Regional retention of plutonium in the respiratory tract of four acutely-exposed workers can be described 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

April 28, 2022

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

LA-UR-22-21135

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

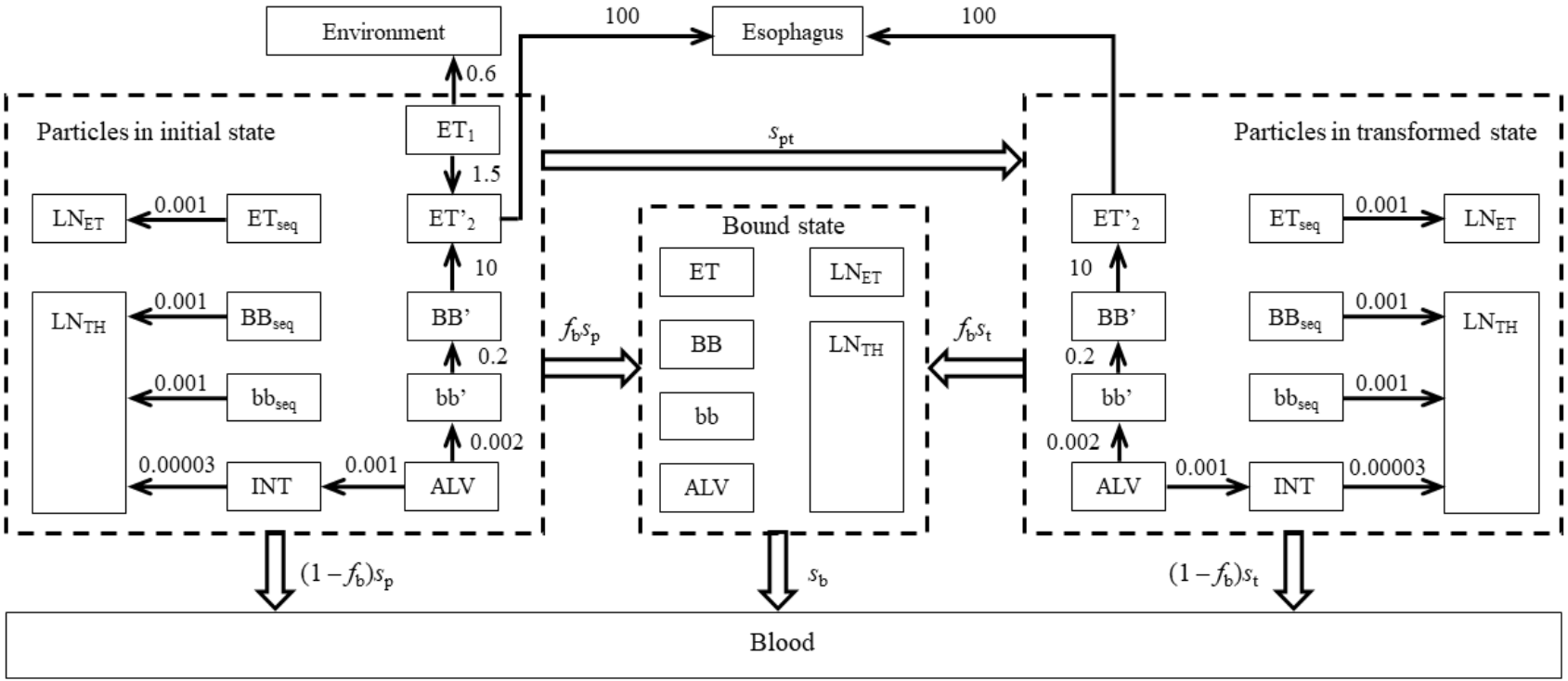
Modelling of long-term retention of high-fired plutonium oxide in the human respiratory tract: importance of scar-tissue compartments

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)

Chemical binding

- 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]: $f_b = 0.002$, $s_b = 0$

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%

[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.

Physical binding

- Encapsulation of Pu in scar tissues
- Mechanism not discussed in HRTM but evidence in the literature[7-14]
- Not as dosimetrically significant as chemical binding

[7]Bair et al. Radiat. Res. 82(3), 588-610 ; 1980.
[8]Guilmette et al. Radiat. Prot. Dosim. 99(1-4), 457-461; 2002.
[9]Hahn et al. Radiat. Res. 161(5), 568-581; 2004.
[10]Nielsen et al. Cancer Res. 72(21), 5529-5536; 2012.
[11]Nielsen et al. Int. J. Radiat. Biol. 90(1), 60-70; 2014.
[12]Sanders et al. Int. J. Radiat. Biol. 64(4), 417-430; 1983
[13]Talbot and Moores. Radiat. Res. 103(1), 135-148; 1985
[14]Wilson. Health Phys. 96(2), 175-185; 2009

Objectives

- Extent of physical or chemical binding is important for dosimetry (and epidemiological and dose response modelling)

- Objectives:
  - Discuss the inconsistencies of the chemical binding model
  - Analyze the data using a scar-tissue model

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.

