Modeling the long-term retention of plutonium in the respiratory tract using scar-tissue compartments

Deepesh Poudel[1], Maia Avtandilashvili[2], John Klumpp[1], Luiz Bertelli[1], Sergei Tolmachev[2]

[1]Internal Dosimetry, Los Alamos National Laboratory

[2]USTUR, Washington State University

Los Alamos NATIONAL LABORATORY EST. 1943

July 28, 2021

NNSA National Nuclear Security Administration

Managed by Triad National Security, LLC for the U.S. Department of Energy's NNSA

LA-UR-21-26612

Further reading

Paper

Long-term Retention of Plutonium in the Respiratory Tracts of Two Acutely-exposed Workers: Estimation of Bound Fraction

Deepesh Poudel,[1] Maia Avtandilashvili,[2] Luiz Bertelli,[1] John A. Klumpp,[1] and Sergei Y. Tolmachev[2]

Journal of Radiological Protection

Official journal of the Society for Radiological Protection

ACCEPTED MANUSCRIPT

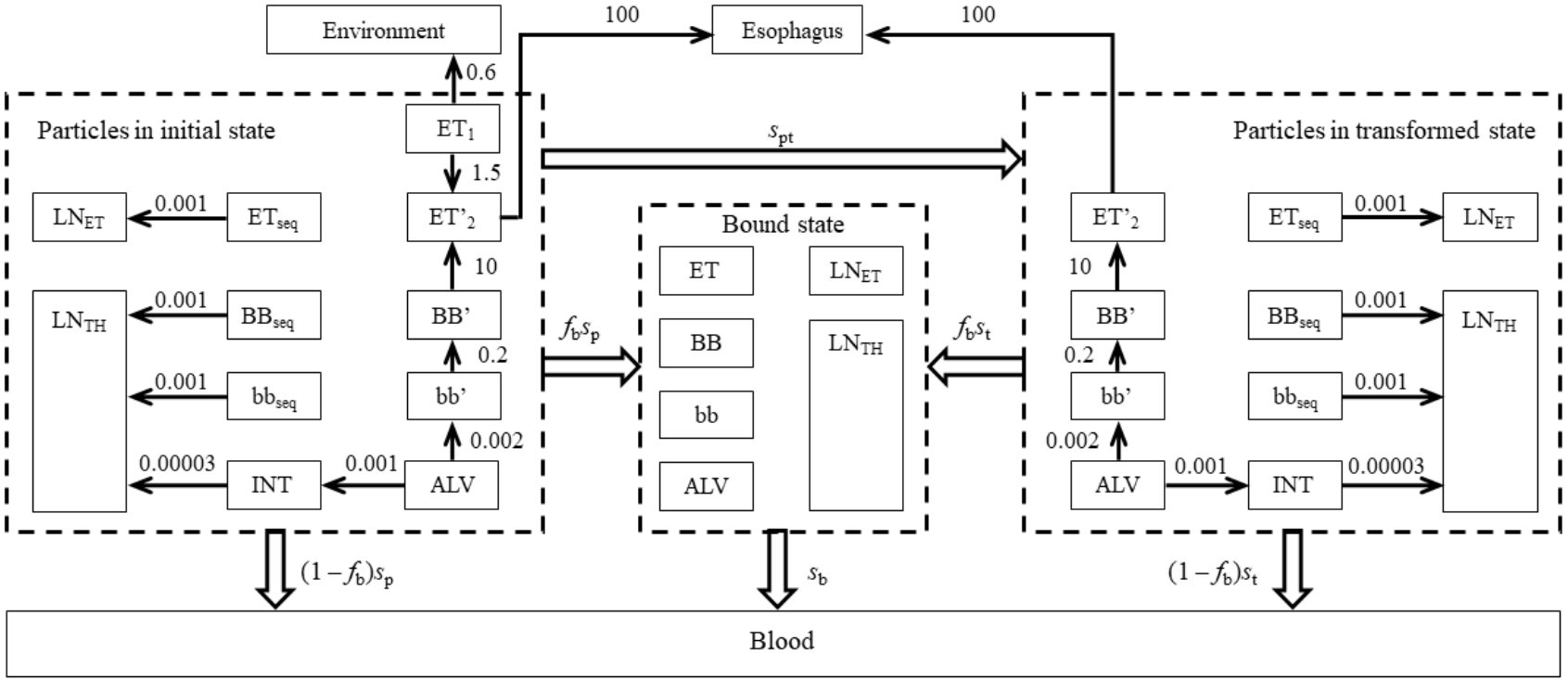
Modelling of long-term retention of high-fired plutonium oxide in the human respiratory tract: importance of scar-tissue compartments

