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TITLE: DISTRIBUTION OF ^{239}PU AND ^{241}AM IN THE HUMAN SKELETON

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DISTRIBUTION OF ^{239}PU AND ^{241}AM IN THE HUMAN SKELETON*

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INTRODUCTION

The soft tissues and bones of two whole bodies donated to the United States Transuranium Registry (USTR) have been analyzed for their plutonium and americium content. The USTR is funded through the Hanford Environmental Health Foundation, Richland, Washington, by the United States Department of Energy. A major objective of the Registry program is to study the distribution, concentration, and retention of plutonium and other transuranic elements in tissues of occupationally-exposed individuals.

The Registry relies on voluntary donation of selected organs and bones at the time of death from individuals who have a potential internal deposition of transuranic elements and have been followed with a health physics surveillance program. Whole body donations are sought from workers with a known internal deposition of 10% of maximum permissible body burden of an actinide, such as plutonium, determined by bioassay techniques in common use in the industry. It was recognized that whole body donations with radiochemical analysis of the entire skeleton as well as all major organs would provide more information than obtained from the limited number of specimens

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taken routinely for the Registry cases. At present the USTR has about 850 donors for a limited-tissue autopsy and 22 donors for the whole body program.

The number of bone samples obtained in a routine autopsy is limited to two ribs, the sternum, clavicle, a vertebral wedge, and a patella. The radiochemical analyses of these osseous tissues, weighing usually a few hundred grams, are extrapolated to estimate the total deposition in the entire skeleton (~10Kg). Generally, for lack of better information, the concentrations of the available bone specimens are averaged and this value used to estimate the skeletal deposition, assuming a uniform distribution. We recognize potential for errors in this method and expect that complete skeletal analyses will provide information to more accurately estimate the total skeletal burden from limited bone samples.

The two individuals whose total skeletons have been analyzed were both chemists. The first individual (Case I) was tall and lean (182 cm tall and weighed, while healthy, 65 Kg). In 1979, at the age of 49, he died from a metastatic malignant melanoma. Past medical history revealed a diagnosis of dermatitis herpetiformis which was treated with sulfapyridine. He also had a malabsorption syndrome treated with gluten-free diet in 1974. A wide excision of a malignant melanoma lesion on his back was performed in 1975. There was a recurrence of melanoma in 1978 with a 1.2 cm nodule in the right lung. Subsequently, there was pleural effusion and widespread metastases with a fatal outcome in 1979. He was a marathon runner, a bicyclist, and hiker who remained active until two months before death. At autopsy there was widespread metastases of melanoma throughout the tissues of the body including bone, especially the ribs.

This donor was a research chemist from 1950 to 1979. He worked with significant amounts of ^{241}Am early in his career (1952-1954) and continued in research with other radionuclides until his death. There was no documented history of radionuclide inhalation, ingestion or wound; however, a routine monitoring urine collection in 1958 showed positive alpha activity, later identified as ^{241}Am (HE85). Following whole body counting and urine bioassays, the total skeletal burden was estimated then to be 107 nCi ^{241}Am. The route of entry was unknown but was presumed to be inhalation. At the time of radiochemical analysis of his tissue samples, the soft tissue of the left hand showed a high level of ^{241}Am activity which raised the possibility of an unrecognized contaminated wound as the route of entry.

The second individual (Case II) was a 173 cm tall, 78 kg chemical engineer. Previous surgery included bilateral hernia repairs and appendectomy. His general health was good until he suffered a coronary occlusion in 1968 at age 48. He subsequently increased his physical activities with walks and by riding a stationary bicycle four kilometers per day, five days per week. A second coronary occlusion occurred in 1976 with an uneventful recovery. He continued work and retired about one year before suffering fatal pneumonia and heart failure in 1981 at age 61. All laboratory data including hematological values were normal in available occupational records.