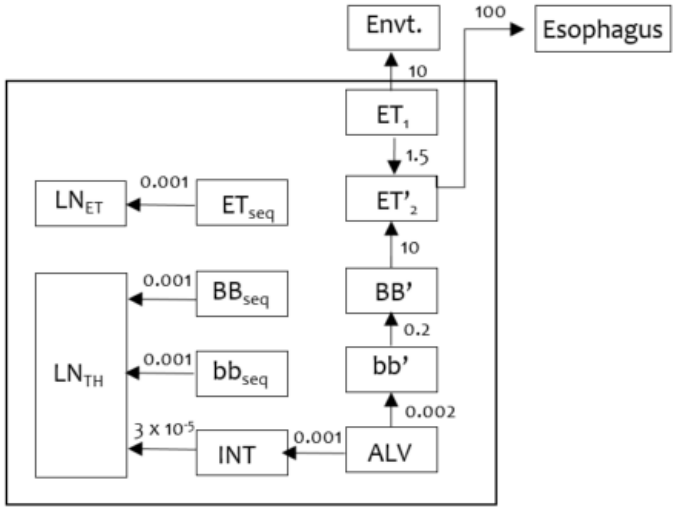
Need for binding

- USTUR Case 0269:
  - ~1% of intake retained in the lungs several years after intake[15]
  - 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.



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

Issues with chemical binding

- Estimated bound fraction found to be dependent on solubility

Table 5. Some published values of bound fraction

Study	Nitrates	Mixtures	Oxides
Puncher et al. (2017)[16]	0.14%		4.7%
Khokhryakov et al. (2005)[17]	3%	3-7%	15-19%
USTUR Regional retention study [2, 18, 19]	0.40%	1-4%	Cannot be described

[16]Puncher et al. Radiat. Prot. Dosim. 176(1-2), 62-70; 2017
[17]Khokhryakov et al. Health Phys. 88(2), 125-132; 2005
[18]Poudel et al. Health Phys. 120(3), 258-270; 2021
[19]Poudel et al. J. Radiat. Prot. 41(4), 940-961; 2021

Issues with chemical binding

- Autoradiography for USTUR Case 0269 showed alpha star aggregates localized within connective tissue[10,11]: inconsistent with presence of bound state

- Data for USTUR Case 0407 cannot be 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

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

Other arguments for physical 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[21]
    - Study of Rocky Flats worker showed individuals with lung doses > 0.5 Gy likely to have abnormal chest x-ray[22]
    - Fibrosis also observed in mice[13], rats[12], dogs[14] and baboons[7]

[21]Azizova et al. Health Phys. 118 185-192; 2020
[22]Newman et al. Radiat. Res. 164 123-131; 2005

