	21 9 65	922	
M033P0.0C	503	11.70	18 11 65	864	
M034P0.0B	525	13.50	26 1 67	430	
M034P0.0C	484	12.70	22 3 67	375	
M035P0.0B	484	12.50	22 3 67	375	
M035P0.0C	484	13.10	22 3 67	375	
M036P0.0B	489	11.00	25 5 67	311	
M036P0.0C	489	12.20	25 5 67	311	
M037P0.0B	507	11.70	22 6 67	283	
M037P0.0C	493	10.40	22 6 67	283	
M038P0.0B	529	10.70	16 11 67	136	
M038P0.0C	529	12.20	16 11 67	136	
M039P0.0B	503	10.70	21 12 67	101	
M039P0.0C	503	10.10	21 12 67	101	
F013P0.1	515	9.46	4 3 64	1488	

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 OBTURATING PULMONARY EMBOLISM
F007P0.0
M008P0.0 CIRCULATORY FAILURE
F009P0.0 PULMONARY EMBOLISM, NEPHRITIS
F010P0.0 LEUKEMIA
M011P0.0 FIBROSARCOMA (SPLEEN)
M012P0.0 TESTICULAR CARCINOMA
F013P0.0
F014P0.0
M015P0.0
M016P0.0
M017P0.0
F018P0.0
M019P0.0
F020P0.0
M021P0.0
F022P0.0
M031P0.0B
M031P0.0C
M032P0.0B
M032P0.0C
M033P0.0B
M033P0.0C
M034P0.0B
M034P0.0C
M035P0.0B
M035P0.0C
M036P0.0B
M036P0.0C
M037P0.0B
M037P0.0C
M038P0.0B
M038P0.0C
M039P0.0B
M039P0.0C

F013P0.1

DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (CM)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
F014P0.1	452	10.30		0.00055	12 5 64	1419	
M015P0.1	536	9.67		0.00071	23 10 64	1255	
M016P0.1	501	12.00		0.00059	7 4 65	1089	
M017P0.1	551	12.20		0.00057	18 11 66	509	
F018P0.1	536	9.28		0.0007	29 11 66	488	
M019P0.1	536	11.60		0.00063	29 11 66	488	
F020P0.1	536	9.80		0.00075	29 12 66	458	
M021P0.1	538	11.30		0.00059	26 1 67	430	
F022P0.1	489	9.80		0.00059	25 5 67	311	
M031P0.1B	517	12.20		0.00068	4 3 64	1488	
F032P0.1B	549	10.40		0.00059	18 11 65	864	
M033P0.1B	549	10.80		0.00079	18 11 65	864	
F034P0.1B	533	11.10		0.00058	18 11 66	509	
M035P0.1B	489	10.30		0.00059	25 5 67	311	
F036P0.1B	493	9.79		0.0006	22 6 67	283	
M037P0.1B	493	11.30		0.00059	22 6 67	283	
F038P0.1B	513	9.52		0.00057	21 12 67	101	
M039P0.1B	490	10.50		0.00058	21 12 67	101	
F013P0.2	517	9.44		0.00206	4 3 64	1488	
F014P0.2	516	7.44		0.00173	12 5 64	1419	
M015P0.2	505	10.90		0.00201	23 10 64	1255	
M016P0.2	500	11.40		0.00163	7 4 65	1089	
M017P0.2	533	11.80		0.00171	18 11 66	509	
F018P0.2	530	9.46		0.002	29 11 66	488	
M019P0.2	530	12.10		0.00198	29 11 66	488	
F020P0.2	532	8.30		0.00224	29 12 66	458	
M021P0.2	538	12.10		0.00181	26 1 67	430	
F022P0.2	485	8.30		0.00176	25 5 67	311	
M031P0.2B	515	10.70		0.00185	4 3 64	1488	
F031P0.2C	452	11.90		0.00169	12 5 64	1419	
F031P0.2D	429	9.35		0.00186	12 5 64	1419	
M032P0.2B	549	13.60		0.00178	18 11 65	864	
F032P0.2C	494	10.10		0.00183	4 2 65	1151	
F032P0.2D	490	8.04		0.00193	4 2 65	1151	
M033P0.2B	513	14.50		0.00178	18 11 65	864	
F033P0.2C	549	12.50		0.00176	18 11 65	864	
F033P0.2D	513	12.70		0.00178	18 11 65	864	
M034P0.2B	533	12.70		0.0017	18 11 66	509	
F034P0.2C	533	11.50		0.00172	18 11 66	509	
F034P0.2D	519	9.92		0.00167	18 11 66	509	
M035P0.2B	489	11.20		0.00173	25 5 67	311	

DOG
NUMBER

COMMENTS ON DEAD DOGS

F014P0.1
M015P0.1
M016P0.1
M017P0.1
F018P0.1
M019P0.1
F020P0.1
M021P0.1
F022P0.1
M031P0.1B
F032P0.1B
M033P0.1B
F034P0.1B
M035P0.1B
F036P0.1B
M037P0.1B
F038P0.1B
M039P0.1B

F013P0.2
F014P0.2
M015P0.2
M016P0.2
M017P0.2
F018P0.2
M019P0.2
F020P0.2
M021P0.2
F022P0.2
M031P0.2B
F031P0.2C
F031P0.2D
M032P0.2B
F032P0.2C
F032P0.2D
M033P0.2B
F033P0.2C
F033P0.2D
M034P0.2B
F034P0.2C
F034P0.2D
M035P0.2B

DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (CM)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68	DEATH	DOSE TO SKELETON (RADS)
F035P0.2C	507	10.50		0.00175	22 6 67	283		
F035P0.2D	507	9.10		0.00175	22 6 67	283		
M036P0.2B	479	12.90		0.00177	25 5 67	311		
F036P0.2C	493	10.40		0.00177	22 6 67	283		
F036P0.2D	569	8.74		0.00146	16 11 67	136		
M037P0.2B	529	10.60		0.00149	16 11 67	136		
F037P0.2C	529	10.10		0.0015	16 11 67	136		
F037P0.2D	529	7.14		0.00153	16 11 67	136		
M038P0.2B	517	10.00		0.00152	16 11 67	136		
F038P0.2C	503	7.95		0.00211	21 12 67	101		
F038P0.2D	499	9.08		0.00176	21 12 67	101		
F039P0.2C	499	9.46		0.00173	21 12 67	101		
F039P0.2D	499	9.34		0.00176	21 12 67	101		
F013P0.5	517	9.93		0.0054	4 3 64	1488		
F014P0.5	516	9.98		0.00493	12 5 64	1419		
M015P0.5	505	8.41		0.00627	23 10 64	1255		
M016P0.5	501	12.60		0.00521	7 4 65	1089		
M017P0.5	533	13.40		0.00506	18 11 66	509		
F018P0.5	530	8.98		0.00594	29 11 66	488		
M019P0.5	530	11.90		0.00645	29 11 66	488		
F020P0.5	532	9.30		0.00553	29 12 66	458		
M021P0.5	538	9.80		0.00526	26 1 67	430		
F022P0.5	485	8.10		0.00525	25 5 67	311		
M031P0.5B	515	10.50		0.00549	4 3 64	1488		
M032P0.5B	549	13.60		0.00546	18 11 65	864		
F032P0.5C	494	8.44		0.00571	4 2 65	1151		
F033P0.5B	503	10.10		0.00559	18 11 65	864		
M034P0.5B	530	12.50		0.00642	29 11 66	488		
F035P0.5B	501	9.54		0.0052	22 6 67	283		
M036P0.5B	479	11.50		0.00527	25 5 67	311		
F037P0.5B	517	8.39		0.00454	16 11 67	136		
M038P0.5B	517	10.50		0.00448	16 11 67	136		
F039P0.5B	490	10.90		0.00528	21 12 67	101		
M001P1.0	442	9.41		0.015	1 12 52	4572		98
F002P1.0	422	6.85		0.0163	2 3 53	4810		112
M003P1.0	515	8.00		0.0165	1 6 53	4292		102
M004P1.0	608	9.97		0.0139	16 9 53	4549		91
F005P1.0	620	8.80		0.0142	14 10 53	1539		30

DOG
NUMBER

COMMENTS ON DEAD DOGS

F035P0.2C
F035P0.2D
M036P0.2B
F036P0.2C
F036P0.2D
M037P0.2B
F037P0.2C
F037P0.2D
M038P0.2B
F038P0.2C
F038P0.2D
F039P0.2C
F039P0.2D

F013P0.5
F014P0.5
M015P0.5
M016P0.5
M017P0.5
F018P0.5
M019P0.5
F020P0.5
M021P0.5
F022P0.5
M031P0.5B
M032P0.5B
F032P0.5C
F033P0.5B
M034P0.5B
F035P0.5B
M036P0.5B
F037P0.5B
M038P0.5B
F039P0.5B

M001P1.0 OSTEOSARCOMA
F002P1.0 CIRCULATORY FAILURE
M003P1.0 OSTEOSARCOMA
M004P1.0 BILE DUCT CARCINOMA
F005P1.0 COLITIS, ENTERITIS + SECONDARY HEPATIC NECROSIS

DOG NUMBER	AT INJECTION AGE WEIG HT (DAYS) (KG)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
F005P1.0A	472 11.00	0.0168	3 9 58	3497	
F006P1.0	410 7.38	0.014	12 5 54	4292	86
F007P1.0	510 6.36	0.0167	25 10 54	3981	96
M008P1.0	453 10.60	0.0172	15 3 55	3367	83
F009P1.0	556 7.87	0.0168	9 9 55	2257	60
F010P1.0	641 12.00	0.0152	22 11 55	3649	80
M011P1.0	602 8.90	0.0157	24 4 56	4359	
M012P1.0	629 9.67	0.0167	29 5 56	2374	60
M013P1.0	504 12.70	0.0153	3 9 58	3497	
M001P1.7	657 8.72	0.0475	26 6 56	3025	210
F002P1.7	527 8.62	0.0431	22 11 55	3430	215
M003P1.7	642 8.63	0.0495	26 6 56	3430	246
M004P1.7	673 8.37	0.0484	10 10 56	3312	233
F005P1.7	642 11.60	0.0493	26 6 56	2659	190
F006P1.7	642 10.30	0.0459	26 6 56	2221	170
F007P1.7	756 9.73	0.0481	10 10 56	3353	234
M008P1.7	673 13.60	0.0479	10 10 56	3282	229
F009P1.7	756 9.72	0.0485	10 10 56	2500	180
F010P1.7	739 10.60	0.0495	10 10 56	467	40
F010P1.7A	472 8.07	0.0457	3 9 58	3497	
M011P1.7	599 11.60	0.0486	24 4 56	2777	200
M012P1.7	673 9.41	0.0491	10 10 56	2973	213
M013P1.7	504 10.60	0.0473	3 9 58	3497	
M001P2.0	442 7.61	0.0853	1 12 52	2985	370
F002P2.0	422 7.73	0.112	2 3 53	2780	460
M003P2.0	485 10.50	0.094	1 6 53	3185	420
M004P2.0	608 9.84	0.0862	16 9 53	2948	380
F005P2.0	594 8.12	0.0846	14 10 53	2423	310
F006P2.0	417 7.54	0.0902	12 5 54	2947	370
F007P2.0	485 8.40	0.0996	25 10 54	2093	310
M008P2.0	406 9.73	0.0957	15 3 55	1761	250
F009P2.0	552 9.72	0.101	9 9 55	2014	300
F010P2.0	551 7.94	0.0968	22 11 55	2912	410
M011P2.0	599 10.30	0.0961	24 4 56	1617	230
M012P2.0	622 9.98	0.1	29 5 56	2284	370

DOG
NUMBER

COMMENTS ON DEAD DOGS

F005P1.0A
F006P1.0 CARCINOMA OF COLON
F007P1.0 TRAUMA LYMPHADENOPHATHY
M008P1.0 OSTEOSARCOMA
F009P1.0 OSTEOSARCOMA
F010P1.0 MAMMARY CARCINOMA
M011P1.0
M012P1.0 CHRONIC PANCREATITIS
M013P1.0

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
M011P1.7 BILE DUCT CARCINOMA
M012P1.7 LEUKEMIA
M013P1.7

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

DOG NUMBER	AT INJECTION			DATE			DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIG (KG)	HT (μ C/KG)	INJECTED	INJECTED	INJECTED		
M001P3.0	417	8.00	0.261	1	12	52	1476	580
F002P3.0	422	6.85	0.312	2	3	53	1947	900
M003P3.0	485	8.74	0.291	1	6	53	1604	700
M004P3.0	608	8.51	0.292	16	9	53	1950	840
F005P3.0	650	8.22	0.288	14	10	53	1504	630
F006P3.0	415	8.38	0.282	12	5	54	1617	670
F007P3.0	485	9.00	0.314	25	10	54	1627	750
M008P3.0	406	9.73	0.3	15	3	55	1771	780
F009P3.0	552	7.67	0.3	9	9	55	1894	840
F010P3.0	533	8.94	0.298	22	11	55	1547	700
M011P3.0	599	10.50	0.309	24	4	56	1198	550
M012P3.0	622	10.20	0.308	29	5	56	1659	760
M001P4.0	442	7.61	0.823	1	12	52	1724	2100
F002P4.0	567	8.65	1.03	2	3	53	1556	2380
M003P4.0	485	9.36	0.929	1	6	53	1198	1680
M004P4.0	566	8.74	0.974	16	9	53	1066	1560
F005P4.0	650	7.05	0.872	14	10	53	1245	1650
F006P4.0	420	9.26	0.811	12	5	54	1357	1660
F007P4.0	485	8.45	0.963	25	10	54	1198	1730
M008P4.0	651	9.22	0.887	15	3	55	1157	1560
F009P4.0	552	8.58	0.96	9	9	55	1343	1920
F010P4.0	527	6.48	0.868	22	11	55	1241	1660
M011P4.0	596	9.56	0.927	24	4	56	1288	1790
M012P4.0	598	11.40	0.838	29	5	56	1463	1840
M001P5.0	417	8.86	2.67	1	12	52	1324	5370
F002P5.0	1150	8.75	3.3	2	3	53	1576	7830
M003P5.0	515	8.10	3.0	1	6	53	499	2340
M004P5.0	566	9.18	3.17	16	9	53	1562	7380
F005P5.0	691	8.77	2.77	14	10	53	2059	8690
F006P5.0	407	7.90	2.57	12	5	54	1194	4620
F007P5.0	482	8.33	2.99	25	10	54	1491	6630
M008P5.0	497	9.55	2.69	15	3	55	1192	4840
F009P5.0	552	9.45	2.73	9	9	55	1145	4750

DOG
NUMBER

COMMENTS ON DEAD DOGS

M001P3.0	OSTEOSARCOMA
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

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
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

C. RADIUM-228 (MESOTHORIUM)*

DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68	DEATH	DOSE TO SKELETON (RADS)
F001M0.0	732	7.33			4 1 54		3451	
F002M0.0	545	6.94			29 11 54	4871		
M003M0.0	579	13.00			13 3 56	4401		
M004M0.0	601	10.30			15 1 57	4093		
F005M0.0	671	11.20			5 3 57	4044		
M006M0.0	492	7.56			23 4 57	3995		
F007M0.0	395	8.71			4 6 57		1414	
F007M0.0A	594	10.90			15 1 63	1902		
F008M0.0	654	11.60			9 3 60	2944		
M009M0.0	575	12.40			13 4 60	2909		
M010M0.0	581	13.30			17 7 62	2084		
F011M0.0	475	9.31			18 9 62	2021		
M012M0.0	695	10.00			22 12 60	2656		
F001M0.5	492	9.47		0.0173	17 7 62	2084		
F002M0.5	492	9.15		0.0173	17 7 62	2084		
M003M0.5	493	10.80		0.0199	18 9 62	2021		
M004M0.5	475	12.80		0.0199	18 9 62	2021		
F005M0.5	534	7.83		0.0172	23 10 62	1986		
M006M0.5	510	10.30		0.0171	23 10 62	1986		
F007M0.5	492	8.87		0.0172	17 7 62	2084		
F008M0.5	654	12.60		0.0159	9 3 60	2944		
M009M0.5	485	11.90		0.017	13 4 60	2909		
M010M0.5	492	10.60		0.0174	17 7 62	2084		
F011M0.5	505	7.82		0.0202	18 9 62	2021		
M012M0.5	510	10.60		0.0165	23 10 62	1986		
F001M1.0	718	7.75		0.0463	4 1 54		2952	196
F001M1.0A	590	8.07		0.0512	23 10 62	1986		
F002M1.0	459	8.25		0.0324	29 11 54	4871		
M003M1.0	575	13.80		0.0589	13 3 56		3157	306
M004M1.0	601	9.90		0.0481	15 1 57	4093		
F005M1.0	658	8.80		0.049	5 3 57	4044		
M006M1.0	521	10.60		0.0468	23 4 57		3402	272
F007M1.0	534	9.89		0.0489	4 6 57		2159	149
F008M1.0	654	12.40		0.0491	9 3 60	2944		
M009M1.0	485	10.10		0.0504	13 4 60	2909		
M010M1.0	492	9.43		0.0501	17 7 62	2084		
F011M1.0	505	8.91		0.0613	18 9 62	2021		
M012M1.0	528	9.27		0.0498	23 10 62	1986		

DOG NUMBER	COMMENTS ON DEAD DOGS
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F001M0.0	PURULENT MENINGOENCEPHALITIS
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F002M0.0	
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M003M0.0	
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M004M0.0	
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F005M0.0	
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M006M0.0	
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F007M0.0	STATUS EPILEPTICUS
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F007M0.0A	
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F008M0.0	
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M009M0.0	
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M010M0.0	
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F011M0.0	
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M012M0.0	
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F001M0.5	
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F002M0.5	
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M003M0.5	
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M004M0.5	
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F005M0.5	
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M006M0.5	
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F007M0.5	
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F008M0.5	
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M009M0.5	
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M010M0.5	
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F011M0.5	
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M012M0.5	
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F001M1.0	SARCOMA (SPLEEN)
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F001M1.0A	
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F002M1.0	
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M003M1.0	OSTEOSARCOMA
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M004M1.0	
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F005M1.0	
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M006M1.0	EPIDERMOID CARCINOMA (PENIS)
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F007M1.0	SARCOMA (HEART)
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F008M1.0	
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M009M1.0	
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M010M1.0	
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F011M1.0	
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M012M1.0	
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DOG NUMBER	AT INJECTION		INJECTED (μ C/KG)	DATE INJECTED			DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIG (KG)		D	MO	YR		
F001M1.7	510	7.52	0.151	23	10	62	1986	
F002M1.7	560	9.90	0.183	13	3	56	2383	733
M003M1.7	576	11.00	0.18	13	3	56	2709	723
M004M1.7	601	8.94	0.143	15	1	57	2864	424
F005M1.7	658	12.80	0.141	5	3	57	3234	625
M006M1.7	521	10.00	0.144	23	4	57	3424	393
F007M1.7	534	10.20	0.146	4	6	57	2646	600
F008M1.7	654	10.80	0.148	9	3	60	2486	386
M009M1.7	485	12.60	0.149	13	4	60	563	762
M010M1.7	492	10.10	0.124	17	7	62	2084	
F011M1.7	505	10.70	0.179	18	9	62	2021	
M012M1.7	524	9.28	0.153	23	10	62	1986	
F001M2.0	676	7.60	0.276	4	1	54	1780	870
F002M2.0	517	8.25	0.194	29	11	54	965	198
M003M2.0	576	11.00	0.358	13	3	56	619	355
M004M2.0	601	9.88	0.282	15	1	57	2282	1033
F005M2.0	509	8.30	0.295	5	3	57	2688	928
M006M2.0	502	12.40	0.306	23	4	57	2674	1382
F007M2.0	534	10.10	0.298	4	6	57	2239	1064
F008M2.0	654	12.40	0.3	9	3	60	2386	928
M009M2.0	630	9.99	0.302	13	4	60	1254	561
M010M2.0	430	11.20	0.311	17	7	62	2084	
F011M2.0	505	7.03	0.381	18	9	62	2021	
M012M2.0	524	9.47	0.306	23	10	62	1986	
F001M3.0	519	10.40	0.858	4	1	54	918	1833
F002M3.0	460	6.70	0.612	29	11	54	1856	2075
M003M3.0	579	10.40	0.965	13	3	56	1185	2464
M004M3.0	601	10.20	0.916	15	1	57	1176	1592
F005M3.0	531	8.51	0.94	5	3	57	1869	2148
M006M3.0	502	9.09	0.953	23	4	57	1421	1906
F007M3.0	534	9.94	0.907	4	6	57	1463	3145
F008M3.0	633	11.80	0.95	9	3	60	1447	2158
M009M3.0	630	9.83	0.918	13	4	60	1570	2277
M010M3.0	581	10.40	1.0	17	7	62	1575	2318
F011M3.0	499	11.00	1.19	18	9	62	1395	2467
M012M3.0	510	12.90	0.987	23	10	62	1638	2365

DOG
NUMBER

COMMENTS ON DEAD DOGS.

