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SUMMARY

Progress in a number of interrelated investigations is reviewed in this report.

VOLUME I

✓ Investigation of the Retention and Distribution of Americium-241 in the Baboon and the Enhanced Removal of Americium-241 from the Body by Diethylenetriaminepentaacetic Acid (DTPA)

Experiments have been performed to study the metabolism and distribution of intravenously administered ^{241}Am in the adult and juvenile baboon; in addition, decorporation therapy using $\text{Na}_3\text{-CaDTP}$ was performed on selected baboons to assess the efficacy of this drug in removing systemic burdens of ^{241}Am from this primate species. Determination of the kinetics of ^{241}Am was accomplished principally by in vivo methodologies and by radiochemical analysis of ^{241}Am activity of biological material.

The major sites of deposition of ^{241}Am are the liver and the skeleton. Upon intravenous injection of americium as the citrate, the nuclide is cleared rapidly from the circulation; less than 10% of the injected dose remains in the blood one hour post-injection while less than 1% ID remains 24 hours later.

VOLUME II

Estimation of the Skeletal Content of "Bone-Seeking" Radionuclides from *In Vivo* Scintillation Measurements of Their Activity in the Skull

Utilization of in vivo head counting techniques holds considerable promise for estimating the total skeletal burden of various "bone-seeking" radionuclides more easily and with greater precision than has been possible in the past. Anatomical features of the head (skull) make this structure an ideal site for scintillation measurements of those radionuclides emitting photons of relatively low energy, e.g. <100 keV. The present section discusses specific techniques for performing these measurements with particular reference to those physical, biological, and anatomical parameters which are significant for estimating skeletal body burdens. It is concluded that once the skeletal content of the radionuclide has been determined it will be possible to estimate the amount of bone contribution to in vivo anterior thorax measurements which, in turn, should help to define the partition of activity between the lung and rib cage structure. Various important radionuclides that have already been measured by this technique include Pb-210, Am-241, Pu-238, Pu-239, Sr-90 and U-235.

Additional *In Vivo* Measurements and Bioassay of ^{210}Pb in the Blood and Urine of Former Uranium Miners; UM-3

The present report gives the most recent results in our ongoing program of Pb-210 measurements in the skeleton, blood, and excreta of a former uranium miner. In vivo detection of Pb-210 in a former uranium miner (UM-3) indicates a decrease in body burden between 1972 and 1975 from 9.2 ± 0.8 to 8.4 ± 0.03 nCi. The effective half-life of Pb-210 in the skeleton as calculated from this change in body burden is approximately 15 ± 0.6 years.

From this measured body burden of Pb-210 in the skeleton, an estimate of the radon and radon daughter exposure in cumulative working level months (CWLm) was calculated using the empirically-derived relationship of R. Holtzman. The calculated cumulative exposure value of 7190 CWLM is in good agreement with the estimated value of 6315 CWLM that was supplied by the Department of Health, Education and Welfare (PHS).

Bioassay for Pb-210 in blood and urine was correlated with the in vivo head measurements and provided relationships between Pb-210 concentrations in bone and blood as well as between bone and urine.

Design of a Continuous Digital-Output Environmental Radon Monitor

A new field instrument for the continuous measurement of radon concentrations has been developed to investigate the magnitude and variability of environmental levels of Rn-222.

Passive diffusion of radon, but not its daughters, occurs through an open pore polyurethane foam into a sensitive volume where a static electric field directs the positively ionized radon daughter products to a central collecting electrode. Pulses in a ZnS(Ag) scintillator, resulting from the alpha emission of ^{218}Po and ^{214}Po , are observed with a photomultiplier tube and counted using standard NIM electronics. The detector unit has been fabricated into a small, convenient package for indoor air sampling without the use of air movers or pumps. The unit is unobtrusive and acceptable into a daily routine without disrupting normal family or business activities. The monitor can detect as little as 0.5 pCi/l for a 40-min. count ($\alpha = .05$). The equilibrium detection efficiency of the instrument is 0.7 cpm/pCi/l.

Non-Occupational Radiation Exposures from ^{222}Rn and Daughters to Residents of Grand Junction, Colorado

Six individuals from Grand Junction, Colorado were examined for ^{210}Pb body burdens as a result of living in homes where concentrations of ^{222}Rn were elevated due to the presence of uranium mill tailings beneath the building foundation. In vivo detection for ^{210}Pb using three NaI-CsI(Tl) thin crystals in the standard NYU head geometry identified two persons with estimated body burdens above 1.1 nCi. Bioassay for ^{210}Pb was also performed to compare with the in vivo analysis and to further substantiate the relationship between ^{210}Pb in bone, blood and urine.

Estimates of exposure (in cumulative working level months (CWLM)) based on indoor radon concentrations were used to calculate expected body burdens of Pb-210 as a comparison to measured values. The NYU continuous readout radon monitor provided diurnal measurements of Rn-222 in the homes of the volunteer subjects so that, considering assumptions about ventilation and residence times, actual exposures could be determined.

Enhanced Removal of ^{241}Am by DTPA Chelation Therapy in an Adult and Teenage Subject - Continuation Study

During the past year we have witnessed a series of $\text{Na}_3(\text{Ca-DTPA})$ chelation treatments on two human subjects, an adult man and a teenage boy, who have long-term body burdens of Am-241. We have coordinated in vivo whole-body counting, bioassay of urine and feces, and various blood chemistry measurements to coincide with this therapy schedule. Decreases in total body burdens for this treatment period were measured as 5% in the adult and 30% in the youth. High concentrations of zinc in urine and a corresponding decrease of activity of the zinc-dependent erythropoietic enzyme, ALAD, has also been observed.

Is Liver a "Critical Organ" in Man for Isotopes of Americium?

Generation of electrical power by nuclear means will result in the production of substantial quantities of the transplutonium elements. Largely regarded as a waste product,

americium may eventually find some function, resulting undoubtedly, in an increase in the number of contamination incidents involving man. To date, there are about 15 documented cases of internal deposition of americium (without plutonium) in man. Experimental results describing the early deposition and rate of removal of Am-241 from the liver of the mouse, rat, Chinese Hamster, beagle, cynomolgus monkey, baboon, and man are reviewed. It is concluded that there are marked differences in the rate at which Am-241, injected intravenously in the monomeric form, is excreted from the liver with the specified species (orders) falling into two distinct groups according to life expectancy. The mouse, rat, cynomolgus monkey, and baboon eliminate Am-241 from the liver rapidly in an exponential fashion and almost completely with biological half times between 10 and 150 days. The Chinese Hamster and beagle eliminate Am-241 more slowly with half times of approximately 1000 days for the Chinese Hamster and 3600 days for the beagle. The mechanism(s) responsible for these differences remain to be defined. It is not yet clear that deposition of americium nuclides in the liver is as radiobiologically important as deposition in bone.

Completion of a New Laboratory and Animal Housing Unit for Radionuclide Studies

A description of the completion of a combination radiochemical laboratory and baboon housing unit for radionuclide studies is presented. The use of this laboratory has become

an integral part of the physical space that is available for this study. Its location is advantageous since it is an integral part of the LEMSIP facility and, thereby, provides a convenient basis for cooperation between the separate entities of Environmental Medicine and the surgical staff of the Laboratory for Experimental Medicine and Surgery in Primates.

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(Vol. II)
SECTION I

✓
Estimation of the Skeletal Content of "Bone-Seeking"
Radionuclides from In Vivo Scintillation Measurements
of Their Activity in the Skull

Norman Cohen and Henry B. Spitz

ABSTRACT

In vivo scintillation measurement of the head has been determined to be an extremely useful and practical method for estimating the total skeletal burden of various "bone-seeking" radionuclides. ~~Specific techniques for making this measurement~~ are described with particular reference to those physical, biological and geometrical parameters which are significant for accuracy and precision considerations.

Introduction and Rationale

The head represents a body structure of major bone mass concentration, comprising 22 individual bones of the skull, with relatively little overlying soft tissue cover, defined by the scalp, hair, facial muscles and skin. These two anatomical features, in particular, make the head an ideal site for the in vivo measurement of "bone-seeking" radionuclides emitting photons of relatively low energy, e.g. <100 keV. Furthermore, there are several additional factors which contribute to the applicability and importance of head-site scintillation measurements viz:

- 1) For in vivo scintillation measurements it is possible by judicious use of lead and steel shielding, to isolate the head (skull) and detectors from areas of the body which may contain significant quantities of the radionuclide being measured.
- 2) There is no organ or soft tissue, associated with or in close proximity to the head (skull), that has been reported to specifically concentrate bone-seeking

elements as might, for example, organs such as liver, kidney, spleen and/or lung.

- 3) Of all possible body measurement sites, the head (skull) is one of the least variable anatomical volumes (with respect to relative size and shape) among subjects of different heights and weights.
- 4) The percentage of the total skeleton represented by the skull has been well defined and represents the most concentrated area of available bone in the body (Table 1).
- 5) It is possible to comfortably surround the head structure almost entirely with detector units thereby optimizing geometry for in vivo assay and increasing the precision for any individual measurement (Figure 1).
- 6) The head is relatively easy to approximate with surrogate structure or "phantoms" constructed of tissue equivalent materials; furthermore, actual human skulls are commercially available for purchase.
- 7) In the experimental laboratory animal of our choice, i.e. the baboon, it has been a routine procedure to obtain biopsy samples from the frontal bones of the calvarium by trephine techniques (Cohen and Wrenn, 1973).

Table I-1

Relative Weights of Individual Bones of the Skeleton
(% of Whole Skeletal Weight)

Bone Type	Dry Fat Free (1)	Dry Fat Free (2)	Dry Wt. (3)	Dry Wt. (4)	Fresh Wt. (5)	Ash Wt. (6)	Fresh Wet Wt. (7)	Ash Wt. (7)	(Ash Wt./Fresh Wt.) (7)
1. Skull	17.1	18.9	18.4	13.1	11.5	15.3	13.0±1.64	18.7	31.4
2. Femur	32.0	31.0	8.9	9.2	---	---	15.3±1.46	18.0	24.0
3. Tibia			(1) 5.08	(1) 5.39	---	---	11.3±1.36	12.3	23.3
4. Fibula			(1) 1.25	(1) 1.16	---	---			
5. Humerus	11.9	10.1	(1) 3.33	(1) 3.62	---	---	(2) 5.3±0.49	(2) 6.1	24.4
6. Ulna			(1) 1.47	(1) 1.35	---	---	3.6±0.55	4.7	28.5
7. Radius			(1) 1.21	(1) 1.09	---	---			
8. Vertebrae	10.5	13.2	---	9.36	---	10.0	19.0±1.59	10.4	12.1
9. Ribs	6.3	6.3	(24) 4.4	6.6	---	5.7-6.5	7.0±0.42	7.8	24.2
10. Clavicle	---	---	(1) 0.50	0.54	---	---	(2) 0.8±0.13	(2) 0.8	23.1
11. Scapula	---	---	(1) 1.51	1.56	---	---	(2) 3.6±0.23	3.6	21.8
12. All other bones (i.e. pelvis, feet, hands, etc.)	22.2	20.6	---	---	---	---	---	---	---

- (1) Trotter, M. and R. Peterson, Library of Congress, Doc. ADI 7153 (1962) (10 skeletons).
 (2) Lloyd, E. and D. Hodges, Clinical Orthopaedics, Vol. 78, pg. 230-250 (1971) (1 skeleton).
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 (6) Rivera, J. and J. Harley, HASL-163, pg. 21 (1965) (for two males aged 40 and 60 yrs.).
 (7) Borisov, B. K. and A. N. Marei, Health Phys. 27: 224-229 (1974) (10 males aged 37-50 yrs.).

Numbers in parentheses within the table are the number of bones represented by the given value.

Fig. I-1 Subject to detector standard NYU in vivo head
counting geometry; three NaI-CsI(Tl) detectors,
Be entrance windows - 0.25 mm.

Subject-Detector Standard N.Y.U. Head Counting Geometry

- 8) Metabolic parameters of bone remodeling and resorption have been defined for the skull bones for comparison to other bone structures in the body (Howells, 1972).

Application

It has already been shown that it is or may be possible to measure various radionuclides in vivo in the skull bones, by the use of two or three dual-thin crystal (Phoswich) detectors positioned about the head viz.---

- 1) Pb-210, a bone volume-seeking calcium congener (alkaline earth-like material), present in greater than normal levels in those individuals who have been exposed to abnormally high concentrations of radon and radon daughters, i.e. uranium miners (Cohen, Jaakkola, and Wrenn, 1973), inhabitants of "uranium tailing homes" in Grand Junction, Colorado (Section IV) and in individuals and experimental animals directly exposed to higher than average levels of ^{210}Pb , i.e. heavy cigarette smokers (Holtzman and Ilcewicz, 1966) and adult baboons administered intravenous doses of ^{210}Pb (Cohen and Wrenn, 1972).
- 2) Am-241, a bone surface-seeking actinide (transuranic nuclide) whose deposition in bone approximates that of other transuranic nuclides by initially concentrating along periosteal and endosteal sites. In vivo measurements of this nuclide have been performed in workers

engaged in nuclear fuel reprocessing procedures and in two individuals who became accidentally contaminated in their home during experiments with ^{241}Am for instrument development purposes (Wrenn, Rosen and Cohen, 1972).