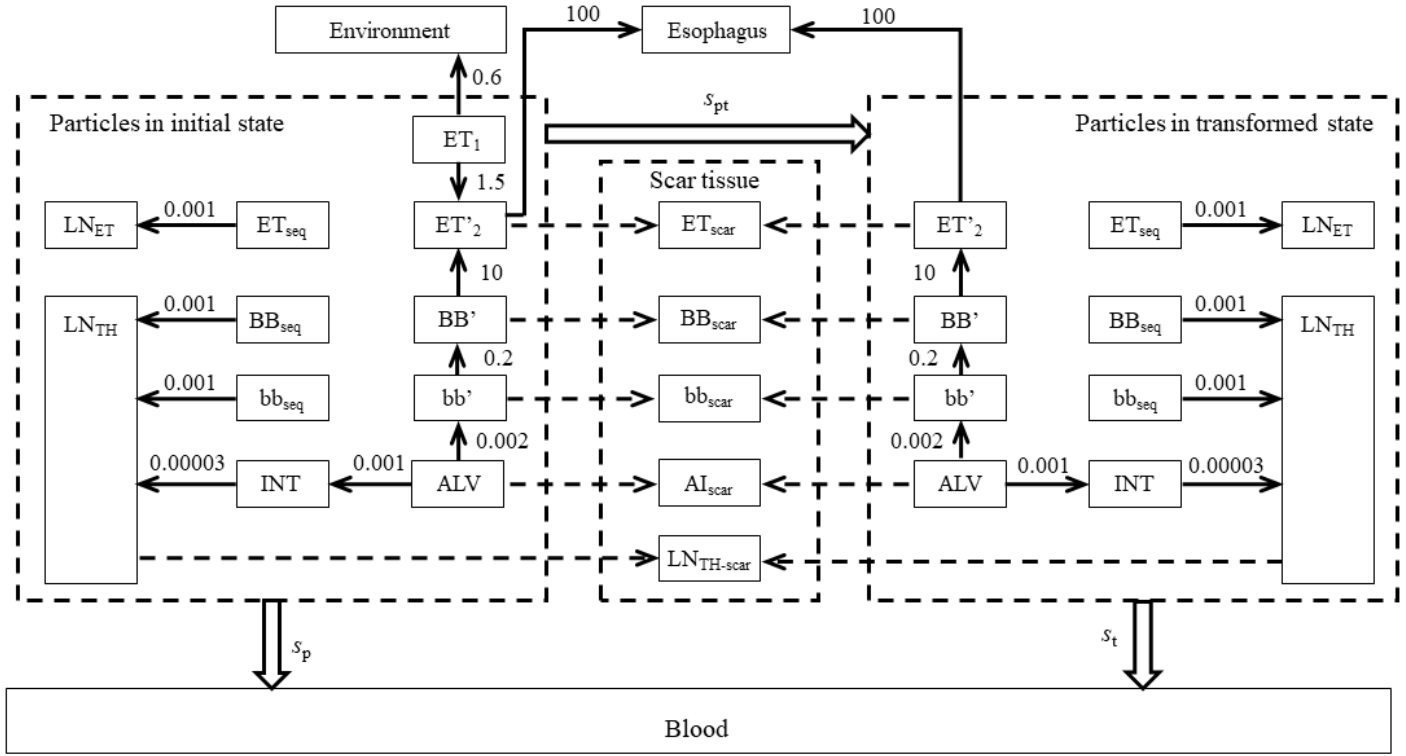
The scar-tissue approach

- 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[8-9, 23]
  - Fibrosis of tissue immobilizes plutonium

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

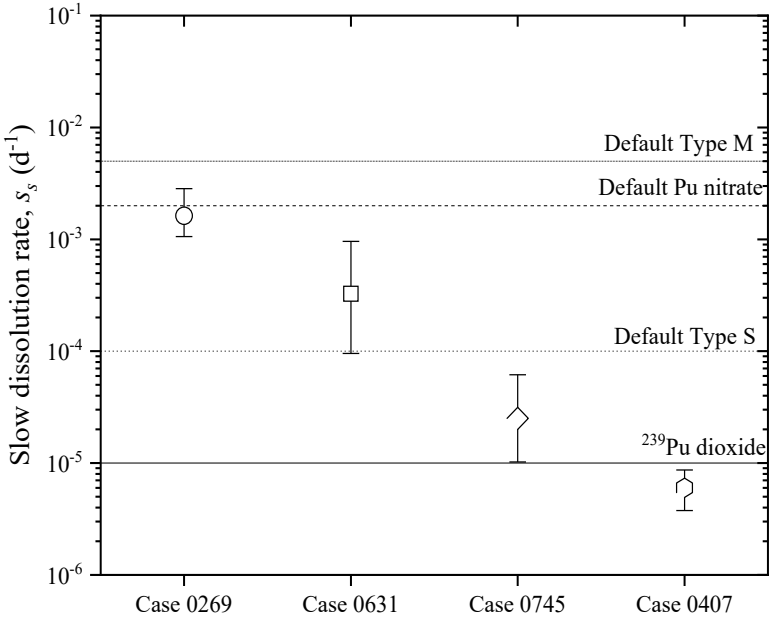
[23]Hahn et al. Radiat. Res. 161(5), 568-581; 2004