F001M1.7	
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	
F011M1.7	
M012M1.7	

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	
F011M2.0	
M012M2.0	

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
M010M3.0	OSTEOSARCOMA
F011M3.0	OSTEOSARCOMA
M012M3.0	OSTEOSARCOMA

DOG NUMBER	AT INJECTION			DATE			DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIG (KG)	HT (μC/KG)	INJECTED	D	MO	YR	
F001M4.0	510	7.56	2.6		4	1	54	841
F002M4.0	460	6.95	1.86		29	11	54	778
M003M4.0	579	9.65	3.37		13	3	56	418
M003M4.0A	494	7.34	2.64		4	6	57	1063
M004M4.0	609	7.84	2.47		15	1	57	896
F005M4.0	509	9.63	2.67		5	3	57	1064
M006M4.0	502	9.49	2.66		23	4	57	1121
F007M4.0	544	8.40	2.67		4	6	57	1253
F001M5.0	494	7.77	8.11		4	1	54	232
F002M5.0	460	7.35	5.46		29	11	54	780
M003M5.0	579	8.87	10.4		13	3	56	688
M004M5.0	482	7.29	7.89		15	1	57	561
F005M5.0	658	11.10	8.48		5	3	57	770
M006M5.0	580	7.53	8.67		23	4	57	792
F007M5.0	494	7.35	8.92		4	6	57	966

* ($\mu\text{C Th}^{228} / \mu\text{C Ra}^{228}$) 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.

DOG
NUMBER

COMMENTS ON DEAD DOGS

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 (RADIOTHORIUM)

DOG NUMBER	AT INJECTION AGE WEIG HT (DAYS) (KG)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
M001T0.0	493 8.24		8 2 54	4895	
M002T0.0	488 7.28		28 9 54	4933	
F003T0.0	797 11.60		6 6 55	2592	
M004T0.0	591 8.10		18 10 55	3072	
M005T0.0	458 10.40		14 10 58	3456	
F006T0.0	489 9.64		10 1 61	171	
F006T0.0A	688 8.61		15 12 60	2663	
M007T0.0	517 10.50		7 2 61	1412	
M008T0.0	533 10.80		24 5 61	2503	
F009T0.0	569 8.28		29 6 61	2467	
F010T0.0	536 10.40		28 7 61	2438	
F011T0.0	530 9.45		4 6 63	1762	
F012T0.0	492 9.09		9 7 63	1727	
M001T0.2	682 11.40	0.00164	27 3 62	2196	
M002T0.2	682 10.40	0.00166	27 3 62	2196	
F003T0.2	478 9.86	0.00163	27 3 62	2196	
M004T0.2	478 10.00	0.00166	27 3 62	2196	
M005T0.2	625 13.80	0.00162	9 2 60	889	10
M005T0.2A	530 13.40	0.00173	4 6 63	1762	
F006T0.2	489 8.85	0.00176	10 1 61	2637	
M007T0.2	532 10.50	0.00159	7 2 61	2609	
M008T0.2	494 13.90	0.00189	24 5 61	2503	
F009T0.2	569 7.82	0.00171	29 6 61	2467	
F010T0.2	508 10.50	0.0017	28 7 61	2438	
F011T0.2	530 9.76	0.00171	4 6 63	1762	
F012T0.2	492 7.37	0.0019	9 7 63	1727	
M001T0.5	699 14.30	0.00496	7 9 56	3471	45
M002T0.5	455 10.50	0.0049	28 9 54	1976	41
F003T0.5	659 8.59	0.00485	6 6 55	3032	44
M004T0.5	516 8.58	0.0054	18 10 55	2159	46
M005T0.5	513 8.46	0.00522	14 10 58	3456	
F006T0.5	489 9.66	0.0051	10 1 61	2637	
M007T0.5	532 9.11	0.00491	7 2 61	2609	
M008T0.5	533 9.53	0.00562	24 5 61	2503	
F009T0.5	569 8.62	0.00529	29 6 61	2467	
F010T0.5	508 10.20	0.0051	28 7 61	2438	
F011T0.5	530 7.78	0.00518	4 6 63	1762	
F012T0.5	492 9.94	0.00567	9 7 63	1682	45

DOG NUMBER	COMMENTS ON DEAD DOGS
M001T0.0	RETICULUM CELL SARCOMA (SOFT TISSUE)
M002T0.0	
F003T0.0	BRAIN HEMORRHAGE
M004T0.0	LYMPHOSARCOMA
M005T0.0	
F006T0.0	TRAUMA
F006T0.0A	
M007T0.0	BRAIN HEMORRHAGE
M008T0.0	
F009T0.0	
F010T0.0	
F011T0.0	
F012T0.0	
M001T0.2	
M002T0.2	
F003T0.2	
M004T0.2	
M005T0.2	STRANGULATION ON VOMITUS + GRAND MAL
M005T0.2A	
F006T0.2	
M007T0.2	
M008T0.2	
F009T0.2	
F010T0.2	
F011T0.2	
F012T0.2	
M001T0.5	CEREBRAL INFARCTION HEMORRHAGE
M002T0.5	STRANGULATION ON VOMITUS + GRAND MAL
F003T0.5	PYOMETRITIS + SECONDARY PERITONITIS
M004T0.5	STATUS EPILEPTICUS + PNEUMONIA
M005T0.5	
F006T0.5	
M007T0.5	
M008T0.5	
F009T0.5	
F010T0.5	
F011T0.5	
F012T0.5	LIVER DEGENERATION, ANESTHETIC REACTION

DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (CM)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
M001T1.0	493	9.36		0.0146	8 2 54	3172	132
M002T1.0	699	9.27		0.0146	7 9 56	4223	
F003T1.0	723	8.84		0.0145	7 9 56	4142	133
M004T1.0	699	8.27		0.0146	7 9 56	3217	132
M005T1.0	513	11.90		0.0146	14 10 58	2886	130
F006T1.0	489	8.81		0.015	10 1 61	2637	
M007T1.0	532	9.18		0.0147	7 2 61	2609	
M008T1.0	533	8.69		0.0166	24 5 61	2503	
F009T1.0	527	10.00		0.016	29 6 61	2467	
F010T1.0	508	10.20		0.015	28 7 61	2438	
F011T1.0	521	7.55		0.0154	4 6 63	1762	
F012T1.0	472	9.96		0.0167	9 7 63	1263	118
M001T1.5	699	7.95		0.0289	7 9 56	2894	258
M002T1.5	458	10.00		0.0293	28 9 54	2576	257
F003T1.5	609	10.30		0.0303	6 6 55	1921	249
M004T1.5	591	8.59		0.0299	18 10 55	2309	257
M005T1.5	598	9.65		0.0286	9 2 60	1624	223
F006T1.5	489	8.14		0.0292	10 1 61	2373	252
M007T1.5	517	8.83		0.0292	7 2 61	384	95
M007T1.5A	521	9.08		0.0311	4 6 63	1762	
M008T1.5	494	11.60		0.0324	24 5 61	2503	
F009T1.5	527	8.80		0.0306	29 6 61	2467	
F010T1.5	508	11.60		0.0296	28 7 61	1859	241
F011T1.5	518	11.40		0.0305	4 6 63	1762	
F012T1.5	465	7.56		0.0329	9 7 63	1727	
M001T2.0	491	10.20		0.0976	8 2 54	1282	693
M002T2.0	483	9.16		0.0875	28 9 54	1234	611
F003T2.0	474	7.87		0.0908	6 6 55	1541	695
M004T2.0	553	13.00		0.09	18 10 55	78	70
M004T2.0A	650	10.60		0.0899	7 9 56	1222	625
M005T2.0	598	9.12		0.0848	9 2 60	1085	556
F006T2.0	451	8.65		0.0879	10 1 61	1108	583
M007T2.0	517	8.85		0.0881	7 2 61	1015	558
M008T2.0	533	10.70		0.0981	24 5 61	1078	641
F009T2.0	527	8.09		0.0979	29 6 61	1209	677
F010T2.0	508	10.70		0.0919	28 7 61	1022	584
F011T2.0	518	10.80		0.0904	4 6 63	1038	579
F012T2.0	464	8.92		0.1	9 7 63	1499	748

DOG
NUMBER

COMMENTS ON DEAD DOGS

M001T1.0	OSTEOSARCOMA
M002T1.0	
F003T1.0	UNDIFFERENTIATED MALIGNANCY (SOFT TISSUE)
M004T1.0	OSTEOSARCOMA THYROID CARCINOMA PERIANAL ADENOCARCINOMA
M005T1.0	STATUS EPILEPTICUS
F006T1.0	
M007T1.0	
M008T1.0	
F009T1.0	
F010T1.0	
F011T1.0	
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	
M008T1.5	
F009T1.5	
F010T1.5	OSTEOSARCOMA
F011T1.5	
F012T1.5	

M001T2.0	OSTEOSARCOMA
M002T2.0	OSTEOSARCOMA
F003T2.0	OSTEOSARCOMA
M004T2.0	TRAUMA
M004T2.0A	OSTEOSARCOMA
M005T2.0	OSTEOSARCOMA
F006T2.0	OSTEOSARCOMA
M007T2.0	OSTEOSARCOMA
M008T2.0	OSTEOSARCOMA
F009T2.0	OSTEOSARCOMA
F010T2.0	OSTEOSARCOMA
F011T2.0	OSTEOSARCOMA
F012T2.0	OSTEOSARCOMA

DOG NUMBER	AT INJECTION AGE WEIG HT (DAYS) (KG)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
M001T3.0	314 9.15	0.301	8 2 54	988	1879
M002T3.0	458 11.90	0.301	28 9 54	859	1736
F003T3.0	471 12.00	0.272	6 6 55	547	1164
M004T3.0	606 9.69	0.285	18 10 55	801	1575
M005T3.0	571 10.70	0.269	9 2 60	890	1584
F006T3.0	451 8.83	0.282	10 1 61	1156	1909
M007T3.0	427 9.90	0.266	7 2 61	861	1536
M008T3.0	494 10.10	0.313	24 5 61	685	1566
F009T3.0	511 11.50	0.298	29 6 61	1062	1933
F010T3.0	508 9.26	0.28	28 7 61	971	1732
F011T3.0	518 10.30	0.29	4 6 63	791	1591
F012T3.0	459 11.50	0.32	9 7 63	804	1773
M001T4.0	480 8.32	0.882	8 2 54	645	4237
M002T4.0	458 8.32	0.916	28 9 54	833	5185
F003T4.0	461 7.25	0.8	6 6 55	763	4290
M004T4.0	606 8.81	0.835	18 10 55	793	4587
M001T5.0	480 9.48	2.76	8 2 54	212	5457
M002T5.0	483 8.22	2.63	28 9 54	97	2535

DOG NUMBER	COMMENTS ON DEAD DOGS
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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	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (CM)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68	DEATH	DOSE TO SKELETON (RADS)
F001S0.0	502	8.48			18 1 55	4821		
M002S0.0	600	11.10			14 2 56		3838	
M003S0.0	493	9.03			11 9 57		3516	
F004S0.0	520	8.19			15 10 57	3820		
M005S0.0	542	10.60			19 11 57	3785		
M006S0.0	466	9.68			27 5 58	3596		
F007S0.0A	462	9.46			7 1 59		3303	
F008S0.0	483	9.29			19 5 59	3239		
F009S0.0	549	12.40			11 8 59		708	
F009S0.0A	535	11.20			4 6 63	1762		
M010S0.0	522	13.90			29 9 59	3106		
F011S0.0	541	9.60			3 11 59	3071		
M012S0.0	605	8.99			6 1 60	3007		
F001S1.0	1524	6.84		0.573	18 1 55		308	21
F001S1.0A	521	9.38		0.588	14 2 56	4429		
M002S1.0	567	8.81		0.606	14 2 56	4429		
M003S1.0	493	10.90		0.572	11 9 57	3854		
F004S1.0	525	8.96		0.56	15 10 57	3820		
M005S1.0	555	10.20		0.532	19 11 57		2705	69
M006S1.0	466	9.56		0.581	27 5 58	3596		
F007S1.0	524	9.94		0.517	11 11 58	3428		
F008S1.0	483	10.80		0.697	19 5 59		2784	77
F009S1.0	549	11.60		0.534	11 8 59	3155		
M010S1.0	522	11.50		0.558	29 9 59	3106		
F011S1.0	543	10.30		0.55	3 11 59	3071		
M012S1.0	607	13.70		0.559	6 1 60	3007		
F001S1.7	526	7.41		1.78	14 2 56	4429		
M002S1.7	567	11.60		1.84	14 2 56		4297	421
M003S1.7	493	9.19		1.69	11 9 57	3854		
F004S1.7	522	9.60		1.68	15 10 57	3820		
M005S1.7	560	9.85		1.6	19 11 57		1715	161
M005S1.7A	493	11.40		1.78	6 3 63	1852		
M006S1.7	466	10.60		1.72	27 5 58	3596		
F007S1.7	488	10.20		1.6	11 11 58	3428		
F008S1.7	472	8.47		2.03	19 5 59		1973	215
F009S1.7	549	10.00		1.62	11 8 59	3155		
M010S1.7	519	13.60		1.66	29 9 59		2947	311
F011S1.7	543	11.00		1.68	3 11 59	3071		

DOG
NUMBER

COMMENTS ON DEAD DOGS

F001S0.0

M002S0.0

M003S0.0

F004S0.0

M005S0.0

M006S0.0

F007S0.0A

F008S0.0

F009S0.0

F009S0.0A

M010S0.0

F011S0.0

M012S0.0

BRONCHOGENIC CARCINOMA

OBTURATING AORTIC EMBOLISM, NEPHRITIS

DIABETES MELLITUS

TRAUMA

F001S1.0

F001S1.0A

M002S1.0

M003S1.0

F004S1.0

M005S1.0

M006S1.0

F007S1.0

F008S1.0

F009S1.0

M010S1.0

F011S1.0

M012S1.0

SACRIFICED -IMPROPER INJECTION AGE-

STATUS EPILEPTICUS

PANCREATIC ISLET CELL CARCINOMA

F001S1.7

M002S1.7

M003S1.7

F004S1.7

M005S1.7

M005S1.7A

M006S1.7

F007S1.7

F008S1.7

F009S1.7

M010S1.7

F011S1.7

HEMANGIOSARCOMA (SOFT TISSUE ORIGIN)

COMA OF UNKNOWN ETIOLOGY (NO BONE TUMOR)

STATUS EPILEPTICUS, CHRONIC PANCREATITIS

OBTURATING PULMONARY EMBOLISM, NEPHRITIS

DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (KG)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
M012S1.7	607	11.90		1.68	6 1 60	3007	
F001S2.0	502	5.59		3.7	18 1 55	3269	480
M002S2.0	567	8.97		3.42	14 2 56	3768	639
M003S2.0	494	7.82		3.39	11 9 57	3854	
F004S2.0	522	9.68		3.41	15 10 57	3820	
M005S2.0	560	8.72		3.24	19 11 57	3253	516
M006S2.0	466	9.19		3.5	27 5 58	3596	
F007S2.0	488	11.20		3.19	11 11 58	3421	459
F008S2.0	465	9.49		4.14	19 5 59	3239	
F009S2.0	473	14.10		3.28	11 8 59	2467	564
M010S2.0	508	10.70		3.34	29 9 59	3106	
F011S2.0	543	10.40		3.41	3 11 59	3071	
M012S2.0	607	11.60		3.49	6 1 60	3007	
F001S3.0	468	7.36		11.6	18 1 55	4821	
M002S3.0	565	9.62		11.6	14 2 56	4263	2695
M003S3.0	494	11.40		10.8	11 9 57	3854	
F004S3.0	527	9.17		10.6	15 10 57	3101	1469
M005S3.0	557	8.90		10.1	19 11 57	3785	
M006S3.0	466	9.44		10.9	27 5 58	3596	
F007S3.0	486	9.80		10.1	11 11 58	3428	
F008S3.0	465	12.50		12.9	19 5 59	3239	
F009S3.0	468	10.00		10.1	11 8 59	3155	
M010S3.0	519	12.50		10.3	29 9 59	2898	2107
F011S3.0	541	9.00		10.8	3 11 59	3071	
M012S3.0	605	8.43		10.2	6 1 60	3007	
F001S4.0	468	8.74		33.3	18 1 55	3682	6832
M002S4.0	567	11.20		32.6	14 2 56	2093	5806
M003S4.0	593	9.83		32.1	11 9 57	2781	4052
F004S4.0	526	8.24		32.1	15 10 57	3820	
M005S4.0	562	9.65		30.6	19 11 57	3785	
M006S4.0	504	16.00		32.7	3 9 58	3497	
F007S4.0	478	10.90		30.9	11 11 58	3428	
F008S4.0	465	10.90		40.6	19 5 59	2206	7801
F009S4.0	468	9.56		30.6	11 8 59	3155	
M010S4.0	517	8.20		31.3	29 9 59	3106	

