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BIOKINETICS OF HIGHLY ENRICHED URANIUM IN A FEMALE NUCLEAR WORKER

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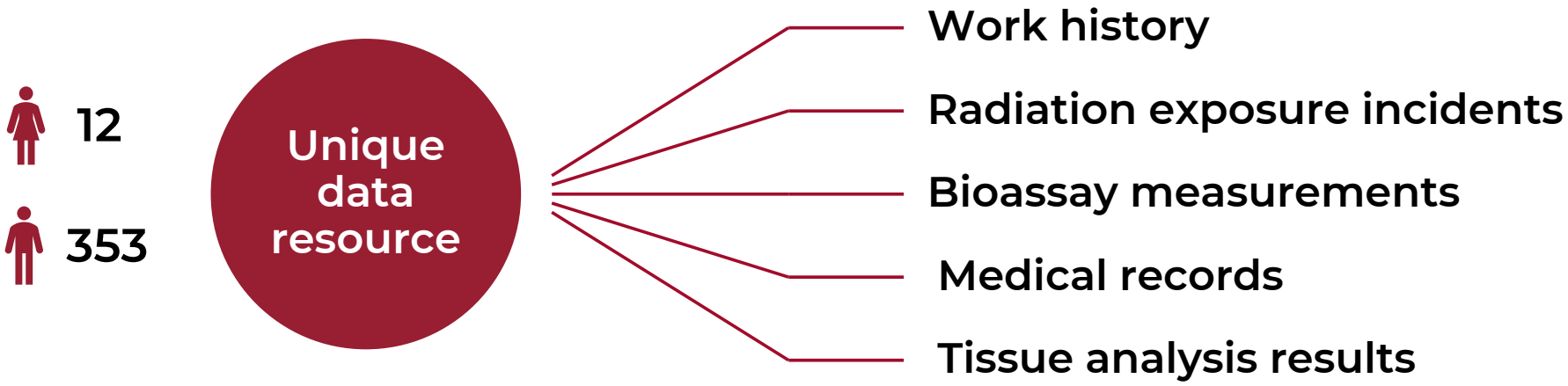
U. S. Transuranium and Uranium Registries

- Established by U.S. Atomic Energy Commission in 1968
- Since 1992, operated by Washington State University as a research grant funded by U.S. Department of Energy
- Follows up occupationally-exposed individuals (volunteer Registrants) by studying the biokinetics and tissue dosimetry of uranium and transuranium elements, such as plutonium, americium, curium, and neptunium
- Tissue donors (posthumous): whole-(48) and/or partial-body (317) donations

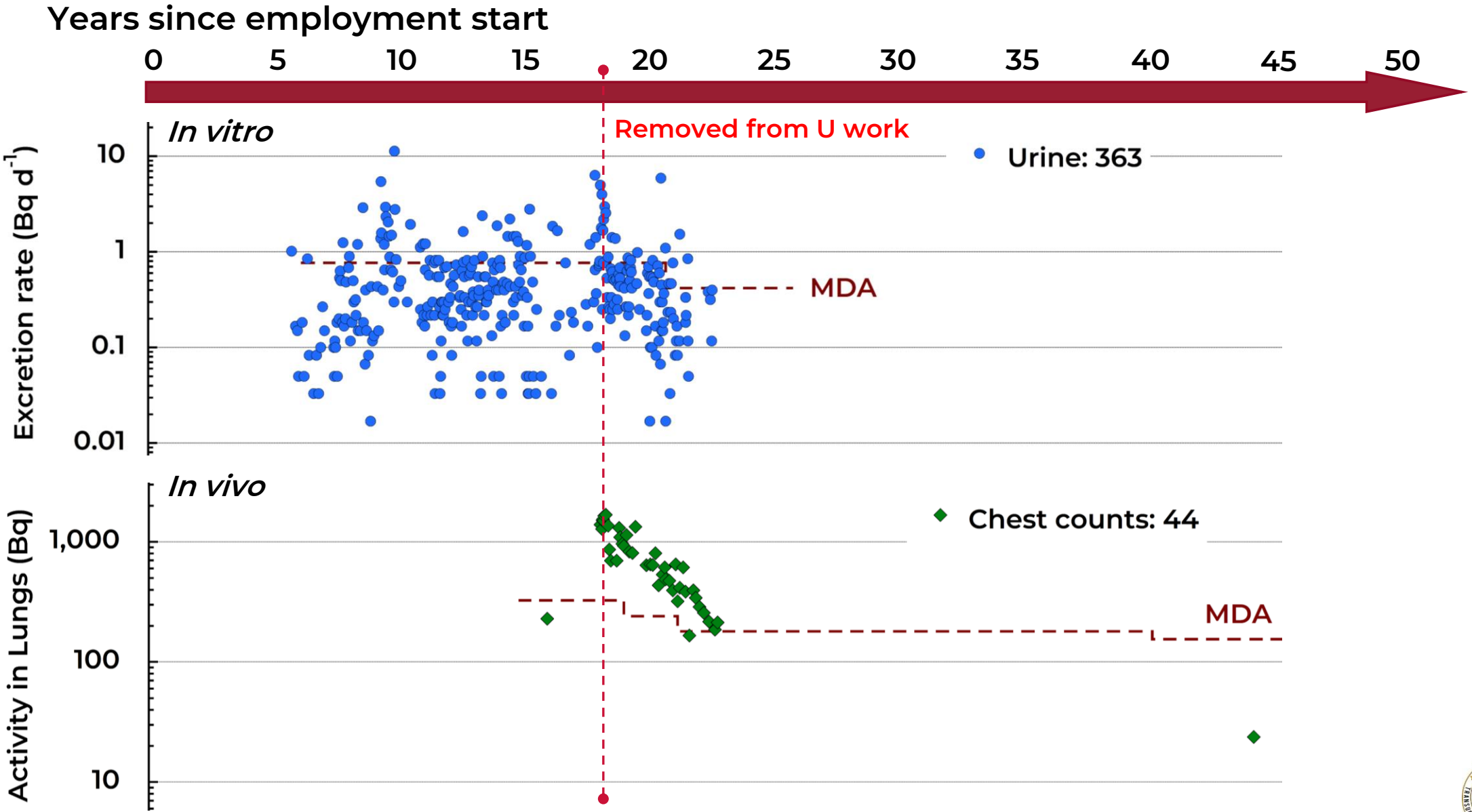


USTUR Case 1028: Summary

- Female whole-body tissue donor
- Involved in enriched uranium processing operations for 17 years
  - ✓ ^{235}U: from 20% to > 93%
- Handled large quantities of uranium material
- High potential of chronic inhalation
- No acute inhalation incidents documented
- 25-year bioassay monitoring
- Heavy smoker for 38 years: 2+ packs per day
- Died at age 86 from acute myocardial infarction