To cite this article before publication: Deepesh Poudel *et al* 2020 *J. Radiol. Prot.* in press https://doi.org/10.1088/1361-6498/abca49

MODELLING THE LONG-TERM RETENTION OF PLUTONIUM IN THE HUMAN RESPIRATORY TRACT USING SCAR-TISSUE COMPARTMENTS

Deepesh Poudel[1,*], Maia Avtandilashvili[2], John A Klumpp[1], Luiz Bertelli[1], Sergei Y Tolmachev[2]
[1]Radiation Protection Division, Los Alamos National Laboratory, Los Alamos, NM, USA
[2]United States Transuranium and Uranium Registries, Washington State University, Richland, WA, USA

The Human Respiratory Tract Model[1]



[1]ICRP 130. Ann. ICRP 44(2)

Studies on Binding of Plutonium

- Plutonium bound fraction inferred from three studies
  - USTUR Case 0269 autopsy and bioassay data[2,5]: $f_b = 0.037$
  - Lung-retention data from 15-year life-span beagle study[3,5]: $f_b = 0.0023$
  - Autopsy data from 40 Mayak workers[4,5]: $f_b = 0.0014$

- ICRP recommendation[6]: $f_b = 0.002$, $s_b = 0$

[2]Puncher et al. Radiat. Prot. Dosim. 176(1-2), 50-61; 2017
[3]Puncher et al. Radiat Prot. Dosim. 176(1-2), 32-44; 2017
[4]Puncher et al. Radiat. Prot. Dosim. 176(1-2), 62-40; 2017
[5]Birchall et al. Health Phys. 117(2), 133-142; 2019
[6]ICRP 141. Ann. ICRP. 48(2/3); 2019.

Dose Consequence of Binding

Table 1. Impact of bound fraction assumption (0.2% vs 0) on 50-y committed dose for inhalation of Pu nitrates

Target region	% increase
ET region (ET)	23.1%
Basal cells of anterior nasal passages (ET1-bas)	-0.06%
Basal cells of posterior nasal passages + pharynx (ET2-bas)	23.1%
Lung	41.0%
Basal cells of bronchi (Bronchi-bas)	99.6%
Secretory cells of bronchi (Bronchi-sec)	181%
Secretory cells of bronchioles (Brchiol-sec)	49.2%
Alveolar-interstitium (AI)	9.88%
Lymph nodes, total	3.47%
Lymph nodes of the ET region (LN-ET)	6.03%
Lymph nodes in the thoracic region (LN-Th)	5.93%
Systemic lymph nodes (LN-Sys)	-0.20%
Effective dose	7.67%

Objectives

- Epidemiological studies show association between lung cancer and lung doses
- Important to characterize critical parameters such as binding
- Objectives:
  - Compare current model of binding against observations (USTUR data and literature)
  - Analyze USTUR data using a modified model structure

Data

Table 2. Summary of data

USTUR Case 0269
Incident: internal (and external) contamination following release of plutonium
Reported intake: acidic $Pu(NO_3)_4$ mist
Death: 39y post intake
Data available: 24h urine; blood; feces; sputum; retention in **respiratory tract tissues**, liver, skeleton, other soft tissues.

USTUR Case 0631
Incident: tearing open equipment while working on wet purification process
Reported intake: most likely $Pu(NO_3)_4$
Death: 66y post intake
Data available: **24h urine; retention in respiratory tract tissues, liver, skeleton,** other soft tissues.

USTUR Case 0745
Incident: splattering of solution
Reported intake: soluble $Pu(NO_3)_4$
Death: 59y post intake
Data available: **24h urine; retention in respiratory tract tissues, liver, skeleton,** other soft tissues.