DOG
NUMBER

COMMENTS ON DEAD DOGS

M012S1.7

F001S2.0 BACTERIAL PNEUMONIA
M002S2.0 UNDETERMINED SOFT TISSUE SARCOMA +BRONCHIOGENIC CARCINOMA
M003S2.0
F004S2.0
M005S2.0 ULCERATIVE STOMATITIS
M006S2.0
F007S2.0 PANCREATIC ISLET CELL ADENOMA
F008S2.0
F009S2.0 UNDETERMINED (NO BONE TUMOR)
M010S2.0
F011S2.0
M012S2.0

F001S3.0
M002S3.0 NEPHRITIS
M003S3.0
F004S3.0 MAMMARY CARCINOMA
M005S3.0
M006S3.0
F007S3.0
F008S3.0
F009S3.0
M010S3.0 FIBROSARCOMA (GINGIVA)
F011S3.0
M012S3.0

F001S4.0 NOT DETERMINED (NO OSTEOSARCOMA)
M002S4.0 SQUAMOUS CELL CARCINOMA -GINGIVA-
M003S4.0 OBTURATING PULMONARY EMBOLISM
F004S4.0
M005S4.0
M006S4.0
F007S4.0
F008S4.0 UNDETERMINED (NO BONE TUMOR)
F009S4.0
M010S4.0

DOG NUMBER	AT INJECTION			DATE			DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIG (KG)	HT (μC/KG)	INJECTED	INJECTED	INJECTED		
F011S4.0	542	8.86	32.7	3	11	59	2114	3324
M012S4.0	605	10.90	32.3	6	1	60	3007	
F001S4.5	530	9.00	64.2	16	3	66	746	
M002S4.5	530	12.20	63.6	16	3	66	746	
M003S4.5	530	11.90	63.8	16	3	66	746	
F004S4.5	530	9.80	64.5	16	3	66	746	
M005S4.5	496	13.30	61.3	16	3	66	746	
M006S4.5	496	12.00	63.8	16	3	66	746	
F007S4.5	511	9.90	64.5	16	3	66	746	
F008S4.5	511	9.90	64.5	16	3	66	746	
F009S4.5	511	10.30	64.0	16	3	66	746	
M010S4.5	496	14.00	60.9	16	3	66	746	
F011S4.5	496	11.90	63.8	16	3	66	746	
M012S4.5	485	11.40	63.7	16	3	66	746	
F001S5.0	434	9.38	103.0	18	1	55	960	8127
M002S5.0	551	12.20	102.0	14	2	56	255	3202
M002S5.0A	545	11.40	96.6	7	1	59	1740	12007
M003S5.0	507	10.30	102.0	15	10	57	2256	16297
F004S5.0	528	11.40	105.0	15	10	57	1448	9281
M005S5.0	621	8.53	95.2	19	11	57	1285	9930
M006S5.0	504	9.33	98.8	3	9	58	35	647
M006S5.0A	462	11.20	94.2	7	1	59	1021	11616
F007S5.0	478	10.20	92.7	11	11	58	1129	10822
F008S5.0	535	11.20	90.5	7	1	59	1469	10941
F009S5.0	459	8.82	93.5	11	8	59	1982	13569
M010S5.0	517	8.55	95.9	29	9	59	990	7744
F011S5.0	542	8.97	102.0	3	11	59	1667	9956
M012S5.0	606	12.50	99.2	6	1	60	1165	8327

DOG
NUMBER

COMMENTS ON DEAD DOGS

F011S4.0 BLOOD DYSCRASIA, PYOMETRA
M012S4.0

F001S4.5
M002S4.5
M003S4.5
F004S4.5
M005S4.5
M006S4.5
F007S4.5
F008S4.5
F009S4.5
M010S4.5
F011S4.5
M012S4.5

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)

TABLE II. TEST ANIMALS (MAR. 31 1968)

A. RADIUM-226*

DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (CM)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
T001R5.0	995	11.10		10.3	1 12 52	1074	9469
T002R5.0	919	8.40		4.39	12 1 53	1368	4724
T003R5.0	1467	8.29		4.76	12 1 53	428	1316
T004R5.0	459	10.00		10.6	6 7 53	1	24
T005R5.0	126	6.14		11.7	6 10 53	1	25
T006R5.0	126	6.14		11.4	6 10 53	1	24
T007R5.0	126	6.14		11.8	6 10 53	1	25
T008R5.0	290	5.52		1.92	10 5 55	58	488
T009R5.0	2276	10.40		1.94	10 5 55	58	585
T010R5.0	43	1.02		1.98	10 5 55	49	293
T011R5.0	43	1.58		1.91	10 5 55	49	363
T012R5.0	397	12.30		9.72	9 5 56	225	2707
T013R5.0	397	7.59		9.76	9 5 56	188	2319
T014R4.0	674	8.12		3.17	11 7 56	72	380
T015R4.0	672	9.03		3.11	11 7 56	2127	5117
T016R5.0	604	12.40		9.68	11 7 57	12	183
T017R5.0H	383	12.20		9.87	28 10 58	1147	13655
T018R5.0H	383	11.10		10.8	28 10 58	1226	12628
T019R5.0H	383	11.30		10.7	28 10 58	1219	11580
T020R5.0H	383	11.40		10.6	28 10 58	1330	12937
T021R5.0H	381	11.80		10.1	28 10 58	386	3710
T022R5.0H	381	11.90		10.1	28 10 58	587	5911
T023R4.0H	384	9.50		4.05	25 11 58	1471	4340
T024R4.0H	384	11.90		3.24	25 11 58	1505	5593
T025R4.0H	379	11.30		3.42	25 11 58	1309	4672
T026R4.0H	379	11.00		3.48	25 11 58	1780	4719
T027R4.0H	372	11.50		3.34	25 11 58	1414	3382
T028R3.0H	372	11.70		1.11	25 11 58	387	357
T029R5.0	474	13.50		10.4	3 3 59	216	3404

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

DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (CM)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68	DEATH	DOSE TO SKELETON (RADS)
T030R5.0	474	11.50		10.4	3 3 59		178	2851
T031R5.0	471	10.50		10.4	3 3 59		303	4758
T032R3.0	471	11.40		1.13	3 3 59		2294	1864
T033R3.0	471	10.60		1.15	3 3 59		1822	1921
T034R3.0	470	15.70		1.12	3 3 59		1737	1603
T035R3.0J	670	9.44		0.951	5 5 59		8	14
T036R4.0	695	10.20		2.99	22 12 60		1154	3647
T037R4.0	695	9.53		3.0	22 12 60		1627	3234
T038R4.0	695	10.10		3.02	22 12 60		1503	3657
T040R1.0	899	13.00		0.0483	3 4 62		7	1
T041R1.0	899	12.70		0.0487	3 4 62		63	3
T042R1.7	967	14.00		0.146	4 4 62		7	2
T043R1.7	963	13.20		0.145	4 4 62		64	11
T044R3.0	938	11.10		0.937	4 4 62		68	71
T045R3.0	939	13.60		0.941	5 4 62		7	12
T046R3.0	810	12.50		0.928	5 4 62		69	103
T047R6.0	99	5.27		29.4	11 6 62		4	352
T048R6.0	2842	11.20		25.1	27 12 62		49	1597
T049R5.0	485	10.60		7.54	2 5 63		5	111
T050R5.0	485	13.70		7.46	2 5 63		15	274
T051R5.0	418	13.30		8.48	8 5 63		92	1689
T052R5.0	418	10.70		8.57	8 5 63		15	258
T053R5.0	418	12.00		8.5	8 5 63		33	611

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
T053R5.0 SPECIAL STUDY

DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
T054R5.0	417	11.40		8.76	22 5 63	5	88
T055R5.0	417	11.60		8.61	22 5 63	33	534
T056R5.0	417	11.60		8.61	22 5 63	90	1461
T057R4.0	501	12.10		2.72	15 8 63	14	54
T058R4.0	496	11.70		2.41	15 8 63	61	286
T059R4.0	496	9.64		2.57	15 8 63	63	272
T060R4.0	490	12.10		2.33	15 8 63	117	415
T061R4.0	490	9.48		2.7	15 8 63	371	1567
T062R4.0	490	8.63		2.68	15 8 63	460	1586
T063R3.0	559	8.72		0.899	29 1 64	36	51
T064R3.0	551	8.42		0.919	29 1 64	63	73
T065R3.0	551	11.60		0.922	29 1 64	70	99
T066R3.0	549	10.10		0.904	29 1 64	132	140
T067R3.0	549	12.70		0.898	29 1 64	134	168
T068R3.0	549	12.10		0.917	29 1 64	1523	
T069R3.0	499	8.84		0.919	29 1 64	622	651
T070R3.0	499	14.20		0.922	29 1 64	1523	

*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 Ra^{226} injection was 20.0 μ C for the dogs T17R5H - T22R5H; 6.41 μ C for T23R4H - T27R4H; and 2.16 μ C for T28R3H. Tabulated for each dog are his age at 1st injection, his average weight during the injection period, total μ C/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 μ C Sr^{85} .

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

DOG
NUMBER

COMMENTS ON DEAD DOGS

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	
T069R3.0	SPECIAL STUDY
T070R3.0	

B. PLUTONIUM-239*

DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (KG)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68	DEATH	DOSE TO SKELETON (RADS)
T000P5.0	647	11.40		3.05	24 6 52		1	10
T001P5.0	581	12.70		3.04	13 10 52		29	160
T002P5.0	914	11.90		6.85	15 9 52		44	520
T003P5.0	942	9.65		3.22	13 10 52		610	3040
T004P5.0	1016	8.78		3.02	13 10 52		365	1750
T005P5.0	474	10.40		2.69	14 12 54		400	1720
T006P5.0	527	6.16		2.73	14 12 54		406	1750
T007P5.0	475	7.40		2.68	14 12 54		777	3230
T008P5.0	527	8.32		2.67	14 12 54		863	3540
T009P5.0	551	10.30		2.8	22 11 55		15	80
T010P5.0	534	11.90		2.74	23 11 55		15	70
T011P5.0	516	12.10		2.76	22 11 55		28	140
T012P5.0	487	9.23		2.74	23 11 55		28	140
T013P5.0	587	8.27		3.16	24 4 56		3	20
T014P5.0	587	9.38		2.43	24 4 56		7	30
T015P5.0	737	8.32		2.79	15 10 56		1	10
T016P5.0	673	10.70		2.85	10 10 56		92	440
T017P5.0	739	11.10		3.01	12 2 57		210	990
T018P5.0	739	8.16		2.83	12 2 57		217	960
T019P5.0	688	8.86		2.91	15 12 60		1400	6129
T020P5.0	688	13.00		2.68	15 12 60		474	1970
T021P5.0	688	10.30		2.72	15 12 60		939	3940
T023P1.0	1485	13.10		0.0172	28 7 61		96	3
T024P1.0	559	13.10		0.0172	28 7 61		97	3
T025P1.0	559	13.80		0.0167	28 7 61		467	10
T026P1.0	556	12.00		0.016	28 7 61		647	20
T027P3.0	556	11.50		0.332	28 7 61		755	390
T028P1.0	552	10.50		0.015	9 8 61		559	10
T029P3.0	552	12.10		0.296	9 8 61		560	260

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
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T028P1.0	SPECIAL STUDY
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T029P3.0	SPECIAL STUDY
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DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (CM)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
T030P1.0	548	12.40		0.0148	9 8 61	35	1
T031P3.0	519	13.00		0.305	9 8 61	40	20
T032P1.0	520	8.47		0.0162	9 8 61	274	10
T033P1.0	550	10.70		0.0153	15 9 61	375	10
T034P1.0	550	9.68		0.0154	15 9 61	746	20
T035P3.0	550	11.90		0.303	15 9 61	362	180
T036P1.0	544	10.40		0.0158	15 9 61	5	
T037P1.0	542	8.59		0.0148	15 9 61	186	4
T038P3.0	489	7.96		0.304	15 9 61	187	90
T039P1.0	1534	10.70		0.0151	15 9 61	376	10
T040P1.0	1534	9.92		0.0177	15 9 61	769	20
T041P5.0	543	8.50		3.01	30 11 64	1217	
T042P5.0	510	11.40		2.4	10 2 65	13	57
T043P5.0H	600	14.00		2.86	15 7 65	40	200
T044P5.0H	517	12.00		2.72	21 9 65	35	168
T045P5.0H	420	12.30		2.98	28 10 65	5 hr	1
T046P5.0	420	11.90		3.01	28 10 65	732	3402
T047P5.0	803	12.40		3.02	30 11 65	69	353
T048P5.0	554	8.50		2.61	3 11 66	751	
T049P1.0	103	5.00		0.0162	5 7 66	635	

DOG NUMBER	COMMENTS ON DEAD DOGS
T030P1.0	SPECIAL STUDY
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	
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	
T049P1.0	

DOG NUMBER	AT INJECTION			INJECTED (μ C/KG)	DATE INJECTED			DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIG (KG)	HT		D	MO	YR		
T050P3.0	103	5.30		0.296	5	7	66	635	
T051P5.0	104	4.80		2.73	6	7	66	634	
T052P4.0	437	11.80		0.949	7	7	67	14	24

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

T043P5.0H was given 1.01 μ C Pu²³⁹/kg one day prior to sacrifice.

T044P5.0H was given 0.833 μ C Pu²³⁹/kg and about 9.17 μ C Fe⁵⁹/kg one day prior to sacrifice.

DOG
NUMBER

COMMENTS ON DEAD DOGS

T050P3.0

T051P5.0

T052P4.0 SPECIAL STUDY

C. RADIUM-228 (MESOTHORIUM)*

DOG NUMBER	AT INJECTION			DATE			DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIG (KG)	HT (KG)	INJECTED (μ C/KG)	INJECTED D	MO YR		
T001M4.5	529	9.13	4.23	8	9	54	314	1598
T002M4.5	463	8.93	4.27	8	9	54	755	5097
T003M5.0	579	9.15	10.6	13	3	56	700	15867

* (μ C Th²²⁸/ μ C Ra²²⁸) injected = 0.03.

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 (RADIO THORIUM)*

DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (CM)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68	DEATH	DOSE TO SKELETON (RADS)
T001T5.0	490	9.30	4.88	1	12 53	23		1161
T002T5.0	501	8.48	2.56	8	2 54	77		1979
T003T4.0	429	10.40	0.87	8	2 54	820		4878
T004T5.0	455	8.92	2.59	28	9 54	113		2883
T005T5.0	455	10.10	2.32	28	9 54	65		1524
T006T4.0	591	7.01	0.884	18	10 55	651		4273
T007T3.0	591	9.23	0.298	18	10 55	910		1777
T008T3.0	606	9.23	0.293	14	10 58	1043		1883
T009T3.0	447	11.00	0.285	4	2 59	1		3
T010T3.0	447	14.20	0.289	4	2 59	8		24
T011T3.0	500	8.62	0.335	16	6 59	22		76
T012T3.0	514	10.60	0.302	7	7 59	22		69
T013T3.0	754	13.10	0.298	28	7 59	22		68

*T11, 12, 13T3 received 40, 4, and 0.4 mg Th²³², respectively.

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	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (CM)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68	DEATH	DOSE TO SKELETON (RADS)
T001S0.0	151	7.71			5 3 54		2	
T002S5.0	149	6.85	148.0		5 3 54		11	626
T003S5.0	144	6.19	148.0		5 3 54		18	957
T004S5.0	151	7.05	148.0		5 3 54		41	1945
T005S5.0	144	5.25	148.0		5 3 54		116	4863
T006S5.0	155	7.01	87.0		16 3 54	1 hr		2
T007S5.0	155	6.74	87.0		16 3 54		2	84
T008S0.0	243	7.00						
T008S2.0H	67	3.69	2.74		27 9 55		66	31
T009S2.0H	67	2.79	3.62		27 9 55		66	40
T010S2.0H	67	3.11	3.25		27 9 55		132	93
T011S2.0H	67	3.85	2.62		27 9 55		132	75
T012S3.0	593	10.60	10.5		11 9 57		5	15
T013S4.0	324	10.50	19.1		8 7 60		8	50
T014S5.0	542	10.00	96.1		7 11 61		9	175
T015S5.0	595	9.43	98.4		7 11 61		30	423
T016S2.0	604	9.71	3.27		8 11 61		9	6
T017S6.0	670	7.18	295.0		19 1 62		14	689
T018S6.0	670	5.94	302.0		19 1 62		1369	18913
T019S6.0	670	5.43	284.0		19 1 62		24	637

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)

T019S6.0 LEUKOPENIA, THROMBOCYTOPENIA + PURPURA

DOG NUMBER	AT INJECTION			INJECTED ($\mu\text{C/KG}$)	DATE INJECTED			DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIG (KG)	HT		D	MO	YR		
T020S4.0J	440	8.54	28.9		2	10	63	13	78
T021S2.5J	363	7.20	8.3		2	10	63	13	143

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

T20S4.0J received 0.5 μC Sr^{85} .

T21S2.5J received 0.5 μC Sr^{85} and 600 μC Sr^{89} .

DOG
NUMBER

COMMENTS ON DEAD DOGS

T02054.0J SPECIAL STUDY

T02152.5J SPECIAL STUDY

F. RADIUM-224*

DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (CM)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68	DEATH	DOSE TO SKELETON (RADS)
T001Q3.0J	460	9.55		0.875	26 3 63		4 hr	
T002Q4.0	466	12.00		2.91	27 3 63	1831		
T003Q4.0	466	13.10		2.91	27 3 63	1831		
T004Q5.0	480	9.55		9.71	24 4 63		1462	400
T005Q5.0	455	9.67		9.59	24 4 63		1638	400
T006Q6.0	455	8.29		21.4	17 10 63		13	800
T007Q5.0	465	11.80		8.56	6 11 63	1607		
T008Q5.0	475	9.77		8.62	6 11 63		16	300
T009Q4.0	503	9.80		2.57	4 12 63		1451	100
T010Q4.0	503	10.30		2.57	4 12 63		262	100
T011Q3.0	495	9.10		0.885	4 12 63	1579		
T012Q3.0	495	13.50		0.889	4 12 63	1579		
T013Q3.0	495	11.30		0.912		1213		
T014Q3.0	438	10.30		0.87	4 12 63	1579		
T015Q4.0	515	12.70		2.73	1 2 68	59		
T016Q2.0	515	9.36		0.31	1 2 68	59		
T017Q2.0	515	10.20		0.311	1 2 68	59		
T018Q2.0	502	9.68		0.306	1 2 68	59		

*T001Q3.0J received 18.0 μ C Sr^{85} .
 *The skeletal doses in rads are only from ^{224}Ra and its daughters. In at least some of these dogs, appreciable ^{210}Pb contamination was injected. The dose from the ^{210}Pb has not been included. (See the article ^{210}Pb Contamination of Th^{228} : Its Contribution to Dose in Beagles in Our ^{228}Th Toxicity Studies in this report.)

