



WASHINGTON STATE UNIVERSITY
College of Pharmacy and
Pharmaceutical Sciences



The United States Transuranium and Uranium Registries: 55 Years of Experience in Actinide Research and Radiochemical Analyses

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United States Transuranium and Uranium Registries

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U.S. AEC 1966 Meeting on Plutonium Contamination in Man (Rocky Flats Plant)



“to protect the interests of workers, employees, and the public by ... the acquisition and provision of the latest and most precise information about the effects of the transuranic elements on man.”



National Plutonium Registry: Blue Ribbon Committee (1968)



Standing left to right: Carlos E. Newton, Jr., W. Daggett Norwood, H.D. Bruner, Philip A. Fuqua
Seated left to right: Thomas F. Mancuso, J.H. Sterner, Robley D. Evans, Herbert M. Parker
Not photographed: Clarence C. Lushbaugh, Lloyd M. Joshel



Registrants

Individuals with documented history of exposure to the actinides

- Primary exposure: ^{239}Pu , ^{238}Pu , ^{241}Am , U_{nat} , HEU, DU (^{244}Cm , ^{237}Np , ^{147}Pm)
- Criteria: 4 nCi (10% of the then-Maximum Permissible Body Burden of 40 nCi)
- Mainly former nuclear workers from DOE sites
- Voluntary tissue donors (posthumous)

WANTED

"GANG OF FOUR" NANOCURIES

Anyone who has potential for transuranium deposition $\geq 4\text{nCi}$

Health Physicists

To provide registry information to potential donors

The Registries

- ADMINISTERED BY HANFORD ENVIRONMENTAL HEALTH FOUNDATION
- FUNDED THROUGH U.S. DEPARTMENT OF ENERGY
- VOLUNTARY HUMAN TISSUE PROGRAM
- DOCUMENTED ACTINIDE DEPOSITIONS

Goals

- ESTABLISH NATIONAL DATA BANK
- COMPARE PREMORTEM ESTIMATES WITH TISSUE ANALYSIS
- EVALUATE BIODYNAMIC MODELS
- CORRELATE WITH EXPERIMENTAL DATA
- ASSESS RADIATION PROTECTION STANDARDS

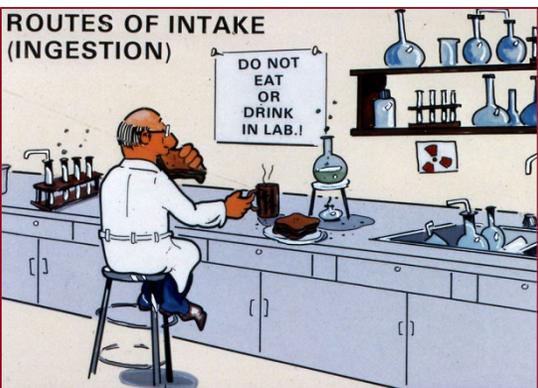
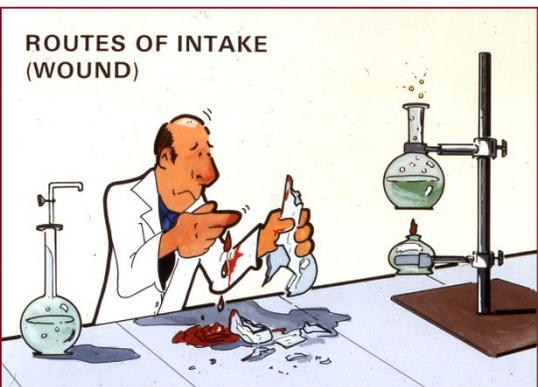
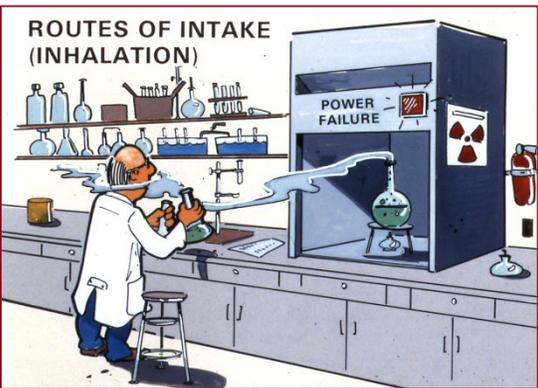
Results