- 3) Pu-238, 239, bone surface-seeking transuranic nuclides whose deposition in bone is characteristic of concentration processes similar to those of thorium and americium. This nuclide has been measured by in vivo techniques in individuals industrially exposed during nuclear reprocessing, research and reactor waste handling operations.
- 4) Sr-90, a bone volume-seeking alkaline-earth nuclide heavily used in research and industry and present in nuclear weapons fallout as well as in reactor waste products. In research concerned with the detection of this nuclide by measurement of bremsstrahlung radiation in the skull, it has been shown that this method is a feasible radiological protection monitoring procedure (Olson, 1972).
- 5) In addition to the radionuclides listed above, it is reasonable to consider the possibility of in vivo measurements of other important nuclides associated with bone tissue such as the gamma or X-ray-emitting radioisotopes of uranium, radium, curium and thorium.

Methodology

A technique has already been developed and used successfully in this laboratory for counting many of the above "bone-seeking" radionuclides in the head (skull). The routine procedure that currently exists entails the use of three 15 cm diameter dual crystal NaI-CsI(Tl) detectors (Laurer and Eisenbud, 1968) with 0.25 mm thick Be windows) positioned above and at the sides of an individual's head for counting times of up to 100 minutes. Electronically, the three detectors are operated in the anticoincidence mode with the total signal fed into a common preamplifier and routed to a multichannel analyzer memory. In all cases the detectors are arranged in a manner such that the subject's ears are at midpoint to the side detector areas and the top of the head (parietal bone) is in contact with the back detector unit. In all cases the detectors are positioned for maximum contact with the subject's head. Long counting times can be employed by allowing individuals to lie prone permitting them to comfortably view a television screen during the measurement period. All counting procedures are performed inside of a 16 cm thick steel graded $\frac{3}{8}$ shield (Pb-Cd-Cu) whole-body counting room with additional lead and steel shielding placed over the subject's trunk and shoulder areas. This technique has been used successfully, to date, in several former uranium miners who were measured for ^{210}Pb content (Cohen, Jaakkola, and Wrenn, 1973) as well as for two individuals inadvertently and non-occupationally exposed to ^{241}Am (Figures 2-3). At the

Fig. I-2 In vivo measurement of ^{210}Pb in the head of a former uranium miner, skull activity = 1.25 nCi - estimated-CWLM = 6315, 60 minutes counting time - gross gamma spectrum.

Fig. I-3 In vivo measurement of ^{241}Am in the head of a 15 year-old boy. Skull activity = 1.8 nCi 30 minutes counting time, gross gamma spectrum.

present time we are in the process of determining the degree to which the precision of an individual measurement is dependent on a subject's head movement within the detection area. Preliminary measurements on one uranium miner indicate that there is no significant difference in count rate (in the 47 keV region) when the side detectors are separated from contact with the subject's head within ± 0.5 cm on each side.

Calibration and Minimum-Significant-Measurable Activity (MSMA)

To determine the total amount of activity present, "phantom" head structures have been fabricated by uniformly painting known quantities of activity on the inner and on the outer bone structures of two matched actual human skulls. Since low energy photons are being measured (e.g. <100 keV), the radioactivity was dispersed in an acrylic paint medium (containing no metals) with food coloring added to delineate nonuniformity in those areas that had been covered by the paint. Physiognomy of tissue equivalent facial structures were approximated by covering each of the described painted skulls with dental paraffin of thicknesses approximating that reported for the human face (Krogman, 1962). Other organs of the head, such as brain, tongue, eyes, etc., were constructed from paraffin, plastics and Lincolnshire Bolus tissue equivalent material. The use of a geometric mean of the count rates from these two phantom skulls, i.e. painted on the inside and on the outside respectively, is employed to account for exponential photon

attenuation as well as to result in a value which should not be too different from any of several possible presumed distributions. Figures 4 and 5 are examples of the photon spectra obtained from the two skulls (painted inside and outside, respectively) used to obtain calibration factor estimates. Thus far, surrogate head structures have been fabricated for ^{210}Pb and ^{241}Am giving overall counting efficiencies of 12.4 cpm/nCi and 119.9 cpm/nCi respectively.

By the use of a mean background count rate value determined from measurements of several individuals, minimum significant measurable activities (MSMA's) (Altshuler and Pasternack, 1963) at this geometry (for a 100-minute counting period at the 95% confidence level) have been determined to be 168 pCi of ^{210}Pb and 19.6 pCi of ^{241}Am .

Background Considerations

At the present time there are two methods in use for choosing an optimum control background to obtain a net subject count rate. Since the subject's head is carefully measured for shape and total volume by height, width and circumference, it is possible to obtain a control whose head size, head shape, hair style, etc., approximates those of the subject and to subtract his count rate from that of the individual in question. By this technique the inherent supposition is that the more subjects measured having similar head size, the better will be the average control value.

Fig.I-4 Head "phantom" gamma spectrum-internal application of ^{241}Am activity--3 NaI=CsI(Tl) detectors.

²⁴¹Am Head "Phantom"
(Internal Application)
3 NaICsI(Tl) Detectors

Fig.I-5 Head "phantom" gamma spectrum external application
of ^{241}Am activity - $^3\text{NaI-CsI(Tl)}$ detectors.

Another possible method for determining background is based on the fact that most of the counts in the region of interest (i.e. <100 keV) that are contributed by the head are due to scattering and other radiological processes involving gamma rays associated with the beta decay of natural ^{40}K (Table 2). Thus, it should be possible to match the 1.46 MeV ^{40}K photoelectric peak for the control and experimental subjects in order to get the best estimate for its contribution to the low energy region of interest. This is accomplished by operating the same detectors as previously described without anticoincidence and calibrated for higher energy photon detection. In fact, it has been possible to make both the low (<100 keV) and high energy (1-2 MeV) measurements simultaneously using the three detector units both in the coincidence and the anticoincidence modes in two separate analyzer inputs. In this way the integrity of the count for this specific geometry is maintained. Since the head acts as both a contributor to background (for the most part from ^{40}K and to a lesser degree from ^{226}Ra , ^{210}Pb , ^{90}Sr , ^{137}Cs , etc.) as well as an absorbing and scattering mass for all radioactive materials outside and inside the head, it is best to employ a background which comprises a combination of both of the methods described above. That is, several people of similar body and head size are chosen to act as controls and an average ratio of counts under the 1.46 MeV ^{40}K peak to the counts in the low energy (<100 keV) region is used to obtain the optimum subject background.

Table I-2
Estimated Stable Potassium and ^{40}K
Content of the Head and Total Body(1)

Specific activity = 853 pCi ^{40}K /g stable potassium

<u>Head Structure</u>	<u>Weight (g)</u>	<u>Stable K (g)</u>	<u>^{40}K (nCi)</u>	<u>Approx. % of Head Activity</u>
1. Skull with teeth	1200-1500	1.8	1.54	19.5
2. Teeth	46	--	--	--
3. Brain	1400	4.2	3.58	45.4
4. Face and neck muscles	803	2.4	2.05	26.0
5. Blood in Head	165	0.26	0.22	2.8
6. Hair	20	0.001	0.00085	0.01
7. Skin and scalp	162	0.38	0.32	4.1
8. Tongue	70	0.20	0.17	2.2
9. Eyes	15	--	--	--
10. Fat	--	--	--	--
11. Cervical vertebrae	--	--	--	--
Total head	3.9-4.2 kg	~9.25	~7.88	
Total body	70 kg	~140	~120	

(1) Determined from Reference Man data - personal communication, Dr. G. P. Howells (1972).

Additional work on the exact distribution of ^{40}K in the skull is currently in progress. At the present time, it can be seen in Table 2 that most of potassium is present in the brain structure and that there is approximately 7.9 nCi of ^{40}K in the head with a stable potassium content of ~ 9.25 g. Contribution factors from the hair content of materials such as ^{210}Pb have been measured and determined to be insignificant compared to natural values of ^{210}Pb in bone. Determination of the absorption of low-energy photons by different quantities and distributions of head-hair are currently in progress. In addition, the possibility of increasing the sensitive detection area by the incorporation of additional detector units, until that time that a maximum S^2/B and an optimum geometry is achieved, are currently under consideration.

Extrapolation to Skeletal Burden

Once the best measurement of the activity content of the skull has been made, it is possible to estimate the total skeletal content as well as retention kinetics in bone by consideration of the following parameters:

- 1) bone to bone variation of radionuclide concentration in the skeleton (see Vol. I).
- 2) percentage of the total skeleton represented by the skull structure (Table 1).

- 3) consideration of the radionuclide content of the dental structures.
- 4) turnover and resorption rates of skull bone compared to other skeletal structures, i.e. temporal considerations.
- 5) surface to volume ratio of the skull bone structures compared to other bones in the body.
- 6) contribution of material in the hair and absorption characteristics of individual hair quantities and styles.
- 7) ~~cortical to trabecular bone ratios for the skull bones compared~~ to other skeletal structures.

Conclusion

Utilization of in vivo head counting techniques holds considerable promise for estimating the total skeletal burden of various bone-seeking nuclides more easily and with greater precision than has been possible in the past.

In addition, once the skeletal content of activity has been determined, it will be possible to estimate the amount of rib, sternum and vertebrae contribution to in vivo thorax measurements. This, in turn, will be extremely useful data for estimating the partition of activity between the lung and these bone structures. In fact, it should be assumed that any estimation of "bone-seeking" activity in the lung be derived from in vivo measurements of the head as well as the thorax.

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SECTION II

Additional ⁹In Vivo Measurements and Bioassay of ^{210}Pb in
the Blood and Urine of Former Uranium Miners; ~~UM-3~~

Henry B. Spitz and Norman Cohen

ABSTRACT

The results of an ongoing program to measure ^{210}Pb in the bone, blood, and excreta of a former uranium miner show a decrease in the ^{210}Pb body burden. In vivo detection of ^{210}Pb in UM-3 indicates that, between 1972 and 1975, his body burden has decreased from 9.24 ± 0.75 to 8.40 ± 0.03 nCi. The effective half-life of ^{210}Pb in the skeleton was calculated from this change in body burden to be 14.7 ± 0.6 years.

From the measured body burden of ^{210}Pb in the skeleton, an estimate of the radon and radon daughter exposure in cumulative working level months (CWLM) was calculated using the empirically derived relationship of R. Holtzman⁽⁴⁾. The calculated cumulative exposure value of 7190 CWLM agrees with the estimated value of 6315 CWLM supplied by HEW.

Bioassay for ^{210}Pb in blood and urine was correlated with the in vivo measurements to provide relationships between ^{210}Pb in bone and blood and ^{210}Pb in bone and urine.

Introduction

The increased incidence of lung cancer observed in former uranium miners has been shown to be related to elevated air concentrations of ^{222}Rn and its daughter products that existed in the underground uranium mine environment⁽¹⁾. With legislation promulgated to reduce concentrations of ^{222}Rn in the mine air, the magnitude of the potential hazard has been considerably reduced in the present day occupational environment. However, for those individuals working underground during the early 1950's, the uranium mine atmosphere often produced cumulative radiation exposures of thousands of Working Level Months (WLM). This was possible since over 25% of the mines surveyed during 1956-1959 had radon concentrations over 10 Working Levels (WL)⁽²⁾.

Statistical analysis of Cumulative Working Level Month (CWLM) exposures in a population of former uranium miners indicates a definitive association between radon daughter exposure and the number of lung cancer deaths in miners whose exposures were greater than 1000 CWLM⁽²⁾. This increase in observed lung cancer mortality over the expected incidence is shown in Figure 1. The data relies heavily upon personal

histories obtained verbally from the miners concerning the duration and site of their employment in the uranium mining industry and upon scanty Public Health Service (PHS) radon and radon daughter measurements in the mine during the early 1950's. Together these two limitations make uranium mine-lung cancer epidemiology difficult to formulate.

Bioassay for ^{210}Pb in Urine and Blood Samples

Historically, the first measurement made to determine the result of exposure to ^{222}Rn progeny upon uranium miners was bioassay for ^{210}Pb in urine, blood and fecal samples. Lead-210 in bone was also examined in autopsy samples⁽³⁾ so that deposition and retention characteristics of this nuclide could be explained. Lead-210 has the longest half-life (22.2 years) of all the components of the ^{222}Rn decay chain and is a chemical congener of calcium. Thus, ^{210}Pb in bone can serve as a cumulative and personal indicator of exposure to the radon decay products. The retention and deposition sites of ^{210}Pb in bone in man are not precisely known, but the effective half-life in the skeleton is estimated to be approximately 15 years⁽⁴⁾.

The body burden of ^{210}Pb is a useful cumulative index of past exposure to radon and its decay products. Early measurements of ^{210}Pb in bone have been shown to correlate with the uranium miners' estimated CWLM exposure⁽⁵⁾. Furthermore,

correlations also have been shown to exist between ^{210}Pb concentrations in blood and bone⁽³⁾. Thus, the bioassay for ^{210}Pb in the blood and urine from former uranium miners should give an indirect estimate of the CWLM exposure. With improved estimates of past exposure, the epidemiology can be updated to provide better predictions concerning somatic and genetic mutations in this well-defined population.

It is important to restrict radiochemical analysis to "former" uranium miners since the amount of ^{210}Pb inhaled directly or via ^{222}Rn daughters a short time before measurement may substantially influence the blood concentrations. One might then expect the blood concentrations of active miners to exceed that of former miners due to the presence of ^{210}Pb not just from the body skeletal reservoir but also from the freshly inhaled activity. Once exposure is terminated (i.e. the miner retires or no longer actively mines uranium) the body pool of ^{210}Pb in bone will decrease normally and daily urinary excretion will be a good indicator of the skeletal burden.

