USTUR Whole Body Case 0269: Demonstrating Effectiveness of Ca-DTPA for Pu

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1. THE CASE

Accidental, single acute inhalation—1956:

- Acidic solution $Pu(NO_3)_4$—aerosol 'mist'.
- Chelation treatment (i.v. Ca-EDTA) started day of intake.
- Continued intermittently over 3 months.
- Several other chelating agents tried—also by ingestion.
- 3 years later—i.v. Ca-DTPA administered.
- 400 Pu-in-urine measurements—including periods of chelation—through 31 y after intake!
- 91 Pu-in-faeces measurements—including periods of chelation.

Donor died 38 y after intake:

- Age 79 y.
- Adenocarcinoma of prostrate—extensive carcinomatosis.
- At autopsy all major soft tissue organs harvested.
- Bones from half of skeleton also dissected out—for radiochemistry.
- Tissue contents of ^{238}Pu, $^{239+240}Pu$, ^{241}Am measured.

2. THE BIOASSAY DATA

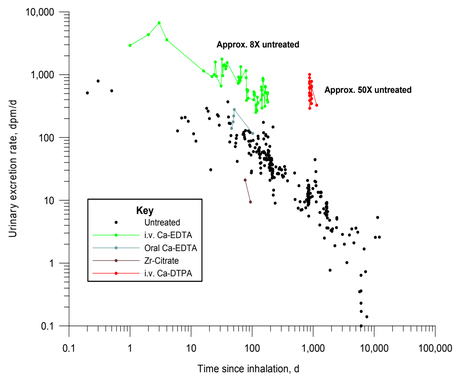


Figure 1. Pu-α excretion in urine

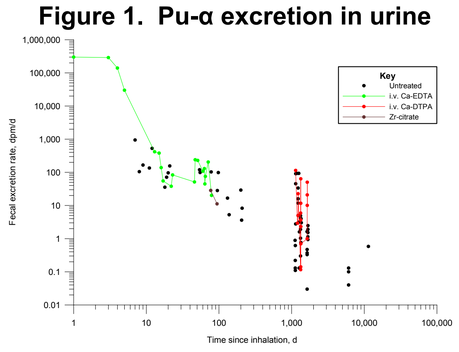
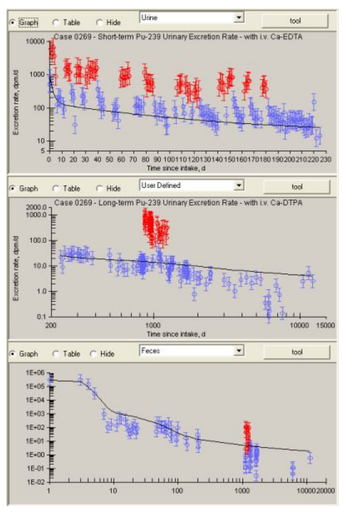


Figure 2. Pu-α excretion in faeces

3. ANALYSIS OF INTAKE

IMBA Expert™ USDOE-Edition code used to assess intake:

- Exclude data affected by chelation.
- 'Hard-wired' with ICRP Publication 67 Pu biokinetic model.
- Maximum likelihood estimate of intake and absorption parameters constrained to fit simultaneously urinary and faecal excretion data (un-treated) AND total Pu lung/LNTH activities measured at death.
- **RESULT—Intake ~58 kBq; AMAD ~2 μm; f_1 ~0.0005; s_p ~10 d^{-1}; s_{pt} ~100 d^{-1}; s_t ~0.02 d^{-1}; f_b ~8%; s_b ~2 × 10^{-4} d^{-1}.**



ACKNOWLEDGEMENT/DISCLAIMER

Acknowledgment: This material is based upon work supported by the U.S. Department of Energy, Office of Epidemiology and Health Surveillance, under Award Number DE-FG06-92EH89181".