- IMPROVED UNDERSTANDING OF HUMAN ACTINIDE METABOLISM
- ENHANCED OCCUPATIONAL RADIOLOGICAL SAFETY

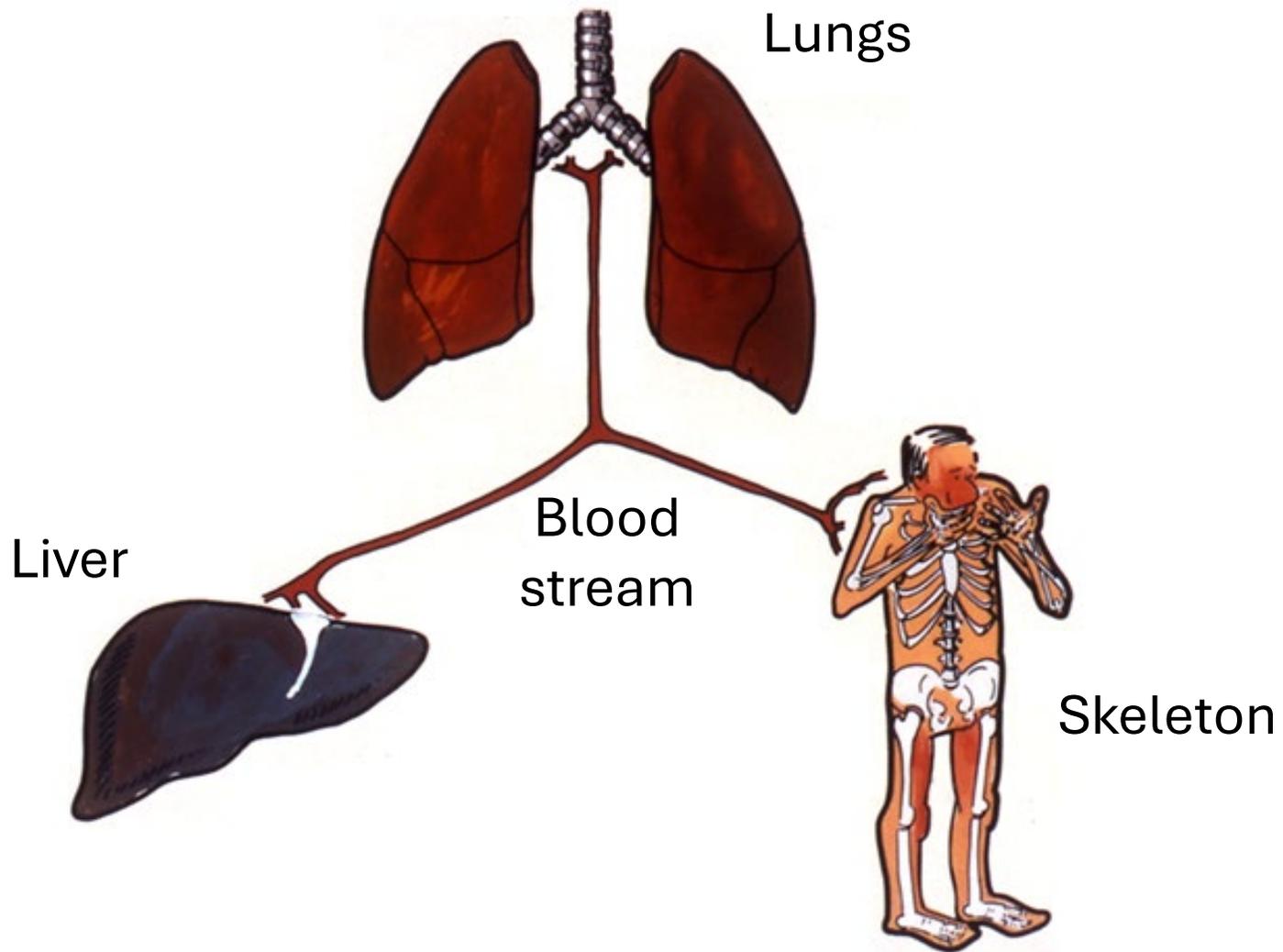
UR
UNITED STATES URANIUM REGISTRY

We're Looking for URANIUM

Likely Sites:
LUNG-BONE-KIDNEY

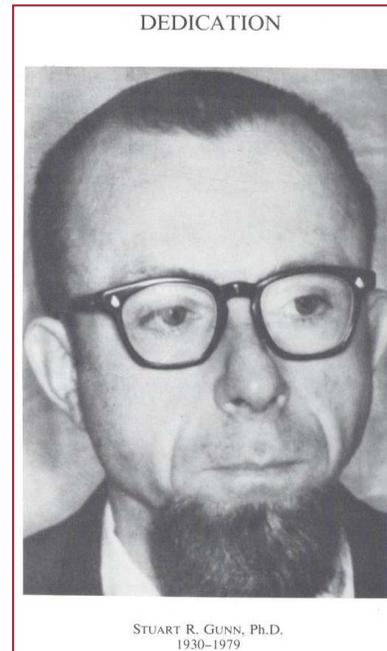
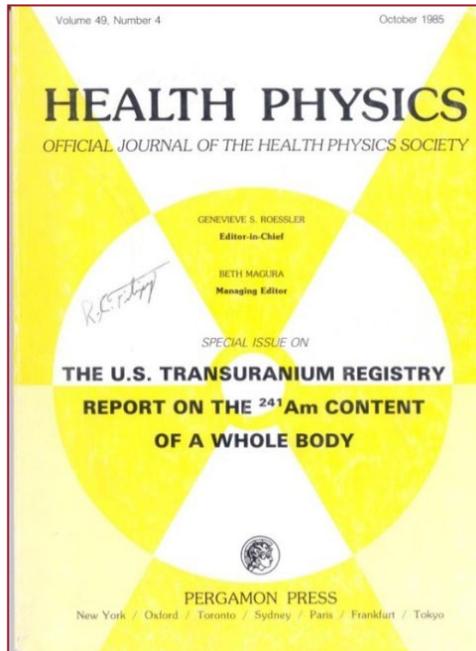