DOG
NUMBER

COMMENTS ON DEAD DOGS

T001Q3.0J SPECIAL STUDY

T002Q4.0
T003Q4.0

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

T006Q6.0 PURPURA HEMORRHAGICA

T007Q5.0
T008Q5.0 PURPURA HEMORRHAGICA

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

T011Q3.0
T012Q3.0
T013Q3.0
T014Q3.0

T015Q4.0

T016Q2.0
T017Q2.0
T018Q2.0

DOG NUMBER	AT INJECTION			INJECTED (μ C/KG)	DATE INJECTED			DAYS SINCE INJECTION 31/3/68	DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIG (KG)	HT		D	MO	YR		
T019Q1.0	515	11.80		0.0475	1	2	68	59	
T020Q1.0	515	10.40		0.0472	1	2	68	59	
T021Q1.0	502	9.08		0.0447	1	2	68	59	

DOG
NUMBER

COMMENTS ON DEAD DOGS

T019Q1.0

T020Q1.0

T021Q1.0

G. AMERICIUM-241

DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (KG)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
T001W5.0	517	10.40	2.78	28 6 66	401	1430	
T002W5.0	517	12.70	2.83	28 6 66	449	1630	
T003W4.0	517	12.60	0.897	28 6 66	642		
T004W4.0	517	9.40	0.911	28 6 66	642		
T005W3.0	561	15.00	0.305	15 9 66	563		
T006W3.0	561	11.90	0.31	15 9 66	563		
T007W2.0	561	12.60	0.0952	15 9 66	563		
T008W2.0	561	11.70	0.0957	15 9 66	563		
T009W1.0	517	8.60	0.016	15 9 66	563		
T010W1.0	517	9.90	0.0162	15 9 66	563		
T011W0.5	526	8.17	0.00532	13 10 66	535		
T012W0.5	526	11.90	0.00539	13 10 66	535		
T013W0.2	526	10.60	0.00179	13 10 66	535		
T014W0.2	526	14.90	0.00178	13 10 66	535		
T015W5.5	858	11.50	4.53	23 10 67	1	10	
T016W5.0	461	10.70	2.78	29 1 68	22	80	
T017W4.0	523	9.87	0.924	21 3 68	10		

DOG
NUMBER

COMMENTS ON DEAD DOGS

T001W5.0 LIVER DEGENERATION
T002W5.0 LIVER DEGENERATION

T003W4.0
T004W4.0

T005W3.0
T006W3.0

T007W2.0
T008W2.0

T009W1.0
T010W1.0

T011W0.5
T012W0.5

T013W0.2
T014W0.2

T015W5.5 SPECIAL STUDY

T016W5.0 SPECIAL STUDY

T017W4.0

DOG NUMBER	AT INJECTION AGE (DAYS)	WEIG (KG)	HT (CM)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68	DEATH	DOSE TO SKELETON (RADS)
T018W3.0	523	8.60		0.307	21 3 68	10		
T019W2.0	513	13.40		0.097	21 3 68	10		
T020W1.0	513	10.80		0.0161	21 3 68	10		
T021W1.0	513	9.36		0.0166	21 3 68	10		
T022W1.0	487	11.60		0.0164	21 3 68	10		
T023W0.5	487	12.20		0.0053	21 3 68	10		
T024W0.2	477	11.30		0.00181	21 3 68	10		

DOG
NUMBER

COMMENTS ON DEAD DOGS

T018W3.0

T019W2.0

T020W1.0
T021W1.0
T022W1.0

T023W0.5

T024W0.2

H. ANCILLARY*

DOG NUMBER	AT INJECTION AGE WEIG HT (DAYS) (KG)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68	DOSE TO SKELETON (RADS)
F001A				1383	
F002A				2492	
M003A				1451	
M004A				3345	
M005A				4713	
M006A				5266	
M007A				3896	
M008A				3746	
F009A				3719	
F010A				2605	
F011A				4198	
F012A				4219	
F013A				4527	
F014A				3777	
F015A				4874	
F016A				4415	
F017A				2145	
F018A				5521	
F019A				4166	
F020A				2464	
F021A				5388	
F022A				4350	
M023A				1741	
M024A				3074	
F025A				5350	
M026A				4133	
M027A				2130	
M028A				3114	
M029A				5339	
F031A				5339	
F032A				1990	
F033A				3282	
F034A				2584	
M035A				529	
M036A				1971	
M037A				4089	
F038A				3802	
M039A				4554	
M040A				4666	
F041A				4704	
M042A				1265	
F043A				3881	
F044A				4767	
F045A				4763	

DOG
NUMBER

COMMENTS ON DEAD DOGS

F001A	SPECIAL STUDY
F002A	SPECIAL STUDY
M003A	SPECIAL STUDY
M004A	NOT DETERMINED
M005A	TRANSITIONAL CELL CARCINOMA, NEPHRITIS, PNEUMONIA
M006A	BRAIN HEMORRHAGE
M007A	LYMPHOSARCOMA
M008A	PROGRESSIVE PARALYSIS, CAUSE UNKNOWN
F009A	VAGINAL FIBROMA
F010A	SPECIAL STUDY
F011A	MAMMARY CARCINOMA
F012A	SEVERE OSTEOARTHRITIS
F013A	SPECIAL STUDY
F014A	OBTURATING EMBOLISM OF PORTAL VEIN
F015A	TRANSITIONAL CELL CARCINOMA URINARY BLADDER
F016A	SPECIAL STUDY
F017A	TRAUMA
F018A	
F019A	MAMMARY GLAND CARCINOMA
F020A	SPECIAL STUDY
F021A	
F022A	LYMPHOSARCOMA
M023A	OBTURATING PULMONARY EMBOLISM
M024A	SPECIAL STUDY
F025A	
M026A	SEMINOMA
M027A	SPECIAL STUDY
M028A	SPECIAL STUDY
M029A	
F031A	
F032A	LYMPHOSARCOMA
F033A	OBTURATING PULMONARY EMBOLISM
F034A	SPECIAL STUDY
M035A	SPECIAL STUDY
M036A	SPECIAL STUDY
M037A	SPECIAL STUDY
F038A	MAMMARY CARCINOMA
M039A	OBTURATING PULMONARY THROMBO EMBOLISM
M040A	EPIDERMICOID CARCINOMA (GINGIVA), PNEUMONIA
F041A	LEIOMYOSARCOMA (SPLEEN)
M042A	STATUS EPILEPTICUS
F043A	SPECIAL STUDY
F044A	
F045A	

DOG NUMBER	AT INJECTION AGE WEIG HT (DAYS) (KG)	INJECTED (μ C/KG)	DATE INJECTED D MO YR	DAYS SINCE INJECTION 31/3/68 DEATH	DOSE TO SKELETON (RADS)
F047A				1732	
F048A				3981	
F049A				4151	
M050A				2264	
F051A				1089	
F052A				509	
F053A				3915	
F054A				3190	
F055A				3571	
M056A				701	
F057A				3544	
M058A				767	
M059A				567	
M060A				3722	
M061A				3680	
F062A				3625	
F063A				3625	
F068A				3484	
F070A				3036	
M073A				5695	
F074A				5553	
M075A				5046	
F076A				2946	
F077A				2931	
F078A				2665	
F079A				2576	
F080A				2520	
F081A				2520	
M082A				2283	
F083A				2207	
M084A				2207	
M085A				2477	
M086A				499	
F087A				1715	
F088A				1715	
F089A				1871	
F090A				1655	
F091A				1645	
F092A				1645	
M093A				1590	
F094A				1590	
F095A				1575	
F096A				1558	
F097A				1558	

DOG
NUMBER

COMMENTS ON DEAD DOGS

F047A	SPECIAL STUDY
F048A	
F049A	
M050A	SPECIAL STUDY
F051A	SPECIAL STUDY
F052A	SPECIAL STUDY
F053A	
F054A	SPECIAL STUDY
F055A	
M056A	VOLVULUS + PERITONITIS
F057A	
M058A	SPECIAL STUDY
M059A	SPECIAL STUDY
M060A	
M061A	
F062A	
F063A	
F068A	
F070A	
M073A	DEGENERATION OF ADRENAL GLAND + DIABETES MELLITUS
F074A	LYMPHO SARCOMA
M075A	
F076A	
F077A	
F078A	
F079A	
F080A	
F081A	
M082A	
F083A	
M084A	
M085A	
M086A	SPECIAL STUDY
F087A	
F088A	
F089A	
F090A	
F091A	
F092A	
M093A	
F094A	
F095A	
F096A	
F097A	

DOG NUMBER	AT INJECTION			DATE		DAYS SINCE		DOSE TO SKELETON (RADS)
	AGE (DAYS)	WEIG (KG)	HT (CM)	INJECTED (μ C/KG)	INJECTED D MO YR	INJECTION 31/3/68	DEATH	
F098A							1464	
F099A								479
M100A								476
M101A								290
F102A								243
M103A								217
M104A								188
F105A								157
F106A							1159	
F107A							1068	
F108A							1305	

*Time interval shown here is the animal's age.

DOG
NUMBER

COMMENTS ON DEAD DOGS

F098A	
F099A	SPECIAL STUDY
M100A	SPECIAL STUDY
M101A	SPECIAL STUDY
F102A	SPECIAL STUDY
M103A	SPECIAL STUDY
M104A	SPECIAL STUDY
F105A	SPECIAL STUDY
F106A	
F107A	
F108A	

Symposium on
BONE-SEEKING RADIONUCLIDES

(Modified from the report in Bioscience 18:3, 239-240, March 1968)

Charles W. Mays (Editor-in-Chief)

Radiation-induced cancer was the central theme of the international symposium, Delayed Effects of Bone-Seeking Radionuclides, held on 12-14 September 1967 at Sun Valley, Idaho. Six countries were represented in the 28 invited papers. Comments on some of the papers follow:

H. D. BRUNER (Division of Biology and Medicine, U.S.A.E.C.) stated that the investigators of long-term toxicity studies and the supporting agencies both have a mutual responsibility to carry these experiments on to their natural conclusions, which is to the time that all of the animals shall have died. The supporting agencies must be resolved and able to provide sufficient funds on a regular basis, but should not feel compelled to fund projects that are percolating trivia. He noted that we should not shrink from additional experiments with other radionuclides as warranted.

JOHN H. MARSHALL (Argonne National Laboratory) contrasted the radionuclides which deposit throughout bone volume (i.e., the volume-seekers) against those which deposit on bone surfaces (i.e., the surface-seekers). For surface deposits of ^{239}Pu , about 50% of the α -particle energy is absorbed in cellular regions. However, for a volume deposit of ^{226}Ra , uniformly distributed throughout typical bone trabeculae 150 microns thick, only about 5% of the α -energy reaches cells. Experimentally, 100 rads from ^{239}Pu (averaged over the whole skeleton) has been found equivalent to about 900 rads from ^{226}Ra in

producing osteosarcomas in Beagles at the U. of Utah.

CONSTANTINE J. MALETSKOS (New England Deaconess Hospital and Harvard Medical School: work done at MIT) found that when humans swallowed synthetic dial paint, about 20% of the radium but only about 0.02% of the thorium was absorbed. Hence, for the ^{228}Ra (MsTh) dial painters, the swallowed ^{228}Th can be disregarded. MALETSKOS estimated that an injection of 1 μCi of ^{224}Ra delivers a total average radiation dose between 0.05 and 0.5 rads to the 7-kg skeleton of a standard adult. For children the corresponding dose limits are 0.3 to 0.9 rads multiplied by the factor (70 kg/body weight of child). These values are useful in estimating the dose to the German ^{224}Ra cases (presented later in the symposium by SPIESS).

JAN MULLER and JOSEF THOMAS (Institute of Radiation Hygiene, Prague, Czechoslovakia) analyzed the ^{90}Sr excreta from Czechoslovakian dial painters. Their data, coupled with that of other workers, indicate that the injection of 1 μCi of ^{90}Sr into an adult results in a 50-year dose of about 4 rads to a 7-kg skeleton.

BETTY I. BLEANEY (Bone-Seeking Isotopes Unit, Oxford, England) evaluated the local distribution of ^{239}Pu in tissue using a recent innovation. Tissue sections in contact with polycarbonate films were neutron-irradiated. Fission fragments from the ^{239}Pu pierced the polycarbonate film. These tracks were then etched and counted. The method is 100 times more sensitive than conventional autoradiography.

ROBLEY D. EVANS (Massachusetts Institute of Technology) summarized the studies at MIT on persons exposed to ^{226}Ra and ^{228}Ra . There have been 28 bone sarcomas plus 9 head carcinomas in the 90 persons whose

skeletal doses exceeded 1200 rads. However, none of these tumors have yet been observed in the 406 persons of this series whose doses were lower. A linear non-threshold relationship for the induction of these tumors seems extremely unlikely. EVANS calculates that for a residual content of 1 μCi of ^{226}Ra in the body after 40 years, the cumulative average dose to the 7-kg skeleton of a standard man is about 2300 rads, and it is about 3200 rads to the 5-kg skeleton of a standard woman.

ASHER J. FINKEL (Argonne National Laboratory) reported 23 bone sarcomas plus 16 neoplasms of the skull in 217 radium-containing persons. In all but one of these tumor cases, the residual content of ^{226}Ra in the body exceeded 0.5 μCi . In this one case, the content at tumor diagnosis (about 40 years after the start of exposure) was about 0.16 μCi . Her peak content while dial painting was an estimated 1.2 μCi . FINKEL suggests that the estimated peak content may be of greater significance than the terminal content in evaluating tumorigenesis.

HEINZ SPIESS (University Childrens' Clinic, Göttingen, Germany) outlined his follow-up of about 1000 of some 2000 German patients injected with ^{224}Ra in the years 1944 to 1951. This was the first presentation of these studies to an English-speaking audience, and there was very keen interest in this paper. To date, 50 bone sarcomas have appeared, 35 of them in the 206 patients injected as children. For the bone sarcoma cases, the smallest total injected activity was about 400 μCi of ^{224}Ra (in an 8-year old child and also in a 70-year old adult). Using the dose-conversion factors of MALETSKOS, the radiation dose for the adult's skeleton was between 20 and 200 rads. Short-lived (3.6 day) ^{224}Ra appears considerably more toxic rad-for-rad than the

long-lived (1600 year) ^{226}Ra . The greater effectiveness of ^{224}Ra may be because it decays quickly before the apposition of new bone mineral can shield the living cells from α -irradiation.

ROBIN MOLE (Harwell, England) assembled experimental data supporting his hypothesis that the radiation dose from a given radionuclide required to produce a set incidence of bone cancer is rather similar for a variety of mammals including man.

WILLIAM J. CLARKE (Battelle-Northwest Laboratory, Richland, Washington) reported 29 myelo-lympho proliferative disorders (hematopoietic neoplasms) in 605 Pitman-Moore miniature swine, contaminated with ^{90}Sr via their mother's diet from conception through weaning, and then fed 1 to 125 μCi of ^{90}Sr per day until death. Five of these pigs (all at 125 $\mu\text{Ci/day}$) also developed osteosarcomas. The skeletal doses at death ranged from 300 to 15,000 rads for the hematopoietic neoplasms, and 8000 to 14,000 rads for the osteosarcomas. There were 3 hematopoietic neoplasms, but no osteosarcomas in 64 pigs fed 1 to 125 μCi of $^{90}\text{Sr/day}$ starting at 9 months of age. No hematopoietic neoplasms nor osteosarcomas have yet occurred among 270 control pigs. For these pigs, the risk from hematopoietic neoplasms exceeded that from bone cancer.

LEO K. BUSTAD (U. of California, Davis, California) described effects in Beagles given ^{90}Sr continually from mid-gestation until adulthood (18 mo). He reported 9 myelogenous leukemias in 60 Beagles fed 3.3 μCi of $^{90}\text{Sr/gCa}$; 2 myelogenous leukemias in 65 Beagles fed 1.1 μCi of $^{90}\text{Sr/gCa}$; but no leukemias (yet) in 399 Beagles fed lower levels. Furthermore, no osteosarcomas have yet appeared at any of these levels. For continuous intake of ^{90}Sr by the very young Beagle (at 1.1 and 3.3 $\mu\text{Ci } ^{90}\text{Sr/gCa}$) the indicated risk from hematopoietic neoplasms exceeds

that from bone cancer.

JANET VAUGHAN (Bone-Seeking Isotopes Unit, Oxford, England) summarized her laboratory's ^{90}Sr studies in Dutch rabbits during the past 20 years. In 50 rabbits given a single injection of 50 to 1000 μCi of $^{90}\text{Sr}/\text{kg}$ at various ages, 26 developed osteosarcomas and 14 developed squamous cell carcinomas in the ear region, but no leukemias were observed.

ROGER O. McCLELLAN (Lovelace Foundation, Albuquerque, New Mexico) presented an excellent and detailed review of the neoplasms induced by high doses of ^{90}Sr in experimental animals. When single high doses of ^{90}Sr are given to adult experimental animals, osteosarcomas frequently predominate. However, when repeated doses of ^{90}Sr are received early in life, the hematopoietic neoplasms may form a greater risk.

GLENN N. TAYLOR (U. of Utah) reported that in Beagles injected as adults: squamous cell carcinomas in the head sinuses have been induced from ^{239}Pu , ^{226}Ra , and ^{90}Sr ; liver tumors from ^{239}Pu ; and eye melanomas from ^{228}Ra and ^{226}Ra . In all cases these tumors arose within heavily-irradiated tissue. The induction of these soft-tissue tumors was much less frequent than the induction of osteosarcomas.

MARCIA ROSENTHAL (Argonne National Laboratory) showed that monomeric ^{239}Pu (which deposits on bone surfaces) was about twice as effective in inducing bone cancer in mice than an equal skeletal activity of polymeric ^{239}Pu (which deposits in aggregates throughout the marrow as well as on bone surfaces). Local deposition patterns determine the severity of the resulting effects.

YURI I. MOSKALEV (Ministry of public Health, Moscow, USSR) provided the concluding paper, which was read in English by CYRIL COMAR

(Cornell University). For many in the audience, this was a first introduction to Russian radiobiology. Experiments on the delayed effects of internally-deposited radionuclides were reported for 5000 animals, mostly rats. Whereas no osteosarcomas were observed in 722 control rats nor in 1365 rats injected with 0.005 to 2.5 μCi of $^{90}\text{Sr}/\text{kg}$; osteosarcomas developed in 5 (7.4%) of 68 rats orally given 0.5 μCi of ^{239}Pu per day from 3 months of age until death 370 days later. The average radiation dose to the bone was only 57 rads at death and the inducing dose was likely much lower. Skeletally-deposited ^{239}Pu is very effective in inducing bone cancer. Radiation protectionists throughout the world should take note of this finding.

Other senior authors were MARVIN GOLDMAN, TOMISLAW DOMANSKI, F. W. SPIERS, BETSY J. STOVER, PATRICIA W. DURBIN, DAVID M. TAYLOR, CHARLES W. MAYS, LEONIDAS D. MARINELLI, MIRIAM P. FINKEL, WEBSTER S. S. JEE, JEAN H. DOUGHERTY and DAVID L. BERLINER.

This symposium was organized under the direction of THOMAS F. DOUGHERTY, Head of the Radiobiology Division of the Anatomy Department at the University of Utah. It was supported by the U. S. Atomic Energy Commission. The proceedings, published by the University of Utah Press, should appear about October 1968.

