To be published in the Proceedings of the International Radiation Protection Association 8th Congress, to be held in Montreal, Canada, May 1992.

THE EFFECT OF ISOTOPE ON THE DOSIMETRY OF INHALED PLUTONIUM OXIDE

Raymond A. Guilmette[1], Albert W. Hickman[2] and William C. Griffith[1]
1. Inhalation Toxicology Research Institute, P. O. Box 5890, Albuquerque, NM 87185
2.University of Florida, Gainsville FL

ABSTRACT: Results of experimental studies in which animals inhaled $^{238}PuO_2$ or $^{239}PuO_2$ aerosols have shown that the biokinetics and associated radiation dose patterns for these two isotopes differ significantly due to differences in *in-vivo* solubility caused by the 260-fold difference in specific activity between $^{238}PuO_2$ and $^{239}PuO_2$. We have adapted a biokinetics and dosimetry model derived from results of the ITRI dog studies to humans and have calculated dose commitments and annual limits on intake (ALI) for both Pu isotopes. Our results show that the ALI calculated in this study is one-third that for class Y ^{238}Pu from ICRP 30, and one-half or equal to that for class Y ^{239}Pu, depending on how activity in the thoracic lymph nodes is treated dosimetrically.

CONF-920501--9

DE92 004257

INTRODUCTION: Inhalation has been shown to be the most likely route of occupational exposure to plutonium. Nonoccupational inhalation exposures to Pu aerosols have also occurred as a result of atmospheric nuclear weapons testing. Despite these exposures, information from studies of people have not been adequate to define the dosimetry of inhaled Pu aerosols. Consequently, data from experiments with animals are used to augment our knowledge of Pu biokinetics and dosimetry and to identify important dose- and effect-modifying factors. This report summarizes results obtained from studies at ITRI in which adult dogs inhaled monodisperse aerosols of either $^{238}PuO_2$ or $^{239}PuO_2$ having similar aerodynamic sizes, produced in the same way, and having the same chemical form. Therefore, the two exposure materials differed only in specific activity.

MATERIALS AND METHODS: The materials and methods used in these studies have been reported in detail (1,2). Briefly, adult male and female beagle dogs (15 - 41 mo of age) received a single brief pernasal inhalation exposure to a monodisperse aerosol of $^{238}PuO_2$ (1.7 or 2.7 μm AMAD) or $^{239}PuO_2$ (1.4 or 2.9 μm AMAD). Each aerosol was produced by heat-treating droplets of a nebulized suspension of $Pu(OH)_4$ at 1150°C, thus forming PuO_2. After exposure, each animal was maintained in a metabolism cage for excreta collection and in a kennel run until the dog was either sacrificed, euthanized or died. Sacrifice times ranged from 4 hr to 4 y after exposure. Additional data from dogs that inhaled $^{239}PuO_2$ as part of a dose-response study were also included in this analysis (3). Radiochemical analysis of Pu in tissue and excreta samples provided the data for determination of the biokinetics of ^{238}Pu and ^{239}Pu following inhalation deposition of Pu in oxide form.

Fifty-year dose commitments for lung, liver and bone surfaces of humans were obtained from different models for ^{238}Pu and ^{239}Pu. In the former case, the doses were calculated using the canine-based model of Mewhinney and Diel (1) that was modified for application to man. Four changes in metabolic parameters from those of the canine model were made: 1) The partitioning of Pu that reached the blood from solubilization of the deposited Pu particles was 45% liver, 45% bone, 4% muscle and 0.4% kidney, values which were derived from the analyses of McInroy *et al.* (4

and are similar to those suggested in ICRP 30 (5). 2) A ratio of Pu in urine to Pu in feces of 1 was used based on the systemic model of Leggett (6). 3) Biological retention half times of 40 y for liver and 100 y for skeleton, as proposed in ICRP 30 (5) and supported by analyses of exposed humans (7) were used. 4) The particle size of the inhaled aerosol was assumed to be 1.0 μm diameter.

The calculation of human dose commitments for ^{239}Pu was based on retention equations obtained from the ITRI dog studies modified to include the 40-y biological half time for liver and 100-y half time for skeleton. These equations are:

$$R_{lung}(t)=0.18e^{-0.024t}+0.82e^{-0.0.00045t}$$

$$R_{liv}(t)=0.010e^{-4.7x10^{-5}t}(1-e^{-0.12t})$$

$$R_{skel}(t)=0.0017e^{-1.9x10^{-5}t}(1-e^{-0.12t})$$

$$R_{thor}(t)=0.17e^{-0.027t}+0.83e^{-0.00016t}$$

where $R_i(t)$ is the retention in organ i (where i = lung, liver, skeleton and thoracic = lung + lung-associated lypmth nodes,LALN, respectively) expressed as fraction of the initial lung burden, and time t is in days after exposure. For all dose calculations, the organ masses used were those specified in ICRP 30 (5), i.e. lung = 1000 g, liver = 1800 g, and bone surfaces = 120 g.