Simplified Pathways for Plutonium



Historical Landmarks (I): First Whole-Body Donation

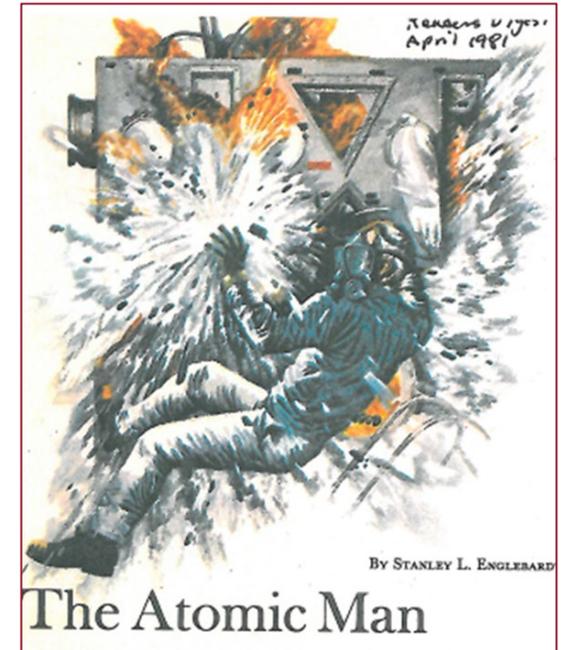
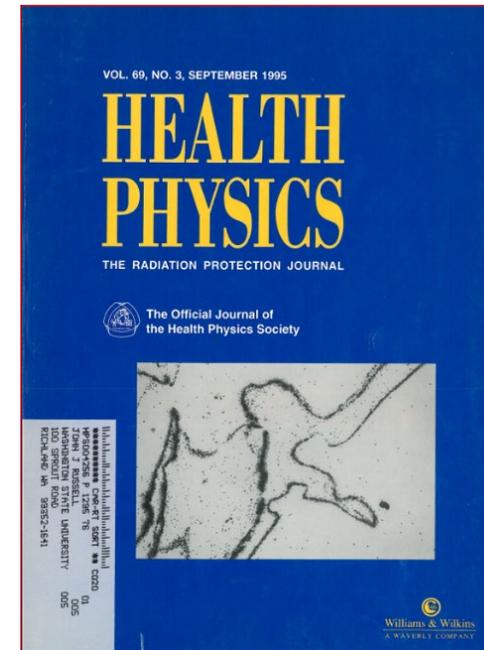
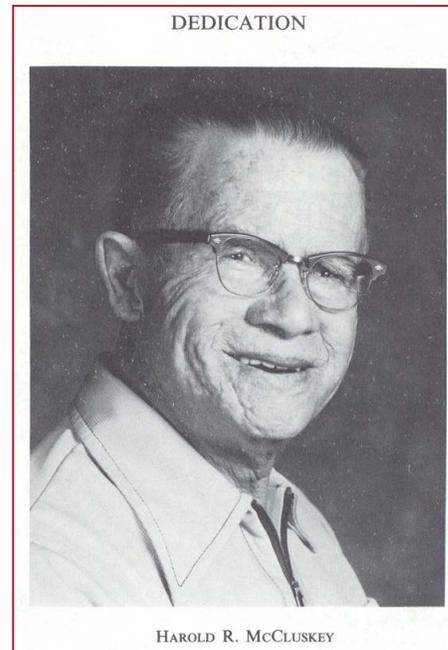
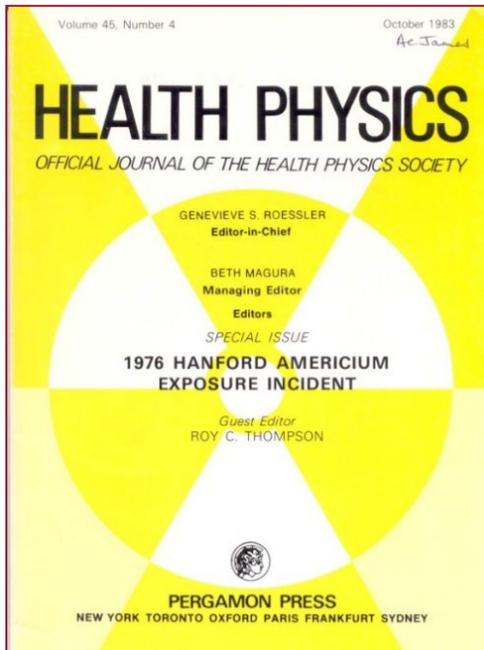
- Worked with unsealed ^{241}Am source for 2 years
- ^{241}Am was detected later in routine urine samples
- Contemporary estimate of intake: 8 – 40 kBq
- Systemic deposition: 82% skeleton, 6.3% liver; 11% other tissues
- *In vivo* calibration phantoms of skull, torso, arm and leg



Historical Landmarks (II): The Atomic Man

Largest recorded Am intake !!!

- Explosion of ion-exchange column with ~ 100 g of ^{241}Am
- Estimated uptake > 40 MBq
- Extensive Ca/Zn-DTPA chelation therapy
- Systemic deposition after treatment – 0.5 MBq



Genealogy of the Registries

REGISTRIES MANAGEMENT

ANALYTICAL SUPPORT

1968 National Plutonium Registry (NPR)
Hanford Environmental Health Foundation

Rocky Flats
Facility

Pacific Northwest
Laboratory

1970 United States Transuranium Registry (USTR)
Hanford Environmental Health Foundation

Los Alamos
Scientific Laboratory

1971

1978 United States Uranium Registry (USUR)
Hanford Environmental Health Foundation

1978

1992 United States Transuranium and Uranium Registries (USTUR)
College of Pharmacy, Washington State University

1993



Mission

- Follow up occupationally-exposed individuals (volunteer Registrants) by studying the biokinetics (deposition, translocation, retention, and excretion) and tissue dosimetry of **uranium** and transuranium elements, such as **plutonium, americium, curium, and neptunium**
- Obtain, **analyze**, preserve, and make **available for future research**, materials from individuals who had documented intakes of uranium and transuranium elements
- Apply USTUR data to refine dose assessment methods in support of reliable epidemiological studies, radiation risk assessment, and regulatory standards for radiological protection of workers and public