USTUR Case 0407
Incident: inhalation of aerosols released from plutonium glove-box fire
Reported intake: high-fired PuO_2
Death: 42y post intake
Data available: **24h urine**; 24h feces; **lung counts; retention in respiratory tract tissues, liver, skeleton,** other soft tissues.

Data

- Data on regional retention in lungs

Table 3. Post-mortem data

Region	^{239}Pu retention at death (Bq)			
	Case 0269	Case 0631	Case 0745	Case 0407
Respiratory tract				
Larynx (ET_2)	2.16 ± 0.02	0.18 ± 0.01	0.44 ± 0.02	0.17 ± 0.01
Bronchi (BB)	5.62 ± 0.03	0.64 ± 0.00	3.49 ± 0.11	145.6 ± 6.1
Bronchiole (bb)	2.08 ± 0.01	0.24 ± 0.02	1.47 ± 0.06	87.2 ± 3.8
Alveolar-interstitium (AI)	16.79 ± 0.11	2.54 ± 0.11	29.4 ± 0.7	704.4 ± 43.5
Thoracic lymph nodes (LNTH)	0.45 ± 0.06	2.71 ± 0.08	21.8 ± 0.5	1135.6 ± 20.4
Liver + Skeleton	2120 ± 22[a]	234.8 ± 83.4	454 ± 55	299.5 ± 74.6

[a]Not used in modeling because the systemic activity is affected by several chelation treatments.

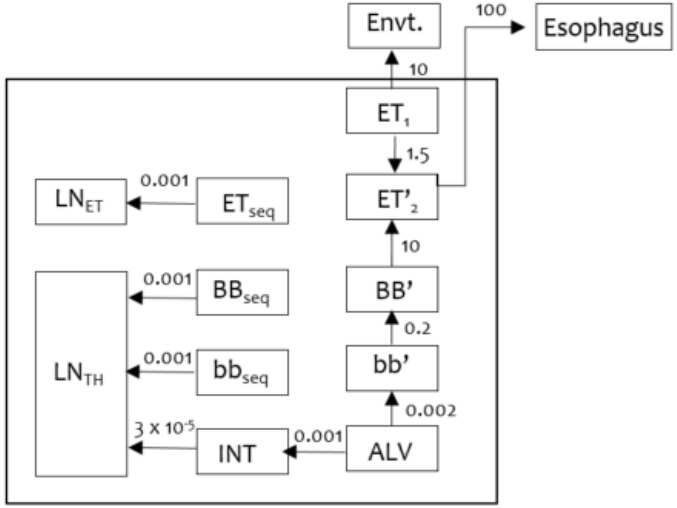
Need for binding

- USTUR Case 0269:
  - ~1% of intake retained in the lungs several years after intake[7]
  - Inconsistent with known behavior of soluble plutonium
  - Regional retention shows activity in the upper respiratory tract

Table 4. Effects of different model assumptions on retention in upper respiratory tract after inhalation of 5 µm AMAD plutonium nitrate

	$A_{URT/RT}$
No binding and:	
default model parameters	2.5×10^{-8}
$f_{seq} = 0.01$[a]	1.3×10^{-7}
K_{PT}, $K_{PT(seq)} = 0.2$[b]	1.9×10^{-3}
Measured for Case 0269	0.364 ± 0.002
Binding, f_b=0.002	0.07

[a]The fraction deposited into ET_{seq}, Bb_{seq} and bb_{seq} compartments was increased from 0.002 to 0.1.
[b]All mechanical transport rates in the ET, BB and bb compartments were decreased by five times.



[7]James et al. Radiat. Prot. Dosim. 127(1-4), 449-455; 2007

Issues with Binding

- Estimated bound fraction found to be dependent on solubility

Table 5. Published values of bound fraction

Subject(s)	Material	f_b(%)
ICRP default[6]	Independent of solubility	0.2
USTUR Case 0269[2, 5]	Nitrate	0.7[a]
	Nitrate	0.4[b]
Beagles[3, 5]	Nitrate	0.2[c]
	Nitrate	0.8[d]
Mayak workers[5]	Nitrate	0.1
Mayak workers[8]	Nitrate	0.3[e]
"Case 110"[9]	Type M	5.3[f]
USTUR Case 0631[10]	Mixture	1[g]
USTUR Case 0745 [10]	Mixture	4[g]
Mayak workers[8]	Mixture	3-7[e]
"Case 080"[9]	Type S[e]	56.2[f]
Mayak workers[11]	Oxides	4.7
Mayak workers[8]	Oxides	15-19[e]
USTUR Case 0407[12]	High-fired Oxide	cannot be explained

