Health Physics Vol. 52, No. 2 (February), pp. 179–192, 1987
Printed in the U.S.A.

701378

0017-9078/87 $3.00 + .00
© 1987 Health Physics Society
Pergamon Journals Ltd.

● *Paper*

ACTINIDE DISTRIBUTION IN THE HUMAN SKELETON

Ronald L. Kathren*
Pacific Northwest Laboratory and United States Transuranium Registry, Richland, WA 99352

and

James F. McInroy**
Los Alamos National Laboratory, Los Alamos, NM 87545

and

Margery J. Swint†
United States Transuranium Registry, Richland, WA 99352

(*Received* 21 *June* 1985; *accepted* 8 *September* 1986)

***Abstract*—Radiochemical analysis of two half skeletons donated to the United States Transuranium Registry from individuals with occupationally incurred depositions, one of ^{241}Am and the other of ^{239}Pu, revealed an inverse proportionality between the concentration of actinide in the bone ash and the fraction of ash (or the calcium content of the ash). A similar relationship was observed in a third case suffering from osteoporosis, but the slope was shallower. These results suggest that accurate estimates of the total skeletal content of actinide can be made from radiochemical analysis of only a few bone samples.**

INTRODUCTION

THE UNITED States Transuranium Registry (USTR) was established in 1968 to evaluate human experience with Pu and other transuranic elements (Br81; Sw84). From radiochemical analyses of selected donated tissues or the whole body, the distribution patterns of actinides within the body can be determined and estimates made of internal deposition. These data are useful in determining the validity of existing biokinetic models, possibly leading to refinements or to the development of new models.

To date, two whole-body contributions have been received and analyzed by the USTR. The first was obtained in1979. The results of postmortem radiochemical analyses of the tissues of this donor, along with health physics implications and the development of sophisticated biokinetic models based on the analytical results, have been reported (Br85; Du85a; He85; Mc85a; Mc85b; Pa85). Radiochemical analysis of the second whole body contribution, received in 1983, has only recently been completed; data analysis is now in progress.

Skeletal distributions of Pu and other actinides have been studied widely in experimental animals and to a much lesser degree in humans and have been the subject of several excellent reviews (Du62; Du73; ICRP72a; Je72; Ne79; Va73). The earliest studies (Ha47) described the deposition of both Pu and Am on the bone surfaces, a finding many times confirmed, with the actual quantity deposited in the skeleton a function of the amount and route of intake, physico-chemical form of the material, and certain biological factors such as the age of the animal (Du62; Je72; Ll72; Ne79; St69; St72; Va73). Studies show that skeletal uptake is smaller in older animals and the growth activity of the bone exerts a significant influence on the deposition (An83; Du73; Du76). Moreover, initial deposits of Pu are non-uniform, localizing primarily on the endosteal surfaces and, to a lesser extent, the periosteal surface and vascular channels of cortical bone (Je72). Bone remodelling, which varies inversely with the age of the animal, results in decreased concentration of Pu on trabecular surfaces as well as a decreased total dose to cells. Of interest is the fact that the remodelling rate is variable, being approximately twice as fast in vertebrae as in the distal end of the femoral shaft (St72). Remodelling is also decreased, at least in dogs, at high levels of exposure (St72).

Following intake, the greatest uptake and deposition are generally thought to initially occur at sites of high growth activity, such as in the metaphyses of young animals, with rapid burial or displacement as endochondral ossification progresses. Although bone remodelling ulti-

* Work performed for the U.S. Department of Energy under contract DE-AC06-76RLO1830.
** Work performed for the U.S. Department of Energy under contract W-7405-ENG36.
† Work performed for the U.S. Department of Energy under contract EY-AC06-76RLO1837.

0005608

LANL

mately tends to move the actinide to the bone volume from the surface, initial uptake inside of cortical bone is minimal or absent (Pr78). More recently, studies of the mouse have shown that the rate of Pu deposition is determined by the blood supply, at least for deposition on the endosteal surfaces (Hu82). In studies of seriously ill humans injected with Pu experimentally, deposition was found on the endosteal surfaces, with the greater concentrations observed in the axial skeleton as compared with the appendicular skeleton at 15–17 mo postinjection (La79; La81a; La81b; Sc81).

On a macrodistribution scale, concentrations of actinides are expectedly greater in trabecular than in compact bone. Thus, in studies of ^{241}Am metabolism in the baboon, concentrations were greatest in the vertebrae and sternum and smallest in the long bones (Gu80). Similar findings have been made in studies of Pu in beagles (At58; St69; St72; St74). Plutonium has also been known to deposit in marrow as well as in mineralized bone (Bl71; La50). Human studies of the macrodistribution of actinides in bone have of necessity been rare but tend to confirm the findings in animals (La81a; La81b). However, at present there is no clear model of the macrodistribution of Pu and other actinides in the human skeleton. Such a model could be of considerable practical value for bone dosimetry and would also be of value to the USTR and others by providing the means for accurate estimation of the skeletal deposition from analysis of a single or small number of bone samples, rather than analysis of the entire or half skeleton.

DESCRIPTION OF CASES

Two whole bodies donated to the USTR were radiochemically analyzed for actinide content. The first of these (Case 1) was a 49-y-old Caucasian male radiochemist, 1.82 m tall who weighed, when healthy, 65 kg. Until 2 mo before death from metastatic malignant melanoma, this individual had regularly engaged in strenuous aerobic exercises as a runner, bicyclist and hiker. Past medical history revealed a diagnosis of dermatitis herpetiformis that had been treated with sulfapyridine and a malabsorption syndrome treated with a gluten-free diet since 1974. Melanoma was diagnosed in 1975, and a wide excision of a malignant lesion on his back was performed. In December 1978, a 12-mm-diameter nodule was observed in the right lung, and subsequent pleural effusion and metastases followed, resulting in death in March 1979. Widespread melanoma metastases were observed at autopsy throughout the body tissues including bone, especially the ribs and sternum.

The donor (Case 1) had been a research chemist from 1950–1979 and had worked with significant amounts of ^{241}Am early in his career (1952–54). Although he had no documented history of actinide intake, a routine radiourinalysis performed in 1958 revealed the presence of ^{241}Am (He85); follow-up urinalyses and *in-vivo* counting led to an estimated skeletal deposition of 3.96 kBq (107 nCi), based on inhalation as the presumed route of intake. Postmortem radiochemical analysis of the body resulted in an estimated total body deposition of 5.44 kBq (147 nCi) of ^{241}Am, of which 82% or 4.44 kBq (120 nCi) was estimated to reside in the skeleton (Br85; Mc85a). An elevated level of ^{241}Am was found in the soft tissues of the left hand which raised the possibility of a hitherto unrecognized contaminated wound as a route of entry.

