Bayesian Analysis of Bioassay and Autopsy Data from 18-y Follow-up of an Acute Accidental Inhalation of Refractory PuO_2

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Introduction

The International Commission on Radiological Protection (ICRP) is currently reviewing and updating its biokinetic and dosimetric models, including the Human Respiratory Tract Model (HRTM) recommended in Publication 66 (1994).

Recently, Gregoratto et al. (in press) have derived a simplified model of particle transport in the alveolar-interstitial and bronchial regions that substantially reduces the complexity of the HRTM.

It is important to test and verify proposed changes to the HRTM against available human data for various intake scenarios.

USTUR Partial-Body Donor 0202

- Process Operator in Metal Production at the Rocky Flats Plant for 20 y
- Highest exposed of 18 USTUR Registrant tissue donors involved in the 1965 Pu fire accident at the Rocky Flats Plant (RFP)
- Highly refractory PuO_2 aerosol with measured 0.32 µm mass median diameter (1.0 µm AMAD)
- Initial Am:Pu Mass Ratio: 1830 ppm
- Average Pu-in-Air Concentration at the registrant's workplace: > 1.5 kBq/m^3
- Treated with Ca-DTPA: 1 g on each 5 days following the fire
- RFP estimate of Pu activity in lungs (1973): 668% of MPLB (3.96×10^3 Bq)

Bioassay Data

- In-vivo Lung Counts – 38 results (over 2,868 days post-intake)
  - ^{239}Pu activity calculated from the original ^{241}Am 59 keV count rate
  - Decreasing from 289 nCi in 1965 to 145 nCi in 1973
- Urinary Excretion Rates of Pu – 40 valid results (over 2,797 days post-intake)
  - 28 results exceeding the LOD = MDA/2 (0.27 dpm/24-h)
  - Data affected by DTPA treatment not used in calculations
- Fecal Excretion Rates of Pu – 16 results (over 220 days post-intake)
  - No information on sample volumes available
  - Not used in analysis

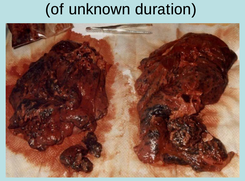
Autopsy and Pathology

Died in 1983, at age 74, y from Emphysema and Acute Myocardial Infarction.

Portions of the lungs, tracheo-bronchial lymph nodes, liver, adrenals, kidneys, spleen, testes, thyroid, gall bladder, clavicle, rib, and sternum were taken at autopsy and analyzed radiochemically for $^{239/240}$Pu, ^{238}Pu and ^{241}Am.

Worker's respiratory tract was likely compromised due to:

- History of COPD
- Exposure to coal dust:
  Coal Miner prior to RFP
- 1 pack/day cigarette smoker (of unknown duration)



Case 0202's lungs at autopsy showing heavy carbon pigmentation

Table 1. Summary of $^{239+240}$Pu tissue analysis

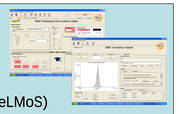
Organ or Tissue	Sample mass, g	Concentration, Bq/kg	Organ Content, Bq
Lungs	1,008	7,225 ± 123	7,283
LN_{TH}	12.8	19,816 ± 689	254
Liver	1,022	100.6 ± 2.7	103
Adrenals	10	20.3 ± 1.5	0.203
Kidneys	300	1.81 ± 0.08	0.54
Spleen	150	92.7 ± 4.0	13.9
Thyroid	15	1.50 ± 0.31	0.023
Gall Bladder	8.3	4.02 ± 0.54	0.033
Testes	23.3	2.16 ± 0.24	0.05
Skeleton - based on:		24.0 ± 10.5	210.9[a]
Clavicle (shaft)	24.1	13.7 ± 0.6	-
Rib	28	26.0 ± 1.1	-
Sternum	102.5	32.8 ± 1.2	-

[a] Based on total skeletal weight (8.8 kg) predicted from height (164 cm) (ICRP 2002)

Objectives

- Examine the applicability of the current ICRP HRTM and Gregoratto et al.'s model.
- Optimize the parameter values for particle transport in both models to represent USTUR case 0202 data.
- Calculate the probability distributions on intake, biokinetic model parameters and doses according to both models.

Methods



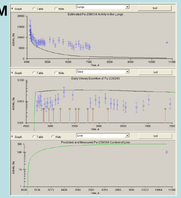
- Maximum Likelihood Method
  - IMBA Professional Plus (IPP) (Birchall et al 2007)
- Bayesian Statistical Analysis using
  - Weighted Likelihood Monte-Carlo Sampling Method (WeLMoS) (Puncher and Birchall 2008)

IPP Maximum Likelihood Assessment

IPP maximum likelihood assessment of the case 0202 data was performed, assuming the measured aerosol characteristics (AMAD = 1 µm, PuO_2 particles).