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4. BIOKINETIC MODEL SYSTEM

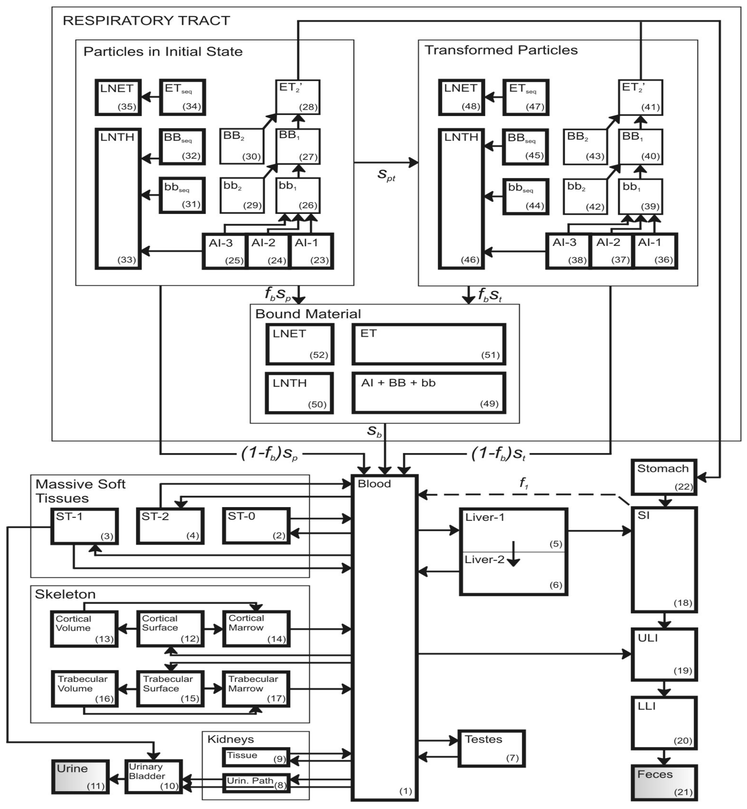


Figure 3. Combined implementation of ICRP 66 HRTM and ICRP 67 systemic Pu model

Method used to solve overall biokinetic model — and to predict Pu excretion rates and tissue contents as a function of time:

- Exact (analytical) solution using 'rate matrix' method—Birchall A, James AC. "A microcomputer algorithm for solving first-order compartment models involving recycling." Health Phys. 56:857-869; 1989.
- Solved sequentially—time-steps defined by excreta collection periods—keeping track of whether or not Ca-EDTA **OR** Ca-DTPA therapy is currently being applied.

5. MODELING EFFECTS OF CHELATION

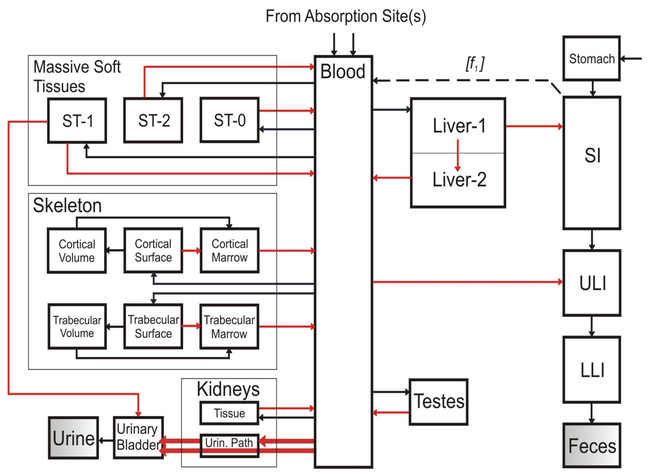
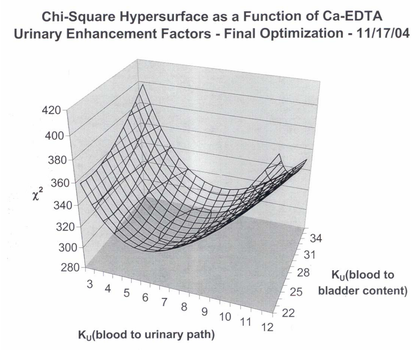


Figure 4. Hypothetical chelation pathways considered



- ICRP-recommended values of principal biokinetic rate constants multiplied by test factor [K(pathway)].
- Values of K(pathway) varied iteratively (in pairs)—to minimize total X^2-sum for whole dataset—avoiding false (local) minima.
- ALL excretion data (with lognormal errors) AND measured Pu tissue compartmental distribution at time of autopsy, *e.g.*, derived total trabecular and cortical bone contents, INCLUDED in calculated X^2-sum.