RESULTS AND DISCUSSION: Model curves describing the retention of ^{238}Pu and ^{239}Pu in dogs exposed to PuO_2 aerosols are shown in Figure 1 for lung and skeleton. The retention of Pu in liver (not shown) was similar to that in skeleton. The biokinetics of the two Pu isotopes were significantly different. Whereas ^{239}Pu was retained in lung and LALN for very long times, ^{238}Pu translocated from the lung mainly to liver and bone at an accelerated rate beginning at about 100 days after exposure. The accumulation of ^{238}Pu in liver and bone was about 200 times larger than that seen with ^{239}Pu.

The observed difference in biokinetics of inhaled ^{238}Pu and ^{239}Pu aerosols has been explained based on the 260-fold difference in specific activity of equivalently sized aerosol particles. The much higher specific-activity $^{238}PuO_2$ particles incur a proportionately higher amount of energy deposition within the particle itself, particularly from the recoil nuclei. This energy deposition results in damage to the crystalline structure of the PuO_2, presumably lattice defects that accumulate with time, and that ultimately are expressed in an aqueous environment as fragmentation and accelerated dissolution (8). This theory is supported by autoradiographic observation of particle breakup (8). The dissolved ^{238}Pu was then available for translocation to blood and redistribution to the major deposition sites for systemic Pu, i.e., liver and bone. In contrast, the much lower decay rate of ^{239}Pu has yet to provide concrete evidence that fragmentation of these particles occurs to any significant extent, at least through 3 y after exposure.

The consequences of the different radiation dose patterns found for the two Pu isotopes are shown in Table 1 with respect to the 50-y dose commitments predicted for man, as calculated using the ITRI models and using ICRP 30 methods (5). It can be seen for ^{238}Pu that the highest dose commitments were to the bone surfaces for both methods of calculation, the difference being in the threefold higher dose

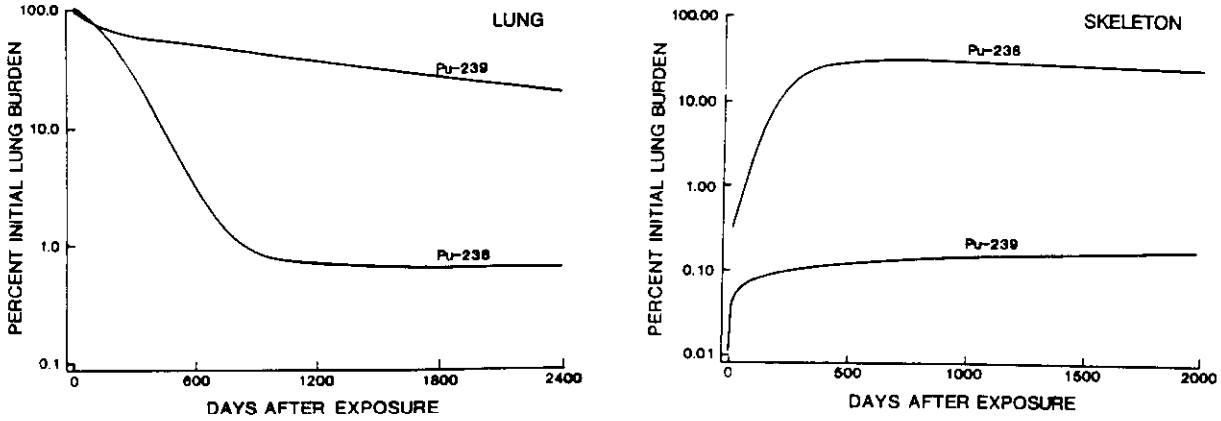

Figure 1: Model curves for the uptake and retention of ^{238}Pu and ^{239}Pu in lung and skeleton of dogs that inhaled Pu dioxide aerosols (data points for individual dogs not shown). Retention of Pu in liver was similar to those shown for skeleton.