The second donor (Case 2) was a 62-y-old Caucasian metallurgist, 1.73 m tall and weighing 78 kg, who enjoyed good general health until 1968 when he suffered a coronary occlusion at age 48. His subsequent physical activity included walking and riding a stationary bicycle the equivalent of 4 km daily, 5 d per week. In 1976 a second coronary occlusion occurred and was followed by an uneventful recovery. He continued to work and retired in January 1982, about 1 y before his death from respiratory failure consequent to pneumonia in December 1982. His medical history also showed surgical repair of a bilateral hernia and an appendectomy.

Case 2 was employed in Pu alloy research and Pu weapons work from 1945 until his retirement in 1982. There was potential for moderate inhalation exposure to Pu from 1945–1957; no wounds or ingestions were recorded. Positive nasal wipes with >1 Bq of activity were obtained from this individual on 16 occasions before 1957; the two most significant occurred in 1945 and showed 32.7 and 2.6 Bq in the left and right nostrils, respectively, and 192 and 76.6 Bq (L, R). Exposure potential was probably significantly reduced in 1957 when he assumed supervisory functions. Radiourinalyses were performed at various intervals from 1945–1972, and have been reported previously (as Case 27) in the summary by Voelz and his coworkers (Vo79).

From these data, Case 2 was estimated by operational health physics staff at his place of employment to have a systemic plus lung deposition of 995 Bq (26.9 nCi) of ^{239}Pu and 10 Bq (0.27 nCi) of ^{238}Pu at the time of his retirement. About four-fifths of his ^{239}Pu deposition, some 829 Bq (22.4 nCi), was incurred in the summer of 1945. A total of 17 *in-vivo* chest counts made from 1970–1982 showed an estimated deposition of about 18.5 Bq (0.5 nCi) of ^{241}Am and less than 111 Bq (3 nCi) of ^{239}Pu based on the inferred Am:Pu ratio (Mc85b).

The *in-vivo* estimates of ^{239}Pu deposition were somewhat greater than those obtained from postmortem radiochemical analysis of the tissues, possibly due to uncertainties in the models. The postmortem analyses revealed a total body content of 248 Bq (6.70 nCi) of ^{239}Pu, of which 54% (134 Bq, 3.63 nCi) was resident in the respiratory tract, 20% (49.6 Bq, 1.34 nCi) in the liver and 21% (51 Bq, 1.38 nCi) in the skeleton. The skeleton contained 46% of the non-respiratory tract systemic burden (Mc85b), in rather sharp contrast to Case 1 in which 82% of the systemic deposition was in the skeleton.

ANALYTICAL PROCEDURES

The typical USTR protocol for acquisition and analysis of postmortem bone samples from voluntary whole-

0005669 LANL

body donations is briefly outlined below. A standard autopsy is performed and all the internal organs are removed, frozen and sent for radiochemical analysis to Los Alamos National Laboratory, Los Alamos, NM. The body is then transferred to the USTR facilities in Richland, WA. After assembly of the dissection team, the soft tissues and all bones are wet weighed, frozen and shipped to the radiochemical laboratory at Los Alamos National Laboratory (LANL).

Tissues are either analyzed whole or divided for convenience of analysis as well as to ascertain variation in distribution in larger specimens. The basic radiochemical procedure for Pu and Am in bone began with dry ashing and wet ashing followed by determination of the ash weights. After dissolution of the ash in nitric acid, an aliquot was taken for analysis. Plutonium-242 and ^{243}Am tracers were added followed by Pu and Am separation and isolation by anion exchange and electroplating onto stainless steel disks for quantitative α spectrometry: one blank and one quality control sample were analyzed with each set of 14 bone samples. The mean tracer recovery was 85 ± 7% for the ^{243}Am and 87 ± 9% for the ^{242}Pu. A detailed description of the tissue preparation and analytical procedures for Case 1 has been presented elsewhere in the literature (Bo81; Mc85a); Case 2 was prepared for radiochemical analysis in substantially the same way. The detailed radiochemical methods have likewise been described in these publications.

RESULTS

Individual analytical results are tabulated in Tables 1 and 2 for each of the cases. For Case 1, a total of 74 individual data points are given; for Case 2, 110 are listed. The different number of data points for each case resulted from differences in the way the samples were grouped and is not considered significant.

Examination of the data (Figs. 1 and 2) reveals a clear inverse linear relationship between the fraction of bone ash and the concentration of actinide in both cases. Evaluation of the data by least squares regression produced the following linear equations:

$$\text{Case 1:} \quad C = 2.95 - 3.55f \qquad (r = -0.73)$$

$$\text{Case 2:} \quad C = 0.044 - 0.068f \quad (r = -0.82),$$

in which C is the concentration of ^{241}Am (Case 1) or ^{239}Pu (Case 2) in the bone ash in units of Bq/g, f is the ratio of ash weight to wet weight, and r is the correlation coefficient. Although good correlation was achieved in both cases, there was significantly less variability in the data from Case 2. This could be attributed to several causes but most likely was largely from a power loss to the freezer in which the bones from Case 1 were stored before testing (Mc85b). This resulted in significant and variable losses of bone sample wet weights between the time of dissection and the analyses (Mc85b). In addition, there were metastases to bone and replacement of bone tissue with soft tissue.

Nonetheless, the inverse linear relationship is clear in both cases, and if the equations are normalized to a constant concentration at a specific value of f are found to have approximately the same slope. Grouping samples according to common structural characteristics in the manner of McInroy and Swint (Mc85b) reduced the number of data points to 21; using this grouping instead of individual bone samples did not, in fact, yield an appreciably different result.

DISCUSSION

The relationship of concentration in the ash to the ash fraction is not too surprising since Pu and Am deposit on the bone surfaces. The structure of cancellous or spongy bone expectedly would have larger surface area to mass ratio than compact bone and thus would be expected to have a higher actinide concentration per unit mass of ash. Thus, the observed relationship may simply be a reflection of the surface area to mass ratio of each of the bone samples, which in itself might be useful to know from the standpoint of anatomical studies or application to Reference Man data. However, as the bones or their subdivisions were analyzed *in-toto*, without removal of marrow, the amount of marrow in the bone samples could be a confounding factor, particularly if the marrow contained significant quantities of actinide.

Perhaps of greater significance is the quantity of marrow relative to the wet weight, which may be a major factor in determining the fraction of bone ash. In fact, the greater the marrow content, the smaller the bone ash fraction. Using available data on the distribution of human bone marrow (El61; ICRP75; Wo60), no correlation was found between the fraction of marrow as determined from the literature and the concentration of actinide in bone ash. Preliminary results of a joint study by USTR, LANL and Pacific Northwest Laboratory (PNL) to evaluate the actinide content of the marrow suggest that the quantity of Pu in human bone marrow relative to that in the mineral bone is comparatively small, indicating the relationship observed between concentration and bone ash fraction is indeed dependent on the bone rather than on the marrow.

The relationship between actinide concentration and bone Ca was also examined. The Ca content of 18 representative samples from Case 2 was determined and shows a mean weight fraction of Ca in the bone ash of 0.373 ± 0.069 (Table 3). This is in good agreement with the value of 0.357 calculated from the Reference Man data, which show a content of 1 kg of Ca in skeleton and an ash weight of 2.8 kg (ICRP75). Since Ca is a constant fraction of the ash, the actinide concentration is also inversely proportional to Ca content of the ash, which again is not an unexpected finding inasmuch as bone with a higher surface area to weight ratio would typically contain a proportionately greater amount of the surface depositing actinides.