6. MODELED EXCRETION BEHAVIOUR

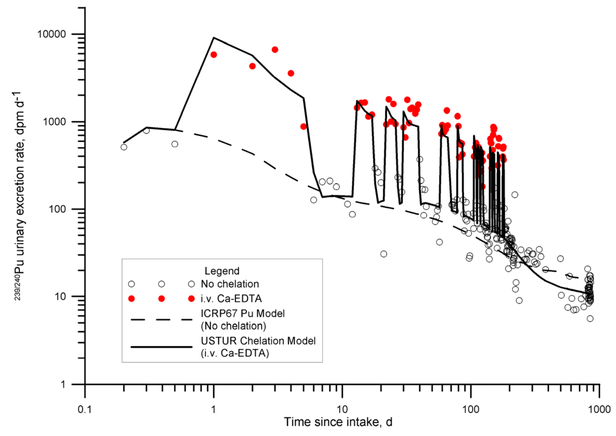


Figure 5. Early i.v. Ca-EDTA—measured and modeled effects on Pu urinary excretion

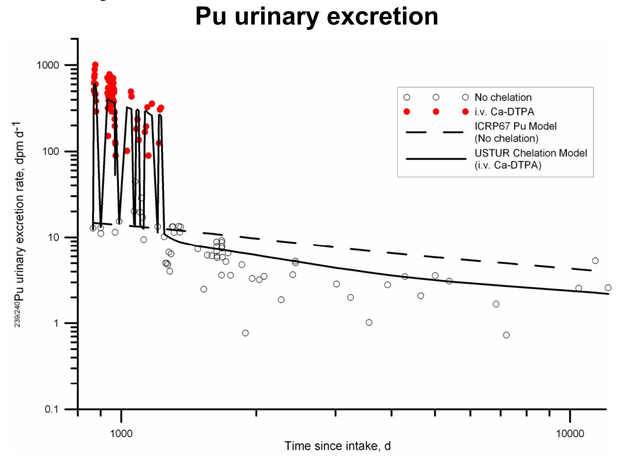


Figure 6. Late i.v. Ca-DTPA—measured and modeled effects on Pu urinary excretion

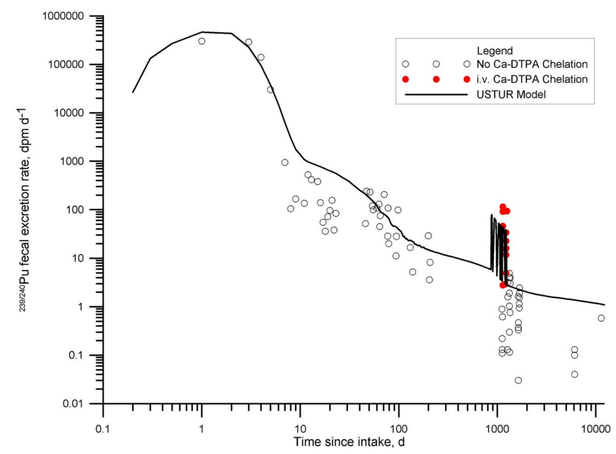


Figure 7. Late i.v. Ca-DTPA—measured and modeled effects on Pu faecal excretion

7. DERIVED EFFECTIVENESS

Tissue	*Tissue Pu Content at Death, kBq*			
	Measured	*USTUR Model*		
		Therapy	*Untreated*	*Saving*
Whole Body	2.29	2.29	4.22	46%
Lungs	0.027	0.027	0.027	0%
LNTH	0.00019	0.00021	0.00021	0%
Liver	0.94	0.81	1.62	50%
Skeleton	1.20	1.21	2.18	45%
Muscle, Skin, *etc.*	0.18	0.23	0.38	39%
Kidneys	0.0017	0.0017	0.0032	47%

Comments:

- *Chelation therapy administered in this case saved significant amounts of tissue and effective dose—**modeled effective dose for no treatment is ~10 Sv (~1,000 rem)**.*
- *Late (3-y delayed) i.v. Ca-DTPA was more effective in removing Pu from tissues than prompt i.v. Ca-EDTA therapy.*
- *USTUR chelation model requires further 'optimization', e.g., to improve prediction of final liver burden, late faecal excretion, and massive soft tissue burden.*
- *USTUR will finalize model development using proposed new ICRP Pu biokinetic model—with modified treatment of early blood and tissue fluid kinetics (Leggett at al. Radiat. Res. 164:111-122; 2005).*

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