Table 1
Dose Commitments for Inhaled ^{238}Pu and ^{239}Pu in Man (mSv/Bq inhaled)

	^{238}Pu		^{239}Pu	
Organ	This Report	ICRP 30	This Report	ICRP 30
Lung	0.079	---	0.65	---
Thoracic*	0.085	0.32	1.75	0.32
Liver	0.50	0.18	0.024	0.21
Bone Surface	2.4	0.83	0.019	0.95

* Includes Pu contained in lung and LALN, since ICRP 30 does not differentiate between activity in these two organs

derived from the ITRI model. This is due to the uptake of a larger fraction of inhaled ^{238}Pu that translocates to bone. For ^{239}Pu, there are several significant differences in the calculated dose commitments: 1) The dose to lung calculated with the ITRI model is either twofold or fivefold higher than that calculated using ICRP 30, depending on whether the activities translocated to the LALN are included in the dose calculation for the former. Although the rationale for including LALN activity with that of the lung as seen in the dog studies is speculative, there is evidence in human exposure cases that there is very long-term retention of insoluble Pu in the thoracic region (~6000 days based on thoracic photon measurement (9)), and the ratio of concentration of Pu in lung to that in lymph nodes is significantly larger in man than in dogs (10).

From Table 2, it is evident that the higher dose to bone surfaces for ^{238}Pu based on the ITRI model has resulted in a limiting ALI that is one third that of ICRP 30, i.e. 200 Bq vs. 600 Bq. For ^{239}Pu, the ITRI-derived ALI is either one half or equivalent to that of ICRP 30, depending on the manner in which the dose to lung is calculated. In either case, however, the limiting ALI for the ITRI model is determined by the stochastic ALI, of which most of the dose contribution comes from the dose to lung. This is more consistent with current data on the biokinetics and dosimetry of inhaled $^{239}PuO_2$ than is the ALI based on the nonstochastic dose to bone

Table 2
Annual Limits on Intake (Bq)

	Stochastic	Nonstochastic		
		Lung	Liver	Bone Surfaces
^{238}Pu				
This Study	450	6300	1000	200
ICRP 30	600	1600	2800	600
^{239}Pu				
This Study	**240**(630)*	**290**(770)*	14000	22000
ICRP 30	600	1600	2500	500

* ALIs in boldtype use dose commitments for lung and LANL: those in parentheses use lung only

surfaces. Whether reductions in the ALIs for Pu isotopes are warranted based on the available experimental data is a matter for discussion.

REFERENCES

1. Mewhinney, J.A., Diel, J.H. "Retention of inhaled $^{238}PuO_2$ in beagles: a mechanistic approach to description" *Health Phys.* 45, 39-60, 1983.
2. Guilmette, R.A., Diel, J.H., Muggenburg, B.A., Mewhinney, J.A., Boecker, B.B., McClellan, R.O. "Biokinetics of inhaled $^{239}PuO_2$ in the beagle dog: Effect of particle size" *Int. J. Radiat. Biol.* 45, 563-581, 1984.
3. Guilmette, R.A., Muggenburg, B.A., Hahn, F.F., Mewhinney, J.A., Seiler, F.A., Boecker, B.B., McClellan, R.O. "Dosimetry of ^{239}Pu in dogs that inhaled monodisperse aerosols of $^{239}PuO_2$" *Radiat. Res.* 110, 199-218, 1987.
4. McInroy, J.F., Kathren, R.L., Swint, M.J. "Distribution of plutonium and americium in whole bodies donated to the United States Transuranium Registry" *Radiat. Protect. Dosim.* 26, 151-158, 1989.
5. International Commission on Radiological Protection, Limits on Intakes of Radionuclides by Workers, ICRP Publication 30, Pergamon Press, Oxford, England, 1979.
6. Leggett, R.W. "A model of the retention, translocation and excretion of systemic Pu" *Health Phys.* 49, 1115-1137, 1985.
7. McInroy, J.F., Kathren, R.L., Voelz, G.L., Swint, M.J. "U. S. transuranium report on the ^{239}Pu distribution in a human body" *Health Phys.* 60, 307-333, 1991.
8. Diel, J.H., Mewhinney, J.A. "Fragmentation of inhaled $^{239}PuO_2$ particles in lung" *Health Phys.* 44, 135-145, 1983
9. Carbaugh, E.H., Bihl, D.E., Sula, M.J. "Long-term follow-up of HAN-1, an acute plutonium oxide inhalation case" *Radiat. Protect. Dosim.* (in press)
10. Kathren, R.L., Strom, D.J., McInroy, J.F., Bistline, R.E. "Distribution of plutonium in the lungs and lymph nodes of USTR registrants and relationship to smoking status" *Health Phys.* 58, sup 1, S48, 1990

ACKNOWLEDGEMENTS: Work performed for the U. S. DOE/OHER under Contract No. DE-AC04-76EV01013 in facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care. A. W. Hickman's practicum at ITRI was supported by the DOE health physics fellowship program.

DISCLAIMER