Did a clarifying principle emerge from the meeting's vast deluge of data and hypotheses? Yes! It is Evans' Law; "Everything is more complicated than most people think".

HEMATOPOIETIC DISORDERS IN BEAGLES INJECTED WITH ^{90}Sr

J. H. Dougherty and G. N. Taylor

Abstract: Fatal blood dyscrasia developed in 2 out of 13 beagles injected at ~ 16 months of age with a single intravenous dose of ~ 100 μCi $^{90}\text{Sr}/\text{kg}$. Death occurred at 990 and 1285 days post-injection, which is within the range of the latent periods observed for osteosarcoma induction by comparable doses of ^{90}Sr . Erythropoietic failure was the most extreme factor and was the ultimate cause of death.

The post mortem changes were characterized by bone marrow hyperplasia, moderate myeloid metaplasia in lymph nodes, spleen and liver and severe infarction in one instance. Neoplasia was not observed.

Introduction

Two of thirteen beagles injected as young adults with approximately 100 μCi $^{90}\text{Sr}/\text{kg}$ developed a severe and progressive blood dyscrasia which resulted in death despite intense therapeutic efforts. Since some hematological deaths have been reported in ^{90}Sr feeding studies in beagles and miniature swine where the exposure was begun while in utero, it is thought important to summarize two strontium injected animals from our laboratory which showed some similarities in the terminal blood picture and similar myeloid metaplastic changes⁽¹⁻²⁾.

Results

The significant findings in dogs M5S5 and M10S5 are divided into (1) clinical events, (2) hematological changes, and (3) post mortem findings.

(1) Clinical events: In both dogs the hematopoietic changes preceded significant clinical abnormalities. The general examination including such factors as lung and heart sounds, EKG, body weight, body temperature, diet, elimination, and general activity remained normal until one to two months prior to death. In one instance (M5S5) the

appetite was normal until three days before death. Radiographic findings were also normal. Both dogs sustained bite wounds at various times after injection and the healing response was normal. Melena and petechiation were prominent terminal features that were associated with severe thrombocytopenia in M10S5.

Terminally both dogs were treated with whole blood for anemia but in each case the transfusions became progressively less effective and ultimately futile. Both animals were eventually sacrificed because of the blood dyscrasia.

Severe infarction was also a contributing factor to death in M5S5. This was manifest clinically by extreme renal and cardiac symptoms. Less severe infarction has also been observed in several other high level strontium dogs, which suggests the possibility of strontium induced auto-hemagglutination.

(2) Hematological findings: These are graphed at monthly intervals in figures 1a and 1b for M5S5 and figures 2a and 2b for M10S5. M5S5 The hematological findings on this dog one month post-injection were as follows: VPRC 39.5, Hgb 12.7, WBC 2,500 and platelets 72,000/mm³. (Fig. 1a and 1b). The red cells returned to preinjection values by 4 months post-injection (VPRC 46.5) whereas leukocyte and platelet values remained well below normal values for the remaining lifespan of the animal. The eosinophils were almost absent for the last twelve months prior to sacrifice. A fall in red cell values occurred at 39 months post-injection (VPRC 30, Hgb 9.3) and they continued to fall despite repeated transfusions. The VPRC was 6.0 prior to the last transfusion which was two days prior to sacrifice. The platelets after the early depression remained within normal limits. Terminally the

Fig. 1a. Changes in the leukocyte values in dog M5S5.

Fig. 1b. Changes in red cell values (VPRC, sedimentation rate, reticulocytes) and platelets in dog M5S5.

Fig. 2a. Change in leukocyte values in dog M10S5.

Fig. 2b. Changes in red cell values (VPRC, sedimentation rate, reticulocytes) and platelets in dog M10S5.

blood smears showed atypical hypersegmented pmns with occasional bizarre promyelocytes and myelocytes.

M10S5 The leukocytes fell to 2,100 cells/mm³ by one month post-injection due to depression of all cell types. The platelets fell from a pre-injection mean of 382,000 to 46,000/mm³. No early period of anemia was noted. The leukopenia and thrombocytopenia persisted with no tendency toward recovery. An anemia appeared 28 months post-injection (VPRC 38.0, Hgb 11.3) which became progressively more severe despite repeated transfusions. Occasional myeloblasts and promyelocytes were found in the blood terminally.

(3) Post mortem findings: Extramedullary hematopoiesis was minimal in organs other than the spleen and lymph nodes. It did not develop in the adrenals and occurred to only a minimal degree in the liver. The most obvious change in the liver was the accumulation of cells in the perivascular region of the central vein. Many of these appeared to be reticulo-endothelial cells, based on their phagocytic activity and their accumulation of hemosiderin. A similar proliferation did not occur in the peri-portal zone and was not seen in the other strontium cases. Limited foci of myeloid metaplasia existed throughout the liver, usually in the sinusoidal areas.

The remainder of the histopathological lesions were primarily those associated with the multiple infarction in M5S5 and the diffuse hemorrhagic lesions of M10S5. Neoplasia of any type was not observed.

Hematopoietic organs of M5S5 - as observed in sections and in imprints stained with May-Grunwald-Giemsa stain.

a) Bone marrow: The marrow was generally hyperplastic with some areas of fibrosis and necrotic foci, particularly in the ends of the bones. Peritrabecular fibrosis, which is also commonly induced by other bone seeking radionuclides, was prominent in both dogs (3). There was a "shift to the left" in developing normoblasts with few mature forms. Abundant developing myeloid cells were present with premature segmentation resulting in hypersegmented mature pmns. Megakaryocytes were abundant. The marrow was extremely fluid so no satisfactory preparations were obtained for making accurate differential cell counts on the smear preparations.

b) Spleen: This organ was removed surgically prior to sacrifice which resulted in abnormal congestion. The white pulp was decreased in amount; the red pulp was greatly increased with large numbers of red cells in the dilated sinusoids. The red pulp showed myeloid metaplasia with mainly erythropoiesis and a larger number of pronormoblasts and basophilic normoblasts as determined by imprint preparations. Numerous megakaryocytes and some early and late myelocytes were also present. Erythrophagocytosis was a prominent feature.

c) Lymph nodes: There was a moderate involution in all nodes. In sections there was greatly decreased lymphocytopoiesis. Abundant erythrophagocytosis was seen in all nodes examined. There was myeloid metaplasia in the medullary cords of several nodes with nests of megakaryocytes - particularly in the submaxillary, retropharyngeal and mesenteric nodes and thymus. Most nodes showed increased numbers of plasma cells.

Hematopoietic organs of M10S5

a) Bone marrow: The marrow was in general hyperplastic particularly in the shafts of long bones where active hematopoiesis is not normally found in the adult animal. As seen in M5S5 there were many early forms of normoblasts and very few late normoblasts. There were many developing white cells with all stages of maturation present. The megakaryocytes were virtually absent in sections and imprint preparations. The myeloid ratio varied from 10.9 to 21.5 in the femur, rib, sternum, costo-chondral junction, and humerus.

b) Spleen: There was again a decrease in white pulp. The red pulp showed abundant myeloid metaplasia with no differentiation to late normoblasts of mature pmns. No megakaryocytes were found in the sections or imprints examined. There were increased amounts of hemosiderin and much evidence of erythrophagocytosis and cellular debris.

c) Lymph nodes: They were slightly to moderately involuted and brown in appearance. On sectioned material there was extreme hemorrhage with hemosiderin and erythrophagocytosis. Plasma cells were increased. Myeloid metaplasia was found in several nodes with many pmns.

Discussion and Summary

Depression of blood cells occurred in the 3, 4 and 5 dose level strontium dogs (4). Other dogs (M6S5A, M12S5) showed changes similar to these two dogs but to a lesser degree. This was noted particularly when the dogs were under additional stress. The latent period of hematological changes which became very severe terminally was slightly less (990 and 1285 days post-injection) than the average for osteosarcoma induction (1480 days post-injection).

While the formation of red cells and white cells is normal in the spleen, lymph nodes, and liver of fetal animals, it only appears after birth in various conditions of stress, including irradiation⁽⁵⁾. The myeloid cell (both red cell and white cell) formation in these adult organs is usually considered to be a compensatory phenomenon due to inadequate blood cell formation in the marrow.

In both of the dogs summarized in this study the most significant factor was erythropoietic failure. This marrow syndrome probably also exists as a latent factor in some of our surviving strontium dogs injected at the next lower dose level ($\sim 33 \mu\text{Ci } ^{90}\text{Sr/kg}$) and in one instance (F11S4) it was unmasked by a toxemia that ordinarily would not produce the progressive fatal anemia that did occur in this instance. It is concluded that the fatal strontium-90 induced anemia presented in this study was a primary radiation induced disease and not a secondary factor resultant to strontium induced myeloid neoplasia. The changes seen in the hematopoietic organs of M5S5 and M10S5 were not leukemic in nature. This conclusion was based on the absence of a leukemic blood picture and lack of evidence of an invasive uncontrolled growth in any of the organs, including those that are potentially hematopoietic. Whether these changes are preleukemic or "pseudo" leukemic cannot be answered at this time because of the lethality of the earlier occurring anemia syndrome.

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DISTRIBUTION OF ^{90}Sr IN THE HUMERUS AND THIRD LUMBAR VERTEBRA
OF THE BEAGLE PUP AFTER SINGLE AND MULTIPLE INJECTIONS

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Abstract: Shortly after intravenous injection of 87 or 148 $\mu\text{Ci } ^{90}\text{Sr/kg}$ the $^{90}\text{Sr}/\text{Ca}$ ratio in the region of the proximal epiphyseal line is 5 to 6 times that of the mid-diaphysis. Later the highest ratio is found in the proximal metaphyseal region.

Shortly after 10 weekly subcutaneous injections of 1 $\mu\text{Ci } ^{90}\text{Sr}$ the $^{90}\text{Sr}/\text{Ca}$ ratio is about the same in the third lumbar vertebra and in the humerus, except in the mid-diaphysis in which it is lower. The ratio then decreases more rapidly in the growing ends of the bone than in the shaft.

Introduction

Two small groups of puppies have been given ^{90}Sr . The first group of 6 received a single high dose which produced marked early hematological and skeletal effects. The second group received 10 small doses which did not produce obvious early effects. This report is concerned with the distribution of ^{90}Sr in the humeri and in the third lumbar vertebrae of these young beagles, and with autoradiographic studies of lumbar vertebral bodies, metatarsals, and tibiae.

Experimental Procedures

Six 5-month old dogs were given a single intravenous injection of ^{90}Sr in citrate buffer of $\text{pH} \sim 3.5$. Four 2-month old dogs received 10 weekly subcutaneous injections of ^{90}Sr in citrate buffer of $\text{pH} \sim 6.2$. Pertinent data are given in Table 1.

The humeri were sawed into 8 pieces and the third lumbar vertebrae into 2 or 3. They are described in Table 2. Each piece was reduced to ash in a muffle furnace, and the weight of ash was determined. The ash was dissolved and aliquots were analyzed for ^{90}Sr .

Three kinds of β - detectors were used, a Geiger tube, a proportional flow counter, and a well-type plastic scintillator.

The second lumbar vertebral body, second metatarsal and tibia were sawed in half longitudinally and fixed in acetone. They were embedded in Selectron (Pittsburgh Paint & Glass Co.) after defatting with ten changes of diethyl ether, and the cut surface of the bone was ground flat with abrasive paper. The flat surfaces of the bones embedded in Selectron were opposed to 25 μ thick Ilford nuclear track film, type K2 (Ilford Limited, Ilford, Essex, England).

Results and Discussion

The distribution of ^{90}Sr in the humerus and the third lumbar vertebra after the single injection are given in Table 3. Both the amount per part and the concentration in bone ash are tabulated. The latter is a measure of the ratio, $^{90}\text{Sr}/\text{Ca}$, since the fractional calcium content of bone ash varies but slightly.

The amounts found in the bones at 1 hour were roughly $3/4$ those at 2 days, which is illustrative of the well known rapid deposition of alkaline earth nuclides. Initially the concentration was highest in the proximal epiphyseal region of the humerus and it exceeded that of the middiaphysis by a factor of 5 to 6. The concentration at the distal end was about half that of the proximal end. The two segments of the vertebra did not exhibit such great variation.

As the time between injection and sacrifice increased two distinct changes in the distribution were noticed. First the region of maximum concentration shifted to the proximal metaphysis and second the concentration in the segments became more uniform. At the longest

interval observed; 141 days, the concentration in the proximal epiphyseal line sample was the lowest and was about 1/2 that of the proximal metaphyseal sample. Thus the variation in concentrations decreased from a factor of 6 to one of 2.

These changes undoubtedly reflect a combination of growth and radiation damage. The initial deposition of ^{90}Sr was highest in the regions of most rapid growth. (Fig. 1). As the bone grew longer, some of the ^{90}Sr was resorbed and a fraction of the resorbed material was reutilized. This led to a more uniform concentration in the segments. However, 148 $\mu\text{Ci/kg}$ was a sufficiently high dose that the resorption process beneath the epiphyseal plate was impeded. (Fig. 2). As a result some of the material which should have been resorbed was not. This abnormal retention led to the higher metaphyseal concentration.

The amounts and concentrations of ^{90}Sr in the pieces of humeri and third lumbar vertebrae from the pups that received multiple injections are given in Table 4. In the bones from the dogs sacrificed three days after the last injection the concentrations were quite uniform. (Fig. 3). The lowest observed were those of the mid-diaphyses which were only 10 and 20% less than those of the total humeri. Thus weekly injections during the beagle pup's third and fourth months resulted in a fairly uniform $^{90}\text{Sr}/\text{Ca}$ ratio at the macroscopic level.

The amounts in the total bones of the pups sacrificed two months after the last injection decreased 20 to 25%. The concentrations decreased by more than a factor of two since considerable skeletal

growth occurred. In the humeri the concentration was no longer uniform. It was highest in the diaphysis and lowest in the proximal epiphyseal region. (Fig. 4). This is consistent with the resorption aspect of the long bone growth process. In the vertebrae the concentration remained uniform. The average increase in bone ash between 66 and 133 days was 83% for the total humerus and 90% for the total vertebra. Thus both bones exhibited about the same gross growth during this period.

Table 1

Dogs, Days, and Doses

Single Intravenous Injection				
Dog	Age at Inj. (d)	Sac. at (d)	$\mu\text{Ci } ^{90}\text{Sr/kg}$	Wt. (kg)
T6S5	155	0.042	87	7.0
T7S5	155	2	87	6.7
T2S5	149	11	148	6.8
T3S5	144	18	148	6.2
T4S5	151	41	148	7.0
T5S5	144	116	148	5.2
10 Weekly Subcutaneous Injections of 1 μCi each				
Dog	Age at 1st Inj. (d)	Sac. at (d after 1st Inj.)	Total μCi	Ave. Wt. during Inj. Period (kg)
T8S2H	67	66	10	3.7
T9S2H	67	66	10	2.8
T10S2H	67	132	10	3.1
T11S2H	67	132	10	3.8

Table 2
Code for and Description of Samples

Code	Description
H-1	proximal epiphysis
H-2	proximal epiphyseal line
H-3	proximal metaphysis
H-4	proximal diaphysis
H-5	mid-diaphysis
H-6	distal diaphysis and metaphysis
H-7	distal epiphyseal line
H-8	distal epiphysis
H	total humerus
V-1	dorsal sponous and caudal articular processes and part of the vertebral arch
V-2	cranial articular process and vertebral arch
V-3	vertebral body and transverse process
V	total 3rd lumbar vertebra

Table 3
Distribution in H and V Following the
Single Injection of ^{90}Sr

Sample Code	T6S5 0.042d	T7S5 2d	T2S5 11d	T3S5 18d	T4S5 41d	T5S5 116d
% dose per sample						
H - 1	0.14	0.17	0.14	0.12	0.12	0.13
H - 2	0.67	0.88	0.74	0.50	0.67	0.18
H - 3	0.26	0.35	0.50	0.53	0.58	0.44
H - 4	0.11	0.20	0.21	0.23	0.20	0.15
H - 5	0.09	0.17	0.23	0.19	0.16	0.15
H - 6	0.12	0.22	0.26	0.27	0.22	0.20
H - 7	0.26	0.34	0.49	0.38	0.39	0.25
H - 8	0.07	0.07	0.09	0.12	0.07	0.16
H	1.73	2.40	2.67	2.34	2.41	1.66
V - 1,2	0.19	0.28	0.33	0.26	0.24	--
V - 3	0.40	0.39	0.44	0.38	0.39	--
V	0.59	0.67	0.77	0.64	0.63	--
% dose per g of bone ash						
H - 1	0.55	0.55	0.50	0.43	0.38	0.22
H - 2	0.68	1.10	0.60	0.46	0.36	0.17
H - 3	0.27	0.41	0.49	0.50	0.39	0.38
H - 4	0.15	0.25	0.24	0.27	0.19	0.22
H - 5	0.11	0.21	0.25	0.25	0.18	0.22
H - 6	0.16	0.27	0.29	0.31	0.22	0.22
H - 7	0.36	0.48	0.45	0.44	0.33	0.33
H - 8	0.25	0.47	0.30	0.35	0.28	0.28
H	0.31	0.46	0.40	0.38	0.30	0.26
V - 1,2	0.24	0.37	0.42	0.40	0.32	--
V - 3	0.36	0.40	0.39	0.38	0.31	--
V	0.31	0.39	0.40	0.39	0.31	--

Table 4
Distribution in H and V Following
the Ten Weekly Injections of ^{90}Sr

Sample Code	T8S2H 66d	T9S2H	T10S2H 132d	T11S2H	T8S2H 66d	T9S2H	T10S2H 132d	T11S2H
	% dose per sample				% dose per g bone ash			
H - 1	0.07	0.09	0.08	0.09	0.40	0.57	0.20	0.18
H - 2	0.26	0.24	0.14	0.13	0.46	0.52	0.15	0.12
H - 3	0.28	0.22	0.15	0.16	0.45	0.55	0.15	0.13
H - 4	0.23	0.23	0.23	0.25	0.44	0.52	0.25	0.26
H - 5	0.22	0.17	0.26	0.21	0.39	0.41	0.29	0.22
H - 6	0.29	0.27	0.21	0.18	0.45	0.50	0.27	0.23
H - 7	0.25	0.25	0.17	0.16	0.42	0.55	0.21	0.18
H - 8	0.08	0.10	0.07	0.10	0.46	0.54	0.24	0.21
H	1.69	1.56	1.30	1.30	0.43	0.51	0.22	0.19
V - 1	0.05	0.03	0.04	0.04	0.49	0.49	0.20	0.16
V - 2	0.10	0.11	0.08	0.07	0.43	0.51	0.19	0.17
V - 3	0.29	0.25	0.19	0.20	0.41	0.51	0.19	0.17
V	0.44	0.40	0.31	0.31	0.43	0.50	0.19	0.17

- Fig. 1 - Contact autoradiograph of a sagittally halved tibia from T7S5 (87 μ Ci of $^{90}\text{Sr}/\text{kg}$ and sacrificed after two days). Note the intense activity at the epiphyseal plates (X 1 1/2).
- Fig. 2 - Autoradiograph from T4S5 (148 μ Ci of $^{90}\text{Sr}/\text{kg}$ and sacrifice after 41 days). Note the stunted growth (arrow points to region of new bone), the intense activity at the growth arrest plates (metaphyses) and the endosteal surfaces of the proximal and distal diaphyses (X 1 1/2).