The significance of this observation is that although the fraction of Ca in bone ash is constant throughout the

0005610

LANL

Table 1. Americium-241 content of bone, USTR Case 1

Sample		Weight (g) Wet	Weight (g) Ash	Weight Ash:Wet	^{241}Am Content (Bq/g ash)
Cranium-1 (occipital, parietal & major portion of frontal bones)		187	87.7	0.47	1.77
Cranium-2 (temporal & portion of frontal bone, maxilla		142	55.7	0.39	2.00
Mandible		51	17.4	0.34	1.62
Hyoid		12	0.91	0.08	2.92
Vertebral Column:					
Cervical-1		17	4.98	0.29	2.12
Cervical-3:	arch	8	2.12	0.27	2.10
	body	7	1.22	0.17	2.15
Cervical-5:	arch	9	2.34	0.26	1.97
	body	7	1.24	0.18	2.28
Cervical-7:	arch	15	3.49	0.23	2.15
	body	10	1.39	0.14	2.27
Thoracic-1:	arch	15	4.30	0.29	1.75
	body	11	1.80	0.16	2.00
Thoracic-3:	arch	16	3.44	0.22	2.15
	body	11	1.86	0.17	2.28
Thoracic-5:	arch	13	3.27	0.25	2.32
	body	12	2.34	0.20	2.22
Thoracic-7:	arch	17	4.31	0.25	2.27
	body	24	3.63	0.15	2.05
Thoracic-9:	arch	15	3.84	0.26	2.27
	body	19	3.16	0.17	2.07
Thoracic-11:	arch	19	4.45	0.23	1.70
	body	43	5.58	0.13	2.33
Lumbar-1:	arch	23	5.74	0.25	1.93
	body	54	6.17	0.11	2.18
Lumbar-3:	arch	28	7.44	0.27	1.92
	body	55	7.02	0.13	2.20
Lumbar-5:	arch	25	7.07	0.28	1.97
	body	48	6.68	0.14	2.12
Sacrum & coccyx		219	31.7	0.15	2.28
Pelvis (ischium & ilium)		373	113.9	0.31	1.33
Clavicle		44	11.0	0.25	1.34
Scapula		139	32.9	0.23	1.67
Rib-1		15	3.31	0.22	1.85
Rib-2		13	3.93	0.30	2.27
Rib-3		16	4.92	0.31	2.14
Rib-4		19	5.57	0.29	2.25
Rib-5		24	6.84	0.29	2.06

(a) Right half of skeleton except for whole of indicated vertebrae, sacrum, coccyx, hyoid and sternum.

LANL

0005611

Table 1. (*Contd.*)

Sample		Weight (g) Wet	Weight (g) Ash	Weight Ash:Wet	^{241}Am Content (Bq/g ash)
Rib-6		23	7.24	0.32	1.89
Rib-7		22	7.13	0.32	1.85
Rib-8		19	6.60	0.35	1.75
Rib-9		22	6.43	0.29	1.82
Rib-10		19	5.37	0.28	1.74
Rib-11		14	3.82	0.27	1.82
Rib-12		3	0.88	0.29	1.86
Costal cartilages		93	1.8	0.02	3.28
Sternum		83	7.3	0.09	1.83
Humerus:	PE	98	11.3	0.12	3.08
	Shaft	139	51.7	0.37	1.39
	DE	62	12.1	0.20	2.48
Radius:	PE	10	1.94	0.19	2.35
	Shaft	50	18.66	0.37	1.25
	DE	21	3.57	0.17	2.28
Ulna:	PE	39	7.03	0.18	2.40
	Shaft	51	20.62	0.40	1.14
	DE	7	1.20	0.17	2.70
Carpals		33	6.34	0.19	2.83
Metacarpals		57	12.73	0.22	2.44
Phalanges (hand)		54	11.22	0.21	2.28
Femur:	PE	266	60.2	0.23	1.88
	PS	136	58.8	0.43	1.63
	MS	115	52.9	0.46	1.60
	DS	137	46.6	0.34	1.63
	DE	225	44.7	0.20	2.70
Tibia:	PE	172	34.6	0.20	2.40
	Shaft	282	127.4	0.45	1.00
	DE	73	22.0	0.30	1.70
Fibula:	PE	18	5.17	0.29	2.00
	Shaft	79	33.1	0.42	0.85
	DE	20	2.78	0.14	2.80
Patella		40	8.00	0.25	2.35
Tarsals		251	56.16	0.22	2.19
Metatarsals		83	20.26	0.24	2.45
Phalanges (foot)		33	7.10	0.22	2.58
	Total	8992	2539.0		
	Mean			0.28	1.75

Notes: MS - medial shaft
VE - vertebral end
SE - sternal end
PE - proximal end
PS - proximal shaft
DS - distal shaft
DE - distal end
P - proximal
D - distal
M - medial

LANL

0005612

Table 2. Plutonium-239 content of bone, USTR Case 1

Sample		Weight (g) Wet	Weight (g) Ash	Weight Ash:Wet	^{239}Pu Content (mBq/g ash)
Cranium					
Occipital		58.6	30.04	0.51	15.4
Parietal		127.1	70.48	0.55	15.7
Temporal 1 & 2		69.4	29.22	0.42	18.1
Frontal 1		44.3	21.92	0.49	16.4
Maxilla		27.4	9.54	0.35	25.5
Frontal 2 & 3		36.4	18.44	0.51	16.1
Temporal 3		32.3	7.78	0.26	29.1
Mandible		32.3	15.12	0.47	11.9
Hyoid		2.90	0.57	0.20	36.8
Vertebral column					
Cervical-1		20.9	7.44	0.36	24.6
Cervical-2:	arch	13.7	3.99	0.29	29.2
	body	12.2	2.49	0.20	33.8
Cervical-3:	arch	8.80	2.56	0.29	26.3
	body	7.80	1.60	0.21	31.8
Cervical-4:	arch	9.04	2.76	0.31	23.3
	body	9.14	1.97	0.22	29.8
Cervical-5:	arch	8.20	2.62	0.32	23.8
	body	8.50	1.92	0.23	30.3
Cervical-6:	arch	10.2	3.17	0.31	23.8
	body	9.37	2.08	0.22	30.3
Cervical-7:	arch	13.1	3.92	0.30	24.5
	body	9.50	2.08	0.22	30.6
Thoracic-1:	arch	19.5	5.66	0.29	25.6
	body	11.8	2.08	0.18	38.3
Thoracic-2:	arch	16.5	4.81	0.29	24.7
	body	12.6	2.07	0.16	37.5
Thoracic-3:	arch	14.3	4.16	0.29	23.8
	body	12.5	1.91	0.15	36.8
Thoracic-4:	arch	14.1	3.76	0.27	26.0
	body	13.5	2.18	0.16	37.3
Thoracic-5:	arch	14.8	3.58	0.24	28.2
	body	14.7	2.51	0.17	37.9
Thoracic-6:	arch	15.4	3.97	0.26	28.0
	body	18.7	2.72	0.15	39.3
Thoracic-7:	arch	15.9	4.36	0.27	28.0
	body	20.5	2.45	0.12	40.9
Thoracic-8:	arch	17.0	4.38	0.26	28.5
	body	21.6	3.18	0.15	40.9
Thoracic-9:	arch	20.7	4.98	0.24	29.1
	body	22.3	3.92	0.18	40.8
Thoracic-10:	arch	23.8	5.87	0.25	26.1
	body	32.8	5.26	0.16	35.3
Thoracic-11:	arch	22.2	5.61	0.25	23.1
	body	37.7	5.48	0.15	36.5
Thoracic-12:	arch	24.1	6.04	0.25	25.4
	body	42.8	5.73	0.13	39.9