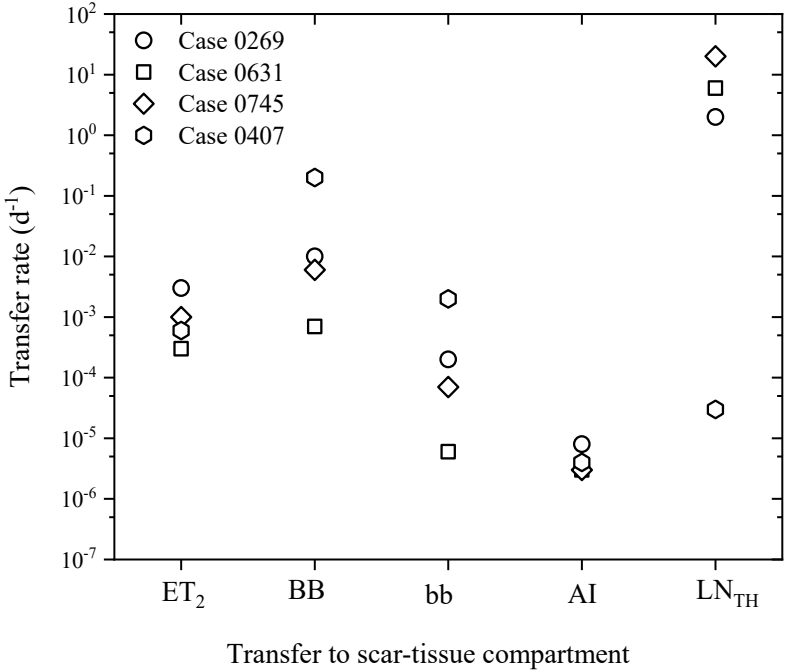
Proposed model



Results and discussion

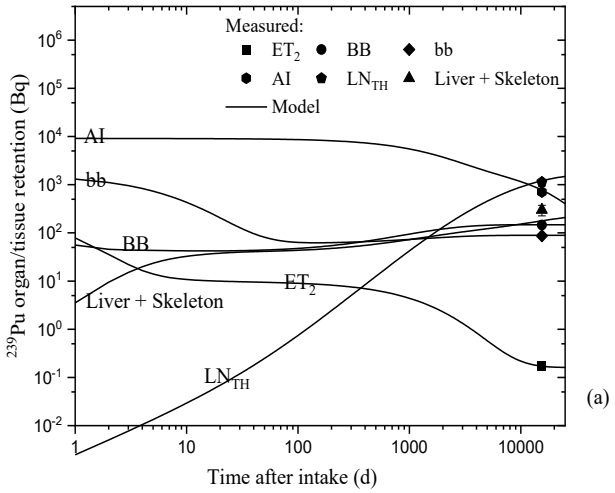
- Priors from several previous studies
- Posterior distributions obtained from Markov-chain Monte Carlo analysis



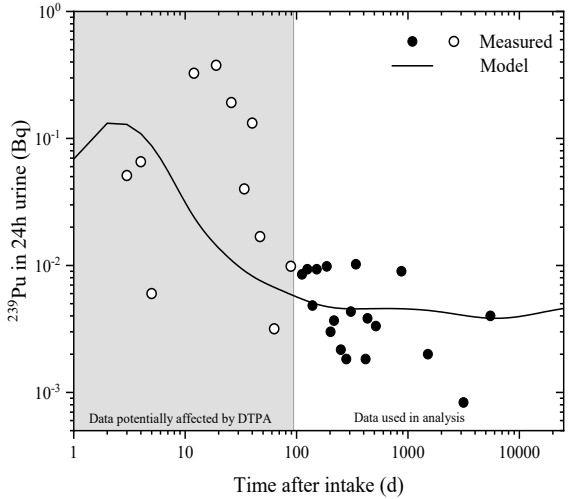


Results and discussion

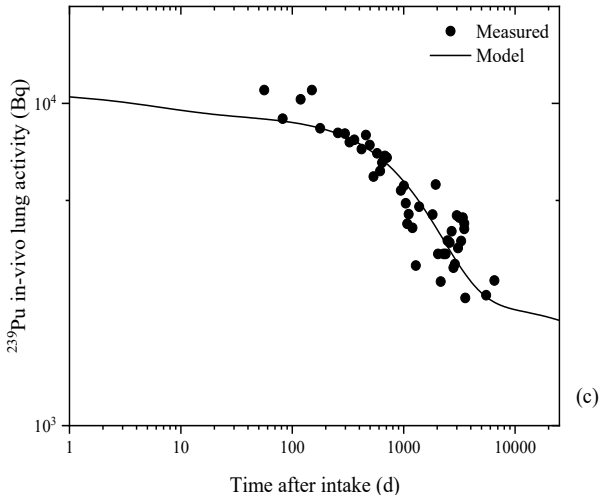
- Case 0407 as an example:



(a)



(b)

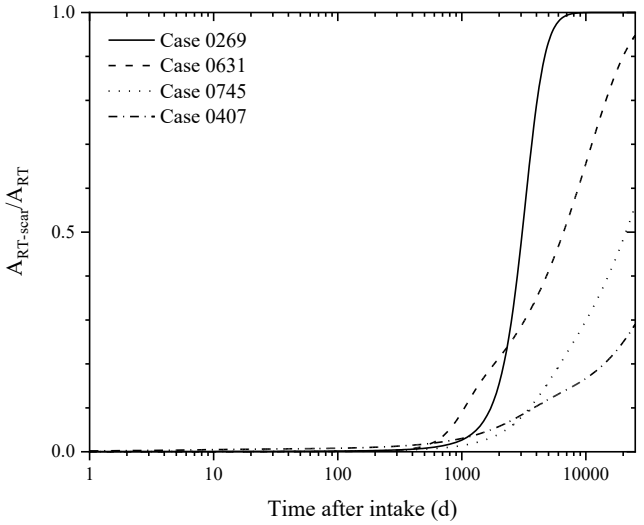


(c)

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

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

- Other mechanisms can also be responsible
  - combination of physical and chemical binding
  - systemic uptake of plutonium by the lungs

Questions?

dpoudel@lanl.gov