This donor was employed from 1945-1980 in plutonium alloy research and development and in plutonium weapons work. Records show he had moderate plutonium exposure from 1945 to 1957. No wounds were recorded. Two nose counts were positive in 1945: 1962 dis/min (L)/156 dis/min (R); 7696 dis/min (L)/4598 dis/min (R). A total of 16 nose counts over 50 dis/min were noted in his records. After 1957, he assumed supervisory duties and probably did not have a subsequent exposure to plutonium. A 1970 count of the ^{241}Am in his lungs indicated less than 3 nCi ^{239}Pu, based upon the inferred Am/Pu concentration ratio. His total body burden in 1976, estimated from urine excretion values, was 27 nCi ^{239}Pu(VO79).

METHODS

A complete description of the dissection and chemical analysis of Case I was presented at the "International Conference on Radiobiology of Radium and Actinides in Man", held at Lake Geneva, Wisconsin in 1981 and has been submitted to Health Physics (MC85). Case II was dissected and analyzed in the same way.

Briefly, the internal organs were removed at autopsy, frozen, and shipped to Los Alamos for radiochemical analyses. The bodies were taken to the USTR laboratories in Richland, Washington and preserved by freezing. A team of researchers was assembled to dissect the body. The overlying soft tissue was removed from the skeleton and each bone was cleaned of as much muscle and connective tissue as possible. The bones were weighed whole. Extensive gamma counting was performed on the bones of Case I individually and in various combinations. The 60 Kev x ray of the ^{241}Am was easily measured in statistically significant amounts. The measurement indicated a right-left symmetry in the skeletal deposition of americium. The ^{241}Am activity in this skeleton was at a high enough level that it was decided to preserve one-half of the skeleton to make a phantom that could be used for interlaboratory calibration of detector systems used for whole body counting. The other half of this skeleton was shipped to Los Alamos for radiochemical analysis. The levels of radioactivity in Case II, primarily from plutonium rather than americium, were too low to make the skeleton useful as a phantom.

The bones of the right side of each skeleton were analyzed for their actinide content. They were first subdivided to allow measurement of the distribution of the radioisotope in anatomical regions of interest. In general, larger bones were divided to separate the areas containing cancellous (trabecular) bone from the compact bone since both plutonium and americium deposit primarily on bone surfaces.

The radiochemical procedures used to measure the plutonium and americium in bones have been described in detail elsewhere (MC85, BO81). The bone samples were dry ashed, wet ashed, and the ash weights determined. The resulting ash was dissolved in HNO_3. An aliquot of this solution was removed for analysis and ^{243}Am and ^{242}Pu tracers were added. The plutonium and americium were separated and isolated by anion exchange techniques and electroplated onto stainless steel disks for alpha pulse height spectrometry. The average recovery of the tracers was 85 ± 7% for the ^{243}Am and 87 ± 9% for the ^{242}Pu tracer. One blank and one quality control sample was analyzed with each set of 14 bone samples.

RESULTS

The plutonium and americium contents measured in these skeletons are summarized in Tables 1-2. In Case I, the highest ^{241}Am concentration was in the coccyx and costal cartridges (190 dis/min/g ash); the lowest concentration was in the teeth (46 dis/min/g ash). The total skeletal content in this case was 264,450 dis/min (119.1 nCi), and the weighted-average concentration of ^{241}Am was 105 dis/min/g ash. The ^{241}Am in the bones and teeth was 82.2% of the whole body content of 144.7 nCi (excluding 2.8 nCi in the soft tissues of the left hand). The liver had 6.4% of the whole body content, the respiratory tract had 1.6%, and the striated muscle and skin 8.7%. The remaining tissues contained 1.1% of the total activity.

The highest ^{239}Pu concentrations in Case II were in the coccyx (3.2 dis/min/g ash) and the bodies of the lumbar vertebrae (2.2 dis/min/g ash). The lowest concentrations were in the shafts of the long bones (radius shaft, 0.37 dis/min/g ash; ulna shaft, 0.38 dis/min/g ash; etc.) and the teeth (0.46 dis/min/g ash). The total skeletal content was 3068 dis/min (1.4 nCi), and the weighed-average concentration was 0.98 dis/min/g ash. The skeleton contained 21.0% of the whole-body content of 6.7 nCi, the respiratory tract 54.2%, the liver 20.0%, and the striated muscle and skin 2.4% . The remaining tissues contained 2.4% of the total activity. The fraction of the systemic (whole body minus the respiratory tract) contents found in the liver was 43.6%. The skeleton contained 45.8% of the systemic burden. This is in contrast to the distribution of the ^{241}Am in Case I where 5.5% of the systemic deposition was in the liver and 83.6% was in the skeleton.