LANL

0005613

Table 2. (*Contd.*)

Sample		Weight (g) Wet	Ash	Weight Ash:Wet	^{239}Pu Content (mBq/g ash
Lumbar-1:	arch	29.8	7.42	0.25	27.6
	body	49.8	6.10	0.12	42.6
Lumbar-2:	arch	29.6	7.68	0.26	30.9
	body	53.0	6.13	0.12	42.4
Lumbar-3:	arch	35.3	9.56	0.27	34.2
	body	61.7	6.72	0.11	42.2
Lumbar-4:	arch	37.2	10.50	0.28	28.5
	body	61.1	8.47	0.14	36.7
Lumbar-5:	arch	34.9	10.26	0.29	22.7
	body	52.1	8.77	0.17	31.2
Sacrum & coccyx		256.2	47.52	0.19	35.7
Pelvis:	Ischium	232.2	56.84	0.25	23.9
	Iliac crest	84.9	19.16	0.23	29.0
	Iliac body	127.4	40.16	0.32	22.9
Clavicle:	SE	12.0	2.66	0.22	21.1
	ME	20.5	9.88	0.48	13.6
	Acromial end	14.6	2.67	0.18	31.3
Scapula:	Body 1	26.8	7.28	0.27	19.2
	Body 2	11.5	5.20	0.45	14.7
	Socket 3	23.9	5.96	0.25	21.6
	Spine 4	43.4	15.92	0.37	17.7
	Spine 5	7.90	2.82	0.36	15.7
	Spine 6	17.2	2.06	0.12	50.2
Rib-1:	SE	5.47	0.74	0.13	49.77
	MS	4.44	1.58	0.36	20.15
	VE	7.02	1.06	0.15	18.71
Rib-2:	SE	5.19	1.51	0.29	22.19
	MS	5.44	1.56	0.29	19.02
	VE	4.21	0.95	0.23	25.26
Rib-3:	SE	5.56	1.22	0.22	22.81
	MS	5.20	1.68	0.32	20.04
	VE	6.51	1.74	0.27	22.41
Rib-4:	SE	5.96	1.40	0.23	30.83
	MS	7.55	2.16	0.29	24.54
	VE	8.38	2.34	0.28	26.64
Rib-5:	SE	8.42	1.56	0.18	32.37
	MS	8.08	2.42	0.30	24.52
	VE	10.5	3.36	0.32	21.13
Rib-6:	SE	14.0	2.48	0.18	23.19
	MS	10.9	3.40	0.31	24.80
	VE	11.5	3.92	0.34	23.51
Rib-7:	SE	10.9	2.28	0.21	41.30
	MS	8.87	2.94	0.33	21.15
	VE	14.8	5.08	0.34	19.29
Rib-8:	SE	9.65	2.23	0.23	30.34
	MS	8.13	3.48	0.43	16.04
	VE	12.3	3.98	0.32	19.51
Rib-9:	SE	7.74	0.92	0.12	26.27
	MS	8.20	2.36	0.29	23.94
	VE	12.9	3.36	0.26	25.30

0005614

LANL

Table 2. (*Contd.*)

Sample		Weight (g) Wet	Weight (g) Ash	Weight Ash:Wet	^{239}Pu Content (mBq/g ash)
Rib-10:	SE	4.92	0.78	0.16	34.19
	MS	6.11	2.56	0.42	15.62
	VE	9.12	2.86	0.31	20.75
Rib-11:	SE	2.89	0.56	0.19	23.51
	MS	4.12	1.52	0.37	15.35
	VE	5.67	1.60	0.28	19.17
Rib-12:	SE	1.07	0.28	0.26	22.02
	MS	2.42	0.88	0.36	17.61
	VE	3.42	0.86	0.25	27.91
Sternum		96.4	14.57	0.15	31.18
Humerus:	PE	80.8	15.14	0.19	33.02
	Shaft	122.3	56.45	0.46	11.66
	DE	53.1	16.60	0.31	22.09
Radius:	PE	8.6	2.70	0.31	18.95
	Shaft	43.5	22.25	0.51	7.06
	DE	18.3	4.62	0.25	18.58
Ulna:	PE	34.5	9.55	0.28	20.24
	Shaft	43.7	21.66	0.50	7.26
	DE	6.7	1.39	0.21	25.30
Carpals		29.0	6.98	0.24	28.72
Metacarpals		42.5	13.17	0.31	20.40
Phalanges (hand)		38.0	11.54	0.30	21.42
Femur:	PE	219.6	55.04	0.25	26.71
	Shaft	355.6	171.96	0.48	10.45
	DE	218.4	47.8	0.22	23.36
Tibia:	PE	162.0	36.88	0.23	24.36
	Shaft	222.4	107.72	0.48	9.72
	DE	52.9	14.88	0.28	20.61
Fibula:	PE	14.6	3.22	0.23	24.84
	Shaft	48.3	27.24	0.56	7.83
	DE	15.5	5.10	0.33	17.32
Patella		37.9	8.82	0.23	20.79
Tarsals		194.4	52.44	0.27	22.93
Metatarsals		61.1	21.16	0.35	19.03
Phalanges (foot)		22.7	5.84	0.26	27.80

Notes:
MS - medial shaft
VE - vertebral end
SE - sternal end
PE - proximal end
PS - proximal shaft
DS - distal shaft
DE - distal end
P - proximal
D - distal
M - medial