In Vivo Detection of ^{210}Pb

Another method of estimating the past radon daughter exposure of the former uranium miner was developed to alleviate some of the uncertainty in Working Level estimates and to establish a relationship between the amount of ^{210}Pb excreted and the body burden. In vivo measurements for ^{210}Pb in the skeleton using the dual (thin) NaI(Tl)-CsI(Tl) detector and

pulse shape anticoincidence electronic circuitry have been routinely performed by this laboratory for many years (6,7). Several uranium miners have been examined in the low background counting room at the laboratory and measurements of their respective ^{210}Pb body burdens have been made (7).

A new system employing three NaI-CsI (thin) detectors in a head counting geometry has improved the detection efficiency for ^{210}Pb to 12.4 cpm/nCi from 7.62 cpm/nCi for the earlier system. In addition, further definition of the low energy (i.e. ≤ 100 keV) spectral shape is now possible by simultaneously measuring the ^{40}K head content. This will eventually improve the lower limit of detection for in vivo counting. A more extensive description of this new procedure regarding the simultaneous measuring technique is provided in a separate section of this report. (See Section I.)

UM-3: Uranium Miner Analysis, 1972

In light of the lack of definitive information concerning the relationship between radon daughter exposure and ^{210}Pb body burden and the retention of ^{210}Pb in bone, a follow-up project with a former uranium miner was initiated to explore these parameters using in vivo techniques. In most respects, this project is analogous to an earlier undertaking by this laboratory with subject UM-1 (7). Now, however, with the

improved detection capabilities more decisive results can be expected. In each instance, bioassay for ^{210}Pb in urine and blood is performed so that comparisons with in vivo measurements and relationships between excretion and body burden can be made.

The subject chosen for this project was UM-3 who had originally visited the laboratory in November, 1972. At that time the in vivo ^{210}Pb detection system utilized two thin NaI-CsI(Tl) crystals with 5 mil Be entrance windows. Throughout the period of his visit, several counting geometries were employed to optimize ^{210}Pb detection and attain the most efficient detector to subject configuration. In addition, a lead and steel table was used to shield the remainder of the body during several head counting procedures.

The results of the counting in 1972 indicated that 1.39 ± 0.11 nCi of ^{210}Pb were detected in the head of the subject. If the skull comprises about 15% of the total skeleton and if ^{210}Pb is uniformly distributed among all bones, then UM-3 has a ^{210}Pb skeletal burden of 9.24 ± 0.75 nCi as determined by the in vivo counting technique. The minimum significant measurable activity (MSMA) at the 95% confidence limit for a 100-minute count is 225 pCi with the two crystal geometry. The natural body burden of unexposed persons is about 0.5 nCi⁽⁸⁾ which would provide only 0.075 nCi in the skull, a value below the MSMA.

Since the measured activity is so close to the MSMA, these data are extremely sensitive to the variation imposed by choice of a control subject. An optimum control subject would be the mean value of several subjects that are the same sex and age as the uranium miner, but who were not employed in the underground uranium mining industry. These factors are in addition to the geographic considerations of living in the Colorado plateau area and consuming a diet typical of the western part of the United States. The interest in the ^{40}K content of the head (Section I) will further enable a comparison to be made between subject and control and determine if the physical characteristics are well matched.

UM-3: Uranium Miner Analysis, 1975

Recent arrangements between UM-3 and the laboratory provided the opportunity to re-examine this subject. Since his last measurement the whole body counting facility in the laboratory has been improved by the addition of a third dual (thin) crystal detector and new anticoincidence electronic NIM modules. Prior to his arrival in the laboratory, UM-3 was sent several containers in which 24-hour urine samples were collected. An additional 24-hour urine sample was obtained during his stay in New York as was a 20 ml blood sample. The samples are stored for ingrowth of ^{210}Bi and ^{210}Po for later radiochemical analysis and counting.

The physical characteristics of UM-3 have changed only slightly since the first visit (Table 1). He is a non-smoker and is not taking any medication regularly other than an occasional antihistamine for eye irritation.

Table II-1
Vital Measurements

	<u>3/4/75</u>	<u>11/30/72</u>
Age	62 yrs.	60 yrs.
Weight	177 1/4 lbs.	185 lbs.
Height	72 in.	72 in.
Head Circumference	24 1/4 in.	24 in.
Head Diameter (anterior- posterior)	20 1/2 cm	21 cm
Head Height	22 3/4 cm	23 cm
Chest Circumference	39 in.	39 1/4 in.
Chest Anterior- Posterior	29.7 cm	30.8 cm

The Department of Health, Education, and Welfare (HEW); NIOSH; Western Area Occupational Health Laboratory, Salt Lake City, has supplied the working history and estimated CWLM exposure data.

Table II-2

Occupational History -- UM-3

<u>Date</u>	<u>Estimated Exposure (WLM)</u>
11/50 - 8/52	864.4
8/52 - 12/53	3529.7
1954 - 1955	1150.8
1956 - 1958	510.0
1959 - 1961	169.7
1962 - 1964	80.7
1965 - 1970	0.0
1971 - 1972	10.0
1972 - 1973	0.0
TOTAL EXPOSURE	6314.8

This exposure history obtained from HEW was verified through conversation with UM-3 and is shown on Table 2. In vivo counting consisted of placing the three detectors around the head. The subject lies on a modified plexiglass hospital table with his head slightly elevated. The bed is positioned and locked in place so that a detector is firmly touching the top of the head. The side detectors are located so that the subject's ears are central to the face of the respective crystals.

Depending upon head size, the separation between the side detectors varies; the optimum geometry obtained when the protective plexiglass covers are lightly pressing against the ears. A photograph of the detector geometry shows the actual arrangements (Figures 2 and 3).

Several modifications of the counting geometry were prepared for UM-3. Head counts were performed with and without a lead-steel shielding to determine if ^{40}K from the body, outside the detector geometry, could easily be reduced and, hence, reduce the subject counting background. Figures 4 and 5 show the results in the spectra with and without the shielding. Variations in lateral detector separation indicated a net result that small changes in this dimension (i.e. 1-2 cm), were insignificant. Figure 6 shows that the 19 cm separation between the side detectors made no significant change in the spectrum.

Each counting period was either 60 or 100 minutes in length, times chosen as optimum considering the amount of activity present. For a 60-minute counting interval the MSMA, at the 95% confidence interval, is 217 pCi using the three detector geometry. This level was determined by comparing several control subjects. The MSMA for a 100-minute count is 168 pCi. The net activity determined in this counting procedure was 1.25 ± 0.04 nCi in the head resulting in 8.4 ± 0.03 nCi in the

total skeleton burden of ^{210}Pb . This assumes that all the ^{210}Pb is deposited in the skeleton and that the skull is 15% of the total skeletal ash. The net spectrum is shown in Figure 7. A 3-point moving average has been applied to the data so that the 47 keV photopeak is prominent. Figure 8 is the high energy ($E > 0.1 \text{ MeV}$) spectrum of UM-3 using the three crystal head geometry. Photopeaks due to ^{40}K and ^{137}Cs are identified.

Calculation of Cumulative Exposure from ^{210}Pb Body Burden

Holtzman⁽⁴⁾ has empirically determined the mathematical relationship between cumulative exposure to elevated concentrations of radon daughters in air and the skeletal burden of ^{210}Pb derived from that exposure. The equation

$$\text{pCi/gm (bone ash)} = (8.2 \pm 1.2) \times 10^{-4} \times (\text{WLM}) \quad (1)$$

is not corrected for decay and excretion of ^{210}Pb between the time of exposure and analysis. The effective half life of ^{210}Pb in the skeleton is assumed to be 15 years. The total body burden can be obtained by multiplying the specific concentration in bone ash by 2600 gm, the mass of the total skeletal ash. Table 3 lists body burdens of ^{210}Pb determined by in vivo counting and the estimated and calculated cumulative exposure to UM-3 for the two series of measurements made in the laboratory.

Table II-3

Summary of In Vivo Counting -- UM-3

<u>Date</u>	<u>²¹⁰Pb Head (a) Measured (nCi)</u>	<u>²¹⁰Pb Body (b) Estimated (nCi)</u>	<u>Estimated Cumulative Exposure (c) (CWLM)</u>	<u>Calculated Cumulative Exposure (d) (CWLM)</u>	<u>MSMA (g) (pCi)</u>
1972	1.39±0.11	9.24±0.75	6314.8	7199 (e)	225
1975	1.25±0.04	8.40±0.03	6314.8	7190 (f)	168

(a) measured by in vivo counting.

(b) skull assumed to be 15% of skeleton ash weight; ²¹⁰Pb assumed to be uniformly distributed in the skeleton; all ²¹⁰Pb assumed to be present in the skeleton.

(c) HEW value from Table 2.

(d) calculation follows equation 1.

(e) decay corrected (t=11 yrs.) to last significant exposure.

(f) decay corrected (t=13 yrs) to last significant exposure.

(g) 95% confidence interval, 100-min. count.

The agreement between calculated values for cumulative exposure and those estimations made by HEW may be fortuitous in light of possible differences that may arise from several sources: 1) incorrect assumptions in the CWLM estimates by HEW, 2) choice of effective half-life for ²¹⁰Pb in the skeleton, 3) decay correction of measured body burden of ²¹⁰Pb to last significant exposure period, 4) value for skull percentage of total skeletal mass.

The effective half-life of ^{210}Pb in bone can be calculated by using the measured concentrations of ^{210}Pb in the head from UM-3 in 1972 and 1975. A period of 2 1/4 years elapsed between the two in vivo counting dates. The result of the calculation gives a value of 14.7 ± 0.6 years as the effective half life of ^{210}Pb in the skull.

Bioassay of ^{210}Pb in Urine and Blood

Urine and blood samples were analyzed for ^{210}Pb concentration by measuring ^{210}Bi and ^{210}Po using the method of spontaneous deposition⁽⁹⁾. Urine samples were collected on a 24-hour basis and creatinine was measured to confirm the collection period. Blood was also drawn in 20 ml samples. The MSMA for the ^{210}Bi and ^{210}Po detection systems was 0.49 pCi and 0.05 pCi, respectively, for a 100-minute counting period at the 95% confidence limit. The samples received from UM-3 during the last visit have not had sufficient time for ^{210}Po ingrowth and as such, the results are incomplete. The urine samples were analyzed for ^{210}Bi since the equilibrium activity between ^{210}Pb and ^{210}Bi occurs in about 30 days. Table 4 gives the available urine and blood results.

Table II-4

Bioassay for ^{210}Pb in Urine and Blood

<u>Date</u>	<u>Urine Bi-210 pCi/l</u>	<u>Urine Po-210 pCi/l</u>	<u>Blood Po-210 pCi/l</u>	<u>Blood Pb-210 pCi/l</u>
1/71	2.7 ± 0.4	0.24 ± 0.2	10.8 ± 0.6	19.4 ± 1.3
3/75	3.8 ± 0.7	--	--	--

Summary

The in vivo detection system for measuring ^{210}Pb in the head was used to estimate the skeletal burden of ^{210}Pb in a former uranium miner due to the occupational exposure to elevated concentrations of ^{222}Rn and its daughter products. From the quantity of ^{210}Pb in the skeleton an estimate of cumulative exposure was made that is in excellent agreement with the HEW estimates for exposure. Sequential in vivo measurements made on UM-3 indicate an effective half-life of 14.7 ± 0.6 years for ^{210}Pb in the skeleton.

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Fig. II-1 Observed and expected lung cancer mortality
per 10⁴ miners.

Figure 1. Observed and Expected Annual Lung Cancer Mortality per 10,000 Miners and 95-percent-Confidence Limits in Relation to Exposure

Fig. II-2 Head count geometry for ^{210}Pb in UM-3.

Fig. II-3 Standard chair detection geometry for high energy emitting nuclides.

Fig. II-4 Low energy spectrum using head counting geometry from UM-3.

Fig. II-5 Low energy spectrum using head counting geometry from UM-3 and remainder of body shielded by a lead-steel table.

Fig. II-6 Low energy spectrum using head geometry from UM-3;
lateral detectors separated to 19 cm.

Fig. II-7 Net spectrum of UM-3.

Former Uranium Miner UM-3
Head Measurement - 60 Min. Net.
3 NaICsI (TI) Detectors

Fig. II-8 High energy spectrum in the head geometry taken simultaneously with the low energy spectrum seen in Figure II-4.

Former Uranium Miner: UM-3

3 Detector: NaI-CsI Dual (thin) Crystals

Skull Geometry, 60 minutes, 3/04/75

Crystal Separation = 18cm

Gross Spectrum, High Energy Calibration

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SECTION III

Design of a Continuous Digital-Output
Environmental Radon Monitor

McDonald E. Wrenn, Henry Spitz, and Norman Cohen

ABSTRACT

A new field instrument for the continuous measurement of radon concentrations has been developed to investigate the magnitude and variability of environmental levels of ^{222}Rn . Passive diffusion of radon, but not its daughters, occurs through an open pore polyurethane foam into a sensitive volume where a static electric field directs the positively ionized radon daughter products to a central collecting electrode. Pulses in a $\text{ZnS}(\text{Ag})$ scintillator, resulting from the alpha emission of ^{218}Po and ^{214}Po , are observed with a photomultiplier tube and counted using standard NIM electronics. The detector unit has been fabricated into a small, convenient package for indoor air sampling without the use of air movers or pumps. The unit is unobtrusive and acceptable into a daily routine without disrupting normal family or business activities. The monitor can detect as little as 0.5 pCi/l for a 40-min. count ($\alpha=.05$). The equilibrium detection efficiency of the instrument is 0.7 cpm/pCi/l.