DISCUSSION

As outlined above, the two individuals studied differ in age, physical characteristics and exposure parameters. To evaluate observed differences in the skeletal distribution of americium and plutonium, it is useful to compare their skeletal characteristics with Reference Man (ICRP75), keeping in mind, however, that Reference Man is a composite of data representative of healthy young adult (20 to 30 year old) male Caucasions. The wet and ash weights of various bones from the bodies of Case I and II are listed in Tables 1 and 2. Reference Man has a skeletal weight of 10 kg, representing 14.3% of the total body weight (70 kg). The ash weight of the skeleton is 2800 g, or 28% of the wet weight of the skeleton. Case I had a skeletal mass of 8992 g. This is 13.8% of his healthy whole body weight of 65 kg. The ash fraction of his skeleton was 28.2%, very close to that of Reference Man.

Case II had a skeletal mass of 8700 g or 11.2% of his healthy whole body weight. The fraction of ash in this skeleton was 35.6% of the skeletal weight, slightly higher than Reference Man and Case I. Case I was described as being tall and lean and was, in fact, 7% taller and 7% leaner than Reference Man. Case II was 1.8% taller than Reference Man but was 11.1% heavier. Apparently the age related mineral loss in the bones of Case II, even though he was 12 years older, was not as great, proportionally, as that in Case I. This may have been due, in part, to the extended terminal illness of Case I as compared to Case II.

Durbin has compared the ash weights of the skeletal parts of Case I to data for 10 male Caucasians of comparable age (DU85). The latter individuals (mean age 51.3 ± 7.2 years), hereinafter referred to as age controls, were from the central United States (TR62). The total ash weight of the skeleton of Case I was nearly the same as the mean of this age control group (Table 3). The ashed weights of the bones of the upper body were, however, lighter than the control mean, in some cases by more than one S.D., while the ash weights of the bones of the pelvis, legs and feet were heavier than the age controls.

The ash weights of the bones of Case II were all heavier than the bones for the age controls except for the mandible (Table 3). Most ash weights of the bones of the upper body were within one standard deviation of the age controls. Of these bones, only the clavicles and cervical vertebrae varied by more than one standard deviation. In the lower body, the bones of the legs and feet and, consequently, the total skeleton also had ash weights that were heavier than the age controls by slightly more than one standard deviation.

The ash weights of the bones of the upper body of Case II then, were generally heavier than Case I and the age control group and the legs of both individuals were relatively alike and heavier than the control group.

The amount of americium and plutonium in the bone specimens having common structural similarities is shown in Tables 1 and 2. The bones comprising the head (skull, mandible and teeth) contained 14.1% of the ^{241}Am and 13.2% of the ^{239}Pu in the respective skeletons. Bones of the axial skeleton (vertebral column, including the sacrum, coccyx and pelvis) contained 17.8% of the ^{241}Am and 27.5% of the ^{239}Pu with the largest differences observed in the lumbar vertebrae and pelvis. However, all bones in this group had a larger fraction of skeletal plutonium compared with the americium distribution. Similarily, all the bones comprising the shoulder and rib cage contained relatively more plutonium than americium; 11.7% of the skeletal plutonium and 9.0% of the americium. Conversely, the bones of the appendicular skeleton (arms, hands, legs and feet) contained a significantly larger fraction of the americium as compared to the plutonium distribution. The arms and hands had 13.1% of the americium and 11.4% of the plutonium; the legs and feet had 46.0% of the americium and 36.2% of the plutonium.