- Fig. 3 - Autoradiograph from T8S2H (10 weekly injections of 1 μCi of ^{90}Sr and sacrificed 66 days after the first injection). Note the relative uniform distribution of ^{90}Sr except for the quantity in both epiphyses (X 1 1/2).
- Fig. 4 - Autoradiograph from T10S2H (10 weekly injections of 1 μCi of ^{90}Sr and sacrificed 132 days after the first injection). Note the reduction of ^{90}Sr at the metaphyses due to growth and the persisting concentration of ^{90}Sr in the diaphyses (X 1 1/2).

^{210}Pb CONTAMINATION OF Th^{228} : ITS CONTRIBUTION TO DOSE
IN BEAGLES IN OUR ^{228}Th TOXICITY STUDIES

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Abstract: Beagles injected with our 1st stock of ^{228}Th were virtually free of ^{210}Pb contamination, but for the 2nd and 3rd stocks, the injected contamination ranged from 0.08 to 0.24 $\mu\text{Ci } ^{210}\text{Pb}/\mu\text{Ci } ^{228}\text{Th}$.

Preliminary studies of 7 Beagles intravenously injected with ^{210}Pb in citrate solution suggest that its total body retention is somewhat similar to that for ^{90}Sr , dropping to about 1/4 of the injected activity at 3 months post injection. At 10 years after injection the estimated skeletal dose in rads from ^{210}Pb relative to that from ^{228}Th is 0%, 1% and 3% for the toxicity dogs receiving the lowest, median, and highest $^{210}\text{Pb}/^{228}\text{Th}$ ratios. Thus, the skeletal dose from the ^{210}Pb contamination in our ^{228}Th -injected dogs is negligible.

However, in some of our test dogs injected with ^{224}Ra prepared from contaminated ^{228}Th stock, the ^{210}Pb accounts for the major fraction of the radiation dose.

Introduction

A long-lived γ -ray emitter was observed in a recent injection solution of short-lived ^{224}Ra . This led to the discovery of ^{210}Pb contamination in the ^{228}Th stock from which this solution was obtained.

All 3 of our ^{228}Th stock solutions were purchased from the Radiochemical Centre, Amersham, England. This supplier extracts ^{228}Th from "technical mesothorium", which is a mixture of ^{228}Ra , ^{226}Ra and their daughter products. The supplier recognized that the ^{228}Th so derived was likely to contain ^{210}Pb and ^{210}Po contamination and proposed to remove these contaminants by electrolysis. (1)

Our analyses of ^{228}Th stocks #1 and #2 indicated negligible ^{232}Th , ^{230}Th , ^{228}Ra , and ^{226}Ra contamination (2, 3).

Evaluation of ^{210}Pb

^{210}Pb was first identified by its 47keV γ -ray which despite its low abundance (4 γ -rays/100 disintegrations of ^{210}Pb) was prominent

in ^{228}Th stocks #2 and #3, but virtually absent in stock #1. The identity of ^{210}Pb was confirmed and quantitated by electrodeposition on copper of its granddaughter (^{210}Po) from equilibrated samples of each stock solution. Solid-state α -particle spectroscopy revealed that the only α -particles evident in the electrodeposits had the ^{210}Po α -energy of 5.30 MeV. The ^{210}Po activity was evaluated by α -counting in a 2π gas-flow proportional counter.

Our observed $^{210}\text{Pb}/^{228}\text{Th}$ activity ratios, adjusted to the dates of the supplier's evaluation of ^{228}Th , are shown in Table 1. (A ^{210}Pb half-period of 20.4 years and a ^{228}Th half-period of 1.91 years were used to adjust for radioactive decay.)

Table 1. Original $^{210}\text{Pb}/^{228}\text{Th}$ ratios as of the time of the supplier's evaluation of ^{228}Th .

Stock	Calendar date	Julian day	$\mu\text{Ci } ^{210}\text{Pb}/\mu\text{Ci } ^{228}\text{Th}$
1	23 July 1953	4582	0.000040
2	29 July 1959	6779	0.0662
3*	19 June 1963	8200	0.238

*The difference in stocks #2 and #3 appears due to the effect of radioactive decay alone: this is as it ought to be because the supplier⁽⁴⁾ stated that stock #3 would be from the same batch as stock #2.

From the values in Table 1, the activity ratios on the dates of injection have been computed for all of our ^{228}Th -injected dogs (Table 2).

Table 2. ^{210}Pb contamination in ^{228}Th dogs at injection.

^{228}Th (RdTh) Dogs	^{228}Th Purchase Number	Julian Day of Injection	Injected $\frac{\mu\text{Ci } ^{210}\text{Pb}}{\mu\text{Ci } ^{228}\text{Th}}$
T1T5	1	4713	0.000045
M1T1, M1T2, M1T3, M1T4, M1T5, T2T5, T3T4	1	4782	0.000048
M2T0.5, M2T1.5, M2T2, M2T3, M2T4, M2T5, T4T5, T5T5	1	5014	0.000059
F3T0.5, F3T1.5, F3T2, F3T3, F3T4	1	5265	0.000074
M4T0.5, M4T1.5, M4T2, M4T3, M4T4, T6T4, T7T3	1	5399	0.000083
M1T0.5, M1T1.5, M2T1, F3T1, M4T1, M4T2A	1	5724	0.000112
M5T0.5, M5T1, T8T3	1	6491	0.000223
T9T3, T10T3	1	6604	0.000247
T11T3	1	6736	0.000278
T12T3	1	6757	0.000283
T13T3	1	6778	0.000289
M5T0.2, M5T1.5, M5T2, M5T3	2	6974	0.0789
F6T0.2, F6T0.5, F6T1, F6T1.5, F6T2, F6T3	2	7310	0.1068
M7T0.2, M7T0.5, M7T1, M7T1.5, M7T2, M7T3	2	7338	0.1095
M8T0.2, M8T0.5, M8T1, M8T1.5, M8T2, M8T3	2	7444	0.1205
F9T0.2, F9T0.5, F9T1, F9T1.5, F9T2, F9T3	2	7480	0.1245
F10T0.2, F10T0.5, F10T1, F10T1.5, F10T2, F10T3	2	7509	0.1277
M1T0.2, M2T0.2, F3T0.2, M4T0.2	2	7751	0.1588
F11T0.2, F11T0.5, F11T1, F11T1.5, F11T2, F11T3, M5T0.2A, M7T1.5A	1	8185	0.001026
F12T0.2, F12T0.5, F12T1, F12T1.5, F12T2, F12T3	3	8220	0.242

The activity ratio of $^{210}\text{Pb}/^{228}\text{Th}$ was negligible in the 37 toxicity and 13 test dogs injected with stock #1. It varied from 0.08 to 0.24 $\mu\text{Ci } ^{210}\text{Pb}/\mu\text{Ci } ^{228}\text{Th}$ in the 44 toxicity dogs injected with stocks #2 and #3. Similar activity ratios were obtained by comparing the excess γ -ray count rate at 47 keV in injection duplicates filled and sealed at each injection time against the count rate from a ^{210}Pb standard which we had calibrated by absolute γ -ray counting. Thus, little or no selective hold-back of ^{210}Pb or ^{228}Th appears to have occurred from stock solution to injection. The skeletal dose resulting from injected ^{210}Pb will now be estimated.

^{210}Pb Dosimetry

The skeletal dose from ^{210}Pb depends upon its retention. While our data on the biological retention of ^{210}Pb are limited, they are sufficient to show that the skeletal contribution from ^{210}Pb is negligible in the ^{228}Th -injected dogs.

Our last seven ^{224}Ra dogs (T15Q4, T16Q2, T17Q2, T18Q2, T19Q1, T20Q1, and T21Q1) were injected with approximately 1 $\mu\text{Ci } ^{210}\text{Pb}/\mu\text{Ci } ^{224}\text{Ra}$. The 3.62 day ^{224}Ra quickly decayed away, leaving 20.4 year ^{210}Pb plus a small residual ^{228}Th contamination whose contribution at 47 keV was stripped out. Assuming that for total body counting, the (dog/injection standard) calibration factor for ^{210}Pb (47 keV γ -rays) is about the same as that for ^{241}Am (60 keV γ -rays) the following average total-body retentions for ^{210}Pb were observed (Table 3).

The retention of ^{210}Pb is low, and appears to approximate that of ^{90}Sr . Provisionally we assumed that (a) all retained ^{210}Pb is in skeleton, (b) the effective retention of ^{210}Pb equals that of ^{90}Sr ,

Table 3. Biological retention* of ^{210}Pb and other radionuclides injected i.v. in citrate solution into young adult Beagles.

Days after Injection	^{210}Pb	^{90}Sr	^{226}Ra	^{239}Pu	^{228}Th
35†	0.35	0.32	0.44	0.62	0.69
62	0.27	0.29	0.39	0.61	0.68
99	0.22	0.27	0.34	0.60	0.68

*The ^{210}Pb values are for the total body based on 7 injected Beagles. Values for the other nuclides are for skeletal biological retention (transformed from the equations for effective skeletal retention listed on pg.10).

†Only T15Q4 was counted on this date (35 days). His actual retention (36.6%) was multiplied by the ratio (av. retention/T15Q4 retention) observed on the other dates (62 and 99 days).

(c) each ^{210}Pb decay series releases 5.30 MeV of α -energy plus 0.32 MeV of β -energy plus 0.10 MeV of recoil energy to the skeleton (a total of 5.72 MeV), compared to 0.893 MeV of β -energy from the ^{90}Sr decay series. Then, the skeletal dose from ^{210}Pb was estimated by multiplying the skeletal dose from ^{90}Sr (based on its retention equation on pg.10 of this report) by the absorbed energy ratio (5.72 MeV/0.893 MeV). The computed skeletal doses (rads for each injected $\mu\text{Ci/kg}$) are shown at various years after injection in the second column of Table 4.

The ratio of ^{210}Pb dose in rads/ ^{228}Th dose in rads is about 1% in the median contaminated (F6) group, and ranges from virtually zero in

Table 4. Estimated $^{210}\text{Pb}/^{228}\text{Th}$ dose to skeleton.

Years After Injection	^{210}Pb [rads $\mu\text{Ci/kg}$]	^{228}Th [rads $\mu\text{Ci/kg}$]	X 1.00 [^{210}Pb dose ^{228}Th dose]	X 0.24 most contam. group (F12)	X 0.1 ¹ median contam. group (F6)
1	261	3137	0.083	0.020	0.008
2	421	5214	0.081	0.019	0.008
3	552	6589	0.084	0.020	0.008
4	667	7499	0.089	0.021	0.009
5	770	8102	0.095	0.023	0.010
6	862	8501	0.101	0.024	0.010
7	944	8765	0.108	0.026	0.011
8	1018	8940	0.114	0.027	0.011
9	1084	9055	0.120	0.029	0.012
10	1143	9132	0.125	0.030	0.012

dogs injected with ^{228}Th stock #1 to about 3% in the most contaminated (F12) group. THUS, THE SKELETAL DOSE FROM ^{210}Pb CONTAMINATION IN OUR ^{228}Th -INJECTED DOGS IS NEGLIGIBLE.

Much additional work is needed to evaluate accurately the ^{210}Pb dose to the ^{224}Ra test dogs. For example, Table 4 indicates that the injection of 1 μCi $^{210}\text{Pb}/\text{kg}$ might deliver roughly 1000 rads to the skeleton in about 8 years, while the injection of 1 μCi $^{224}\text{Ra}/\text{kg}$ only delivers about 40 rads⁽⁵⁾. Certainly, in the last seven ^{224}Ra dogs (T15Q4 $\rightarrow$ T21Q1) injected with about 1 μCi $^{210}\text{Pb}/\mu\text{Ci}$ ^{224}Ra the vast majority of the skeletal dose will be from ^{210}Pb . In the earlier ^{224}Ra -injected dogs, the degree of ^{210}Pb contamination remains to be quantitated, but in at least some of these dogs it appears to be much lower.

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DISTRIBUTION OF ^{241}Am IN THE BEAGLE

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Abstract: Measurement of the amounts and concentrations of ^{241}Am in a variety of tissues of the beagle have been made at 1, 22, 401, and 449 days after the intravenous injection of 4.53, 2.78, 2.78 and 2.83 $\mu\text{Ci/kg}$, respectively. Animals surviving 400 or more days died of extreme liver degeneration. Retention measurements were done serially on these and 4 animals receiving 0.897, 0.911, 0.305, and 0.310 $\mu\text{Ci } ^{241}\text{Am/kg}$. The measurements are continuing on the latter 4 dogs. The americium concentration was measured in something over 25 tissues in each of the 4 animals. The concentration was higher in the liver than in the skeleton. In addition the concentration was greater in the thyroid than in the skeleton in 3 of the 4 animals studied. Whole body measurements suggest that part of the ^{241}Am lost from the liver is redeposited in the skeleton while measurements of liver biopsies taken serially on one of the dogs show, at most, a slight decrease in ^{241}Am concentration in that tissue.

It has been previously reported(1) that pilot studies of chronic toxicity of ^{241}Am were initiated in June of 1966. The retention and gross distribution studies described in that report are continuing. A total of 24 dogs have thus far been entered in these studies, the 2 animals given 2.8 $\mu\text{Ci/kg}$ died of severe liver degeneration 401 and 449 days after their americium injection. Two animals were sacrificed at 1 and 22 days for studies of initial retention and distribution.

In this report an attempt will be made to summarize the short term findings.

Retention and gross distribution, as determined by whole and partial body counting(1), of the injected americium are shown in Fig. 1. Fig. 1a describes the whole body, liver and non-liver retention of two 3-level ($\sim 0.3 \mu\text{Ci/kg}$) dogs through 565 days following americium injection.

Figure 1.

Fig. 1b shows the data for two 4-level ($\sim 0.9 \mu\text{Ci/kg}$) dogs. Note that non-liver retention is quite possibly increasing during the final 6 months or so of the 644 day period of observation.

The same measurements, as described above, made on two 5-level ($\sim 2.8 \mu\text{Ci/kg}$) dogs are shown in Fig. 1c. Notable here is the increasing rate of americium loss from the liver and the concurrent increase in non-liver retention during the 401 and 449 days of these observations.

Information generated by the observation of 2 dog groups is entirely inadequate to describe retention with very great precision. However these figures give the impression that a dose-effect has been observed. The 3-level animals appear to have a higher retention than the 4- and 5-level animals, the higher retention being due to a larger fraction of the dose being deposited and retained in the liver.

The longest of these studies has continued for 642 days as of this report with all animals surviving except the two 5-level dogs. They died of extreme liver degeneration accompanied by portal hypertension and ascities which were related to marked alteration of the general vascular architecture of the liver.

An interesting feature of liver retention by these two animals is that while the liver retention decreased by a factor of something approaching 3 during the period of observation, the concentration decreased by no more than about $1/4$, as can be seen in Table 1. This was demonstrated by measuring americium concentrations in liver specimens obtained by biopsies at 41 and 245 days after injection.

The explanation for the non-parallel decline of total retention and concentration is that the loss of americium from liver proceeds

with a somewhat concurrent loss of liver mass; instead of a normal 350 g liver, the two 5-level animals contained 144 and 146 g livers terminally.

Table 1
TLW5: ^{241}Am Liver Concentrations

	Days After Injection	% Dose Kg
Liver Biopsy	41	201
Liver Biopsy	245	134
Residual (Post Mortem) Liver	401	150

Two dogs injected for short term retention and distribution studies and the two 5-level animals who died of degenerative liver disease were analyzed in considerable detail. Something over 50 samples of each animal were evaluated, the results were combined, where appropriate, and the most interesting features are tabulated in Tables 2, 3, and 4.

The most obvious feature of Table 2 is that the vast majority of the injected dose is found in the liver and skeleton with kidneys, spleen and muscle accounting for most of the rest retained.

Because radiation dose is proportional to concentration of deposited radionuclide, the values for percent of dose per kilogram of tissue are tabulated in Tab. 3. Values shown here appear to indicate that the liver is the critical organ with skeleton, kidney, thyroid and perhaps other tissues as candidates for secondary mention. This is in some contrast to the Handbook 69(2) tabulation which lists kidney and bone as the critical organs in man.

Table 2

Part	Δt (days)	1	22	401	449
	Dog	T15W5.5	T16W5	T1W5	T2W5
% of Dose/Part					
Skeleton		28.3	28.1	45.4	50.5
Liver		48.7	53.9	23.6	15.5
Thyroid		0.094	0.0204	0.072	0.029
Kidneys		1.30	0.362	1.28	1.13
Spleen		---	0.0488	0.495	0.94
Lymphatic Tissue		0.103	0.0249	0.071	0.071
Aorta		0.057	0.0173	0.049	0.046
Lung		0.654	0.345	---	0.393
Adrenals		0.005	---	---	0.006
Prostate		0.032	0.0106	0.016	0.037
Testes		0.018	0.0075	0.014	0.015
Muscle		2.40	---	1.07	2.24
Brain		0.002	0.0034	0.009	0.007

Table 3

Part	Δt (days)	1	22	401	449
	Dog	T15W5.5	T16W5	T1W5	T2W5
% of Dose/Kilogram					
Skeleton		24.6	27.5	43.7	39.8
Liver		175.3	203.9	164.0	106.1
Thyroid		115.6	20.4	134.0	80.1
Kidneys		27.4	9.68	18.7	17.4
Spleen		---	2.96	10.7	22.3
Lymphatic Tissue		15.1	7.39	16.3	16.8
Aorta		11.2	2.00	4.3	6.0
Lung		7.4	4.95	---	4.9
Adrenals		4.8	---	---	3.4
Prostate		3.0	1.24	2.4	7.8
Testes		1.9	0.57	0.8	1.2
Muscle		0.56	---	0.4	0.8
Brain		0.03	0.04	0.1	0.08

Table 4

Part	Δt (days) Dog	1	22	401	449
		T15W5.5	T16W5	T1W5	T2W5
		$\frac{\% \text{ Dose}}{\text{g}}$	Part / $\frac{\% \text{ Dose}}{\text{g}}$	Skeleton	
Skeleton		1.00	1.00	1.00	1.00
Liver		7.13	7.41	3.74	2.67
Thyroid		4.66	0.742	3.06	2.01
Kidneys		1.11	0.352	0.428	0.437
Spleen		---	0.108	0.245	0.560
Lymphatic Tissue		0.614	0.269	0.373	0.422
Aorta		0.456	0.073	0.098	0.151
Lung		0.301	0.180	---	0.123
Adrenals		0.195	---	---	0.085
Prostate		0.122	0.045	0.055	0.196
Testes		0.077	0.021	0.018	0.030
Muscle		0.023	---	0.009	0.021
Brain		0.001	0.001	0.003	0.002

The same data are presented once more in Table 4, this time the concentration of each part is compared to the concentration in the skeleton. Once again it is seen that liver and thyroid may be at greater risk than bone. This, of course, is dependent on the distribution of americium within a specific organ and the relative radiosensitivity of the cells ultimately irradiated. One should remember in using these figures that the values for liver and skeleton concentration are terminal values and that, as shown in Fig. 1c, at this level, the liver has lost more than 1/2 its initial burden with only slightly lowering its americium concentration. Concurrently the skeletal burden has increased and therefore the concentration has increased substantially, thus lowering the liver concentration to skeletal concentration ratio.