Introduction

The Institute of Environmental Medicine of the New York University Medical Center has an extensive history in research relating to human exposures to ^{222}Rn and its progeny.^{1,2,3,4} Measurements in uranium mines have been made with a device developed earlier at

New York University that performs as a personal dosimeter for high levels of mine air.⁵ Finally, uranium mine atmospheres have been characterized with respect to radon daughter concentrations, differential equilibria and attachment as a function of particle size.⁶

A new radon monitor, capable of measuring low level, diurnal fluctuations of ^{222}Rn concentration inside residential structures has been developed and is described in the present text. The device was designed in response to a need for a rapid and simple method for analyzing the atmosphere in residential structures that were believed to have uranium mill tailings incorporated into the building materials. Radon concentrations in some of these houses are not elevated above "normal" average indoor background values.

Accordingly, the instrument described herein was specifically designed to give a continuous record of radon concentration which would allow investigation of fluctuations over time with a sensitivity sufficient to detect radon indoors at natural concentrations. Our results show that a limited number of grab samples are inadequate to characterize indoor radon levels because of the large diurnal effect observed.

Theory and Design

Radon-222 decays through four short-lived daughters, two of which are alpha emitters, to ^{210}Pb , a relatively long-lived nuclide. Each decay of ^{222}Rn will eventually produce three alpha particles.

Radon, a noble gas, decays to ^{218}Po which is normally formed as a positive ion. The ^{218}Po grows into 50% of its equilibrium activity in three minutes in an environment which is initially free of daughters. The ingrowth of ^{214}Po from ^{222}Rn decay requires close to an hour to be reasonably complete.

The present radon monitor operates by electrostatically collecting the daughter products of ^{222}Rn and observing the alpha decay events from ^{218}Po and ^{214}Po . Radon, but not its daughters, diffuses through a porous foam filter and enters a sensitive volume. The degree of "passive diffusion" is determined by the differential radon concentration gradient inside and outside the detector. Costa-Ribeiro measured an average value of $0.032 \text{ cm}^2/\text{sec}$ for the diffusion coefficient of radon in polyurethane foam.⁷ From this we have calculated that about ten minutes is required for passive diffusion to establish 90% of equilibrium inside the sensitive volume.

The design of the central electrode consists of a hemispherical lucite light pipe painted with a $\text{ZnS}(\text{Ag})$ coating and then covered with aluminized mylar to obtain an electrically conductive surface. Most of the ^{218}Po is initially formed as a positive unattached ion and is thereby attracted toward the central electrode by the electrostatic field applied within the sensitive volume. The ^{218}Po attached to the aluminized mylar will decay by alpha emission, a fraction of which (roughly 40%) penetrates the mylar. The scintillations produced in the underlying ZnS are detected by a 19 mm photomultiplier tube optically coupled to the light pipe.

Since the density of the aluminized mylar covering the central electrode is about $2 \text{ mg}/\text{cm}^2$, part or all of the alpha particle

energy may be deposited in the mylar depending on the angle of entrance.

The instrument was calibrated by exposing the sensitive volume to various known concentrations of radon and observing the equilibrium response of the detector. Several exposures to different concentrations of ^{222}Rn were made to insure that detector response is independent of concentration.

The monitor, Fig. 1, is constructed in a cylindrical shape 36.5 cm high, 25.5 cm in diameter and weighs 2.5 kg. The bulk of the volume contains a preamplifier, photomultiplier tube, and batteries to supply the constant collecting potential for the electric field in the sensitive volume.

A hemispherical region atop the cylinder defines the sensitive volume, Fig. 2. A 7.7 cm radius hemispherical screen functions as the anode while a centrally located lucite cathode is the site at which positively ionized radon daughters are collected. A concentric screen covers the anode and functions only to secure the polyurethane foam. In addition to its diffusive properties. The foam also seals the photomultiplier tube from light reaching the central electrode. The 19 mm diameter lucite light pipe is optically coupled to a 19 mm amperex XP1110 photomultiplier tube.

Scintillation pulses are detected with standard NIM type electronics and recorded on paper tape for predetermined counting periods. A 40-minute interval has been selected for routine observations but this can be altered to any predetermined time period.

The diurnal fluctuation of radon is observed by plotting average count rate versus time of day. A typical pattern is

indicated in Fig. 3. A cyclic repetitive pattern is observed in all residential structures monitored with this radon sampler even at control locations where no tailings were present.

The fact that all construction materials have some natural alpha contamination partially accounts for the background activity of the radon monitor when it is exposed to "aged-air", presumably free of radon and its daughters. In addition to this activity there are spurious electrical pulses inherent in the detection modules and photomultiplier tube. Measurements of the instrument background over an extended time period are indicative of a buildup of activity on the central electrode especially when exposure to high radon concentrations has been made for long periods of time. The buildup is gradual due to the ingrowth of ^{210}Po from the relatively long-lived parent, ^{210}Pb . When the instrument contamination background has increased to an objectionable level, it is a simple procedure to replace the aluminized mylar conductor.

A calibration and background determination were made after one instrument underwent extensive field operation (about nine months) in Grand Junction, Colorado. The calibration factor remained a constant value of 0.72 cpm/pCi/l and the instrument background increased to 0.61 cpm from 0.47 cpm.

The minimum significant measurable activity (MSMA)⁸ in a 40-minute counting period at the 95% confidence level is 0.48 pCi/l. This value can be improved by application of a lower background ZnS(Ag) scintillator and installation of new aluminized mylar over the light pipe. A new model of the detector has now been built that has a significantly larger sensitive volume and incorporates a lower-background ZnS(Ag) preparation. It is expected to be capable

of measuring radon concentrations as low as 0.10 pCi/l.

The response of the monitor is linear with radon concentration. The collection efficiency appears to be unaffected by normal fluctuations of relative humidity and unaffected by gamma radiation fields up to 85 μ R/hr. One does expect a variation in collection efficiency with voltage applied for collecting potential. Figure 4 indicates that collection of the ^{210}Po ions is complete above 300 VDC. This voltage is easily supplied by a standard battery pack.

The response time of the monitor was determined by observing count rate, as radon was initially injected into the test chamber. A steady state condition between the radon concentration in the atmosphere and the sensitive volume was achieved within 15 minutes. There is a time lag between a change in the ambient radon concentration and the instrument response which is related to the diffusion time and the time necessary for buildup of the short-lived daughters on the central electrode.

Only a small fraction of the alpha particles from the direct decay of ^{222}Rn itself are observed since their mean range in air is 3.25 cm, and most of the sensitive volume is beyond this range. Thus, for each ^{222}Rn atom that decays within the sensitive volume, two alpha particles from the short-lived daughters are potentially observed.

It has been standard practice to bring the radon monitor to the observation site immediately upon arrival and subsequently connect the counting electronics. To simplify operation, the collecting potential is always applied to the monitor regardless of the status of the unit. Thus, within this initial period the monitor has usually achieved the steady state condition.

Conclusion

The successful field employment of this new continuous readout radon monitor has provided a simple and accurate method to determine the natural environmental concentrations of ^{222}Rn in residential and other occupied structures. Its ease of operation simplifies the measuring procedure and provides not only a value for mean concentration of ^{222}Rn , but also indicates the variation of the concentration over the measuring period.

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We would like to acknowledge the general support of a center program supported by NIEHS grant ES00260 and support for construction of a field model from the State of Colorado.

Support for the construction and field implementation of this device was received from the State of Colorado as part of the uranium mill tailings removal and reconstruction project for Grand Junction. Inclusion of this section into the Annual Report is to supply background information on the design and operation of the NYU continuous readout radon monitor and to indicate the manner in which radon sampling was performed in Grand Junction.

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Fig. 1 - Continuous environmental sampling with radon monitor in office. The sampler and associated counting electronics are shown at a monitoring site.

DETECTOR CROSS-SECTION

Fig. 2 - Cross-section of radon monitor sensitive volume. Radius of the volume is 7.7 cm. Central electrode diameter is 19 mm.

Fig. 3 - Typical diurnal variation in radon concentration observed with continuous-readout environmental radon monitor. Measurements obtained in occupied residential structure with uranium mill tailings incorporated into building materials.

Fig. 4 - Efficiency vs. collecting potential. Evaluation of monitor efficiency at different collecting potentials in steps of 300 volts, d.c.

Figure 5

Detector Efficiency as Function of Collecting Potential

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Non-Occupational Radiation Exposures from ^{222}Rn
and Daughters to Residents of Grand Junction, Colorado

Henry B. Spitz, Norman Cohen, and McDonald E. Wrenn

ABSTRACT

Six individuals from Grand Junction, Colorado were examined for ^{210}Pb body burdens as a result of living in homes where concentrations of ^{222}Rn were elevated due to the presence of uranium mill tailings beneath the building foundation. In vivo detection for ^{210}Pb using three NaI-CsI(Tl) thin crystals in the standard NYU head geometry identified two persons with estimated body burdens above 1.1 nCi. Bioassay for ^{210}Pb was also performed to compare with the in vivo analysis and to further substantiate the relationship between ^{210}Pb in bone, blood and urine.

Estimates of exposure in cumulative working level months (CWLM), range 85-566 CWLM, were used to calculate expected body burdens of ^{210}Pb . The NYU continuous readout radon monitor provided diurnal measurements of ^{222}Rn in the homes of the volunteer subjects so that, considering assumptions about ventilation and residence times, actual exposures could be determined.

Introduction

The development in this laboratory of a continuous readout radon monitor and its successful field employment in Grand Junction, Colorado, has provided a simple and accurate device for identifying structures where large sources of radium enriched sands were incorporated into building materials (see Section III). Grand Junction, Colorado is a former uranium mill city where numerous residential and commercial structures were built with materials that include uranium mill tailings. The result of this factor was the construction of several houses where indoor radon concentrations have been shown to exceed 150-200 pCi/l on a daily average. The mean concentration for all involved homes in the area usually falls between the range of 2.5 to 75 pCi/l, but higher anomalies are not uncommon. Indoor radon concentration in non-contaminated structures is usually less than 1.5 pCi/l. Each location is unique with respect to its ventilation characteristics and hence will exhibit a different diurnal variation in radon concentration. A typical pattern of the variation observed is indicated in Figure 1.

In order to obtain a meaningful value for the concentration of radon in a typical home environment, it is necessary to observe and characterize the diurnal concentration pattern. One must determine the actual concentration of the nuclide in air at the time when residents are exposed to the environment. This would depend upon their living habits. Hence, a 24-hour mean value is insufficient for evaluating inhalation exposure unless the fluctuations in radon concentration are of small magnitude.

Diurnal Fluctuations of ^{222}Rn

Figure 1 is typical of the diurnal pattern exhibited when the radon concentration is examined on a continuous basis. Each point represents a 40-minute integration period. At this location the maximum period of exposure occurred when the radon concentration was at a minimum. The average value for ambient radon concentration would be a biased estimate of the actual exposure received by the family. The continuous readout capability of the radon monitor provides a method heretofore unavailable to estimate exposure to radon.

It is understood that the source of dose is from radon daughter activity (i.e. RaA and RaC') rather than from the ^{222}Rn (1). However, by making assumptions about the nature of the ventilation and structure configuration an estimate of the equilibrium ratio between the daughters and the parent activity can be made. An intercomparison between daughter

activity in working level concentrations (WL) and actual ^{222}Rn concentration was made using the NYU radon monitor and samplers designed and operated by the AEC's Health and Safety Laboratory (HASL) (2). Results of this analysis defined the relationship between estimates of exposure (WL) and radon concentration. The multicomponent radon fluctuation observed at the time of the intercomparison was due to intentional changes in space heating conditions. During the intercomparison several attempts to observe changes due to the cycling of the forced air heating were made.

Magnitude of Tailings Involvement in Grand Junction

In all, about 4800 residences in Grand Junction have tailings under or near the foundation. The magnitude of the sampling program to measure and document the radon or radon daughter concentrations in these homes is extensive and costly. The New York University radon monitor has been extremely successful in quickly identifying locations where gamma radiation levels are below the Surgeon General's recommended guidelines for remedial action (Table 1) but the radon and radon daughter levels may exceed those guidelines.

Table IV-1

Surgeon General's Guidelines

External Gamma Radiation (above natural background of 0.014 mR/hr)

Greater than 0.1 mR/hr	remedial action indicated
From 0.05 mR/hr to 0.1 mR/hr	remedial action suggested
Less than 0.05 mR/hr	no action indicated

Indoor Radon Daughter Products (above the natural background of 0.004 WL)

Greater than 0.05 WL	remedial action indicated
From 0.01 to 0.05 WL	remedial action suggested
Less than 0.1 WL	no action indicated

Of the approximately 4800 Grand Junction residences that are suspected of having uranium mill tailings under or near the structure about 2400 exceed the Surgeon General's lower guidelines and about 250 exceed the upper guideline. The AEC risk estimates for the Grand Junction population predict minimal, if any, elevation over the natural incidence of somatic and genetic mutations.

Classification of Exposure

An indirect measurement of cumulative exposure to elevated concentrations of the ^{222}Rn decay chain is the body burden of ^{210}Pb . Continuous and ongoing studies with former

uranium miners have relied upon bioassay for ^{210}Pb in blood and urine samples to determine cumulative past exposure. This laboratory has been instrumental in development of programs to monitor former uranium miners by in vivo detection for ^{210}Pb in the skull (see Section II). A natural extension of the ^{210}Pb measuring program is the analysis of non-occupational exposures like those incurred by Grand Junction residents.

The exposure received by residents of Grand Junction who live in homes with elevated radon concentrations is similar to that incurred by uranium miners, but of considerably smaller magnitude. It is estimated that, living in a home where the average radon concentration is 100 pCi/l could provide a chronic exposure equivalent to about 350 cumulative working level months over a period of ten years. This exposure can be shown to be equivalent to a skeletal body burden of 750 pCi ^{210}Pb (see Table 2).