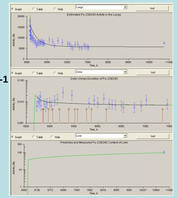
- Implementation of ICRP particle transport and Type S absorption models along with the ICRP Publication 67 model for Pu systemic biokinetics (ICRP 1993) resulted in a non-credible fit to the data.
- Gregoratto et al. particle transport model (GPT) coupled with customized absorption model parameters resulted in a credible fit for urinary excretion data and predicted the liver and skeletal activities measured post-mortem. However, the fit to the lung retention data did not predict the lung data for this case.

- **Current HRTM**
- **Absorption Type S**



χ^2 = 3,050
P-value = 0

- **GPT**
- **Absorption:**
  f_r= 0.0064
  s_r=1.98 d^{-1}
  s_s= 5.3×10^{-6} d^{-1}



χ^2 = 317
P-value ~ 10^{-31}

Bayesian Analysis Results

Bayesian statistical analysis of the case 0202 data was performed using the WeLMoS methodology implemented in a software tool IMBA Uncertainty Analyzer (Puncher and Birchall 2008).

The software samples the selected model parameters from user-defined prior probability distributions and uses the IMBA Professional Plus (IPP) as a "code library" to solve the biokinetic models and calculate the posterior probability distributions.

Assumptions

For both models, the alveolar-interstitial compartmental deposition fractions and particle transfer rates were optimized in order to represent the case 0202 data using the IPP code.

Particle transport rate constants are assumed to be correlated and can be modeled by scaling them by a single factor, K_{PT}.

HRTM absorption model applies to both models, with user-defined parameters and no chemical binding, e.g. f_b = 0.

The systemic biokinetics of Pu represented by the ICRP 67 model was assumed for optimized HRTM, while the optimized Gregoratto et al. model was coupled with the Pu systemic biokinetics model of Legget et al. (2005).

Prior Distributions

The following parameters were varied in this study: intake; rapidly absorbed fraction, f_r; rapid absorption rate, s_r; slow absorption rate, s_s; and particle transport rate factor, K_{PT}. The assumed prior probability distributions of model parameters for both optimized models are presented in Table 2.

Table 2. Assumed Prior Distributions of Model Parameters

Parameter	Distribution	Range
Intake, Bq	Lognormal	OHRTM: Median = 7.2 × 10^4, σ_g = 1.05
		OGPT: Median = 8.2 × 10^4, σ_g = 1.10
Rapid Fraction f_r	Log-uniform	0.001 – 0.02
Rapid Rate s_r, d^{-1}	Log-uniform	0.1 - 10
Slow Rate s_s, d^{-1}	Log-uniform	1 × 10^{-6} - 1 × 10^{-4}
Particle Transport Factor K_{PT}	Lognormal	Median = 1, σ_g = 1.17

Posterior Distributions

The Latin Hypercube sampling algorithm was used to sample parameters from the prior probability distributions (McKay et al. 1979). The posterior probability distributions of input parameter values and resulting doses were calculated with 10,000 input parameter vector realizations. The results are summarized in Table 3.

Table 3. Posterior Probability Distributions of the optimized HRTM and GPT models

Quantity	OHRTM		OGPT	
	Mean	GSD	Mean	GSD
Intake, Bq	71,500	1.02	81,500	1.01
Rapid fraction (f_r)	0.0064	1.27	0.0068	1.24
Rapid rate (s_r), d^{-1}	1.98	3.77	2.06	3.61
Slow rate (s_s), d^{-1}	5.3 × 10^{-6}	1.21	4.7 × 10^{-6}	1.23
Particle transport factor (K_{PT})	0.729	1.35	0.932	1.30
Effective dose (H_E), mSv	7,100	1.05	7,300	1.02
Weighted equiv. lung dose [H_E(lung)], mSv	6,860	1.06	7,070	1.02
Equiv. lung dose (H_{lung}), mSv	57,200	1.06	58,900	1.02
AI dose (H_{AI}), mSv	149,000	1.05	162,000	1.02
LN_{TH} dose (H_{LNTH}), mSv	1,540,000	1.31	805,000	1.28
Liver dose (H_{liver}), mSv	1,640	1.14	1,820	1.14
Bone surface dose (H_{BS}), mSv	7,650	1.14	6,790	1.14
RBM dose (H_{RBM}), mSv	415	1.14	370	1.15
MST dose (H_{MST}), mSv	12.9	1.13	10.5	1.14
Terminal LN_{TH} dose rate (D_{LNTH}), mGy y^{-1}	863	-	606	-