It will be recalled that our 3-level animals (Fig. 1a) show a loss of americium from the liver sufficiently slow to prevent any increase in the skeletal retention. It would therefore seem probable that at this and lower levels, the liver may continue to be the critical organ in the dog.

References

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MICROSCOPIC DISTRIBUTION OF AMERICIUM-241 IN THE BEAGLE THYROID GLAND

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Abstract: Americium-241 deposition in the beagle thyroid gland occurred principally in the interfollicular areas. Lesser amounts were also retained in the tunica media and/or intima of some of the arterioles. Retention in the follicular epithelium, the colloid, and the collagenous structures such as the capsule and interlobular septa was low. There was no significant change in this general distribution pattern over a period of 448 days.

Introduction

Relatively high retention of ^{241}Am in the skeleton and liver of some species is well known⁽¹⁻⁵⁾. More recently, canine studies at this laboratory have demonstrated an additional site of relatively high deposition, the thyroid, where the concentration exceeded that of the skeleton during post injection intervals extending up to 448 days - the longest time studied thus far⁽⁶⁻⁷⁾.

It is the purpose of this report to present the microscopic distribution of the ^{241}Am thyroid burden as observed in the Beagle.

Methods

Thyroids from four purebred Beagles given a single intravenous injection of approximately 2.8 to 4.5 $\mu\text{Ci } ^{241}\text{Am/kg}$ in a citrate buffer (pH 3.5) were available for study. They were from dogs sacrificed at 1 day, 22 days, 401 days, and 448 days post injection. The latter two animals were moribund at the time of sacrifice from severe radiation-induced liver changes. All of the animals were approximately 16 months of age at the time of injection.

The autoradiograms are from acetone fixed tissues that were prepared according to procedures described by Arnold and Jee⁽⁸⁾. The silver impregnations were made according to Nassar's method⁽⁹⁾.

Results

The autoradiographic studies indicated that most of the thyroid americium was localized extracellularly within the interfollicular region (Figs. 1-2). Thus in addition to other components, it was in association with a dense mesh work of argyrophilic reticulum fibers, some PAS positive staining material, and a rich capillary bed (Fig. 3). Blood flow in the thyroid on a weight basis is the highest of any gland⁽¹⁰⁾. Retention in the follicular epithelium and the colloid was very low. The collagenous structures such as the capsule and interlobular septa also contained very little activity.

A second but lesser region of americium concentration in the thyroid was the inner aspect of some of the larger arterioles. The α -activity was usually highest in those vessels with at least several annular layers of smooth muscle and most of the α -tracks appeared to emanate from this zone - the tunica media or possibly the intima (Fig. 4). Activity in the larger thyroid arteries was not observed. The retention was lower than the interfollicular region and the percentage of the total thyroid burden retained in this vascular site was low.

There was no obvious difference in the thyroid-americium distribution pattern in dogs observed at short post-injection times (1-22 days post-injection) as compared to the longer intervals (448 days post-injection). However, within a given thyroid gland there were significant regional differences in concentration of the radionuclide. Some of this non-uniformity appeared to have a lobular pattern. However, this was inconclusive. Significant variation also occurred within a given lobule, including some foci of very intense hot spots (Fig. 5).

Thus far (448 days post-injection) unequivocal ^{241}Am -induced thyroid lesions have not been noted. However, in both of the terminal dogs, the thyroid weights were below average - especially in the 448 day animal. Nevertheless, except for the smaller size, the gross appearance was unremarkable and the microscopic features were normal. Clinical symptoms related to the thyroid were not observed.

Discussion

Liver disease was the principal cause of the relatively early death in both of the dogs in this study that died from americium toxicity (T1W5 and T2W5). The syndrome was similar to that observed in some of the acute deaths in our high-level plutonium groups. Reports of this liver syndrome, even at significantly higher dose levels, have not been reported in other species such as the rat probably because of their much higher excretion rates, ⁽²⁾ However, in the dog where liver retention is greater and more prolonged, ^(6,7) approximately $2.8 \mu\text{Ci } ^{241}\text{Am/kg}$ of body weight appears to be very near or in excess of the LD_{100} dose, with death due to liver failure at approximately 400 to 500 days post-injection. It remains to be seen if thyroid disease in the dog will also become an important end point, especially at the longer latent periods of some of our lower dose levels. Certainly the relatively high thyroid retention and the deposition of the radionuclide immediately adjacent to the follicular epithelium tend to make this a likely possibility.

Fig. 1. Autoradiogram from beagle injected with $2.83 \mu\text{Ci } ^{241}\text{Am/kg}$ and sacrificed 448 days post-injection which shows retention of americium within the thyroid to be primarily in the interfollicular region (I). Retention in the colloid (C) and the follicular epithelium (arrow) is low. 50 day exposure. H & E. X 600.

Fig. 2. Higher magnification of thyroid autoradiogram from same dog as Fig. 1 showing localization of the americium burden to be primarily in the interfollicular region. 14 day exposure. H & E. X 1100.

Fig. 3. Microphotograph of normal beagle thyroid showing the relatively dense argyrophilic reticulum (arrow) of the interfollicular region. Nasser Reticulum stain. X 600.

Fig. 4. Autoradiogram of thyroid arteriole from beagle injected with $4.53 \mu\text{Ci } ^{241}\text{Am/kg}$ and sacrificed 24 hours post-injection showing localization of americium within the inner aspect of the arteriole wall (arrow). 50 day exposure. H & E. X 600.

Fig. 5. Autoradiogram of thyroid gland of same dog as Fig. 4 showing foci of intense activity within the interfollicular area. 50 day exposure. H & E. X 600.

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SOME OBSERVATIONS ON THE DEPOSITION OF ^{241}Am IN THE THYROID GLAND

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The observation that the concentration of ^{241}Am in the thyroid gland is significant was quite unsuspected. The concentration found in this organ ranged from 0.7 to 4.7 times the skeletal concentration (Atherton, D. R., et al., 1968). For this reason a study was initiated to determine the factor or factors responsible for this deposition as well as a study of its intraorgan and intracellular distribution.

A beagle dog was injected with 2.78 $\mu\text{Ci/kg}$ of ^{241}Am and sacrificed 22 days later. The thyroid was removed immediately and frozen in liquid N_2 . The parathyroids were dissected away from the thyroid. A small portion of one thyroid was taken for radioautography.

The thyroid was thawed to 0°C and then homogenized in cold 0.9% saline with 10 strokes at low speed in a teflon homogenizer. The homogenate was centrifuged at 100 RPM for 5 minutes. The resulting supernatant (I) was decanted and samples were taken for counting. The remaining sediment contained fibrous connective tissue (residue I). This was then counted. The supernatant (I) was then centrifuged at 1000 g to remove nuclei, whole cells and cell membranes. The sediment was added to the original fibrous sediment. The resulting supernatant (II) was fractionated into mitochondrial and microsomal fractions. The activities associated with these different fractions are shown in Table I. The major part of the activity was found in the original connective tissue residue. The amount of activity associated with the subsequent fractions was not significant when compared with the total amount found in the connective tissue residue.

TABLE I

FRACTION	WEIGHT	% INJECTED DOSE	COUNTING ERROR (%)
Whole Frozen Thyroid	1.147g	0.02336	1.17
Total Homogenate		0.02085	1.16
Supernatant I		0.004	2.4
Residue I		0.01761	1.7
Supernatant II			
Mitochondria		0.0012	
Microsomes		0.009	3.5
105,000 g Supernatant			
Residue II		0.002	2.2
Total Residue (I + II)	0.215g	0.01961	

The high concentration of ^{241}Am in the thyroid (0.7 - 4 times that of the skeleton and exceeded only by that of the liver) is undoubtedly related to the high vascularity and large blood flow of this organ. The deposition in the connective tissue may be related to binding by the anionic groups of the mucopolysaccharides of the ground substances. Experiments are under way to isolate and identify the compound or compounds responsible for this binding.

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^{241}Am IN THE BLOOD: IN VIVO AND IN VITRO OBSERVATIONS.

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Abstract: After AmIII is given intravenously to the beagle, the concentration in blood decreases at a rate similar to those of divalent alkaline earths. Very little ^{241}Am was found in association with blood cells. No binding of ^{241}Am with plasma proteins could be demonstrated in samples obtained 30 minutes after injection. Complexes of ^{241}Am with both transferrin and albumin were obtained in vitro using normal and abnormal human blood. They were sufficiently stable to be isolated in low yield by gel filtration plus ion exchange chromatography. Further studies with dogs indicated that these complexes are formed in vivo very soon after injection.

Introduction

Trivalent ^{241}Am was shown to leave the blood of the rat at a rate more comparable with that of divalent ^{45}Ca than that of tetravalent ^{239}Pu when the nuclides were given intravenously(1). Early work had shown that ^{239}Pu was associated with serum proteins and more recently a PuIV transferrin complex has been isolated from serum(2). The complex has been observed in the blood of rats, beagles, and humans(2,3,4). In addition to the transferrin bound PuIV, varying amounts of PuIV were found in the low molecular weight fraction of serum, and the distribution between the two fractions was related to the degree of saturation of transferrin with iron(4). In the beagle the low molecular weight fraction decreased more rapidly after intravenous injection than that bound to transferrin(3).

The distribution of AmIII in human serum has been studied in vitro (5). AmIII was bound by proteins but the complexes appeared to be less stable than the PuIV transferrin complex(5). In this paper further studies of AmIII in blood are presented. They include the rate at which AmIII leaves the blood, the association of AmIII with blood cells and the constituents of serum following intravenous injection in the

beagle, and in vitro studies using both normal human serum and sera deficient in iron and albumin.

Materials and Methods

Young adult beagles were injected intravenously with ^{241}Am in 0.08M citrate buffer of pH 3.5. There were two dogs at each of the dose levels 0.9, 0.3, and 0.1 $\mu\text{Ci/kg}$. Blood samples were drawn at intervals ranging from 5 minutes to 24 hours after injection. The blood was weighed and the packed cell volume was measured. The weight of plasma was derived from those two measurements, since preliminary measurements indicated little association of ^{241}Am with cells. An additional dog was given 4.5 $\mu\text{Ci/kg}$ and blood was obtained at 1 and 5 minutes.

Three human sera from two donors were incubated with ^{241}Am or ^{241}Am and ^{59}Fe in vitro for 30 minutes. The first serum was normal with respect to its constituents. In the second iron and albumin were depleted artificially by treatment with citrate at pH 4.5 and subsequent dialysis. The third was a clinically abnormal serum in which the iron concentration was 10 $\mu\text{g}/100\text{ ml}$ and the total iron binding capacity was 110 $\mu\text{g}/100\text{ ml}$. Albumin was very low (37% of total protein).

^{241}Am and ^{59}Fe were measured in a well-type NaI(Tl) crystal gamma detector(6). The concentration of ^{241}Am in blood cells was measured by a dilution method(7). Determination of ultrafilterable ^{241}Am in serum was attempted using the method for calcium(8).

Serum constituents were separated by gel filtration and ion exchange chromatography. High and low (< 5000 MW) molecular weight fractions were obtained using a short column, 25 cm x 1 cm, of Sephadex G-25, which was eluted with a buffer of 0.01 M tris

(hydroxymethyl)aminomethane (TRIS) + 0.15 M NaCl, pH = 8. Serum proteins were separated from low molecular weight species and into three groups using a double column of Sephadex G-100 → G-200 which was eluted with 0.1 M TRIS + 0.7 M NaCl + 0.0015M NaN₃, pH = 7.5(9). Peak I contained macroglobulins and high molecular weight lipoproteins, the bulk of the globulins comprised peak II, and peak III included albumin, transferrin and some α -globulins(10).

Serum proteins were separated into three different peaks using the ion exchange resin, DEAE-Sephadex. The serum was put on a column containing 7.5 g of resin at pH = 8, and a linear gradient of 0.1 M TRIS → 0.1 M TRIS + 0.5 M NaCl was applied. The first peak contained β - and γ -globulins including the β -globulin transferrin, the second was mainly α -globulins plus some β -globulins, and the third was albumin and traces of α - and β -globulins(11). A similar method was used to separate transferrin and albumin obtained in peak III from the G-100 → G-200 columns. The pooled peak III material was diluted by 20, adsorbed on DEAE-Sephadex and eluted using the linear gradient 0.1 M TRIS → 0.1 M TRIS + 1 M NaCl. Protein concentration in the various eluates was determined spectrophotometrically by measuring the optical density at 280 m μ .

Results

The rapid rate of decrease in concentration of ²⁴¹Am in plasma after intravenous injection is shown in Fig. 1. The first three and the last two points are the average of six determinations, and the intermediate ones are the average of two or four. The average weight of the dogs was 12.2 kg. The mean plasma volume is (51.4 ± 12.4) ml/kg(12). Thus at 5 minutes, 1 hour, and 1 day an average of 39, 9.8, and 0.28% of the injected ²⁴¹Am, respectively, was circulating.

A preliminary in vitro study with canine blood showed that after 30 minutes incubation the concentration of ^{241}Am in blood cells was only 0.005 times that in plasma. The lack of appreciable association with the cells was confirmed in vivo. The ratio of the concentration in cells to that in plasma was 0.025 in a sample obtained at 8 hours and 0.069 in one at 24 hours.

The ultrafiltration method, which was developed for calcium in serum, was found unsuitable for tripositive americium. After ultrafiltration a significant fraction of the ^{241}Am was adsorbed in the membrane that separated the plasma concentrate and ultrafiltrate. This interaction of the membrane with AmIII made it impossible to obtain valid quantitative results.

Beagle blood (30 ml) was incubated with 0.1 ml of the ^{241}Am citrate solution that was used for the injections. A portion of this tagged serum was separated on a G-25 column. 62% of the ^{241}Am was eluted with the proteins, about 4% was eluted in the lower molecular weight range, but 34% remained on the resin. These results showed that in vitro ^{241}Am is associated with serum proteins or large colloidal particles and also that the resin interacts with Sephadex resin in the system. When the G-100 → G-200 gel filtration columns were used, most of the ^{241}Am stayed on the resin. The ^{241}Am that was eluted appeared in three peaks. The first and largest was between protein peaks I and II, the second was in the descending part of peak III, and the third in the low molecular weight range. Further separation of peak III material by ion exchange was attempted, but no ^{241}Am was recovered.

When the whole serum was separated on DEAE-Sephadex, about 55% of the ^{241}Am was eluted in three overlapping peaks. The first fell

between the second protein peak and the albumin peak, and the second and smallest coincided with albumin. The third was essentially beyond the protein range, and it did not drop sharply but trailed out as long as elution was continued. Of the 45% left on the resin about half was in the upper tenth of the column.

These separation methods were also used on serum obtained 30 minutes after injection, but no significant results were obtained.

Since losses on the resins were high and interpretation of elution patterns was difficult, four ^{241}Am solutions were studied by gel filtration and ion exchange. They were (1) the ^{241}Am citrate solution described above diluted with physiological saline of pH ~ 7 , (2) ^{241}Am citrate diluted with a physiological phosphate buffer of pH ~ 7.4 , (3) ^{241}Am in 0.1 M HNO_3 + saline, (4) ^{241}Am in 0.1 M HNO_3 + phosphate buffer. The volumes were comparable to those of the sera in above studies. In the G-100 $\rightarrow$ G-200 system, ^{241}Am in (1) was eluted mainly in a single peak in the low molecular weight range with a yield of 37%. The same peak was observed for (2) and there was also a sharp peak at the breakthrough-point of non-adsorbed high molecular weight material as determined by Dextran Blue. 50% of the ^{241}Am in (2) was eluted. In (3) only 2.5% was eluted as the high molecular weight peak, followed by a trailing increase in the low molecular weight range. Of (4) 41% was eluted as the high molecular weight peak followed by a high smear with a suggested peak in the intermediate molecular weight range. The DEAE Sephadex system apparently could not separate hydrolyzed, complexed, and non-complexed Am for all four solutions gave a single large trailing peak at 0.13 M NaCl in the elution gradient. This corresponds to the third ^{241}Am peak in the serum protein elution pattern. The

recoveries were 88%, 17%, 19%, and 23%, respectively.

In the next series of experiments human serum that was artificially deficient in both iron and albumin was used. This serum would accentuate complex formation with transferrin. After incubation with americium citrate, the serum constituents were separated on G-100 → G-200 as shown in Fig. 2. There was a small peak between the first two protein peaks, a larger peak occurring with the third protein peak, and a similar one in the low molecular weight range. The third protein peak was further separated on DEAE-Sephadex and the results are shown in the insert in Fig. 2. A small amount of the ^{241}Am was recovered with albumin and an even smaller amount with transferrin.

When the normal serum was incubated with americium citrate and put directly on DEAE-Sephadex, most of the americium was eluted in two peaks near the albumin peak. This was also about the point in the gradient at which the four protein free americium solutions were eluted.

In a study with purified, lyophilized dog albumin incubated with ^{241}Am in physiological saline solution and chromatographed on DEAE-Sephadex, two closely associated but distinct peaks of ^{241}Am were found. The trailing peak coincided with the albumin. The other peak was not associated with any protein. This albumin eluted later than albumin in fresh serum (Fig. 3).

When the serum that was clinically deficient in iron and albumin was incubated with americium in nitrate solution, i.e., not complexed, an additional peak was found in the high molecular weight elution range of the G-100 → G-200 system. The peak accompanying the third protein peak and the low molecular weight peak were also observed. Recovery was 30%. Separation on DEAE-Sephadex resulted in three ^{241}Am peaks,

each of which reached a maximum on the ascending side of one of the protein peaks (Fig. 4). The third was also at the point at which americium nitrate diluted with phosphate buffer (and the other three solutions) eluted (Fig. 4). Recovery was 80%.

Experiments were then done with tracer and chemically significant amounts of iron. The clinically iron deficient serum was incubated with ^{241}Am in nitrate solution and then with ^{59}Fe in chloride solution. The serum was separated on DEAE-Sephadex, and the maxima of the ^{59}Fe peak and the first ^{241}Am peak coincided as shown in Fig. 5.

Next the clinically iron deficient serum was treated with $\text{Fe}(\text{NH}_4)_2\text{SO}_4$ to increase the amount of iron bound by transferrin. Then it was incubated with ^{241}Am and separated on DEAE-Sephadex. The amount of ^{241}Am in the first peak was reduced markedly with respect to the amounts in the other two.