A typical residential structure will experience 3-5 air changes per hour depending upon occupancy, seasonal conditions, type of air treatment and ventilation employed. Considering that uranium mill tailings are uniformly distributed beneath the foundation, the emanation of radon will rely upon meteorological variables and the exchange rate of air in the house with the outdoor environment. For a well-insulated, vacant house (i.e. doors and windows remain closed) the concentration of ^{222}Rn will be high and will show a diurnal pattern similar to, but not as pronounced as seen in Figure 1. This variation is produced by air exchanges that occur due to differential heating

of outdoor and indoor air.

Exposure, in WLM, can be estimated by first assuming a rate for indoor-outdoor air exchange. This parameter can be used to estimate the degree of equilibrium activity achieved between ^{222}Rn and its daughter products. A factor that describes the percentage of equilibrium between ^{222}Rn and its daughters was calculated for various air exchange rates in a structure. The ratio of WL to ^{222}Rn concentration is plotted as a function of ventilation rate in Figure 2. Note that for less than 0.001 air changes/minute, the ratio WL/pCi/l of radon approaches 0.01 and for an air turnover time of one hour the ratio is 0.005 (or 50% of the equilibrium value). For a typical residential structure the equilibrium ratio of ^{222}Rn to its daughters is about 30%. If 100% equilibrium were attained, then 100 pCi/l of ^{222}Rn would produce an exposure of 1 WL. However, at 30% equilibrium the exposure to the inhabitants from 100 pCi/l of ^{222}Rn would be only 0.33 WL.

Cumulative exposure to elevated concentrations of ^{222}Rn and its daughter products in a home is estimated by first evaluating the occupancy pattern of individual members of the family. Second, the magnitude of the ^{222}Rn concentration during the period of exposure is determined. The WL value is then calculated using the air exchange rate and the WL to ^{222}Rn concentration ratio from Figure 2, as described. Thirdly, for

conversion to CWLM the total hours of exposure per year for each individual is estimated and adjusted to comply with the occupational schedule of 170 hours per working month. (This correction is necessary since occupational exposure occurs only during working hours (i.e. 35 hours/week; 50 weeks/year) whereas non-occupational exposure may be different.) The result of the calculation is the number of occupational working months WLM per year that a person is exposed. The calculation to determine CWLM exposure is shown in Table 2.

Table IV-2

Calculation of Estimated Cumulative Exposure (CWLM)

$$^{222}\text{Rn Concentration (pCi/l)} \times \frac{\text{equilibrium factor (a)}}{\text{factor (a)}} = \text{estimated concentration (WL)} \quad (1)$$

$$\frac{\text{exposure rate (hr/yr)}}{170 \text{ hr/working month}} \times \frac{\text{exposure (yr)}}{\text{duration}} \times \text{estimated concentration (WL)} = \text{CWLM} \quad (2)$$

(a) WL/pCi/l from Figure 2.

Radon-222 Measurements in Grand Junction, Colorado

To assess the effect of living in homes with elevated radon and radon daughter concentrations, several persons from Grand Junction were brought to the Institute of Environmental Medicine in New York. The diurnal variation of radon in their respective

homes has been well documented by measurements made with the NYU radon monitor and, hence, by making some assumptions, their exposure can be estimated.

During field testing of the radon monitor, several locations were identified where concentrations were extraordinarily high. At Location A, a structure with a partial basement used mainly as a sewing room by a mother and her daughter, concentrations of radon averaged 388.3 pCi/l (range 500 pCi/l to 296 pCi/l). The family occupied the house for approximately ten years. That part of the house where the ^{222}Rn concentrations were maximum received restricted use. In fact, the majority of the daylight hours found the house vacant since the family occupation was farming. The primary exposure was confined to the sewing-recreation room. Unfortunately, no sampling was performed in the bedrooms directly above the sewing room. Due to the lack of forced air ventilation, the diffusion of radon into the bedrooms would probably add only slightly to the total exposure estimate. The CWLM estimates have included a factor for this concern. The value for CWLM exposure was derived as a time weighted average by discussing activity patterns with the family members.

Table 3 gives the physiological parameters for Family A.

Table IV-3

Family A

Radon Concentration During Sampling (sewing-recreation room)

14-16 January 1974

Maximum = 500 pCi/l ^{222}Rn

Minimum = 296 pCi/l ^{222}Rn

Mean = 388.6 pCi/l ^{222}Rn

ID	Relation	Age	Height (cm)	Weight (lb)	Head Measurements (cm)			Estimated (CWLM) (a)
					Brow	Anterior- Posterior	Diam.	
GJ-1	Mother	43	157.5	136	10.6	14.8	20	85.0
GJ-2	Son	17	167.6	133	9.8	9.5	21.5	74.5
GJ-3	Daughter	14	155	98	8.7	9.1	19.5	22.4

(a) Values for CWLM were calculated using concepts from Table 2.

Even though the radon levels measured in the home were extraordinarily high, maximum exposure was limited to a few rooms that were occupied only intermittently during the week.

Facilities were not available to monitor the air in other parts of the house. Figure 3 shows the results of the radon sampling in the sewing-recreation room.

Similar high concentrations of radon were found at another site, Location B. This house was an extremely well-sealed structure. The elevated levels prove the merit of building characteristics. Ventilation was by means of forced air

heating and cooling with the addition of electrostatic filtration. Measurements of the radon concentration indicated a mean value of 290.2 pCi/l. Radon daughter measurements were performed simultaneously by a group from Oak Ridge National Laboratory. The results of the intercomparison of radon and radon daughter measurements are shown in Figure 4. It is interesting to note the effect that the electrostatic filters have upon the radon daughter concentrations. On Figure 4, points 6 and 7 show a drop in the daughters but an increase in radon.

Table IV-4

Family B

Radon Concentration During Sampling

2-3 November 1973

Maximum = 428 pCi/l ^{222}Rn

Minimum = 253 pCi/l ^{222}Rn

Mean = 290.2 pCi/l ^{222}Rn

<u>ID</u>	<u>Relation</u>	<u>Age</u>	<u>Height (cm)</u>	<u>Weight (lb)</u>	<u>Head Measurements (cm)</u>			<u>Estimated (CWLM) (a)</u>
					<u>Brow</u>	<u>Anterior- Posterior</u>	<u>Diam.</u>	
GJ-4	Mother	53	153	121	62	56	19	566
GJ-5	Father	55	168	143	66	58	21	416
GJ-6	Son	21	163	134	67	58	20	208

(a) Values for CWLM were calculated using concepts from Table 2.

Unlike Family A, Family B did receive a maximum exposure since the husband and wife operated a business office in the house. The son, however, had been away from home since he reached 18 years of age.

Removal of the uranium mill tailings from beneath the structure at Location A and Location B was completed at least four months before the families traveled to the Institute. Therefore, urine and blood samples should contain ^{210}Pb derived from the skeletal burden rather than from recently inhaled radon daughters. ~~Radon-222 sampling was performed after the tailings removal and reconstruction to confirm the reduction of radon in the air.~~

In Vivo Measurement and Bioassay for ^{210}Pb in Urine and Blood

In vivo measurements and bioassay for ^{210}Pb in urine and blood samples were made for members of both families. Six individuals (GJ-1, GJ-2, GJ-3 from Location A and GJ-4, GJ-5, GJ-6 from Location B) were examined in the low background whole-body counting room using three dual (thin) NaI-CsI(Tl) crystal detectors. Each subject was counted for 100 minutes in our standard head geometry, (see Section I). Apart from anatomical variations inherent in different subjects, it is possible to duplicate this geometry (refer to Figures 5 and 6) and maintain a detector separation between the side crystals of no more than 19 centimeters.

The minimum significant measurable activity (MSMA) is dependent upon the control subject chosen as background. For a 100-minute counting period and using a region of integration of 30 to 60 keV, the MSMA is 168 pCi at the 95% confidence interval. This value is less than the body burden of ^{210}Pb in the skull (head) that one would expect of persons exposed to elevated radon concentrations equivalent to a few hundred working levels.

According to Blanchard⁽³⁾ and Holtzman⁽⁴⁾, the normal body burden of ^{210}Pb is approximately 0.45 nCi. The control subject would then have about 68 pCi of ^{210}Pb in the head if one considers that the ash weight of the skull is about 15% of the total ash weight of the skeleton. The ash weight value is used here since lead is a chemical congener of calcium which in turn is proportional to the ash weight. In vivo counting of an unexposed control subject does not show any indication of a positive ^{210}Pb signal, (since the skull burden is below the MSMA). Any statistically significant positive count rate in the ^{210}Pb photopeak region of the gamma spectrum, after a suitable control subject was used to calculate net data, would imply that the body burden of the individual would be greater than an MSMA of 1.1 nCi, i.e. about twice the "natural" body burden.

Holtzman⁽⁴⁾ has shown empirically that, using regression analysis on concentration of ^{210}Pb in bone vs. exposure, the following equation can determine the body burden of ^{210}Pb from the cumulative working level month estimate:

$$\text{Body burden } ^{210}\text{Pb (pCi)} = (3.2 \pm 0.5) \times 10^{-7} \text{ (WLM)}$$

(3)

This assumes that the effective half-life of ^{210}Pb in human bone is 15 years and that the skeletal mass is 2600 gm of bone (ash) ⁽⁴⁾. For cases where the exposure was received several years before analysis, exponential decay must be considered with an effective half-life of 15 years. Using these assumptions the predicted body burdens of the Grand Junction subjects are given in Table 5. The exposure was of a chronic nature and ended only a few months before the in vivo measurements were made.

Table IV-5

Calculated ^{210}Pb Body Burdens

<u>ID</u>	<u>Calculated Pb-210 Body Burden (a) (pCi)</u>	<u>Calculated Pb-210 Skull Content (b) (pCi)</u>	<u>Estimated CWLM (c)</u>
GJ-1	181.2	27.2	85
GJ-2	158.8	23.8	75
GJ-3	47.8	7.2	22
GJ-4	1206.7	181.0	566
GJ-5	886.9	133.0	416
GJ-6	443.5	66.5	208

(a) as calculated by equation 3.

(b) skull assumed 15% of skeleton.

(c) from Tables 3 and 4.

Results -- Bioassay of ^{210}Pb in Urine

Only preliminary data regarding the bioassay of ^{210}Pb in urine is available at this time since there has only been a six-month period of ^{210}Po ingrowth. Samples were obtained in July 1974 and thus ^{210}Po has grown-in to only 58% of its equilibrium activity. Preliminary analysis was performed upon the first samples from subject GJ-4 and GJ-5. Two 24-hour urine collections were obtained from each subject; one was collected at home and mailed to New York and the other was collected during the period of their visit to the laboratory. For these preliminary results, 24-hour urine samples from control subjects in the New York area were used for comparison. Subsequently, six urine samples from non-exposed individuals in Grand Junction were obtained to help establish the normal excretion of ^{210}Pb for residents of Colorado. The data from these analyses are not available at this time.

To assure that the urine sample is representative of a 24-hour excretion period, creatinine measurements were performed. It is possible, therefore, to report ^{210}Pb urinary excretion as pCi/gm creatinine, pCi/24 hrs., or pCi/ml urine. The creatinine test was particularly important for classification of urine samples from GJ-4 since the volumes produced by this individual were extremely large. Therefore, even though GJ-4 has the highest CWLM exposure, the measured β^- activity in urine on a per ml basis initially appeared to be below the MSMA for ^{210}Bi . The 500 ml sample routinely used in the plating technique was extremely dilute since the overall 24-hour volume was 3930 ml in contrast to Reference Woman's urinary output of 1000 ml/day⁽⁵⁾. In the ^{210}Pb plating technique the

MSMA, at the 95% confidence limit for a 100-minute counting interval, is 0.49 pCi and 0.05 pCi for the beta and alpha systems respectively.

Table 6 lists the preliminary results of the bioassay of ^{210}Pb in urine for GJ-4, GJ-5 and the seven NYU controls. Replicate samples are available but must wait for ingrowth before analysis.

Table IV-6
Bioassay of ^{210}Pb in Urine

<u>ID</u>	<u>^{210}Pb (pCi/l)</u>	<u>^{210}Pb (pCi/day)</u>	<u>Estimated CWLM</u>
NYU Controls (n=7)	0.58±0.55	0.86±0.83	--
GJ-4	0.76±0.67	1.83±1.62	566
GJ-5	1.65±0.65	2.21±0.88	416

Results of *In Vivo* Analysis

Figures 7 through 12 are the gross spectra of the six subjects chosen from Grand Junction. Figure 13 is a control subject that is included only for illustration and is not to be construed as a background. At this time, statistical analysis has identified positive counts in the ^{210}Pb integration region for subject GJ-5. A curve-smoothing technique was applied to the gross spectrum GJ-5 (Figure 14) in order to reduce

the scatter of points in the region of interest. Figure 14 is the result of twice using a three-point moving average and results in a well-defined photopeak due to ^{210}Pb in channel 47. Preliminary results also indicate the possibility of net positive counts in subject GJ-4, but further computer analysis is necessary for confirmation. The magnitude of the exposure received by Family A is such that the ^{210}Pb body burdens would be less than the MSMA for in vivo detection. Analysis performed upon the gross spectra of GJ-1, GJ-2 and GJ-3 confirm the calculations of Table 5, i.e. ~~each subject has a ^{210}Pb body burden less than 1.1 nCi.~~ No detectable ^{210}Pb photopeak was observed with in vivo counting using subjects from Family A. On the figures the region of integration for ^{210}Pb has been emphasized and the location of the expected photopeak has been indicated by an arrow.