https://www.atomicheritage.org/history/women-and-bomb

Bioassay Follow-up



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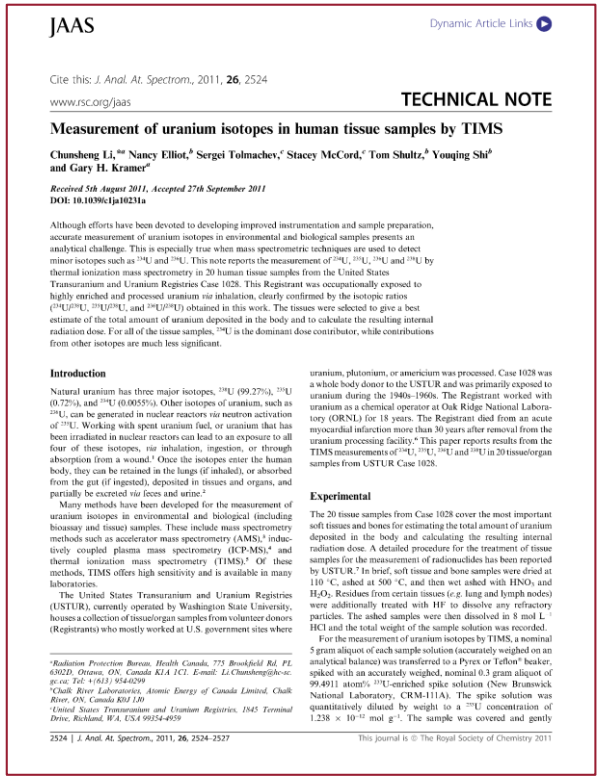
Tissue Radiochemical Analysis

- 129 samples from right side of body: 45 soft tissue and 84 bone samples
- ^{234}U, ^{235}U, and ^{238}U measured using alpha spectrometry
- 20 samples analyzed by mass spectrometry for ^{236}U and isotopic ratios



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www.rsc.org/jaas **TECHNICAL NOTE**

Measurement of uranium isotopes in human tissue samples by TIMS

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Although efforts have been devoted to developing improved instrumentation and sample preparation, accurate measurement of uranium isotopes in environmental and biological samples presents an analytical challenge. This is especially true when mass spectrometric techniques are used to detect minor isotopes such as ^{234}U and ^{236}U. This note reports the measurement of ^{236}U, ^{235}U, ^{236}U and ^{238}U by thermal ionization mass spectrometry in 20 human tissue samples from the United States Transuranium and Uranium Registries Case 1028. This Registrant was occupationally exposed to highly enriched and processed uranium *via* inhalation, clearly confirmed by the isotopic ratios ($^{234}U/^{238}U$, $^{235}U/^{238}U$, and $^{236}U/^{238}U$) obtained in this work. The tissues were selected to give a best estimate of the total amount of uranium deposited in the body and to calculate the resulting internal radiation dose. For all of the tissue samples, ^{234}U is the dominant dose contributor, while contributions from other isotopes are much less significant.

Introduction

Natural uranium has three major isotopes, ^{238}U (99.27%), ^{235}U (0.72%), and ^{234}U (0.0055%). Other isotopes of uranium, such as ^{236}U, can be generated in nuclear reactors *via* neutron activation of ^{235}U. Working with spent uranium fuel, or uranium that has been irradiated in nuclear reactors can lead to an exposure to all four of these isotopes, *via* inhalation, ingestion, or through absorption from a wound.[1] Once the isotopes enter the human body, they can be retained in the lungs (if inhaled), or absorbed from the gut (if ingested), deposited in tissues and organs, and partially be excreted *via* feces and urine.[2]

Many methods have been developed for the measurement of uranium isotopes in environmental and biological (including bioassay and tissue) samples. These include mass spectrometry methods such as accelerator mass spectrometry (AMS),[3] inductively coupled plasma mass spectrometry (ICP-MS),[4] and thermal ionization mass spectrometry (TIMS).[5] Of these methods, TIMS offers high sensitivity and is available in many laboratories.

The United States Transuranium and Uranium Registries (USTUR), currently operated by Washington State University, houses a collection of tissue/organ samples from volunteer donors (Registrants) who mostly worked at U.S. government sites where uranium, plutonium, or americium was processed. Case 1028 was a whole body donor to the USTUR and was primarily exposed to uranium during the 1940s–1960s. The Registrant worked with uranium as a chemical operator at Oak Ridge National Laboratory (ORNL) for 18 years. The Registrant died from an acute myocardial infarction more than 30 years after removal from the uranium processing facility.[6] This paper reports results from the TIMS measurements of ^{234}U, ^{235}U, ^{236}U and ^{238}U in 20 tissue/organ samples from USTUR Case 1028.

Experimental

The 20 tissue samples from Case 1028 cover the most important soft tissues and bones for estimating the total amount of uranium deposited in the body and calculating the resulting internal radiation dose. A detailed procedure for the treatment of tissue samples for the measurement of radionuclides has been reported by USTUR.[7] In brief, soft tissue and bone samples were dried at 110 °C, ashed at 500 °C, and then wet ashed with HNO_3 and H_2O_2. Residues from certain tissues (*e.g.* lung and lymph nodes) were additionally treated with HF to dissolve any refractory particles. The ashed samples were then dissolved in 8 mol L^{-1} HCl and the total weight of the sample solution was recorded.