LANL

0005615

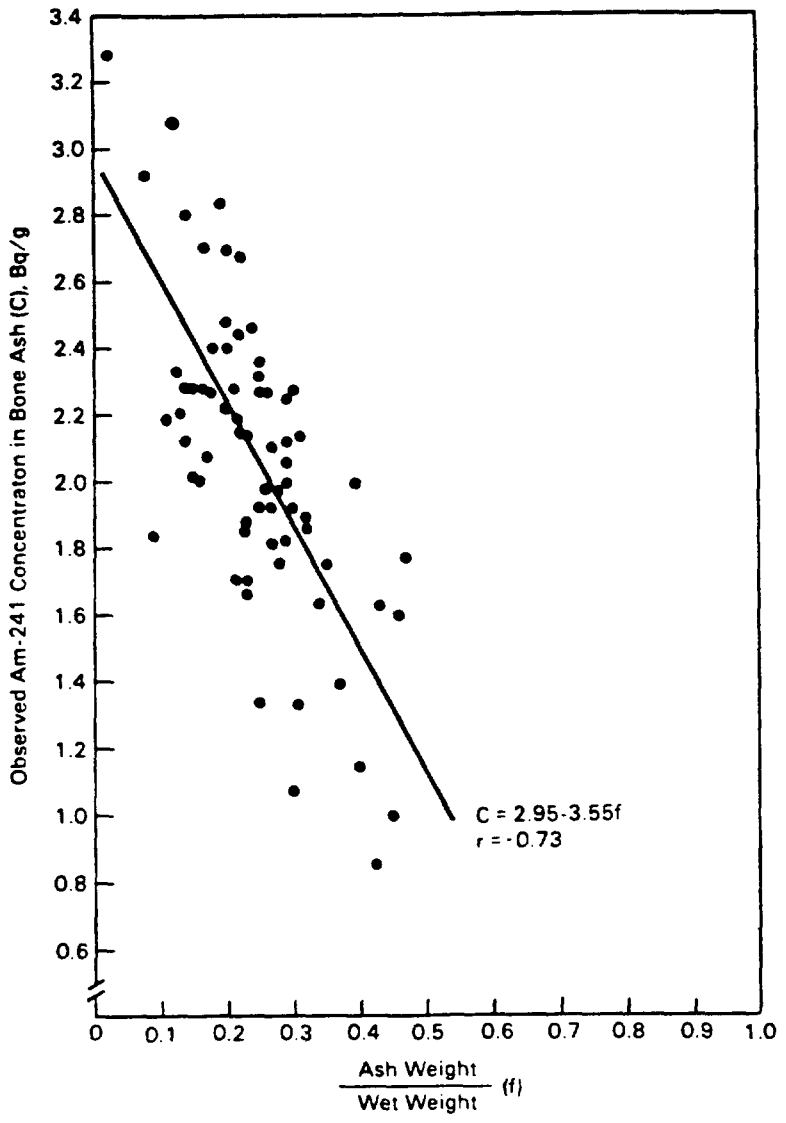

Fig. 1. Relationship of bone ash and ^{241}Am concentration in the skeleton of an occupationally exposed individual (Case 1).

skeleton, the ratio of actinide to Ca is not, and, therefore, the Ca content of the ash cannot be used to estimate the systemic deposition of actinides in the skeleton. The relationship between concentration of actinides and fraction of ash or Ca content is consistent with other observations of Pu deposition in the human skeleton and in animals; indeed, in the initial USTR reports, the generally greater concentrations of ^{241}Am in cancellous bone were noted, but the relationship with bone ash content was not determined (Du85a; Mc85a; Mc85b).

Similar observations have been made in postmortem studies of the skeletons of terminally ill individuals experimentally injected with Pu during the mid-1940s, a group that has been extensively studied by Larsen and his co-workers at the Argonne National Laboratory Center for Human Radiobiology (La50; La78; La79; La81a; La81b; Schlenker†). One of these cases was an 18-y-old suffering from Cushing's syndrome, hypertension, nephropathy and osteoporosis who was injected intravenously with 11 kBq (300 nCi) of tetravalent ^{239}Pu in a citrate buffer medium. She died of her original illnesses 2 y later, in 1947. Twenty-six years later the bones were exhumed, weighed, ashed and aliquots taken for radiochemical analysis (La81b). The radiochemical results reported by Larsen *et al.* (La78; La81b) for this case also show that Pu concentration is inversely proportional to the ash fraction in the bone (Fig. 3). Two distinct relationships, one for the cranium and another for the re-

† Personal communication (1984) with R. A. Schlenker, Argonne National Laboratory, 9700 S. Cass Ave., Argonne, IL 60439.

0005016 LANL

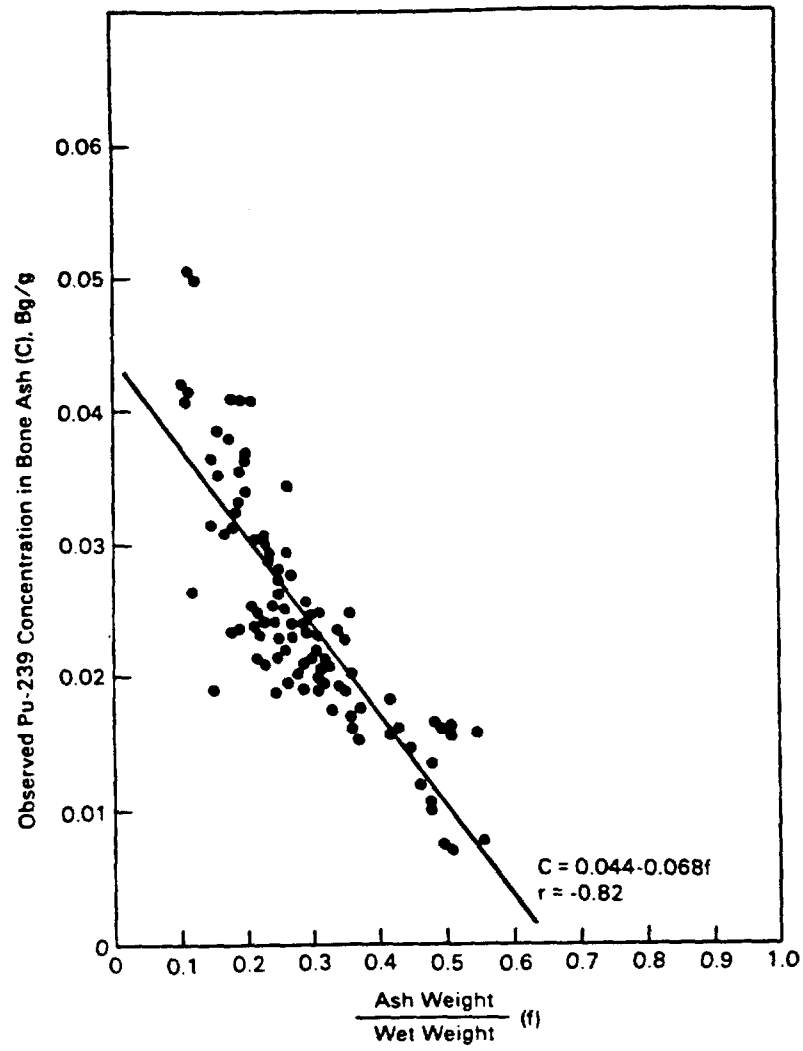

Fig. 2. Relationship of bone ash and ^{239}Pu concentration in the skeleton of an occupationally exposed individual (Case 2).

mainder of the skeleton, were observed; an inverse, albeit somewhat weaker, linear relationship (correlation coefficient = −0.58) was noted between the concentration of Pu in the bone ash and the ratio of ash to wet weight.