[a]Using measured (at autopsy) liver+skeleton activity
[b]Using predicted (without DTPA treatment) liver+skeleton activity
[c]Using DRTM-66 (ICRP 66 HRTM modified for dogs)
[d]Using DRTM-OIR (ICRP 130 HRTM modified for dogs)
[e]Using modified ICRP-66 HRTM
[f]Using ICRP-66 HRTM
[g]Solubility between that of plutonium nitrate and mixed oxides

[9]Khokhryakov et al. Health Phys. 88(2), 125-132 (2005).
[10]Poudel et al. Health Phys. 120(3), 258-270; 2021
[11]Birchall et al. Radiat. Prot. Dosim. 105(1-4), 85-90; 2003
[12]Poudel et al. J. Radiat. Prot. In press; 2021.

Issues with binding

- Data for USTUR Case 0407 not explained by bound fraction

Table 6. Effects of different assumptions on retention of Pu dioxides in the respiratory tract

	$R_{TB/Lung}$
Measured	0.25 ± 0.01
Default model parameters	5.54×10^{-6}
Assumption:	
$f_{seq} = 0.01$[a]	5.84×10^{-6}
K_{PT}, $K_{PT(Seq)} = 0.2$[b]	5.58×10^{-4}
$f_b = 1$[c]	2.22×10^{-3}

[a]Sequestration increased from default of 0.002 to 0.01
[b]Particle-transport rates decreased by five times
[c]Bound fraction increased from default of 0.002 to 1 as an extreme scenario

- Autoradiography showed alpha star aggregates localized within connective tissue[13,14]
  - Inconsistent with presence of bound state

[13]Nielsen et al. Cancer Res. 72(21), 5529-5536; 2012
[14]Nielsen et al. Int. J. Radiat. Biol. 90(1), 60-70; 2014

“Physical” vs “Chemical” binding?

- Several observations inconsistent with bound fraction
- Could it be scar tissues (“physical” binding)?
  - Significant alpha doses to small volume of tissues may result in scarring/fibrosis
  - Plenty of evidence of fibrotic scar tissues in the literature:
    - Registry of 188 cases of plutonium-induced lung fibrosis among Mayak workers[15]
    - Study of Rocky Flats worker showed individuals with lung doses > 10 Sv or greater likely to have abnormal chest x-ray[16]
    - Fibrosis also observed in mice[17], rats[18], dogs[19] and baboons[20]

[15]Azizova et al. Health Phys. 118 185-192; 2020
[16]Newman et al. Radiat. Res. 164 123-131; 2005
[17]Talbot and Moores Radiat. Res. 103 135-148; 1985
[18]Sanders et al. Int. J. Radiat. Biol. 64 107-130; 1993
[19]Wilson Health Phys. 96 175-185; 2009
[20]Bair et al. Radiat. Res. 82 588-610; 1980