Conclusions

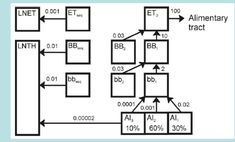
- In order to represent the case 0202 data, substantial modification of the HRTM structure and parameter values is needed:
  Two distinct phases of particle transport from the AI region:
  - ~ 20% of the initial alveolar deposition is transferred to bb_1 with a half-time of ~100 d
  - ~ 80% is cleared to bb_1 (33%) and lymph nodes (67%) with a 'net' half-time of ~63 y
- With appropriate adjustments, Gregoratto et al. model yielded an excellent fit to the data
  - ~ 33% of the initial AI deposit is cleared to the bronchioles with a half-time ~90 d
  - ~ 67% is transferred to thoracic lymph nodes, half-time ~240 y
- PuO_2 particles produced by the plutonium fire are extremely insoluble:
  - ~ 0.6% is absorbed relatively rapidly, half-time ~8 h
  - ~ 99.4% is absorbed extremely slowly, half-time ~400 y
- About 97% of the total committed weighted dose equivalent is contributed by the lungs.
- The committed weighted dose equivalent per unit intake for case 0202 is ~9×10^{-5} Sv/Bq, an order of magnitude higher than the recommended dose coefficient for Type S Pu (8.4×10^{-6}).
- The doses absorbed by this worker's lungs were high: 3 Gy to AI and 6 Gy to LN_{TH}.
- The registrant's lung disease and prior occupational exposure to coal dust are likely to have impaired lung clearance, and thus contributed to the high lung tissue doses.

References

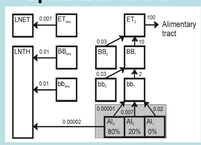
Bailey MR et al. In Proc. 12th International Congress of the IRPA, Buenos Aires, October 2008.
Birchall A et al. Radiat Prot Dosim **125**: 194-197; 2007.
Birchall A et al. In: *Late Health Effects of Ionizing Radiation: Bridging the Experimental and Epidemiologic Divide*, Georgetown University, Washington, DC, May 4-6, 2009 (in press).
ICRP Publication 67. Ann. ICRP **23**(3/4), 1993.
ICRP Publication 66. Ann. ICRP **24**(1-3), 1994a.
ICRP Publication 68. Ann. ICRP **24**(4), 1994b.
ICRP Publication 89. Ann. ICRP **32**(3-4). 2002.
Leggett RW et al. Radiat. Res. 164(2): 111-122, 2005.
Mann JR, Kirchner RA. Health Phys. **13**:877-882, 1967.
McKay MD et al. Technometrics **21**:239-245; 1979.
Puncher M, Birchall A. Radiat. Prot. Dosim. **132**(1): 1-12, 2008.

DISCLAIMER

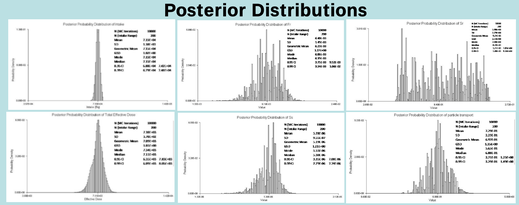
ICRP HRTM



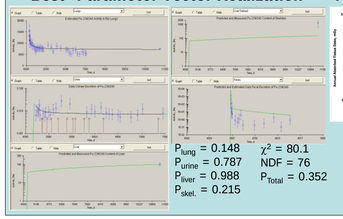
Optimized HRTM



Posterior Distributions

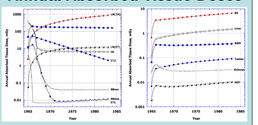


"Best" Parameter Vector Realization



P_{lung} = 0.148
P_{urine} = 0.787
P_{liver} = 0.988
$P_{skel.}$ = 0.215
χ^2 = 80.1
NDF = 76
P_{Total} = 0.352

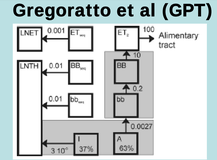
Annual Absorbed Tissue Doses



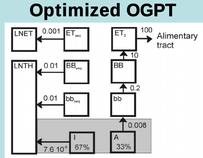
Terminal Dose to LNTH, mGy/y

Measured	Estimated
638 ± 22	863

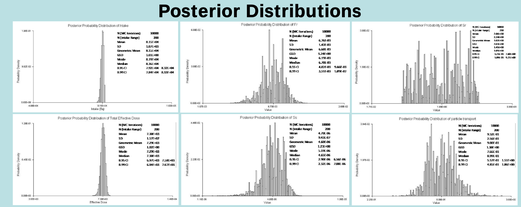
Gregoratto et al (GPT)



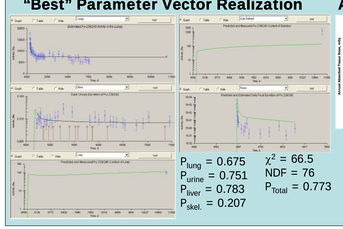
Optimized OGPT



Posterior Distributions

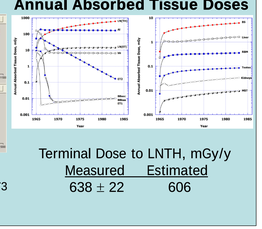


"Best" Parameter Vector Realization



P_{lung} = 0.675
P_{urine} = 0.751
P_{liver} = 0.783
$P_{skel.}$ = 0.207
χ^2 = 66.5
NDF = 76
P_{Total} = 0.773

Annual Absorbed Tissue Doses



Terminal Dose to LNTH, mGy/y

Measured	Estimated
638 ± 22	606