For the measurement of uranium isotopes by TIMS, a nominal 5 gram aliquot of each sample solution (accurately weighed on an analytical balance) was transferred to a Pyrex or Teflon® beaker, spiked with an accurately weighed, nominal 0.3 gram aliquot of 99.4911 atom% ^{233}U-enriched spike solution (New Brunswick National Laboratory, CRM-111A). The spike solution was quantitatively diluted by weight to a ^{233}U concentration of 1.238×10^{-12} mol g^{-1}. The sample was covered and gently

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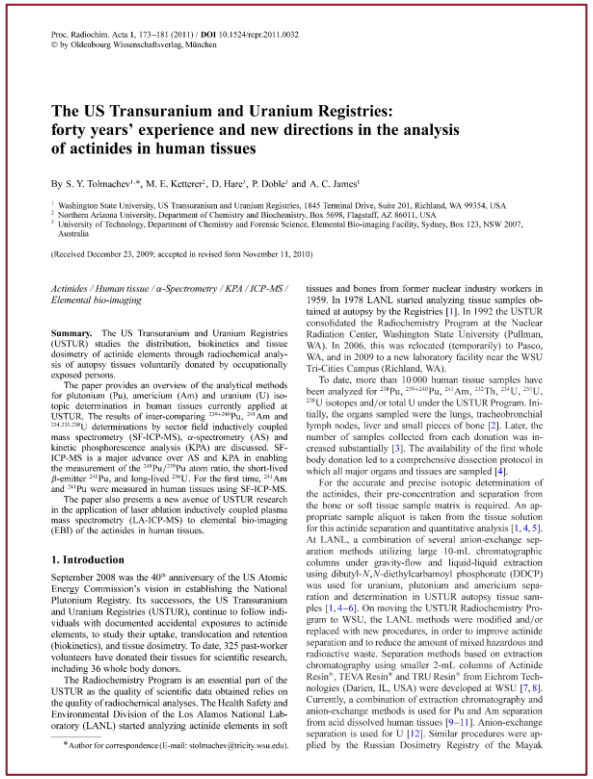

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The US Transuranium and Uranium Registries: forty years' experience and new directions in the analysis of actinides in human tissues

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Actinides / Human tissue / α-Spectrometry / KPA / ICP-MS / Elemental bio-imaging

Summary. The US Transuranium and Uranium Registries (USTUR) studies the distribution, biokinetics and tissue dosimetry of actinide elements through radiochemical analysis of autopsy tissues voluntarily donated by occupationally exposed persons.

The paper provides an overview of the analytical methods for plutonium (Pu), americium (Am) and uranium (U) isotopic determination in human tissues currently applied at USTUR. The results of inter-comparing $^{239+240}Pu$, ^{241}Am and $^{234,235,238}U$ determinations by sector field inductively coupled mass spectrometry (SF-ICP-MS), α-spectrometry (AS) and kinetic phosphorescence analysis (KPA) are discussed. SF-ICP-MS is a major advance over AS and KPA in enabling the measurement of the $^{240}Pu/^{239}Pu$ atom ratio, the short-lived β-emitter ^{241}Pu, and long-lived ^{236}U. For the first time, ^{241}Am and ^{241}Pu were measured in human tissues using SF-ICP-MS.

The paper also presents a new avenue of USTUR research in the application of laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) to elemental bio-imaging (EBI) of the actinides in human tissues.

1. Introduction

September 2008 was the 40th anniversary of the US Atomic Energy Commission's vision in establishing the National Plutonium Registry. Its successors, the US Transuranium and Uranium Registries (USTUR), continue to follow individuals with documented accidental exposures to actinide elements, to study their uptake, translocation and retention (biokinetics), and tissue dosimetry. To date, 325 past-worker volunteers have donated their tissues for scientific research, including 36 whole body donors.

The Radiochemistry Program is an essential part of the USTUR as the quality of scientific data obtained relies on the quality of radiochemical analyses. The Health Safety and Environmental Division of the Los Alamos National Laboratory (LANL) started analyzing actinide elements in soft tissues and bones from former nuclear industry workers in 1959. In 1978 LANL started analyzing tissue samples obtained at autopsy by the Registries [1]. In 1992 the USTUR consolidated the Radiochemistry Program at the Nuclear Radiation Center, Washington State University (Pullman, WA). In 2006, this was relocated (temporarily) to Pasco, WA, and in 2009 to a new laboratory facility near the WSU Tri-Cities Campus (Richland, WA).

To date, more than 10 000 human tissue samples have been analyzed for ^{238}Pu, $^{239+240}Pu$, ^{241}Am, ^{232}Th, ^{234}U, ^{235}U, ^{238}U isotopes and/or total U under the USTUR Program. Initially, the organs sampled were the lungs, tracheobronchial lymph nodes, liver and small pieces of bone [2]. Later, the number of samples collected from each donation was increased substantially [3]. The availability of the first whole body donation led to a comprehensive dissection protocol in which all major organs and tissues are sampled [4].

For the accurate and precise isotopic determination of the actinides, their pre-concentration and separation from the bone or soft tissue sample matrix is required. An appropriate sample aliquot is taken from the tissue solution for this actinide separation and quantitative analysis [1, 4, 5]. At LANL, a combination of several anion-exchange separation methods utilizing large 10-mL chromatographic columns under gravity-flow and liquid-liquid extraction using dibutyl-*N*,*N*-diethylcarbamoyl phosphonate (DDCP) was used for uranium, plutonium and americium separation and determination in USTUR autopsy tissue samples [1, 4–6]. On moving the USTUR Radiochemistry Program to WSU, the LANL methods were modified and/or replaced with new procedures, in order to improve actinide separation and to reduce the amount of mixed hazardous and radioactive waste. Separation methods based on extraction chromatography using smaller 2-mL columns of Actinide Resin®, TEVA Resin® and TRU Resin® from Eichrom Technologies (Darien, IL, USA) were developed at WSU [7, 8]. Currently, a combination of extraction chromatography and anion-exchange methods is used for Pu and Am separation from acid dissolved human tissues [9–11]. Anion-exchange separation is used for U [12]. Similar procedures were applied by the Russian Dosimetry Registry of the Mayak

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Measurement of ^{236}U in human tissue samples using solid phase extraction coupled to ICP-MS

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^{236}U is present at ultra-trace levels in typical environmental and biological samples. Typically, it has been measured by highly sensitive techniques, such as accelerator mass spectrometry. This paper reports the measurement of ^{236}U in 20 human tissue samples using a sector field ICP-MS following automated SPE separation. The tissue samples were selected from one USTUR case, representing tissues/organs that are important for internal radiation assessment. Another uranium isotope, ^{235}U, was also measured in the samples. The results for ^{235}U were compared with those obtained by alpha spectrometry. For most cases, results from the two methods were comparable, indicating that the measurement of ^{236}U in the samples is reliable.