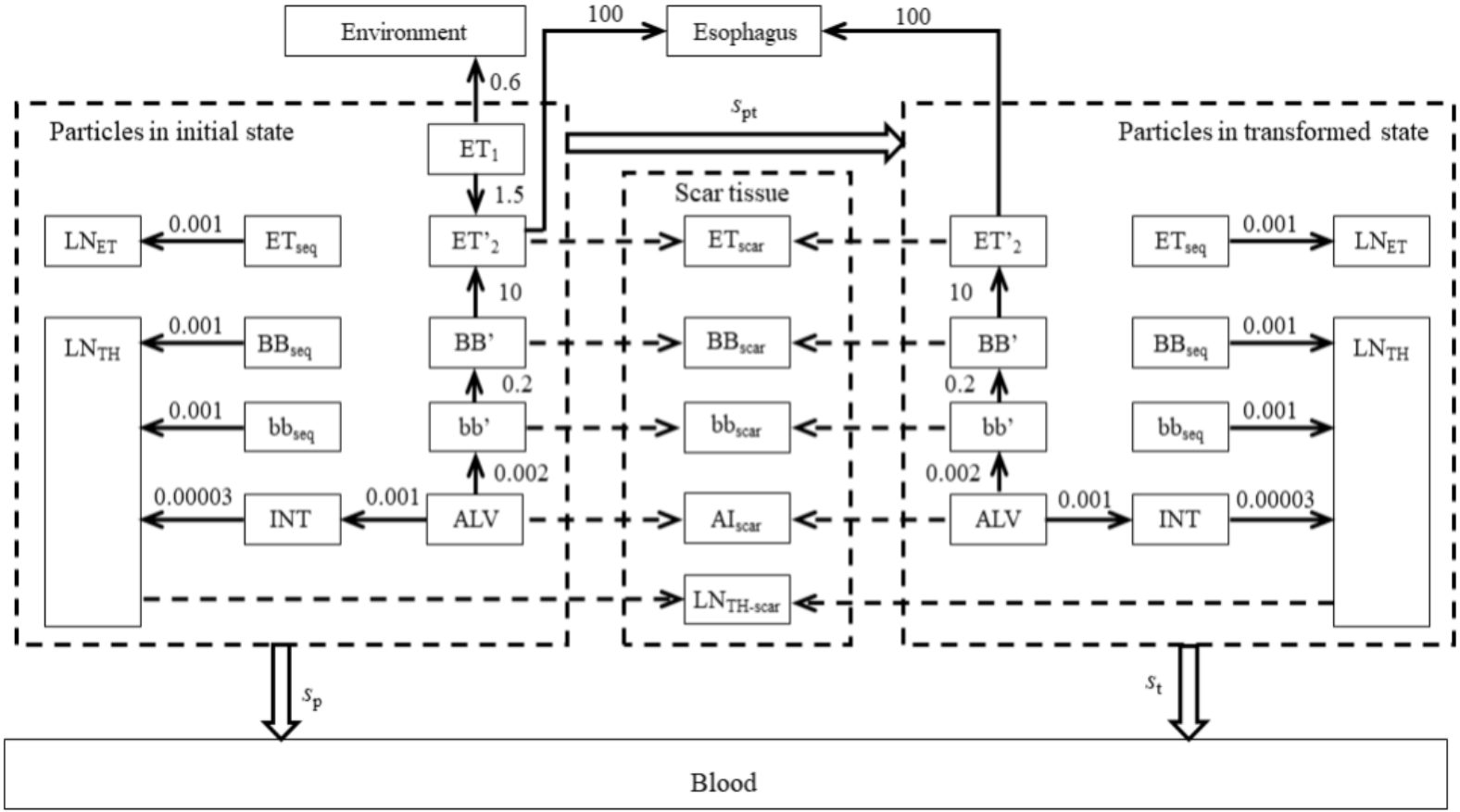
The Scar-tissue Approach

- Encapsulation of plutonium in scar tissues
  - Plutonium ‘hot spots’ deliver high doses to a small volume of tissues resulting in scar tissues
  - Literature review points to the presence of – and significant retention of – plutonium in scar tissues[21-23]
  - Fibrosis of tissue immobilizes plutonium

- “Physical” binding compared to “chemical” binding
  - Less dosimetrically significant
    - Irradiation of scar-tissues vs. sensitive epithelial tissues