There were, however, some striking differences between this case and the USTR cases, which might well be attributable to the osteoporosis suffered by this case, or to the fact that the analyses were not carried out on fresh samples, hence altering the ash-to-wet-weight ratios. Yet another difference relates to the time of intake, which in this case was only 2 y before death as compared with the two USTR cases in which intake occurred many years (approximately 25) prior to death. Thus, the distribution pattern could have been altered as a result of differences in bone formation rates and subsequent translocation, which is controlled to a great extent by remodelling. In adults the remodelling rate is greater for trabecular bone than for cortical bone (Fr69; ICRP72b; Je81). The rate of trabecular bone formation has been reported as four times that of cortical bone (ICRP72b). The kinetics of bone formation, remodeling and removal of calcium and actinides are complex and as yet incompletely understood, but are consistent with the observed pattern. Also, the level of physical activity, weight bearing, and similar factors stimulate retention of bone or Ca and could also account for some of the observed differences, as could the suppression of estrogens and increased androgens associated with Cushing's syndrome, which cause loss of bone mass.

A second case, that of a 65-y-old man injected with 14.1 kBq (380 nCi of ^{239}Pu), showed a similar skeletal distribution of Pu (La79; La81a; La81b; Sc81; Schlenker‡). Unfortunately, the ash:wet weight ratio could

‡ Personal communication (1984) with R. A. Schlenker, Argonne National Laboratory, 9700 S. Cass Ave., Argonne, IL 60439.

0005617

LANL

Table 3. Ash and Ca content of selected bone samples, Case 2

Bone sample	Ashed weight (g)	Calcium content (g)	Ca concentration (g Ca/g ash)
Frontal (partial)	21.9	8.31	0.379
Parietal (partial)	21.9	7.29	0.333
Rib 7, MS	2.94	1.20	0.408
Rib 9, VE	3.36	1.38	0.411
Rib 9, MS	2.36	1.00	0.424
Rib 9, SE	0.92	0.35	0.377
Sternum	14.57	4.75	0.326
Clavicle, SE	2.66	1.01	0.380
Clavicle, acromion	2.67	1.44	0.539
Clavicle, shaft	9.88	3.63	0.367
Vert. T-7, arch	4.36	1.12	0.257
Vert. T-7, body	2.45	1.07	0.437
Vert. L-3, arch	9.56	3.37	0.353
Vert L-3, body	6.72	2.42	0.360
Femur, PE	55.0	11.8	0.215
Femur, MS	55.8	20.5	0.367
Femur, DE	47.8	17.3	0.362
Patella	8.8	3.67	0.416
Mean ± S.D.			0.373 ± 0.069

not be obtained as the samples were dehydrated with alcohol but not defatted (Schlenker‡).

In animals, results are somewhat more ambiguous, which may be related more to the sacrifice and analysis of the skeleton soon after internal administration of the actinide and perhaps the age, dose, and physico-chemical form rather than a species difference. The classical distribution pattern in animals, as described by Jee (Je72), clearly indicates greater concentrations in the highly trabecularized bone and is thus consistent with the linear relationship observed in the USTR cases. Studies in the baboon (Gu80), dog (At58; Je81; St68; St69; Wr80), monkey (Du75; Du83; Du85b), rabbit (Be62), rat (Du69; Ta61) and pig (Bu68) all typically show greater concentrations of actinide in the highly trabecularized bone, which suggests that a similar relationship might exist in these species. Regrettably, the data as reported in the open literature are typically incomplete and do not give wet and ashed weights or ash fraction.

An exception is the study by Stover *et al.* (St69; St72) of the distribution of injected ^{239}Pu(IV) in buffered citrate in beagle dogs, in which ashed and wet weights were given along with concentration data for dogs injected with various levels of Pu and sacrificed at times ranging from 5–769 d post-injection. No linear relationship between concentration and ash fraction could be seen in these data.

A second and highly notable exception is the recent report by Durbin, Jeung and Schmidt (Du85b). In this study, the wet and ashed weights are given along with the percentage of the injected dose per gram of ash for bone specimens from an adult Macaque monkey (>11 y old) sacrificed 67 d after intravenous administration of 11.84 kBq/kg of ^{238}Pu(IV) solution. A clear inverse relationship between ash fraction and concentration in bone ash is observable.

If the two USTR cases are typical of persons with skeletal burdens of actinides, at least for long times after deposition, it is possible to obtain a reasonable estimate of skeletal deposition from analysis of only a few bone samples, which could be of enormous practical significance where only a portion of the skeleton is available. Similarly, by the analysis of more than one sample, the specific relationship for the individual may be obtained, thus resulting in an even more accurate estimate. In general the patellae, clavicles and central ribs are most suitable; in Case 1, the femoral shaft showed large deviation, possibly attributable to his heavy exercise regimen which resulted in a heavy bone shaft. The sternum in this case was also abnormal, due to the presence of a large amount of metastatic neoplasm. Retrospective application of skeletal deposition estimates may also be useful to refine other observations and may also reveal previously unobserved relationships.

CONCLUSION

Radiochemical analysis of half skeletons from the first two whole-body donors to USTR revealed an inverse proportionality between the actinide concentration in the bone ash and the fraction of ash. If this relationship is