The difficulty in deciding upon a definite ^{210}Pb body burden for these subjects is based upon the necessity of choosing a proper control subject. To alleviate any uncertainty in the choice of any single subject as a control, a new procedure has been adopted that compares the ^{40}K content of the head in the subject and control. This procedure gives another parameter that can be applied to the criteria used in choosing a control. The theory is described in Section I of this report.

Conclusion

Six volunteer subjects from Grand Junction, who have lived in homes with elevated ^{222}Rn concentrations, have been examined for ^{210}Pb skeletal burdens. Bioassay for ^{210}Pb in urine

indicates elevated concentrations in comparison to control urines from the New York area. In vivo detection for ^{210}Pb also indicates an elevated body burden for one and possibly two individuals. It is expected that subsequent analysis of the available data and the further examination of the urine and blood samples will extend the findings so that calculations of the body burden of ^{210}Pb can be made.

In addition, the control urine samples from residents of Grand Junction will provide a more sound basis for ~~comparison with the subjects than the New York control urines.~~ Once the body burden of ^{210}Pb has been calculated, an estimate of the cumulative working level-month exposure will be possible.

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Fig. IV-1 Typical diurnal pattern of ^{222}Rn in an occupied house. NYU-AEC intercomparison indicated by arrow.

Fig. IV-2 Working Level--(WL)--to ^{222}Rn concentration (pCi/l)
ratio as a function of ventilation rate.

Calculated Upper Limit of Ratio of "working level" to Radon Concentration in a Ventilated Atmosphere as a Function of Ventilation Rate

Fig. IV-3 Radon sampling at Location A with NYU
continuous readout radon monitor.

Radon Monitor NYU-A
NHPQ-1148 (Pre-reconstruction)
14-16 January 1974

Fig. IV-4 Radon sampling at Location B with NYU continuous readout radon monitor. NYU-ORNL intercomparison data indicated by arrows.

Fig. IV-5 Head geometry for in vivo counting of ^{210}Pb in GJ-5.

Fig. IV-6 Detailed photograph of detector geometry in head counting configuration.

Fig. IV-7 Gross spectrum of subject GJ-1 in head counting geometry.

Subject GJ.1
Head Measurement
 ^{222}Rn Exposure
3 NaICsI(Tl) Detectors
Counting Time = 100 min.

Fig. IV-8 - Gross spectrum of subject GJ-2 in head counting geometry.

Subject GJ.2
Head Measurement
 ^{222}Rn Exposure
3 NaICsI(Tl) Detectors
Counting Time = 100 min.

Fig. IV-9 Gross spectrum of subject GJ-3 in head counting geometry.

Fig. IV-10 Gross spectrum of subject GJ-4 in head-counting geometry.

Subject G.J.4
Head Measurement
 ^{222}Rn Exposure
3 NaICsI(Tl) Detectors
Counting Time = 100 min.

Fig. IV-11 Gross spectrum of subject GJ-5 in head counting geometry.

Fig. IV-12 Gross spectrum of subject GJ-6 in head counting geometry.

Fig. IV-13---Typical control subject spectrum of in vivo
counting for ^{210}Pb .

Fig. IV-14 Gross spectrum of GJ-5 after application of curve smoothing program. Pb-210 peak prominent at 47 keV.

Subject G.J..5

Head Measurement

^{222}Rn Exposure

3 NaICsI(Tl) Detectors

3 Point Moving Average - 2X

Counting Time = 100 min

49553

Vol. II,

SECTION V

Enhanced Removal of ^{241}Am by DTPA Chelation Therapy
in an Adult and Teenage Subject - Continuation Study

Tom Lo Sasso and Norman Cohen

ABSTRACT

During the past year we have witnessed a series of $\text{Na}_3(\text{Ca-DTPA})$ chelation treatments on two human subjects, an adult man and a teenage boy, who have long-term body burdens of ^{241}Am . We have coordinated in vivo whole-body counting, bioassay of urine and feces, and various blood chemistry measurements to coincide with this therapy schedule. Decreases in total body burdens for this treatment period were measured as 5% in the adult and 30% in the youth. High concentrations of zinc in urine and a corresponding decrease of activity of the zinc-dependent erythropoietic enzyme, ALAD, has also been observed.

Introduction

This continuation study is concerned with the effects of diethylenetriaminepentaacetic acid (DTPA) chelation therapy on the old (11 years) ^{241}Am body burdens of a 60 year-old man (Subject 1) and his 15 year-old son (Subject 2). It is part of a more general program ongoing since April 1970 to determine the rate of ^{241}Am loss by whole-body counting and bioassay techniques. In addition, we have attempted to define the gross distribution of the contaminant in their bodies by in vivo scintillation measurements with dual thin crystal NaI-CsI(Tl) detectors positioned over specific regions of the body. Detailed descriptions of our earlier efforts have been previously reported (1,2).

~~Before 1975 there were two series of chelations performed,~~ initially in July 1970 and again in May-June 1973 (see Table 1). The earlier of these treatments consisted of administering one gram doses of $\text{Na}_3[\text{Ca-DTPA}]$ intravenously to each subject three times over a seven-day period; the latter treatments consisted of one gram doses administered intravenously, but given five times over a 26-day period. In both instances of $\text{Na}_3[\text{Ca-DTPA}]$ administration, sharp decreases in lung activity and total

Table V-1

DTPA Dose Administration

Date	# gms/ Injection	DTPA Dose		# of Intravenous Injections	gms	Total Dose	
		μ moles/kg*/ Injection				mmole	
		Subject 1	Subject 2			Subject 1	Subject 2
7/70	1.0	23.6	58.3	3/7 days	3	6.04	6.04
5/11/73	1.0	23.9	49.0	1	5	10.06	10.06
6/1/73	1.0	23.9	49.0	1			
6/7/73	1.0	23.9	49.0	1			
6/18/73	1.0	23.9	49.0	1			
6/25/73	1.0	23.9	49.0	1			
1/17/75	1.0	23.3	41.8	1	4	8.05	8.05
1/24/75	1.0	23.3	41.8	1			
1/31/75	1.0	23.3	41.8	1			
2/7/75	1.0	23.3	41.8	1			

*497 gms $\text{Na}_3[\text{Ca-DTPA}]/\text{mole}$

body burdens, as indicated by in vivo measurements, Figures 1 and 2, occurred for both subjects. As a result of the 1973 chelation treatments, the lung burdens were reduced by 24% in Subject 1 and 50% in Subject 2, with corresponding total body burdens decreasing by 10% for Subject 1 and 32% for Subject 2.

The most recent course of chelation therapy consisted of a series of four, one-gram $\text{Na}_3[\text{Ca-DTPA}]$ doses administered intravenously at one-week intervals during January and February 1975. Concurrent with these treatments, sequential whole-body counting and bioassay of urine and feces for ^{241}Am and the trace element zinc, which is vital to the function of certain metalloenzymes, were conducted. In one instance an attempt was made to measure the effect of DTPA on the zinc dependent erythropoietic enzyme aminolevulinic acid dehydratase (ALAD). Various other blood chemistries and pertinent physiological data are being collected by Drs. S. Piomelli and D. Elmendorf (of New York University Bellevue Hospital and Albany State Department of Health respectively) who supervised and administered the DTPA therapy in this last series of chelations.

These studies are particularly important, not only due to the fact that they represent one of the only non-occupational cases of exposure, but also since probably for the first time in scientific history, a young child has been exposed to a potentially damaging α -emitting actinide material. This last

Fig.V-1 Total body ^{241}Am -meter arc measurement, 2-6" NaI-CsI(Tl) detectors; estimated period of exposure - early 1963 to late 1970.

Total Body ^{241}Am -Meter Arc Measurement, 2 6" NaICsI(Tl) Detectors
Estimated Period of Exposure - Early 1963 to Late 1970

Fig. V-2 ^{241}Am in anterior thorax, 2-6" NaI-CsI(Tl) detectors;
estimated period of exposure - early 1963 to late
1970.

^{241}Am in Anterior Thorax, 2 6" NaICsI(Tl) Detectors
Estimated Period of Exposure - Early 1963 to Late 1970

factor is of particular consideration since: 1) the boy has been undergoing a rapid bone turnover and skeletal growth during this period (see Table 2); 2) ^{241}Am is well-defined as a bone-seeking radionuclide which deposits primarily along the surfaces of trabecular bone and is, for the most part, associated with skeletal and liver structures; and 3) the young of a species has always been shown to be particularly radiosensitive and more subject, therefore, to biological effects from ionizing radiation than their adult counterparts.

Unfortunately, there was not enough time between the days of treatment and the time of writing for this report to allow for complete analysis of ^{241}Am in urine and feces by the time-consuming bioassay procedures. Therefore, we have presented here only the results of the in vivo whole-body counting and the bioassay data presently available.

Results

In Vivo Measurements:

The results of in vivo scintillation measurements are presented in Tables 3 and 4 and Figures 1, 2 and 3. It should be noted that the concentrations of ^{241}Am in the skeletons were obtained by subtracting the lung and liver burdens from the total body burdens and, thereby, represent an estimation which is not definitive, since incorporated in these numbers

Table V-2

Physical Characteristics of the Counting Subjects

<u>Subject</u>	<u>Date</u>	<u>Age (years)</u>	<u>Height (cm)</u>	<u>Weight (kgm)</u>	<u>Chest</u>		
					<u>Circumf. (cm)</u>	<u>Depth (cm)</u>	<u>Width (cm)</u>
#1	3/20/70	57.0	170.2	86.7	101.6	25.0	--
#1	4/10/71	58.0	170.2	84.0	105.4	25.7	31.8
#1	9/1/71	58.0	170.2	--	101.6	24.5	32.0
#1	9/22/72	59.0	170.2	82.7	99.1	24.2	32.8
#1	5/18/73	60.0	167.6	84.3	102.9	25.0	32.0
#1	10/12/73	60.0	169.5	85.9	103.5	26.7	33.7
#1	7/31/74	61.0	168.9	82.6	104.1	26.5	33.5
#1	1/2/74	61.0	168.9	85.9	--	--	--
#1	2/17/74	61.0	169.4	86.4	106.7	--	--
#2	3/20/70	10.5	146.0	33.6	67.0	15.6	--
#2	4/10/71	11.5	150.0	35.4	67.3	15.6	20.3
#2	9/1/71	12.0	--	--	68.6	15.6	22.2
#2	9/22/73	13.0	158.1	38.6	66.0	15.5	22.0
#2	5/18/73	13.0	159.4	41.1	69.9	16.0	23.0
#2	10/11/73	14.0	161.6	39.8	69.9	16.5	24.5
#2	7/31/74	14.0	170.2	45.9	73.7	17.5	25.0
#2	1/2/74	15.0	173.2	48.0	76.8	18.5	26.7
#2	2/17/74	15.0	174.2	48.2	76.2	18.5	27.5

Table V-3

Results of In Vivo Analysis of ^{241}Am
Burdens in Subject 1

<u>Date</u>	<u>Head (nCi)</u>	<u>Lung** (nCi)</u>	<u>Liver (nCi)</u>	<u>Skeleton (nCi)</u>	<u>Total Body (nCi)</u>
2/13/70	6.5±0.2*	18.0±5.0	--	--	--
2/15/70	6.3±0.2	16.7±4.5	--	--	--
3/20/70	6.5±0.2	14.2±4.0	--	--	89.0±4.4*
4/15/70	6.1±0.2	15.1±4.1	5.1±0.7*	65.3±6.0	85.5±4.3
4/10/71	6.6±0.2	12.6±3.4	4.5±0.6	63.8±5.4	80.9±4.1
9/1/71	6.5±0.2	14.0±3.8	5.4±0.7	56.9±5.6	76.3±4.0
9/22/72	6.1±0.2	12.4±3.8	7.0±0.9	72.2±5.7	91.6±4.1
5/18/73	--	14.0±3.9	3.6±0.6	59.6±4.9	77.2±2.9
6/8/73	--	13.9±3.8	6.6±0.9	62.1±5.0	82.6±3.1
10/12/73	--	10.7±3.0	4.4±0.7	57.1±4.3	72.2±3.0
7/31/74	3.5±0.1	10.2±3.0	2.3±0.3	58.3±4.5	70.8±3.3
1/2/75	3.0±0.1	10.8±3.0	2.4±0.3	56.4±4.1	69.6±2.7
2/17/75	3.5±0.1	10.0±2.9	1.5±0.3	--	--
3/12/75	--	--	--	55.7±4.1	67.2±2.8

* 1σ counting errors only.

**Calculated on the assumption that ^{241}Am is distributed uniformly in bone and that the detector "counts" approximately 15% of the total skeleton when the detectors are positioned over the thoracic region.

Table V-4

Results of In Vivo Analysis of ^{241}Am
Burdens in Subject 2

<u>Date</u>	<u>Head (nCi)</u>	<u>Lung** (nCi)</u>	<u>Liver (nCi)</u>	<u>Skeleton (nCi)</u>	<u>Total Body (nCi)</u>
2/15/70	5.81±0.2*	--	--	--	--
3/20/70	5.57±0.2	14.8±2.8	--	--	40.0±2.6*
4/15/70	--	15.0±2.5	13.0±0.8*	7.2±3.7	35.2±2.5
4/10/71	4.07±0.2	9.3±1.4	6.3±0.3	10.0±2.3	25.6±1.8
9/1/71	4.38±0.1	9.3±1.4	6.3±0.3	16.5±2.3	32.1±1.7
9/22/72	3.88±0.2	9.0±1.3	8.9±0.4	11.1±2.4	29.0±1.9
5/18/73	--	9.0±1.3	5.3±0.2	17.2±2.6	31.5±2.2
6/27/73	2.83±0.2	6.6±1.2	7.9±0.4	9.3±2.5	23.8±2.1
10/11/73	--	4.5±1.0	5.1±0.2	10.1±2.4	19.7±2.1
7/31/74	2.22±0.1	1.4±0.6	4.8±0.3	15.1±2.2	21.3±2.0
1/2/75	1.91±0.1	1.4±0.6	3.5±0.2	15.2±1.8	20.1±1.6
2/17/75	1.80±0.1	0.4±0.4	1.8±0.2	--	--
3/12/75	--	--	--	10.5±2.8	12.7±2.7

* 1σ counting errors only.