The mean concentration of americium in 14 cancellous bones containing red marrow (sacrum and coccyx, sternum and 12 vertebral bodies) was 130 ± 9 dis/min/g ash. In 21 compact bones (mandible, 6 cranial bones and 14 pieces of long bone shaft) the mean ^{241}Am concentration was 79 ± 18 dis/min/g ash. The concentration ratio of ^{241}Am in compact bone vs cancellous bone, then was 0.61. The mean concentration of ^{239}Pu in similar bone specimens of Case II was 1.91 ± 0.29 and 0.59 ± 0.19 dis/min/g ash in the cancellous and compact bones, respectively, resulting in a concentration ratio of compact/cancellous bones of 0.31. Durbin has calculated that the concentration ratio for a uniform deposit on bone surfaces, using measured surface-to-volume ratios and the compositions of these two bone types, would be (compact/cancellous) = 0.16 (DU85). This indicates, assuming a uniform distribution of americium and plutonium on all bone surfaces following the initial exposure (T = 0), that there has been a more active turnover of each actinide deposited on the cancellous bone surface than that deposited on the compact bone surface. Further, one can conclude that the americium redistributes at a more rapid rate than the plutonium. If the bone turnover rates for cancellous bone and for compact bone are about equal in these two skeletons, the difference must be due to the rate of circulatory feedback of each element from soft tissue and liver as well as by bone remodeling.

SUMMARY

The ^{241}Am and ^{239}Pu distribution in the skeletons of two former nuclear workers has been measured. The skeletons of both individuals appear to be within normal limits for Caucasian men about 50 y old. Both had lower limb bones that were heavier than the age controls and Case I had upper-body bones that were lighter than the age control group. The distribution of americium in the skeleton of Case I, 25 years post exposure, indicated that a more rapid turnover of initially deposited americium on the bone surfaces of cancellous bone, as compared to that deposited on the bone surfaces of compact bone, had occurred. This resulted in a larger proportion of americium located in the compact bone of the extremities and a lesser quantity in the more cancellous bones of the vertebral column, pelvis and rib cage. A similar shift in the distribution of plutonium occurred in Case II in the 35 y since initial deposition, but at a slower rate than that for americium.

The ratio of each actinide in the liver to that in the systemic system (liver content/systemic system content) was 0.065 and 0.436, for americium and plutonium, respectively, suggesting that a much more rapid turnover of americium in the liver, compared to plutonium, provided a much larger fraction of that nuclide for circulatory feedback to the remodeling skeletal system.

These data have strengthened the ICRP-recommended systemic distribution of actinides (45% in liver, 45% in skeleton, 10% in other tissues) in the body for plutonium, but not for americium (ICRP79). Additional data from whole bodies of occupationally exposed nuclear workers are needed to verify and to extend these findings.

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TABLE 1. MEAN ^{241}Am AND WEIGHTED AVERAGE ^{241}Am CONCENTRATIONS IN BONE SPECIMENS WITH COMMON STRUCTURAL CHARACTERISTICS (Case I)

				^{239}Pu Content		
	Weight (g)				dis/min	Distribution
Skeletal Part	Wet	Ash	% Ash	(dis/min)	g ash	%
Skull	648	291	44.9	32330	111	12.2
Mandible	101	34.8	34.5	3360	96	1.3
Teeth	46	33.7	73.3	1560	46	0.6
Hyoid	12	0.9	7.5	160	175	0.1
Cervical vertebrae	132	29.4	22.3	3730	127	1.2
Thoracic vertebrae	478	91.2	19.1	11600	127	4.4
Lumbar vertebrae	402	69.9	17.4	8550	122	3.2
Sacrum and coccyx	219	31.7	14.5	4350	137	1.6
Pelvis	783	239	30.5	18870	79	7.2
Clavicles	79	19.8	25.1	1590	80	0.6
Scapulae	277	65.5	23.6	6460	99	2.4
Ribs	425	127	29.9	14260	109[a]	5.4
Costal cartilages	155	3.0	1.9	570	190	0.2
Sternum	83	7.3	8.8	803	110	0.3
Humerii	585	147	25.1	16070	109	6.1
Radii	169	50.1	29.6	4480	89	1.7
Ulnae	189	55.9	29.6	5080	91	1.9
Hand bones	291	61.2	21.0	9100	149	3.4
Femora	1770	529	29.9	59100	112	22.4
Tibiae	1100	383	34.8	31400	82	11.9
Fibulae	243	85.3	35.1	5770	68	2.2
Patellae	66	16	24.2	2260	141	0.8
Foot bones	734	167	22.8	23000	138	8.7
Total	8992	2539	28.2	264450	105[b]	99.8

[a] Average ^{241}Am Concentration of ribs does not include the right ribs 2-5.