0005618 LANL

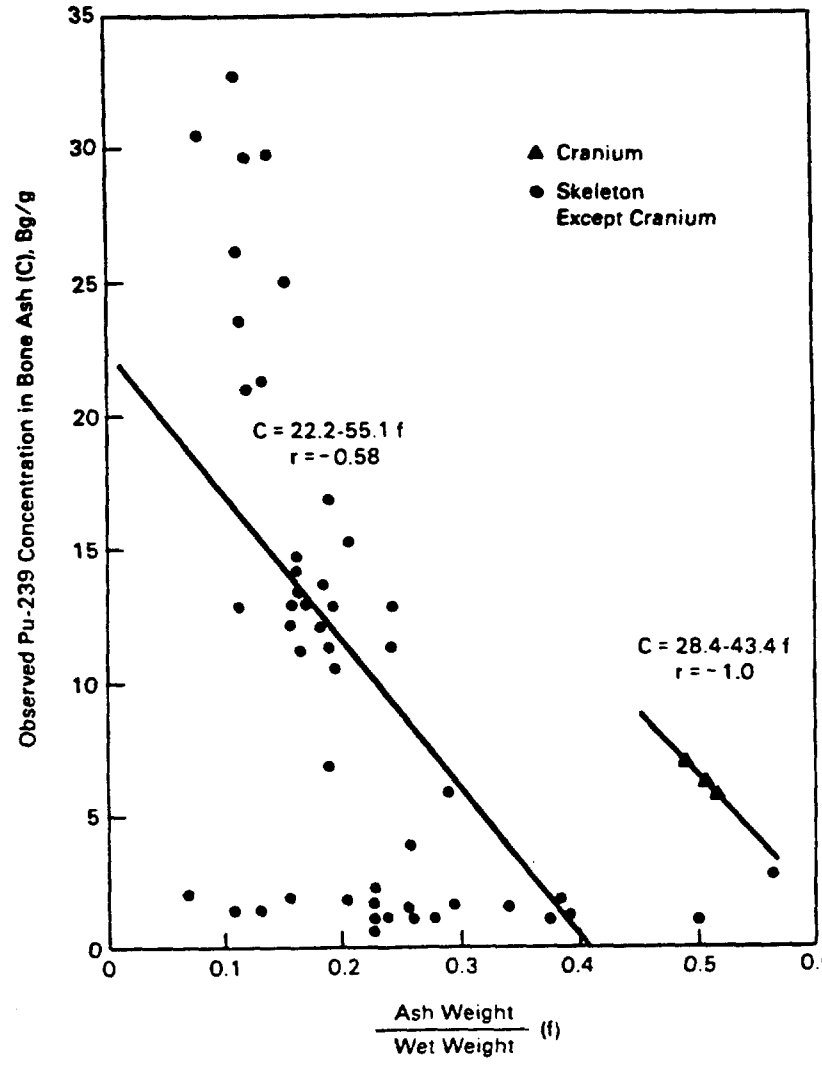

Fig. 3. Relationship of bone ash and ^{239}Pu concentration in the skeleton of an osteoporotic woman experimentally injected with Pu nitrate 2 y before death.

typical, analysis of only a few bone samples, perhaps as few as two, even from the same bone, may establish the specific relationship of the donor and permit an accurate estimate of the total skeletal deposition without the necessity for analyzing all or a major portion of the skeleton. Verification of the relationship will come from analysis of additional USTR total body donors. In the interim, the relationship will be applied to the evaluation of partial body data now in progress by the USTR.

Acknowledgments—The authors are indebted to R. P. Larsen and R. A. Schlenker for supplying data on the Argonne cases and to P. W. Durbin, D. R. Fisher, C. L. Mays and R. C. Thompson for review of the manuscript and helpful comments. The assistance of Patricia Blackburn, CPS, with the preparation of this manuscript is appreciated by the authors.

REFERENCES

An83 Andreozzi U., Clemente G. F., Ingrao G. and Santori G., 1983, "Long-term ^{238}Pu and ^{239}Pu retention and organ distribution in mice at low doses," *Health Phys.* **44**, 505.

At58 Atherton D. R., Mays C. W. and Stover B. J., 1958, "Radionuclide distribution in adult beagle bones," pp. 118–125, in: *Radiobiology Laboratory Semi-Annual Progress Report*, University of Utah, Salt Lake City, UT, Report COO-217.

At78 Atherton D. R., Bruenger F. W. and Stevens W., 1978, "Serial study of ^{239}Pu retention and distribution in the juvenile beagle," pp. 165–168, in: *Research in Radiobiology, Annual Report of Work in Progress in the Internal Irradiation Program*, University of Utah College of Medicine, Salt Lake City, UT, Report COO-119-153.

Be62 Belyayev Y. A., Konstantinova V. A. and Yelkina N. I., 1962, "Plutonium distribution in rabbits," in: *Plutonium-*

0005619 LANL

239: *Its Distribution, Biological Effects and Accelerated Elimination* (edited by A. B. Lebidinskii and Y. I. Moskalev) (Moscow: Mediz); English translation, 1963, U.S. Air Force Report FID-TT63-559.

Bl71 Bleaney B. and Vaughan J., 1971, "Uptake of ^{239}Pu on bone surfaces," *Brit. J. Radiol.* **49**, 67.

Bo81 Boyd H. A., Eutsler B. C. and McInroy J. F., 1981, "Determination of americium and plutonium in autopsy tissue: methods and problems," in: *Actinides in Man and Animals* (edited by M. E. Wrenn), pp. 43–52 (Salt Lake City: RD Press).

Br81 Breitenstein B. D., Jr., 1981, "The U.S. Transuranium Registry," in: *Actinides in Man and Animals* (edited by M. E. Wrenn), pp. 269–272 (Salt Lake City: RD Press).

Br85 Breitenstein B. D., Newton C. E. and Norris H. T., 1985, "The U.S. Transuranium Registry report on the ^{241}Am content of a whole body: Introduction and history of the case," *Health Phys.* **49**, 565.

Bu68 Buldakov L. A., 1968, "The behavior of plutonium (^{239}Pu) in young pigs," *Radiobiologiya* **8**, 1; English translation AEC-TR-6950 (for availability of translation, contact Office of Scientific and Technical Information, P.O. Box 62, Oak Ridge, TN 37831).

Du62 Durbin P. W., 1962, "Distribution of the transuranic elements in mammals," *Health Phys.* **8**, 665.

Du69 Durbin P. W., Jeung N. and Williams M. H., 1969, "Dynamics of ^{241}Am in the skeleton of the rat: A study of the relationship between behavior of bone-seeking elements and bone growth status," in: *Delayed Effects of Bone-Seeking Radionuclides* (edited by C. W. Mays, W. S. S. Jee, R. D. Lloyd, B. J. Stover, H. J. Dougherty and G. N. Taylor), pp. 137–156 (Salt Lake City: University of Utah Press).

Du73 Durbin P. W., 1973, "Metabolism and biological effects of the transplutonium elements," in: *Uranium, Plutonium, Transplutonic Elements* (edited by H. C. Hodge, J. N. Stannard and J. B. Hursh), pp. 739–896 (New York: Springer-Verlag).

Du75 Durbin P. W., 1975, "Plutonium in mammals; influence of plutonium chemistry, route of administration and physiological status of the animal on initial distribution and long-term metabolism," in: *Health Phys.* **29**, 495.

Du76 Durbin P. W. and Jeung N., 1976, "Reassessment of the distribution of plutonium in the human body based on experiments with non-human primates," in: *The Health Effects of Plutonium and Radium* (edited by W. S. S. Jee), pp. 297–313 (Salt Lake City, JW Press).

Du83 Durbin P. W., Jeung N. and Schmidt C. T., 1983, "Distribution and retention of ^{238}Pu in Macaque monkeys," in: *Proc. 7th Int. Cong. Radiation Research* (edited by J. R. Broerse) (Amsterdam: Martin Nyhoff).

Du85a Durbin P. W. and Schmidt C. T., 1985, "The U.S. Transuranium Registry report on the ^{241}Am content of a whole body: Implications for metabolic modelling," *Health Phys.* **49**, 623–661.

Du85b Durbin P. W., Jeung N. and Schmidt C. T., 1985, "^{238}Pu(IV) in monkeys," U.S. Nuclear Regulatory Commission, Washington, DC, Report NUREG/CR-4355.

El61 Ellis R. E., 1961, "The distribution of active bone marrow in the adult," *Phys. Med. Biol.* **5**, 255.

Fr69 Frost H. M., 1969, "Tetracycline-based histological analysis of bone remodelling," *Calcified Tissue Res.* **3**, 211.