**Calculated on the assumption that ^{241}Am is distributed uniformly in bone and that the detector "counts" approximately 15% of the total skeleton when the detectors are positioned over the thoracic region.

Fig. V-3 ^{241}Am in Liver, 2-6" NaI-CsI(Tl) detectors;
estimated period of exposure - early 1963 to
late 1970.

^{241}Am in Liver, 2 $6''\text{NaICsI(Tl)}$ Detectors
Estimated Period of Exposure - Early 1963 to Late 1970

are propagated the errors* inherent in estimations of the lung, liver and total body burdens.

The total body measurements were obtained by a meter arc scintillation count using two NaI-CsI(Tl) detectors**.

Due to the fact that the original exposure was probably obtained by the inhalation route and that ^{241}Am deposits on bone surfaces, it is difficult to estimate that portion of the activity in the thoracic cavity that is associated with the lung and that portion associated with the bone structure of the rib cage. However, by estimating the amount of bone "counted" (✓) the detectors and by deriving an estimation of the concentration of ^{241}Am in the bone from in vivo skull measurements (see Section I), we can determine the lung content by subtracting the rib cage contribution from the thoracic cavity as a whole.

Of all the in vivo measurements described, the one which is most difficult to quantitate is the amount of ^{241}Am in the liver. Although experimental studies in animals indicate long retention half times (~ 10 years) in the beagle dog(3),

* These errors are defined not only as the 1σ counting errors listed in the tables, but also include errors in positioning the detectors and subjects which, due to the changing physical characteristics of the subjects, prohibits precise reproducibility of counting geometries.

** The positioning and calibration techniques used to obtain in vivo measurements have been described in detail in a previous report(1).

relatively short half times (2-4 months) have been measured in the baboon⁽⁴⁾. This may be academic, however, if we consider that there may be a lung "pool" of activity which continually feeds ^{241}Am to other organs causing activity to be present in the liver at a higher level than would be the case with no lung burden. At any rate, using a positioning method previously described (measurements are made over the liver area on the right-hand side of the body with subtraction of a similar measurement over the left-hand side of the body, i.e. an area with the same physiological structures as the right-hand side but without the presence of the liver), it appears that a small fraction of the activity is still present in this organ in both the adult and his teenage son (see Tables 3 and 4)*.

From these tables it can be seen that the lung, liver and total body burdens have decreased over the past five years by 97%, 86%, and 58% respectively in Subject 2 and by 44%, 70% and 24% respectively in Subject 1. The differences in clearance rates between subjects may be expected since Subject 2 is still a young boy and, therefore, had a significantly greater turnover rate for bone and soft tissue cells.

*Note: The values for liver burdens which appeared in the 1974 Annual Report were incorrect due to use of an improper calibration factor; they have been revised for these tables.

If, in fact, the decrease that has been noted by whole-body counting is real, we should see a corresponding amount of ^{241}Am excreted during this period.

Bioassay Measurements:

Although the excretion data have not been completely analyzed for ^{241}Am at this time, some preliminary results are available.

Measurement of ^{241}Am was carried out by two different techniques. At short times after DTPA administration, it is possible to measure activity directly in urine by placing a known volume of material in a three crystal counting geometry and making scintillation measurements over long periods of time by this non-destructive technique. That ^{241}Am was uniformly distributed throughout the sample was ascertained by measuring aliquots of sample as well as the empty container; it was necessary to maintain a pH below 2.0 in order to be assured that the ions remained within solution and did not readily plate out on the container walls. When it was impossible to measure ^{241}Am in this manner, that is, on pre-chelation days and at long times after chelation, alpha counting was performed after sample ashing, chemical ion exchange separation⁽⁵⁾ and electroplating⁽⁶⁾ as outlined in detail at the end of this section. A liquid scintillation technique⁽⁷⁾ was tested and found to be impracticable due to both the low levels of activity encountered here and the long sample preparation time required.

By extrapolation of the excretion data which are available, to those times at which measurements are not yet complete, it appears that Subject 2 excreted a total of approximately 3 nCi in his urine between January 17, 1975, the first day of chelation and March 12, 1975, more than one month after the last chelation date. The activity appears in the urine in the highest concentration on the days of DTPA administration; this is illustrated in Figure 4 for Subject 2. The rate of loss then decreases, averaging 50% on the second day. On the following days the concentration tails off but more slowly so that on the sixth day after DTPA administration, it is approximately 20% of the concentration on the day of chelation. The urine of Subject 1 has been analyzed only for the first week after the initial DTPA dose was administered; here it appears that the amount of ^{241}Am excreted is quantitatively the same as for Subject 2. This is particularly interesting when one notes that the total body content of Subject 2 is about four times higher than that of Subject 1.

As a result of animal experiments (see Volume I), it was found that americium is excreted by the fecal route after DTPA chelation although at a rate much lower than for the urinary component. Fecal samples were analyzed by drying at low temperatures ($\sim 100^\circ\text{C}$), then dry ashing by gradually raising the oven temperature to 500°C , and by subsequent counting using thin crystal scintillation techniques. Enough feces have been analyzed at this time to allow us to estimate the total amount excreted by this route for Subject 2 (see Table 5).

Fig. V-4 ^{241}Am in urine - 24 hour collections, Subject 2

^{241}Am in Urine - 24 hour Collections, Subject 2

Table V-5

 ^{241}Am Excretion Data

Sample	Subject 1	Subject 2	
	Am-241 in Urine (pCi/day)	Am-241 in Urine (pCi/day)	Am-241 in Feces (pCi/day)
→ 1/17-18*	169.3±9.7	152.7±16.6	Bkgd
1/18-19	29.1±9.1	71.7±7.6	Bkgd
1/19-20	40.5±7.5	48.3±6.0	Bkgd
1/20-21	51.9±7.1	51.1±13.1	--
1/21-22	39.2±5.3	33.7±11.2	6.4±1.6
1/22-23	14.9±5.6	62.8±7.0	49.8±7.4
1/23-24	27.3±6.1	20.7±6.2	63.7±9.4
→ 1/24-25		136.9±8.9	25.9±3.1
1/25-26		75.0±5.9	--
1/26-27		57.5±6.3	66.2±7.4
1/27-28		53.3±6.9	--
1/28-29		32.2±7.2	--
1/29-30		39.8±9.6	--
1/30-31		39.2±8.9	--
→ 1/31-2/1		66.7±8.1	39.3±10.2
2/1-2		46.1±6.9	--
2/2-3		26.9±6.8	24.4±5.2
2/3-4		20.8±8.7	73.8±7.7
2/4-5		31.8±6.7	35.9±16.3
2/5-6		9.0±6.5	--
2/6-7		33.7±6.6	44.7±10.9
→ 2/7-8		93.2±5.4	--
2/8-9		37.0±5.9	--
2/9-10		46.9±8.7	--
2/22		38.9±4.6	--
2/23		25.1±5.8	--

* Collections start at 12 Noon and finish at 12 Noon the following day.

→ Days of DTPA administration.

We can estimate the total excretion of ^{241}Am via feces to be approximately 1.5 nCi between January 17, 1975 and March 13, 1975.

Due to the difficulty of collecting 100% of the urine and feces over extended periods of time, a fraction of the excretion was not collected from Subject 2 on weekdays; hence, suitable approximations have been made to account for this loss.

In addition to the excretion of ^{241}Am , the following test was carried out as a check on the possible occurrence of one unwanted side effect of the DTPA chelating agent. As noted in previous papers⁽⁸⁾, there is a distinct possibility of excess and uncompensated zinc ion excretion as a result of DTPA therapy. The many problems resulting from zincuria are related to the inactivation of those necessary metalloenzymes which require zinc for normal activity. Therefore, we proceeded to measure the zinc content of urine during the therapy period by a method which is unique to this laboratory. An aliquot of sample is wet-ashed with concentrated nitric acid, then dry ashed at 500°C. The sample is then finely powdered and pressed into a torus-shaped geometry, and measured for zinc content by X-ray fluorescence techniques⁽⁹⁾. Figure 5 shows the X-ray spectra of two such urine samples, one before chelation and one obtained on the day of chelation. The concentration of zinc in urine can be seen to be approximately 250 times higher in the 24 hours after chelation, than in the pre-chelation

Fig. V-5 Trace metal X-ray fluorescence analysis of urine
from Subject 2 before and after chelation therapy.

X-ray Fluorescence Analysis - Urine Subject 2

sample. The concentration of Zn^{++} then falls off quickly on the day after chelation to less than 10 times normal. Quantitative data on zinc excretion are not available at this time.

On January 17, 1975, the first day of chelation, blood was drawn from both subjects before and 15 minutes after DTPA administration in order to measure the concentration of the zinc-dependent enzyme ALAD. During shipment from Albany, where the DTPA was administered to this laboratory, one of the blood samples was destroyed; however, the other pair of samples from Subject 2 (see Table 6) show a significant decrease in ALAD content probably caused by zinc depletion. Similar decreases in ALAD activity have been observed in baboons administered chelation therapy at this laboratory (see Volume I).

Recommendations for Further Study

With the success of DTPA chelation therapy procedures in this study as well as with other cases of radionuclide exposure in humans and experimental animals, it is more reasonable to assess the benefits vs. risks of further DTPA therapy, bearing in mind the possible toxicological side effects of DTPA administration.

As the analyses of zinc in excreta will shortly be completed, this information together with other physiological parameters of these subjects will play a role in determining the efficacy of further DTPA chelation therapy.

Table V-6

ALAD Concentrations in Blood

		<u>Hematocrit</u> <u>% Red Blood Cells/</u> <u>Whole Blood</u>	<u>Hemoglobin</u> <u>gm/100 ml</u> <u>blood</u>	<u>ALAD</u> <u>nmoles PBG/ml</u> <u>RBC/hr</u>
Subject 1	Pre*	45.5	17.0	603.2
	Post**	50.0	18.0	887.8
Subject 2	Pre	45.0	15.5	1593.7
	Post	41.0	14.5	1154.1

* Blood sample not stored properly before analysis.

** 15 minutes after treatment.

APPENDIX

^{241}Am Ion Exchange Separation Procedure

- 1) Wet ash sample with concentrated HNO_3 , then dry ash.
- 2) Add 30 ml 8 N HCL and heat. Boil 5 minutes, then cool and filter. Discard the precipitate.
- 3) Add 5 cm amberlite CG-400 (100-200 mesh) to an ion exchange column (1 cm diameter). Prepare resin with 50 ml 8 N HCL.
Pour sample solution into column with flow rate of 1.5 cm/min.
- 4) [Am is not absorbed]. Wash the column with 20 ml 8 N HCL and add to the sample.
- 5) Dry the sample, add 30 ml 2 N HCL and heat until all solid is dissolved, then cool.
- 6) Add 10 cm dowex 50x8 (100-200 mesh) to another column. Prepare resin with 50 ml 2 N HCL.
- 7) Pour sample solution into column with flow rate of 1.5 cm/min. [Am is absorbed].
- 8) Wash this column with 20 ml 2 m NaOH followed by 20 ml 0.1 N HCL. Repeat this step. Discard.
- 9) Elute the americium with 40 ml 5 M NH_4 sen.
- 10) Add 5 cm amberlite CG-400 (100-200 mesh) to a third column. Prepare with 50 ml 8 N HCL followed by 10 ml 5 m NH_4 sen.
- 11) Adjust the pH of the sample solution to 1.0, and pour this into the column [Am is absorbed].

- 12) Wash with 20 ml 5 m NH_4SCN followed by 20 ml 2 m NH_4SCN .
Discard these solutions.
 - 13) Elute the americium with 30 ml 0.1 m HCL. Discard the first 5 ml of eluant.
 - 14) Dry the eluant, then dry ash it in oven.
 - 15) Wet ash the sample 2-3 X with concentrated HNO_3 .
- Sample is ready for plating.

^{241}Am Electroplating Procedure

- 1) Wash planchet and rinse with acetone.
- 2) Assemble the plating cell.
- 3) Plate out of 5 ml volume.
- 4) Add two drops methyl red indicator.
- 5) Add 1 drop NH_4OH .
- 6) Adjust color back to red with 2 N HNO_3 and add two drops in excess ($\sim\text{pH}1$).
- 7) Place plating unit in 1000 ml beaker; add water and ice around cell.
- 8) Wash stirrer (anode) and heat over a burner to sterilize.
- 9) Adjust anode to 2-3 mm from planchet.
- 10) Electroplate at 1.1-1.3 amperes, 15-20 volts, for 40-60 minutes.
- 11) Before end of plating add 1 ml NH_4OH to prevent the americium from redissolving.
- 12) Wash planchet with distilled water and dry on a hot plate.
- 13) Count planchet in alpha spectrometer.

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Vol. II
SECTION VI

49554
Abstract of a Presentation
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Is the Liver a "Critical Organ" in Man for Isotopes of Americium?