Introduction

Uranium-236 (^{236}U) is one isotope of uranium. Its natural abundance is extremely low (10^{-14} atom %)[1] so it is not usually considered an isotope of natural uranium. However, ^{236}U can be generated in nuclear reactors through neutron activation of ^{235}U. Working with spent fuel or uranium irradiated in nuclear reactors can lead to occupational exposure to ^{236}U *via* inhalation, ingestion, or wounding.[2] Once it enters the human body, it can be dissolved in the lungs (if inhaled), or cross the gut wall (if ingested), be deposited in tissues and organs, and excreted *via* faeces and urine.[3]

^{236}U is an alpha emitter (4.5 MeV, 74%). In theory, it could be measured by alpha spectrometry; however, its concentration in typical environmental or biological samples is below the detection limit of alpha spectrometry.[4] As its half-life is relatively long ($T_{1/2} = 2.34 \times 10^7$ years), ^{236}U in environmental or human samples can also be measured by atom counting techniques such as accelerator mass spectrometry (AMS).[4–6] AMS provides great sensitivity for the measurement of ^{236}U, but it requires a lengthy procedure for sample preparation. In addition, there are only a small number of AMS laboratories around the world.

Inductively coupled plasma mass spectrometry (ICP-MS), a versatile technology in trace analysis, has been applied widely in health, environmental, and material sciences in the past decades. More recently, it has been used for the measurement of long-lived radionuclides.[7] It requires minimal sample preparation, provides high sample throughput and good sensitivity. In addition, it can be coupled to sample preparation and introduction systems so the measurement process can be fully automated. We previously developed an automated system based on solid phase extraction (SPE) and sector field ICP-MS for the measurement of actinides in environmental and human samples, which has been successfully applied for the measurement of ^{239}Pu in air, urine and faecal samples.[8–10] In this paper, we report on the measurement of ^{236}U in human tissue samples using the automated SPE-ICP-MS system developed in our laboratory. ^{235}U in these samples was also measured at the same time and compared with results previously obtained by alpha spectrometry at the United States Transuranium and Uranium Registries (USTUR).

Experimental

The tissue samples and sample preparation

The 20 tissue samples, all from one case (Case 1028), were provided by the USTUR. The donor was a nuclear worker with known history of exposure to highly enriched uranium (HEU). The 20 tissue samples cover the most important soft tissues and bones used for internal radiation dose assessment. A detailed procedure for the treatment of tissue samples for the measurement of radionuclides has been reported by USTUR.[11] In brief, soft tissue and bone samples were dried at 110 °C, ashed at 450 °C, and then wet ashed with HNO_3 and H_2O_2. Residues from certain tissues (*e.g.* lung and lymph nodes) were additionally treated with HF to dissolve any refractory particles. The ashed samples were then dissolved in 8 mol L^{-1} HCl (specific density of 1.12 g mL^{-1}) and the total weight of the sample solution recorded. For the measurement of ^{234}U and ^{238}U by SPE-ICP-MS in this paper, 10 to 15 mL of the sample solution was used from each digested tissue sample.

Each sample solution was first evaporated to near dryness in a Teflon® vial (Savillex, Minnetonka, MN, USA), and then was converted into 20 mL 3 mol L^{-1} HNO_3 (Optima grade, Fisher Scientific, Ottawa, ON, Canada). During this conversion step, a ^{233}U tracer (Eckert & Ziegler Isotope Products, Valencia, CA, USA) was added to the sample as an internal standard to a concentration of about 1 pg mL^{-1} in the converted sample solution. The exact amount of ^{233}U added to each sample was

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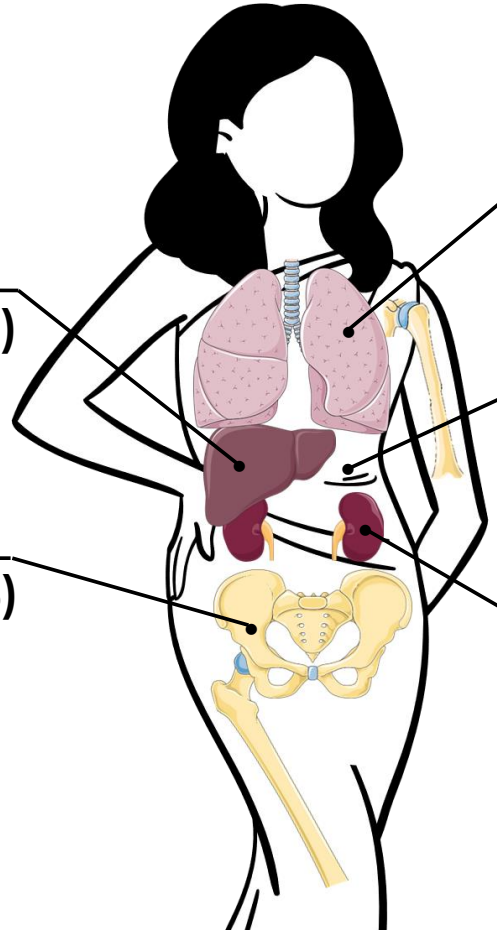
Uranium Distribution in the Body

- Estimated total $^{234,235,238}U$ activity in whole body: 48.0 ± 0.8 Bq



Respiratory tract
28.4 ± 0.8 Bq (59.2%)

Liver
0.059 ± 0.005 Bq (0.12%)

Other soft tissues
1.59 ± 0.03 Bq (3.3%)

Skeleton
17.7 ± 0.2 Bq (36.8%)

Kidneys
0.28 ± 0.01 Bq (0.58%)