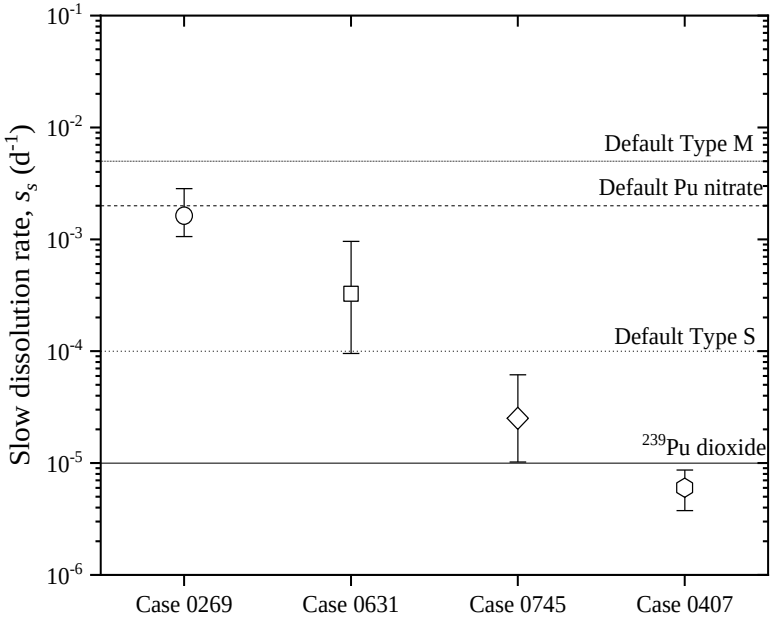
[21]Guilmette et al. Radiat. Prot. Dosim. 99(1-4), 457-461; 2021
[22]Hahn et al. Radiat. Prot. Dosim. 105(1-4), 81-84; 2003
[23]Hahn et al. Radiat. Res. 161(5), 568-581; 2004

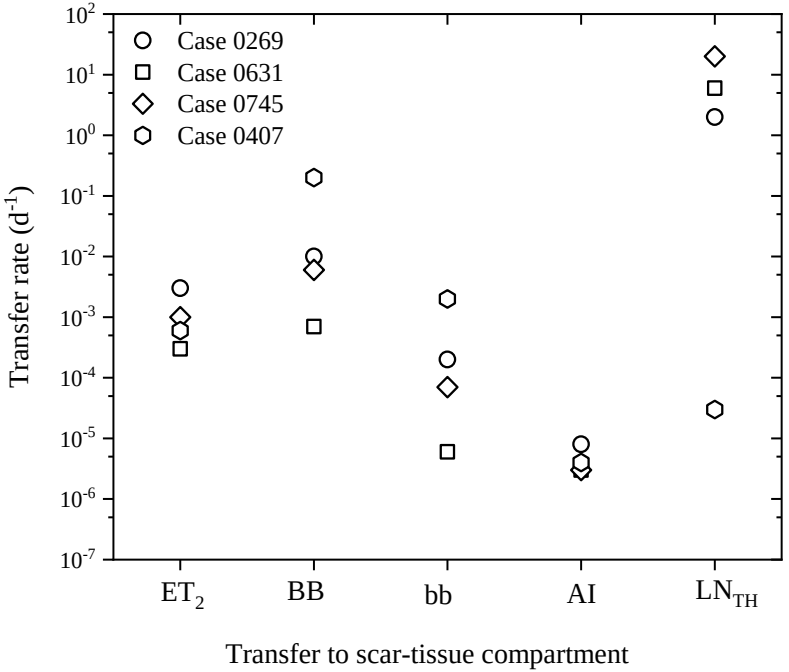
Proposed Model



Results and Discussion

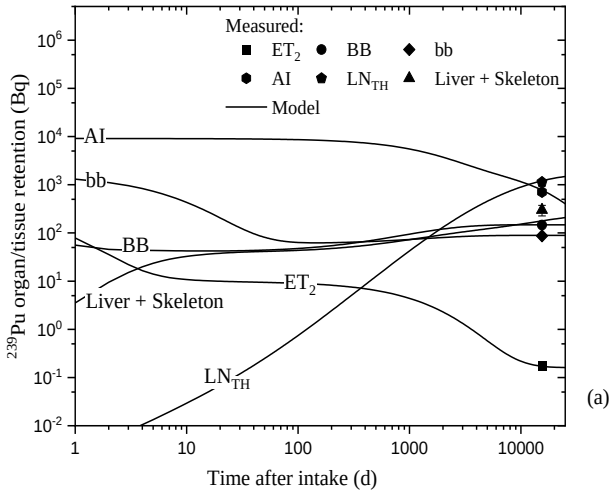
- Priors from several previous studies
- Posterior distributions obtained from Markov-chain Monte Carlo analysis