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ABSTRACT

Generation of electrical power by nuclear means will result in the production of substantial quantities of the transplutonium elements. A significant fraction of the long-lived alpha-emitting nuclides will be in form of the americium isotopes, ^{241}Am and ^{243}Am . Largely regarded as a waste product, americium may eventually find some function, resulting, undoubtedly, in an increase in the number of contamination incidents involving man. To date, there are about 15 documented cases of internal deposition of americium (without plutonium) in man.

Experimental results describing the early deposition and rate of removal of ^{241}Am from the liver of the mouse, rat, Chinese hamster, beagle, cynomolgus monkey, baboon, and man are reviewed^(1,2).

It is concluded that there are marked differences in the rate at which ^{241}Am , injected intravenously in the monomeric form, is excreted from liver with the specified species (orders) falling into two distinct groups when life expectancy is considered. The mouse, rat, cynomolgus monkey, and baboon eliminate ^{241}Am from the liver rapidly in an exponential fashion and almost completely with biological half-times between 10 and 150 days. The Chinese hamster and beagle eliminate ^{241}Am more slowly with half-times of 3600 days for the beagle and ~1000 days for the Chinese hamster. The mechanism(s) responsible for these differences remain to be defined.

It is not yet clear to which group man belongs, although limited evidence seems to indicate that americium may be excreted relatively rapidly from the human liver. It has been noted, however, that ^{241}Am deposited in liver after inhalation of aerosols may be retained for significantly long time periods. The long biological half-times noted for these cases may result from transport of ^{241}Am in particulate form from lung to liver or by a continual translocation from the lung pool. Experimental evidence for this hypothesis is reviewed for two cases of internal contamination in man.

It is not yet clear that deposition of americium nuclides in the liver is as important as deposition in bone.

TRANSCRIPTION

I would like to start off this talk by quickly asking that the question posed by the title of our abstract be considered rhetorical. An alternative and more declarative title should be: "The Liver as a 'Critical Organ' in Man for Isotopes of Americium."

The necessity of defining a "critical organ" becomes evident in any attempt at calculating the maximum permissible body burden for a nuclide. Stated otherwise, the amount or concentration of radioisotope in the body, which produces the maximum permissible RBE dose rate to the "critical body organ" defines the maximum permissible body burden. As we are all aware these days, there is considerable consideration being given to exactly how to calculate this maximum value, particularly as concerns the transuranic nuclide, ^{239}Pu . Of course, the definition of "critical organ" can be extended beyond that having to do with only that organ receiving the "maximum dose rate". (Slide 1) For example, due to non-uniform distributions within a tissue and considering the LET of an alpha particle, it may be the dose or dose rate to some micro-structure within an organ that is critical. Thus, the phrase "critical cell" or even "critical cell component". Referring then to the critical organ as that organ which accumulates the greatest concentration of americium resulting in a gross maximum dose and/or dose rate may be somewhat of an oversimplification.

An alternate or additional definition of "critical" is "that organ of the body whose damage by the radioactive decay of the nuclide in question, results in the greatest damage to the total body". This depends, of course, first on the "essentialness or indispensability of the organ to the well-being of the entire body" and then on the "radiosensitivity of the organ or specific locii within the organ, as for example, that organ or organ site damaged by the lowest radiation dose." Finally, when considering "effect" one must take into account not only the high dose rate, acute damage but the consequences of longer term, lower dose rate, chronic irradiation. There is no certainty that both cases will define the same "critical organ". Thus, under specific circumstances it may be possible to envision a maximum permissible lung burden for ^{241}Am determined by localized dose rates not to a basal cell or the bronchi but, for example, to cells of the liver.

(Slide # 2)

For the case of the transuranic nuclide, ^{241}Am , the principle uptake sites in the body are the skeleton and the liver. (Slide # 3) Of course, since occupational exposure to ^{241}Am occurs chiefly by inhalation or as a result of a puncture wound, the lung, pulmonary lymph nodes and wound site may also be considered as candidates for "critical organ". Depending on particle size and chemical form of the inhaled material, however, there will always be

some degree of translocation and redeposition of inhaled material to bone surfaces and to liver tissue. As seen in this slide, the initial distribution of ^{241}Am in various animal species injected i.v., i.m. or i.p. is present, for the most part, in these two tissues. Since americium is less likely to hydrolyze (and become polymeric in character) than is plutonium, it is possible that material so released from the lung may be partitioned between the liver and bone in a similar manner for man as in experimental animals. Considering that there is a difference of approximately four in the mass of the liver and skeleton in man would result in a difference in the dose rate by this same factor for uniform distributions, equal partitions and equal retention rates of americium in these two tissues. That is, the dose rate to the liver would be a factor of four times as great as that to the skeleton. Which brings me to a classical problem in animal research demonstrated in the next slide. (Slide # 4) As you can see for the case of liver retention, there is a clearcut species, i.e., order difference which cannot be explained as an experimental artifact. (Slide # 5) (Discussion at this point of the possibility of a second, longer-term component for ^{241}Am retention in the liver.) All of these experiments were performed by relatively low dose intravenous injection of ^{241}Am citrate. In the case of our own work in the baboon, (Slide # 6), we used an injection solution prepared in an identical fashion

to that used in the Utah beagle work and followed retention by in vivo counting, sequential liver biopsy and total liver measurement after animal sacrifice at 1 day, 1 month, and 3 months. (Go back to Slide # 4.) As you can see, this half-life is in approximate agreement with that obtained for another primate species, the Cynomolgus monkey, but very different from the rodent, the beagle, and the hamster. A biological explanation for these differences remains uncertain. It is of interest, by the way, (Slide # 7), that almost all the clearance from the liver of the baboon, could be accounted for in the fecal excretion of ^{241}Am . The half-time of ^{241}Am in the bone of the baboon and the dog are both extremely long as seen in the next slide. (Slide # 8)

Very little data currently exists for the uptake and retention of ^{241}Am in the liver of man. Furthermore, as I mentioned before, most human exposures occur as a result of inhalation and puncture wounds. According to the chemical form, solubility and particle size of the inhaled radioactive material, retention in the liver may appear to be long as in the case of the beagle (with the lung acting as a reservoir source of continued exposure) or on the order of months as in the non-human primate. At our own laboratory, we have been measuring the retention of ^{241}Am acquired by inhalation in one man and his son, now 14 years old, for the past three

years. (Slide # 9) Although the body burdens of these two individuals differed by a factor of approximately two in 1970 and by a factor of almost four at the present time, the concentration in the liver is seen as similar and unchanging after the first chelation dose occurred. (Calibration procedures were described here, i.e. positioning the source both in front of and behind the subject, Rando lung phantoms, and right-liver-area-minus-left-adjacent, technique with consideration given to contribution factors from one side to the other.)

It must be remembered, however, that both subjects still have lung burdens which probably continue to contribute to the liver concentration as based on fecal output of ^{241}Am . The implications and speculations that can be drawn based on this data and the experimental animal data are numerous, but should be pondered when considering the current radiological toxicity data for this nuclide in the beagle dog.

Questions from the Audience

One end-of-session question pertained to the fact that the concentration parameter was most often used in defining the critical organ. Q.1: Is there any case that I might know of where any other of the definitions of critical organ that I gave, were used? A.: Although the lymph node has been shown to have the greatest concentration of Pu after an inhalation exposure, it is not usually considered a critical

organ since it's been shown in inhalation toxicity studies to be a relatively radioinsensitive structure. Instead, the skeleton, lungs and the liver are considered the critical organs for Pu. I can't think of any other example offhand, at the moment, although I know that critical organs will change as we learn more about exactly what the effects of alpha-emitting nuclides like ^{241}Am are on the various organs of the body.

Q.2: Might not the spleen have given an additional contribution factor to the in vivo liver area counts? A.: Probably not, based on the distribution of ^{241}Am that we noted in baboons at autopsy. However, the lung might, in fact, give a definite contribution factor and this error although realized has not yet been taken into consideration for the figures that you've seen. This might explain some of the variation that is seen in the liver retention curves for the human subject.

Q.3: How could I know for sure that the material excreted in the feces did, in fact, come from the liver? A.: The amount of material lost from the liver was equal to that excreted in feces. This may not be enough to absolutely guarantee that some material was not depositing in bone and other material being lost from bone to feces, however, it appears biologically sound in that that material could be lost from the liver by a biliary route to the GI tract to then be excreted in feces. Other investigators have made similar assumptions on material being lost from the liver.

References

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2. Durbin, P. A., Metabolism and Biological Effects of the Transplutonium Elements, Handbook of Experimental Pharmacology, Chap. 18, H. C. Hodge, J. N. Stannard, and J. B. Hursh, Eds., Springer-Verlag, Berlin, Heidelberg, NY (1973).

CRITICAL ORGAN:

1. THAT ORGAN WHICH ACCUMULATES THE GREATEST CON-
CENTRATION OF RADIOACTIVE MATERIAL.
2. THAT ORGAN WHICH RECEIVES THE GREATEST DOSE/
DOSE RATE (TOTAL COMMITMENT?).
3. THAT ORGAN WHICH IS THE MOST RADIOSENSITIVE
(DAMAGED BY THE LOWEST DOSE).
4. THAT ORGAN OF THE BODY WHOSE DAMAGE BY THE
RADIATION RESULTS IN THE GREATEST DAMAGE TO
THE TOTAL BODY.

CRITICAL ORGAN

1. CONCENTRATION DISTRIBUTION -- "CRITICAL STRUCTURE"
2. DOSE RATE DISTRIBUTION
3. RADIOSENSITIVITY
4. ESSENTIALNESS
5. TIME-EFFECT RETENTION

GROSS DISTRIBUTION OF ^{241}Am IN LIVER AND SKELETON
AT EARLY TIMES AFTER ADMINISTRATION
 (LOW DOSE, MONOMERIC, SOLUBLE, PARENTERAL)

<u>SPECIES</u>	<u>% OF INJECTED OR ABSORBED DOSE</u>	
	<u>LIVER*</u>	<u>SKELETON*</u>
1. MOUSE	29.0 (4)	44.0 (4)
2. RAT	41.8 (4)	33.8 (4)
3. CHINESE HAMSTER	55.0 (4)	19.0 (4)
4. BEAGLE DOG	48.7 (1-22)	31.0 (1-22)
5. CYNAMOLGUS MONKEY	40-54 (1-8)	27.2 (8)
6. BABOON	24.0 (4)	44.2 (32)
7. MAN	?	?

*Numbers in parentheses = days after injection.

CLEARANCE OF SOLUBLE ^{241}Am FROM THE LIVER*
(LOW DOSE, MONOMERIC, PARENTERAL ADMIN.)

<u>SPECIES</u>	<u>APPROXIMATE HALF TIME OF RETENTION (DAYS)</u>
1. RAT AND MOUSE	8-10
2. CHINESE HAMSTER	1000
3. BEAGLE DOG	3650
4. CYNAMOLGUS MONKEY	70
5. BABOON	40-150
6. MAN	?

* ^{241}Am Citrate

SLIDE # 5

DEPOSITION AND RETENTION OF ^{241}Am
IN THE LIVER; CAUSATION PARAMETERS

1. SPECIES (ORDER)
2. CHEMICAL FORM
3. PHYSICAL FORM
4. AGE
5. ADMINISTRATION ROUTE
6. DOSE

SLIDE # 6

Am-241, Retention in Liver Compared to Cumulative Excretion in Feces

- B-460 *in vivo*
- B-458 *in vivo*
- ◊ B-460 Biopsy
- ⊙ B-458 Biopsy
- ▲ B-460 Feces
- ◆ B-458 Feces

SLIDE # 9

^{241}Am in Liver, 2 $6''\text{NaICsI(Tl)}$ Detectors
Estimated Period of Exposure - Early 1963 to Late 1970

49556

✓

Design of

Vol. II,

SECTION VII

Completion of a New Laboratory and Animal Housing Unit
for Radionuclide Studies

Last year a new combined analytical laboratory and animal housing facility was constructed at the Laboratory for Experimental Medicine and Surgery in Primates (LEMSIP). The original design for this labmobile can be seen in the 1973-1974 Annual Report. By having sample processing facilities in close proximity to the experimental animals, the necessity for transporting biological specimens between LEMSIP and the Institute of Environmental Medicine has been curtailed. In addition, complete radionuclide counting equipment has been installed so that samples need not leave the animal housing site for analysis, a feature based upon our radiological health requirements.

The flexibility of this new laboratory was further enhanced by the installation of a second fume hood that is used primarily for acidifying and radiochemical preparation of urine samples. The inside of the hood has been coated with an epoxy finish to make an acid resistant surface. Figure 1 is a photograph of the radionuclide section of the laboratory. The counting cave and electronic instrument bin and rack are visible. Figure 2 is a view into the animal quarters from the laboratory. Other animals, housed in this section are out of view in this photograph.

The original plans for this laboratory also included a whole-body counting room especially designed for the experimental baboon studies but financial support was insufficient to complete both the radionuclide analytical laboratory and the counting room. In its stead, a sample counting "cave" was installed so that a low background counting system would be available.

At the present time, plastic-coated partitions are being installed between the cages in the animal housing section of the laboratory. This provision is to further prevent cross contamination among excreta samples for the separate animals.

The use of this laboratory has become an integral part of the physical space that is available for this study. Its location is advantageous since it is an integral part of the LEMSIP facility and thereby provides a convenient basis for cooperation between the separate entities of Environmental Medicine and the surgical staff of LEMSIP.

Reference

1. NYU Medical Center, Department of Environmental Medicine
Progress Report, Radioactivity Studies, COO-3382-13,
Section VI (1974).

Fig. VII-1 Radionuclide section of analytical laboratory at
LEMSIP.

Fig. VII-2 Complete view of laboratory and animal housing
facility at LEMSIP.