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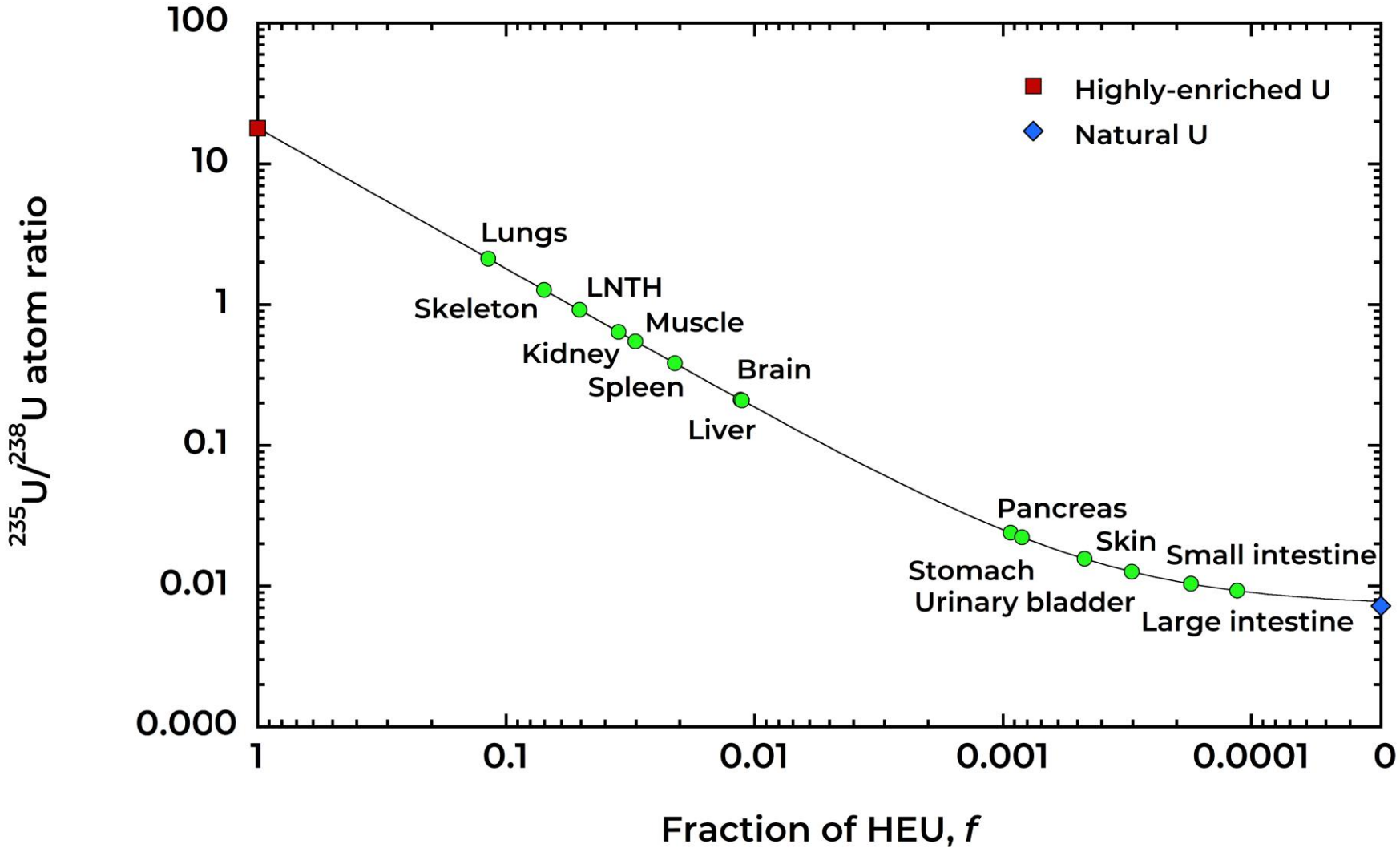
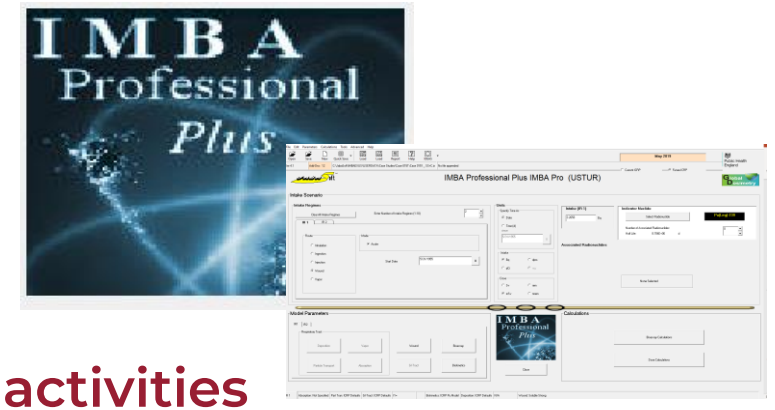
Material Composition Retained in Tissues