[b] Weighted-average concentration = total skeletal ^{241}Am/total skeletal ash; excluding teeth, costal cartilages and hyoid.

TABLE 2. MEAN ^{239}Pu AND WEIGHTED AVERAGE ^{239}Pu CONCENTRATIONS IN BONE SPECIMENS WITH COMMON STRUCTURAL CHARACTERISTICS (Case II)

Skeletal Part	Weight (g) Wet	Weight (g) Ash	% Ash	^{239}Pu Content (dis/min)	^{239}Pu Content dis/min g ash	^{239}Pu Content Distribution %
Skull	804	427.3	53.1	378.8	0.89	12.4
Mandible	77	42.4	55.1	25.8	0.61	0.8
Teeth	5	4.6	92.0	2.1	0.46	0.1
Hyoid	3	0.6	20.0	1.3	2.10	
Cervical vertebrae	142	44.1	31.1	64.6	1.46	2.1
Thoracic vertebrae	480	106.8	22.3	172.3	1.61	5.6
Lumbar vertebrae	450	91.2	20.3	161.1	1.77	5.3
Sacrum & Coccyx	311	54.3	17.5	107.3	1.98	3.5
Pelvis	900	257.8	28.6	338.5	1.31	11.1
Clavicles	96	39.1	40.7	33.2	0.85	1.1
Scapulae	262	87.9	33.5	89.8	1.02	2.9
Ribs	545	165.3	30.3	199.1	1.20	6.5
Costal Cartilages	104	7.5	7.2	8.4	1.12	0.3
Sternum	96	14.6	15.2	27.3	1.87	0.9
Humerii	514	208.8	40.6	181.6	0.87	5.9
Radii	143	74.3	52.0	39.5	0.53	1.3
Ulnae	172	69.0	40.1	42.7	0.62	1.4
Handbones	209	75.4	36.1	85.6	1.14	2.8
Femora	1708	692.0	40.5	561.0	0.81	18.3
Tibia	888	377.2	42.5	269.6	0.71	8.8
Fibulae	158	77.1	48.8	44.2	0.57	1.4
Patellae	75	22.3	29.7	21.7	0.97	0.7
Foot bones	558	183.5	32.9	213.0	1.16	7.0
Total	8700	3123	36.2[a]	3068.5	0.98[b]	99.9

[a]Weighted average percent bone ash = (total skeletal ash weight/total skeletal wet weight) x 100%.

[b]Weighted-average concentration = total skeletal ^{239}Pu/total skeletal ash; excluding teeth, costal cartilages and hyoid.

TABLE 3. Measured Ash Weights of Skeletal Parts of Case I, Case II, and Caucasian Males of Comparable Age.

	Ash Weights (g)			
Skeletal Part	Age Controls[a] (39-59y) Mean	± S.D.	Case I (49y)	Case II (61y)
Cranium	397[b]	83	291	427
Mandible	45[b]	11	35	42
Scapulae	78	16	66	88
Clavicles	26	6	20	39
Sternum	12	4	7	15
Ribs	157	44	127	165
Humerii	176	38	147	209
Radii, Ulnae	132	27	106	143
Hands	67	12	61	75
Cervical vertebrae	38	5	29	44
Thoracic vertebrae	94	18	91	107
Lumbar vertebrae	79	14	70	91
Sacrum	48	13	32	54
Pelvic bones	216	53	239	258
Femora	481	93	529	692
Tibiae, Fibulae	342	80	468	454
Patellae	16	3	16	22
Feet	148	35	167	184
Total[c]	2553	520[d]	2501	3109

[a]Ten male caucasian skeletons obtained in the area of St Louis, Missouri, mean age 51.3 ± 7.2y; designated as age controls. Data of Trotter and Peterson (Tr62)

[b]Includes a variable but usually small number of teeth.

[c]Total skeleton does not include hyoid bone, costal cartilages and teeth.

[d]Standard deviation of summed (total) skeletal ash weights of the ten individuals.