The elution pattern obtained when ^{241}Am in nitrate solution was incubated with serum from a healthy donor is also shown in Fig. 5. Only a little ^{241}Am was eluted with transferrin. In this serum the iron concentration was high and the albumin concentration was normal.

After the above results were obtained in vitro with human sera, an additional in vivo canine experiment was done. Serum from blood that was drawn approximately 1 and 5 minutes after injection of $4.5 \mu\text{Ci } ^{241}\text{Am/kg}$ was separated on the gel filtration and ion exchange systems. When the G-25 Sephadex column was used 56% of the ^{241}Am in the 1 minute serum was eluted with the proteins and a total of 68% was recovered from the column. The concentration of the 5 minute serum had decreased to 0.61 times that of the 1 minute serum, 64% of its ^{241}Am was eluted with the proteins and 75% was recovered from the column.

The results of the separation on G-100 → G-200 are shown in Fig. 6. In the 1 minute sample ^{241}Am peaks were observed with the first and third protein peaks, just preceding the second, and in the low molecular weight range. The ^{241}Am peak at the third protein peak showed an asymmetric broadening in the transferrin region. Total recovery was about 51%. Approximately 4% was found with the first protein peak, 7% preceding and with the second, 7% with the third, and 33% beyond the protein range. In the case of the 5 minute sample recovery was about the same, 47%, with 2% in the first peak, 10% in each of the next two, and 25% beyond the protein range. This suggests that the very high and the low molecular weight forms are being cleared more rapidly.

When the 1 minute sample was separated on DEAE-Sephadex, little ^{241}Am was eluted with the proteins. Two small peaks were observed, one with the first protein peak and one following the second. The same two peaks, slightly enhanced, were observed in the 5 minute serum (Fig. 7).

Discussion

These experiments have been done to identify complexes between large molecules and ^{241}Am formed in the blood and to determine if they are formed in vivo as well as in vitro.

Early association of ^{241}Am with blood cells was shown to be minimal. Determination of the association, or the lack of it, with serum constituents proved difficult for two reasons. First, the interactions of the separation systems with ^{241}Am distorted the distribution pattern so that quantitative results could not be obtained and qualitative results were somewhat limited. Second, the concentration of ^{241}Am in blood decreases so rapidly that only samples obtained shortly after injection contain enough ^{241}Am for the analytical methods used.

The results obtained with canine sera on G-25 Sephadex were the most quantitatively consistent, for 62, 56, and 64% of the ^{241}Am eluted with the proteins in the in vitro and 1 and 5 minute in vivo samples, respectively. Thus, under both sets of conditions more than half of the ^{241}Am is bound to proteins or other chemical entities that are excluded from the gel phase.

The binding of ^{241}Am by transferrin was well established in the experiments with the iron deficient sera. Coincidence of the maxima of the ^{59}Fe and ^{241}Am peaks in the double tracer studies, and the ion exchange separation of the third gel filtration peak into transferrin and albumin (Fig. 2), served to identify the ^{241}Am transferrin complex. The decreased formation of the ^{241}Am complex in normal serum compared with that in the iron deficient serum (Fig. 4), and the decrease in the complex when the deficient serum was pretreated with iron, showed that transferrin bound iron in preference to americium. The specific iron transport function of transferrin and the use of ^{59}Fe greatly facilitated the identification of the AmIII transferrin complex.

Other complexes were less readily identified since several inorganic solutions of AmIII at physiological pH were partly eluted in the protein range in both systems. Uncomplexed AmIII in the presence and absence of phosphate, and AmIII citrate complex to which phosphate had been added, all yielded a high molecular weight peak on G-100 → G-200. These three and AmIII citrate diluted with saline were eluted from DEAE-Sephadex near the point on the gradient at which albumin is eluted. Thus the occurrence of an AmIII peak with the albumin peak when the serum is separated by the ion exchange system does not completely establish the AmIII albumin complex (Fig. 4). In the

presence of hydroxyl and/or phosphate ions AmIII is eluted in this range, probably in colloidal form. However, this colloidal material is eluted much before the third peak (albumin and transferrin) on G-100 to G-200. The subsequent separation of the third peak into transferrin and albumin fractions with coincident ^{241}Am peaks (Fig. 2) adds to the identification of the AmIII albumin complex. Further evidence for this complex was obtained using the lyophilized albumin.

A complex with a third, but yet unidentified, protein appears highly likely. In the gel-filtration separation an ^{241}Am peak was observed on the ascending side of the second protein peak, and in the ion exchange separation there was a peak near the second protein peak. In both systems α -globulins are eluted in these ranges.

In summary, in vitro AmIII forms a complex with transferrin which appears to be less stable than that with FeIII or PuIV. It also is bound to albumin and probably to a third protein which could be an α -globulin. Even though AmIII disappears from the blood very rapidly following intravenous injection, protein complexes are formed in vivo.

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Fig. 1. Comparison of the concentrations of ^{239}Pu , ^{226}Ra and ^{241}Am in plasma during the first day after intravenous administration of the nuclides.

Fig. 2. Distribution of ^{241}Am in vitro in iron and albumin deficient human serum obtained by gel-filtration. Insert, separation of pooled peak III material by anion exchange chromatography.

Fig. 3. Elution pattern of purified dog albumin tagged with ^{241}Am (anion exchange chromatography).

Fig. 4. Elution profile resulting from ion exchange chromatography of in vitro tagged iron and albumin deficient human serum.

Dashed-dotted line shows the elution pattern of a protein-free ^{241}Am preparation under identical experimental conditions.

Fig. 5. Comparison of the elution spectra of iron and albumin deficient serum (top) and normal human serum (bottom) tagged in vitro with ^{241}Am (ion exchange chromatography).

Fig. 6. Distribution of ^{241}Am in dog serum at 1 minute (top) and 5 minutes (bottom) after injection of ^{241}Am in citrate (gel filtration).

Fig. 7. Distribution of ^{241}Am in dog serum of 1 minute (top) and 5 minutes (bottom) after intravenous injection of ^{241}Am citrate (ion exchange chromatography).

NOTE ON THE EXCHANGE OF $^{239}\text{PuIV}$ BETWEEN
TRANSFERRIN AND FERRITIN IN VITRO

F. W. Bruenger, Betsy J. Stover, W. Stevens and David R. Atherton.

Abstract: The transfer of $^{239}\text{PuIV}$ from transferrin, which is the transport protein for iron, to ferritin, which is a storage protein for iron, has been investigated by gel filtration and gel electrophoresis. The results show that the reaction

$\text{PuIV-transferrin} + \text{ferritin} \rightarrow \text{transferrin} + \text{PuIV-ferritin}$
occurs in vitro at pH 8, and that under the specific conditions of this experiment the ferritin complex is more stable than the transferrin complex.

Introduction

Iron in blood serum is complexed by transferrin (1). This protein then carries the iron to the erythroid cells for hemoglobin synthesis as needed. Excess iron is stored primarily in the liver and spleen as ferritin and hemosiderin, two iron storage compounds (2,3). PuIV also complexes with transferrin in blood serum (4,5,6). It does not bind, however, with blood cells to any great extent but it is stored in the liver and skeleton (7). Preliminary analyses of clear liver homogenates free of particulate material (100,000 x g supernatant) indicated that PuIV is also associated with ferritin in the liver. The following experiment was done to determine if the reaction

$\text{PuIV-transferrin} + \text{ferritin} \rightarrow \text{transferrin} + \text{PuIV-ferritin}$
occurred at physiological pH.

Experimental Procedures

Blood (150 ml) from a healthy young beagle was allowed to clot. The serum was separated by centrifugation and divided into 6 roughly equal fractions. A total of $\sim 3 \mu\text{Ci } ^{239}\text{PuIV}$ in $\sim 0.1 \text{ ml } 0.08 \text{ M}$

citrate was added in small quantities to the 6 fractions which were then incubated for 30 minutes at 40° C. The combined fractions were loaded on a column of 35 g DEAE-Sephadex A-50 that had been equilibrated with 0.1 M TRIS, pH 8. The linear elution gradient used was 0.1 M TRIS + 0.1 M NaCl → 0.1 M TRIS + 1 M NaCl, pH 8. The first major protein peak contained the PuIV-transferrin complex, and it was identified visually by the pink color of the Fe-transferrin complex. The fractions comprising the peak were pooled, dialyzed versus distilled H₂O at pH 8, concentrated by pervaporation, and then made approximately 0.9% in NaCl.

A portion of this solution containing the PuIV-transferrin was incubated with commercial equine ferritin at pH 8 for 24 hours. The resulting mixture was analyzed by the following methods:

gel filtration on a column of Bio Gel A-1.5m, eluted

with 0.1 M TRIS + 4% NaCl,

gel filtration on columns of G-100 → G-200, eluted with

0.1 M TRIS + 4% NaCl, and

gel electrophoresis on a 7% acrylamide gel.

The material was applied to the top of the gel columns with blotters. A buffer containing 0.2 M glycine and 0.025 M TRIS of pH 8.6 was used and the applied potential was ~ 30 V/cm. Duplicate samples were run. One was stained with amido-black to locate the bands, then the other was cut into 14 roughly equal slices which were wet ashed and analyzed for ²³⁹Pu. The PuIV-transferrin preparation was also studied by gel electrophoresis.

Protein concentration was determined spectrophotometrically.

A liquid scintillation system was used to measure ^{239}Pu .

Results and Discussion

In prior experiments of a related nature the following results had been established. The first concerns the preparation and separation by ion exchange on DEAE-Sephadex of the solution that contained the PuIV-transferrin complex. The only PuIV eluted in this range was that bound by transferrin so that the solution contained no PuIV either in colloidal aggregates or in association with ions or molecules of low molecular weight. Second, the G-100 $\rightarrow$ G-200 gel filtration separated ferritin (MW $\sim$ 400,000) and transferrin (MW $\sim$ 74,000) into two distinct peaks. However, the ferritin was eluted at the breakthrough point and thus would not be separated from colloidal aggregates of ^{239}Pu . In the Bio-Gel A-1.5m system ferritin was eluted considerably beyond the breakthrough point so that colloidal aggregates would be separated from ferritin. This system did not resolve ferritin and transferrin well.

When the solution containing equine ferritin and canine PuIV-transferrin was separated on G-100 $\rightarrow$ G-200, approximately 3/4 of the recovered ^{239}Pu was found in the ferritin peak and 1/4 in the transferrin peak. When this solution was separated on Bio-Gel A-1.5m, less than 5% of the recovered ^{239}Pu was eluted at the breakthrough point. This is evidence that the following reaction

$\text{PuIV-transferrin} + \text{ferritin} \rightarrow \text{transferrin} + \text{PuIV-ferritin}$
occurs in vitro at pH 8 with little formation of colloidal ^{239}Pu , and probably without formation of intermediates.

TABLE 1
Electrophoretic Distribution of ^{239}Pu in Gels

Slice no.	Canine Transferrin		Canine Transferrin + Equine ferritin	
	Proteins	% ^{239}Pu	Proteins	% ^{239}Pu
1	Front	61.2	Front	21.9
2		8.2		1.3
3		7.1		1.5
4		4.8		1.1
5		3.1		1.1
6		2.1		1.4
7		1.6		1.1
8		1.4		1.2
9		1.1		1.3
10	2 bands of	3.1	2 bands of	3.0
11	transferrin	4.5	transferrin	1.9
12		0.7		2.1
13		0.6	2 bands of	30.8
14		0.7	ferritin	30.4

The results of the gel electrophoreses are summarized in Table 1. Two pink bands of transferrin, one in slice 10 and one in 11, were observed in both gels, and the ferritin was seen as two brown bands which were in the last two slices. (Neither protein is electrophoretically homogeneous.) The PuIV-transferrin dissociated during electrophoresis and 61% of the ^{239}Pu moved with the front. There were decreasing amounts in succeeding slices and then slightly increased amounts in the transferrin bands. In the transferrin plus ferritin sample 22% moved with the front followed by small amounts in the transferrin bands, and then 62% in the ferritin bands. This distribution is consistent with the distribution obtained with the G-100 → G-200 system if it is assumed that only the transferrin complex dissociates in the electric field. (The glycine buffer could also be a factor in the dissociation.)

In summary, PuIV transfers from transferrin to ferritin in vitro at pH 8. This shows that, under the specific conditions of this experiment, the ferritin complex is more stable than the transferrin one. The electrophoretic results support this finding.

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EHPA-SCINTILLATOR METHOD: ANALYSIS OF
BONE SAMPLES FOR ^{239}Pu

David R. Atherton

Introduction

The bones from 1-level ($\sim 0.017 \mu\text{Ci/kg}$) plutonium dogs can be expected to present the Analyst with about 0.0014 dose per gram of ash or about 260 α c/m (2π). Due to the problems of distributing bone salt uniformly on planchets and of making more than a few milligrams adhere to the planchet, one should not attempt to mount anything in excess of about 16 mg of bone ash for 2π α counting. In this case then, the sample would produce about 4 c/m with a perfect mounting. Such samples require very long counting times, in addition to the difficulties referred to above, which makes direct sampling and α -counting quite unreliable for material with a low ^{239}Pu concentration.

The Primene Method* we described in 1963 (Anal. Chem. 35, 11) is somewhat tedious so the method described below was developed.

Materials

Equipment:

Ordinary laboratory glassware including separatory funnels, beakers, volumetric flasks, pipets, 50 ml Erlenmeyer flasks, etc.

A 3" photomultiplier with appropriate electronic gear including preamplifier, amplifier, scaler, timer, and high voltage supply.

A device to shake separatory funnels is desirable.

*The Primene Method also needs some more development work--probably a step for the reduction of plutonium would result in a dependable method.

Supplies:

Concentrated nitric acid (HNO_3); Di-2-ethyl hexyl phosphoric acid (EHPA); toluene; 1,4-bis-2(5-phenyloxazolyl) benzene (POPOP); 2,5-diphenyloxazole (PPO); absolute ethyl alcohol; ammonium carbonate ($(\text{NH}_4)_2\text{CO}_3$); sodium hydroxide (NaOH); and sulfur dioxide (SO_2).

Solutions:

4N NaOH

Saturated solution of $(\text{NH}_4)_2\text{CO}_3$

1N and 4N HNO_3

4.33 x scintillator solution is prepared by dissolving 0.433 g POPOP and 17.32 g PPO per litre of toluene.

1:1 solution of EHPA:toluene is prepared by mixing equal volumes of the two reagents. The EHPA, as obtained from the manufacturer, contains variable but significant and undesirable amounts of iron which are removed as follows:

Wash once with an equal volume of 4N HNO_3 .

Wash once with a 1/2 volume of 4N NaOH. $\text{Fe}(\text{OH})_3$ is precipitated but is not easily separated from the EHPA-toluene solution; therefore, after the H_2O phase has been removed, the organic phase is passed through a roughing filter where most of the $\text{Fe}(\text{OH})_3$ is removed and then through a 1.2 μ millipore filter.

It is then washed twice with an equal volume of a saturated solution of ammonium carbonate, once with an equal volume of 4N HNO_3 , and finally twice with an equal volume of water.

Water saturated with SO_2 is prepared by bubbling SO_2 slowly into water. When the bubbles are no longer absorbed in the water the solution is saturated.

A ^{239}Pu standard is made by placing 1.00 ml of a 1N HNO_3 solution, containing a known amount of ^{239}Pu , in a 50 ml Erlenmeyer flask. To this is added 25.0 ml of EHPA:toluene solution, 15.0 ml of 4.33 x scintillator solution, and 10.0 ml of absolute alcohol. After capping, the flask is shaken until clear.

A sample for measuring background is prepared by placing 1.00 ml 1N HNO_3 in a 50 ml Erlenmeyer flask; 25 ml of EHPA:toluene, 15 ml of 4.33 x scintillator, and 10 ml of absolute ethyl alcohol are then added and, after capping, are shaken until the solution is clear.

Procedure

Bone specimens are ashed in a muffle furnace and put into solution with HNO_3 . Care is taken to have the final solution in the range of 1 to 2 molar with respect to HNO_3 .

If the HNO_3 concentration is not known the sample is dried under an infra-red lamp and redissolved in 1N HNO_3 . The volume of all samples is adjusted to between 40 and 50 ml.

The Pu is reduced by the addition of 2 ml of saturated SO_2 solution, covering (Saran Wrap secured by a rubber band), and standing for 16 to 60 hours. SO_2 is removed by placing the samples in a 90°C (to boiling) water bath for 3 hours.

The volumes of the samples are readjusted to 40 to 50 ml with 1N HNO_3 and then transferred to separatory funnels.

25 ml of a 1:1 solution of EHPA:toluene are added and the funnels shaken for 5 minutes. Following phase separation, the aqueous phase is discarded and the organic phase is transferred to a 50 ml Erlenmeyer flask. The funnel is rinsed first with 15 ml of 4.33 x scintillator solution and once with 10 ml of absolute ethyl alcohol; the rinses

being added to the organic phase. Saran wrap secured by rubber bands is used to cap the samples which are then shaken until clear.

A control sample of bone solution is run with each set so that correction for yield can be made. Pu concentration of the control bone solution is made by α -counting a small aliquot whose mass is taken into account in its evaluation.

The samples are counted by placing them on a 3" photomultiplier tube appropriately connected to pre-amplifier, amplifier, and scaler-timer unit. Pu content is estimated by the relative count rate of the sample and a ^{239}Pu standard.

Discussion

In the development of this method variables were examined with a view to application rather than to a definition of limits. It was found that changes in the method's yield of Pu from bone samples was not affected by changes in: (1) H^+ concentration over the range of 0.1 to 2N HNO_3 ; (2) Bone ash in the range of 0.08 to 2.7 g per 50 ml of aqueous phase; (3) ^{239}Pu concentrations ranging from 10 to 1000 pCi per 50 ml of aqueous phase; and (4) SO_2 reduction times in the range of 16 to 60 hours. 4-hour reduction times appeared to be insufficient.

When very small bone samples are analyzed by this method it was found that phase separation proceeded better if non-radioactive bone ash was added such that each sample contained at least 0.1 g per 50 ml solution.

Aqueous phase to organic phase volume ratios other than about 2:1 were not studied.

The effect of SO_2 on scintillator is drastic. In one experiment it was found that no scintillator remained after contacting a sample

containing SO_2 . In fact its count rate was about $1/2$ the background count rate which is equal to the phototube noise level.

Yields have been about 85% for the first 30 or so runs (~ 100 samples).

With our present electronic gear counting efficiencies are very close to a count per disintegration.

Observed background is due to about equal contribution from tube noise and light flashes in the background blank. The total amounts to about 20 c/m. It is thought that the contribution of tube noise could be reduced to some extent by cooling the photocathode (and sample).

Based on the above, samples containing about 15 pCi can be evaluated to about $\pm 5\%$ if 100 minute counting times are used. This means that the method could be applied to the analysis of whole bones of 0.1 level ($0.0006 \mu\text{Ci/kg}$) plutonium dogs with quite good precision.

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