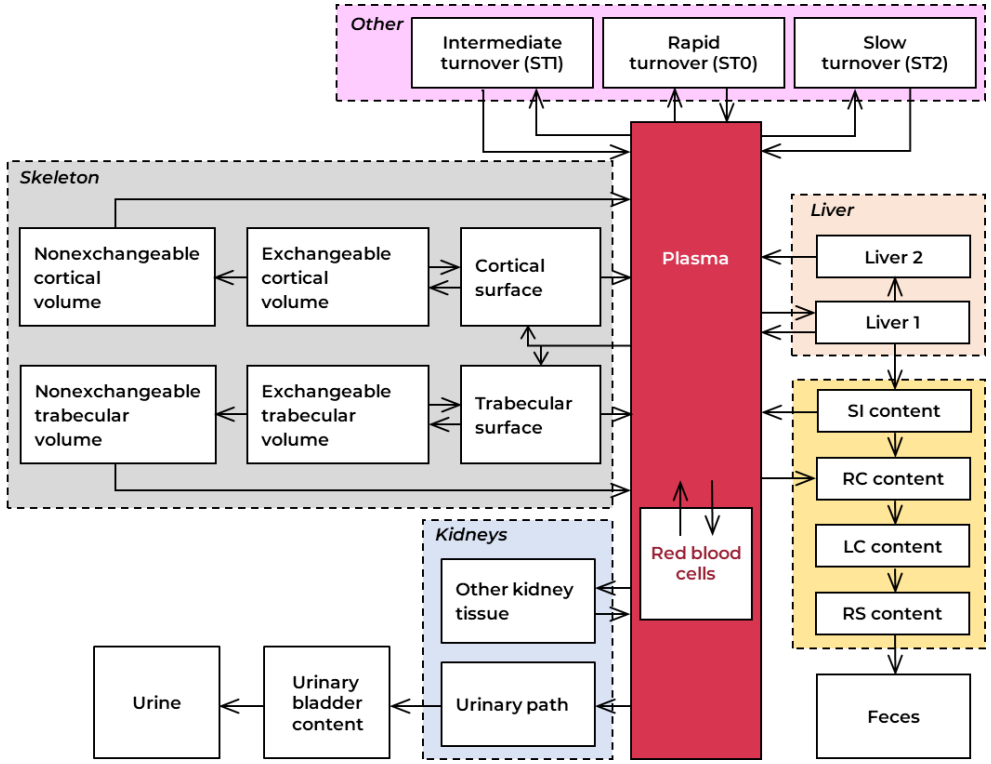


Biokinetic Modeling

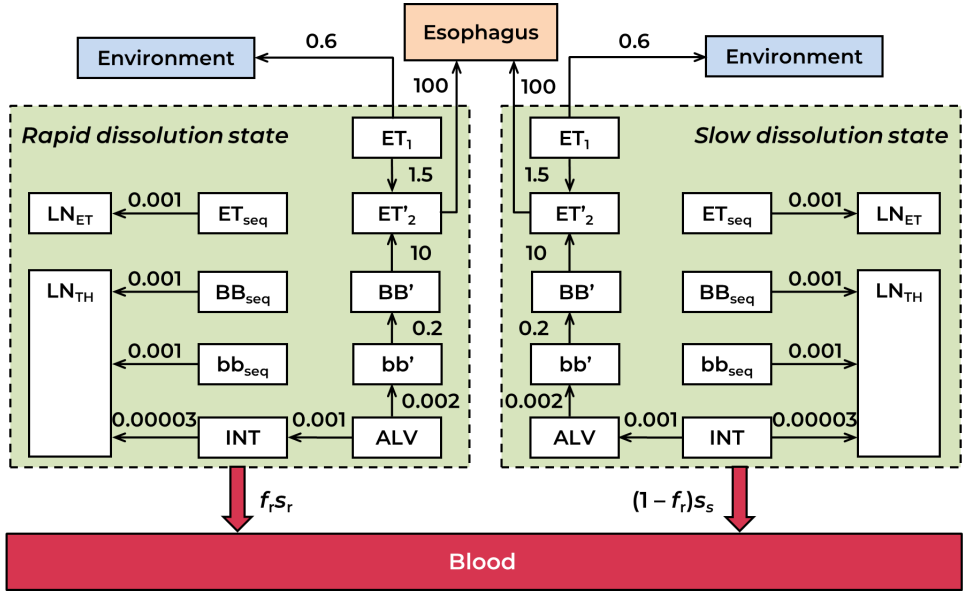


- IMBA Professional Plus: USTUR research version
- Bioassay used: urine, chest counts, post-mortem activities in lungs, liver, kidneys, skeleton

ICRP 137 uranium systemic model



ICRP 130 human respiratory tract model



‘Best Fit’ Intake Scenario

- Chronic inhalation, type M
- Two acute inhalations:
  - I. Year 9, type M
  - II. Year 17, mixture of materials

    86%: Case-specific, ‘Adjusted M/S’

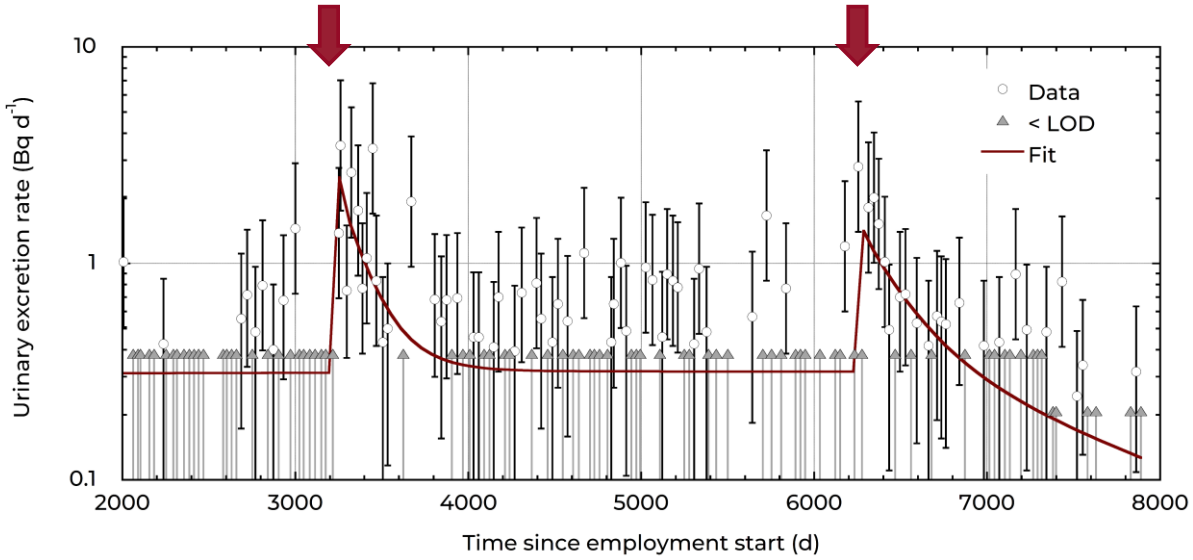
    solubility between M and M/S

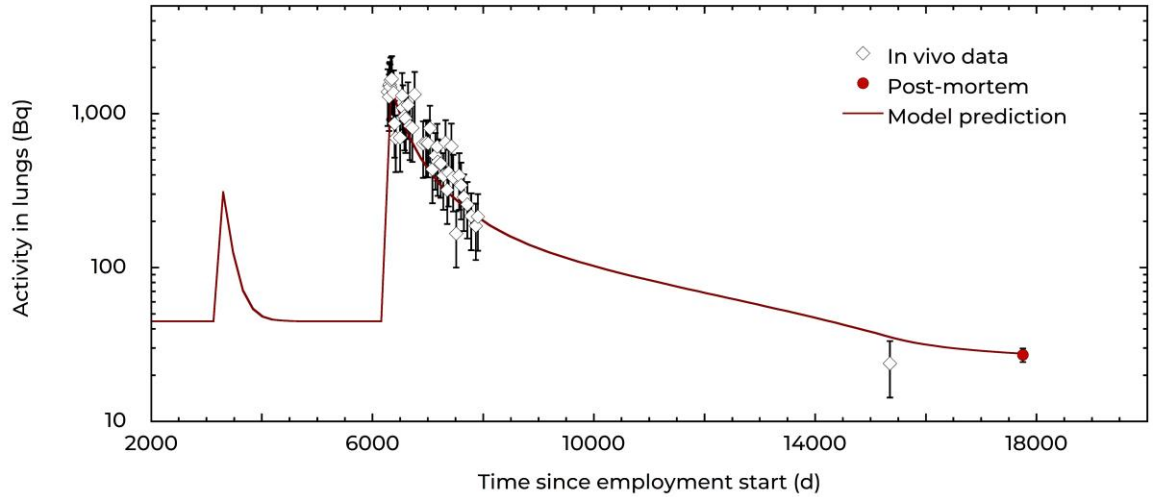
    14%: type S
- Possible U compounds involved:

  Type M: UF_4

  Type M/S: U_3O_8

  Type S: ?