Gu80 Guillmette R. A., Cohen N. and Wrenn M. E., 1980, "Distribution and retention of ^{241}Am in the baboon," *Radiat. Res.* **81**, 100.

Ha47 Hamilton J. G., 1947, "The metabolism of fission products and the heaviest elements," *Radiol.* **49**, 325.

He85 Heid K. R., and Robinson B., 1985, "The U.S. Transuranium Registry report on the ^{241}Am content of a whole body: health physics aspects," *Health Phys.* **49**, 569.

Hu82 Humphreys E. R., Green D., Howells G. R. and Thorne M. C., 1982, "Relationship between blood flow, bone structure, and ^{239}Pu deposition in the mouse skeleton," *Calcified Tissue Int.* **34**, 416.

ICRP72a International Commission on Radiological Protection, 1972, "The metabolism of compounds of plutonium and other actinides," *ICRP Publication* 19 (Oxford: Pergamon Press).

ICRP72b International Commission on Radiological Protection, 1972, "Alkaline earth metabolism in adult man," *ICRP Publication* 20 (Oxford: Pergamon Press).

ICRP75 International Commission on Radiological Protection, 1975, "Report of the task group on reference man," *ICRP Publication* 23 (Oxford: Pergamon Press).

Je72 Jee W. S. S., 1972, "Distribution and toxicity of ^{239}Pu in bone," *Health Phys.* **22**, 583.

Je81 Jee W. S. S., Wronski T. J., Smith J. M., Kimmel D. B., Miller S. C. and Stover B. J., 1981, "Selection of bone samples for ^{239}Pu analyses in man," in: *Actinides in Man and Animals* (edited by M. E. Wrenn), pp. 407–412 (Salt Lake City: RD Press).

La50 Langham W. H., Bassett S. H., Harris P. S. and Carter R. E., 1950, "Distribution and excretion of plutonium administered intravenously to man," Los Alamos Scientific Laboratory Report LA 1151, reprinted in *Health Phys.* **38**, 1031.

La78 Larsen R. P., Oldham R. D., Gacic C. G., Farnham J. E. and Schneider J. R., 1978, "Distribution of injected plutonium in the skeleton and certain soft tissues," pp. 145–153, in: *Radiological and Environmental Research Division Annual Report*, July 1977–June 1978, ANL-78-65, Part II.

La79 Larsen R. P., Oldham R. D. and Martin S. M., 1979, "Distribution of plutonium amongst and within selected bones from an injection case," pp. 115–119, in: *Radiological and Environmental Research Division Annual Report*, July 1978–June 1979, ANL-79-65, Part II.

La81a Larsen R. P. and Oldham R. D., 1981, "Distribution of plutonium in the human skeleton—A comparison of two injection cases," pp. 122–124, in: *Radiological and Environmental Research Division Annual Report*, July 1980–June 1981, ANL-81-85, Part II.

La81b Larsen R. P., Oldham R. D. and Toohey R. E., 1981, "Macrodistribution of plutonium in the human skeleton," in: *Actinides in Man and Animals* (edited by M. E. Wrenn), pp. 191–198 (Salt Lake City: RD press).

Ll72 Lloyd R. D., Jee W. S. S., Atherton D. R., Taylor G. N. and Mays C. W., 1971, "Americium-241 in beagles: Biological effects and skeletal distribution," in: *Radiobiology of Plutonium* (edited by B. J. Stover and W. S. S. Jee), pp. 141–148 (Salt Lake City: The J. W. Press).

Mc85a McInroy J. F., Boyd H. A., Eutsler B. C. and Romero J., 1985, "The U.S. Transuranium Registry report on the ^{241}Am content of a whole body: Preparation and analysis of tissue samples," *Health Phys.* **49**, 587.

Mc85b McInroy J. F. and Swint M. J., 1985, "Distribution of ^{239}Pu and ^{241}Am in the human skeleton," Los Alamos National Laboratory Report LA-UR 85-732.

Ne79 Nenot J. C. and Stather J. W., 1979, *The Toxicity of*

0005620 ANL

Plutonium, Americium and Curium (Oxford: Pergamon Press).

Pa85 Palmer H. E., Rieksts G. A. and Spitz H. B., 1985, "The U. S. Transuranium Registry report on the ^{241}Am content of a whole body: Gamma ray measurements," *Health Phys.* **49**, 559.

Pr78 Priest N. D., 1978, "Plutonium: A bone surface seeker?" *Rad. Prot. Bull.* (England) **24**, 24–29.

Sc81 Schlenker R. A. and Oltman B. G., 1981, "Plutonium microdistribution in human bone," in: *Actinides in Man and Animals* (edited by M. E. Wrenn), pp. 199–206 (Salt Lake City: RD Press).

St69 Stover B. J., Atherton D. R., Bruenner F. W. and Buster D. S., 1969, "^{239}Pu(IV): Its distribution in the beagle," in: *Delayed Effects of Bone-Seeking Radionuclides* (edited by C. W. Mays, W. S. S. Jee, R. D. Lloyd, B. J. Stover, H. J. Dougherty and G. N. Taylor) pp. 109–123 (Salt Lake City: The University of Utah Press).

St72 Stover B. J., Atherton D. R. and Buster D. S., 1972, "Retention of ^{239}Pu(IV) in the beagle," in: *Radiobiology of Plutonium* (edited by B. J. Stover and W. S. S. Jee), pp. 149–169 (Salt Lake City: The J. W. Press).

St74 Stover B. J. and Atherton D. R., 1974, "Kinetics of the skeletal retention of ^{239}Pu(IV)," *Radiat. Pres.* **60**, 525.

Sw84 Swint M. J. and Kathren R. L., 1984, "The U.S. Transuranium Registry: The final contribution or ultimate gift?" *Trans. Am. Nucl. Soc.* **46**, 317.

Ta61 Taylor D. M., Sowby F. D. and Kember N. J., 1969, "The metabolism of americium and plutonium in the rat," *Phys. Med. Biol.* **6**, 73.

Va73 Vaughan J., Bleaney B. and Taylor D. M., 1973, "Distribution, excretion and effects of plutonium as a bone-seeker," Chapter 10 in: *Uranium, Plutonium, Transplutonic Elements* (edited by H. C. Hodge, J. N. Stannard and J. B. Hursh), pp. 349–502 (New York: Springer-Verlag).

Vo79 Voelz G. L., Hempelmann L. H., Lawrence J. N. P. and Moss W. D., 1979, "A 32-y medical follow-up of Manhattan District plutonium workers," *Health Phys.* **37**, 445.

Wo60 Woodard H. W. and Holodny E., 1960, "A summary of the data of Mechanick on the distribution of human bone marrow," *Phys. Med. Biol.* **4**, 57.

Wr80 Wronski T. J., Smith J. M. and Jee W. S. S., 1980, "The microdistribution and retention of injected ^{239}Pu on trabecular bone surfaces of the beagle: Implications for the induction of osteosarcoma," *Radiat Res.* **83**, 74.

LANL

0005621