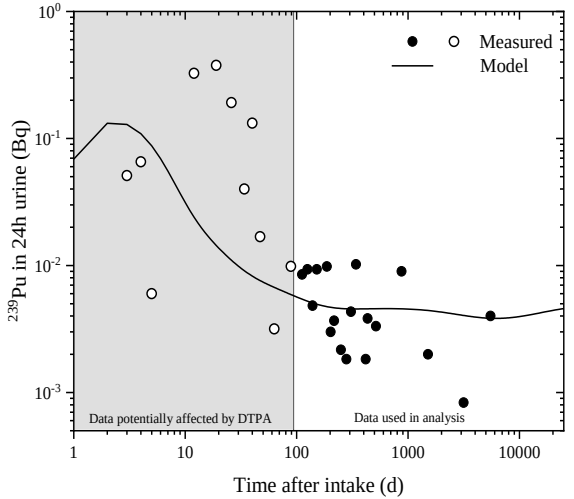


Results and Discussion

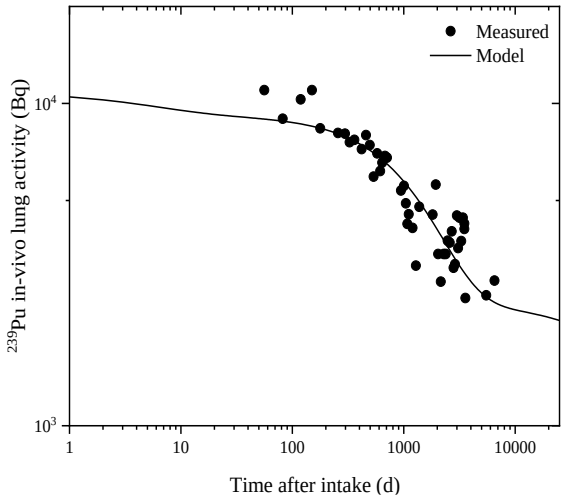
- Case 0407 as an example:



(a)



(b)

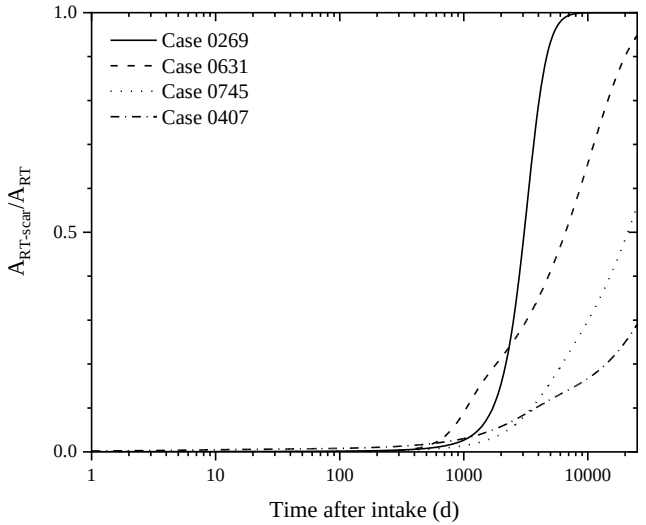


(c)

Results and Discussion

- Very small fraction of intake retained in the scar-tissue compartments
  - 1.5×10^{-4}, 6.2×10^{-5}, 6.7×10^{-4}, and 5.0×10^{-3} for Cases 0269, 0631, 0745, and 0407 respectively

- Significant fraction of activity in the lungs in scar-tissues
  - Consistent with the literature



Conclusions

- Chemical binding alone is not consistent with data and observations in the literature
- A significant fraction of activity in the respiratory tract is found to be retained in scar tissues
- We successfully explained regional retention of plutonium in the respiratory tract of four cases using scar-tissue model

- Other mechanisms can also be responsible
  - Some combination of physical and chemical binding, or systemic uptake of plutonium by the lungs
  - Study of wound case planned to investigate the latter

LANL Disclaimer

The submitted materials have been authored by employees of Triad National Security, LLC (Triad) under contract with the U.S. Department of Energy/National Nuclear Security Administration (DOE/NNSA). Accordingly, the U.S. Government retains an irrevocable, nonexclusive, royalty-free license to publish, translate, reproduce, use, or dispose of the published form of the work and to authorize others to do the same for U.S. Government purposes.

Questions?

dpoudel@lanl.gov