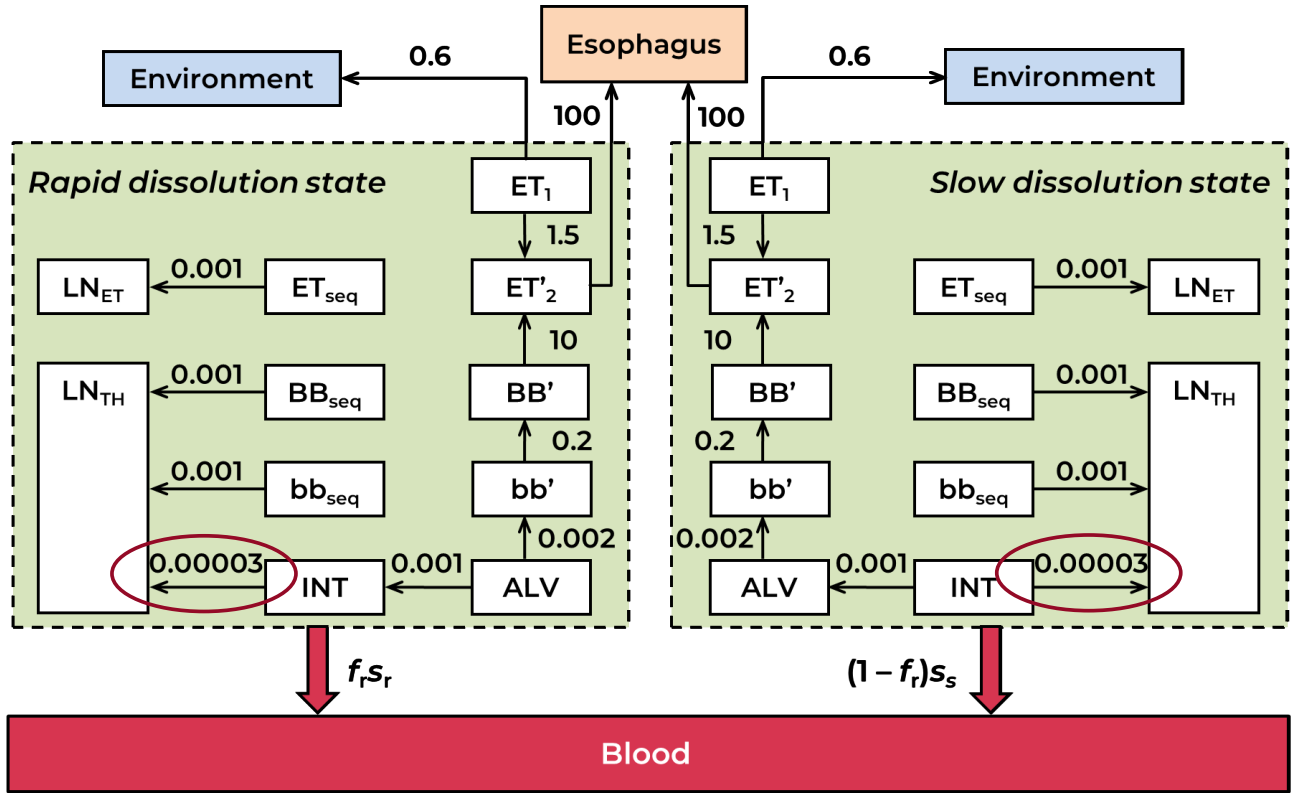


‘High-fired’ UO_2 and/or Scar-tissue encapsulation

Model Parameter Adjustment: *HRTM*

Effect of smoking

- Default *Int* → LN_{TH} transfer rate overestimated post-mortem activity by factor of 9
- Rate adjusted to fit the measurement: $3\times10^{-5} \rightarrow 2.3\times10^{-6}$

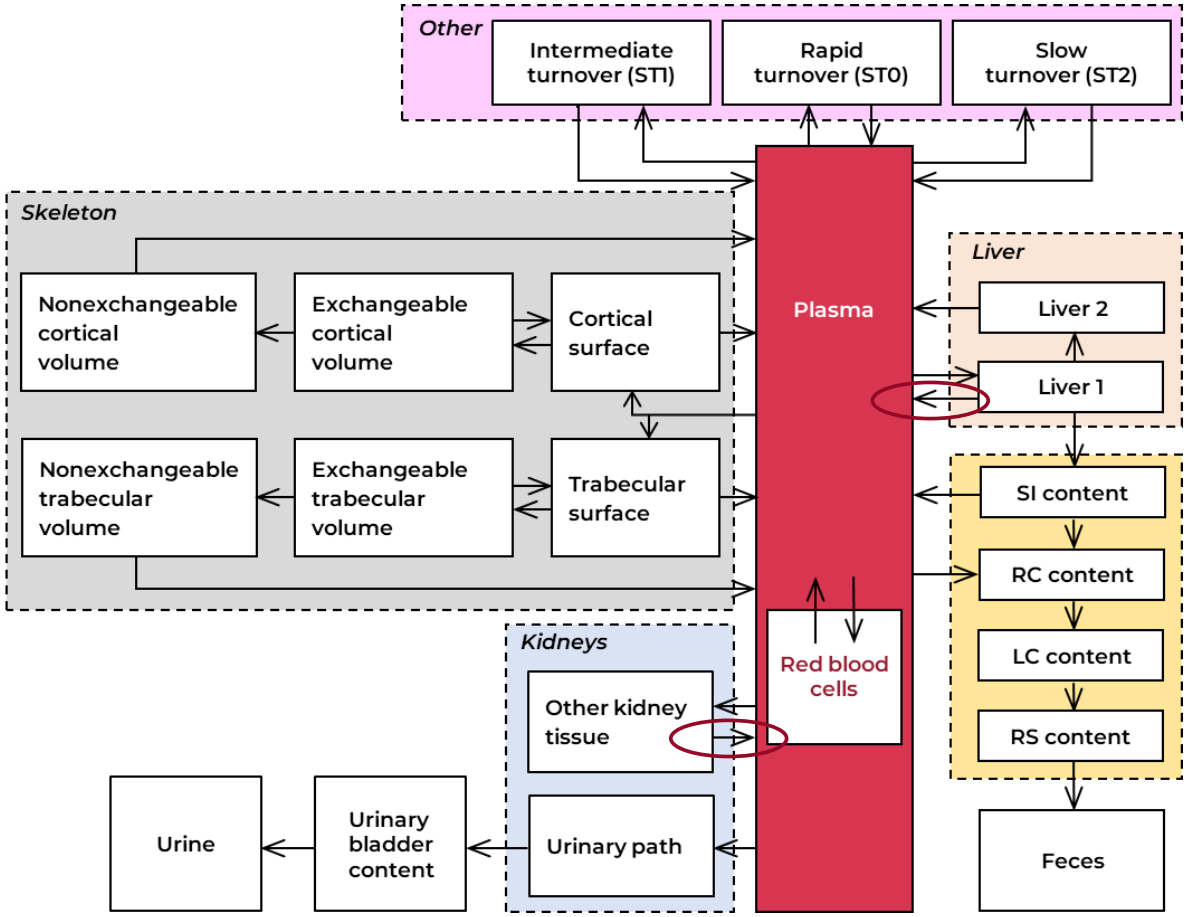


Model Parameter Adjustment: *Systemic*

Default U systemic model mostly based on data from males and may not reflect female physiology

- **Predicted post-mortem activity in skeleton**
- **Overestimated activity in liver by factor of 7**
- **Underestimated activity in kidneys by factor of 6**

Transfer rates adjusted to fit data



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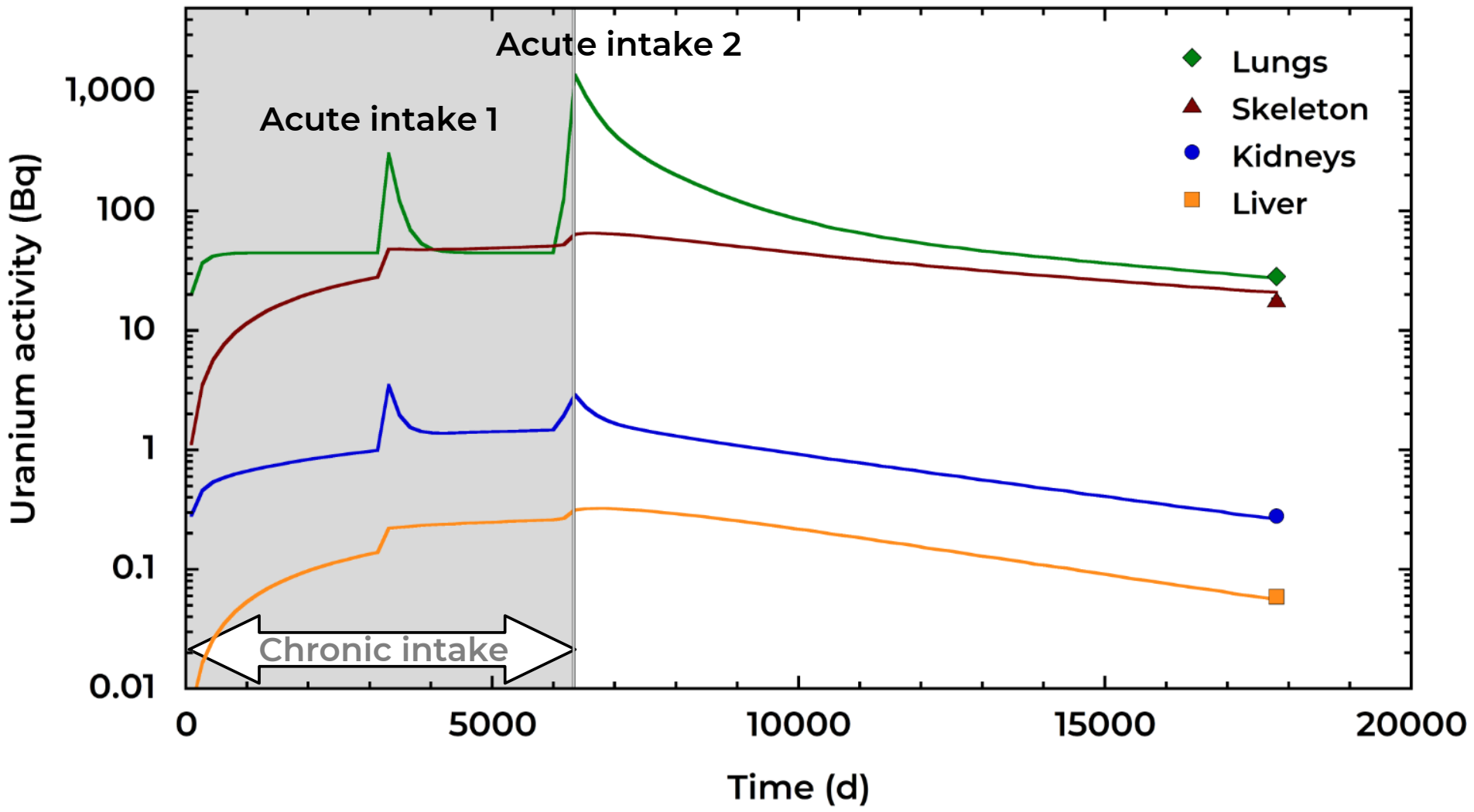
‘Best fit’ Long-term Retention in Tissues



Intake and Dose Estimates

Inhalation	Time (d)		Material	Intake		CED (mSv)*
	Start	End		Rate (Bq d^{-1})	Total (kBq)	
Chronic	0	6,319	M	3.4	21.8	43
Acute 1	3,234		M		4.9	10
Acute 2(*i*)	6,238		M/S adjusted		15.0	115
Acute 2(*ii*)	6,238		S		2.5	52
Cumulative	0	6,319			44.1	220

* IMBA estimate using ICRP60/68 dose coefficients

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Conclusions

- First time, distribution of highly-enriched uranium was studied in whole body of female worker
- Long-term retention of inhaled uranium:

respiratory tract (59.2%) > skeleton (36.8%) > all other tissues (4.0%)

- ICRP models adequately describe uranium biokinetics except retention in liver and kidneys
- Manuscripts in preparation

Tolmachev SY, Avtandilashvili M. *Long-term retention and distribution of highly enriched uranium in occupationally exposed female*. Radiation and Environmental Biophysics; 2022

Avtandilashvili M, Tolmachev SY. *Forty-eight-year follow-up of a female worker exposed to highly enriched uranium via chronic and acute inhalation*. Radiation and Environmental Biophysics; 2022

QUESTIONS?

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