USTUR Today

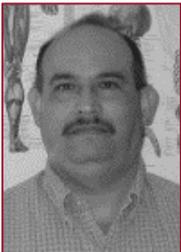
- **Funded:** U.S. Department of Energy, Office of Domestic and International Health Studies (EHSS-13)
- **Managed:** Washington State University, College of Pharmacy and Pharmaceutical Sciences (Award: DE-HS0000073)
- **Operated:** Central DOE IRB #WASU-68-50181



U.S. DEPARTMENT OF
ENERGY



WASHINGTON STATE UNIVERSITY
College of Pharmacy and
Pharmaceutical Sciences



USTUR Facilities: Off WSU Tri-Cities Campus



WASHINGTON STATE UNIVERSITY

**College of Pharmacy and
Pharmaceutical Sciences**



Office



Laboratory



Registrant Statistics

| Primary nuclide | Number |
|-----------------------|--------|
| ²³⁹ Pu | 306 |
| ²³⁸ Pu | 12 |
| ²⁴¹ Am | 5 |
| Uranium (NU, HEU, DU) | 49 |

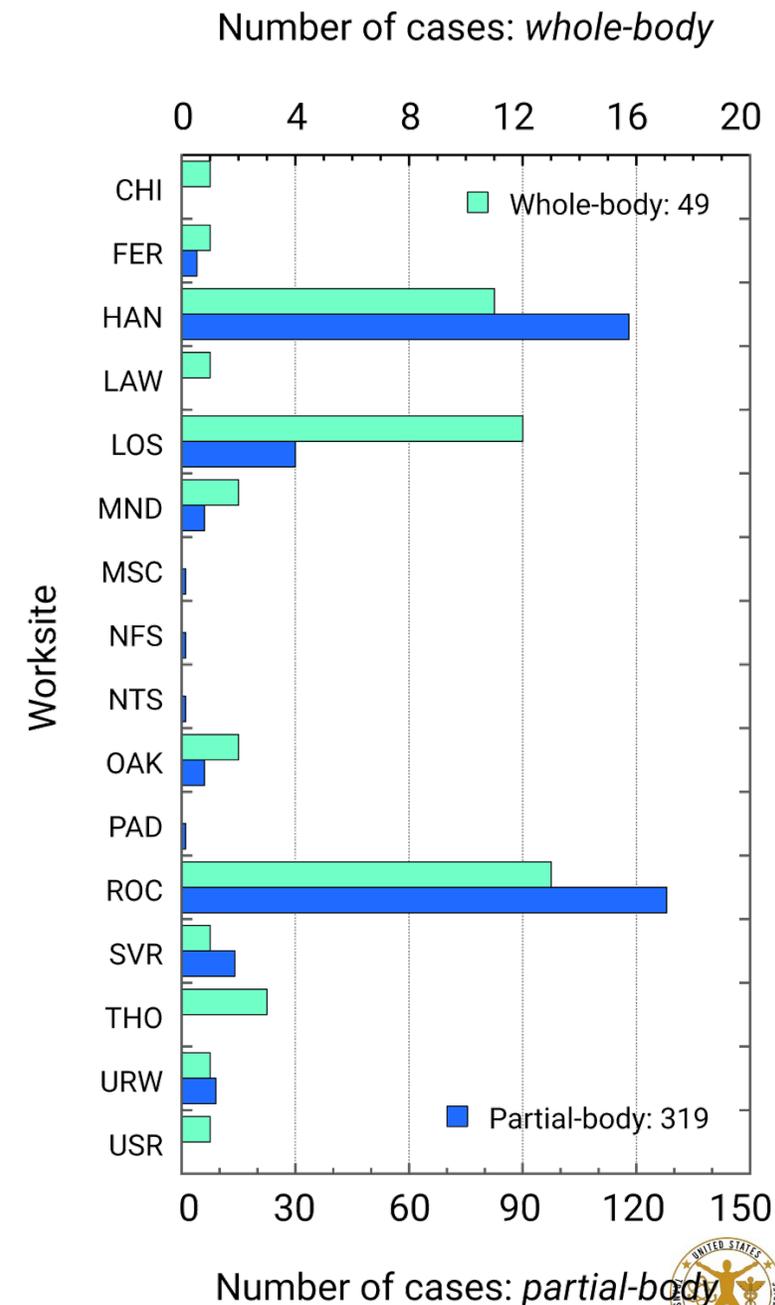


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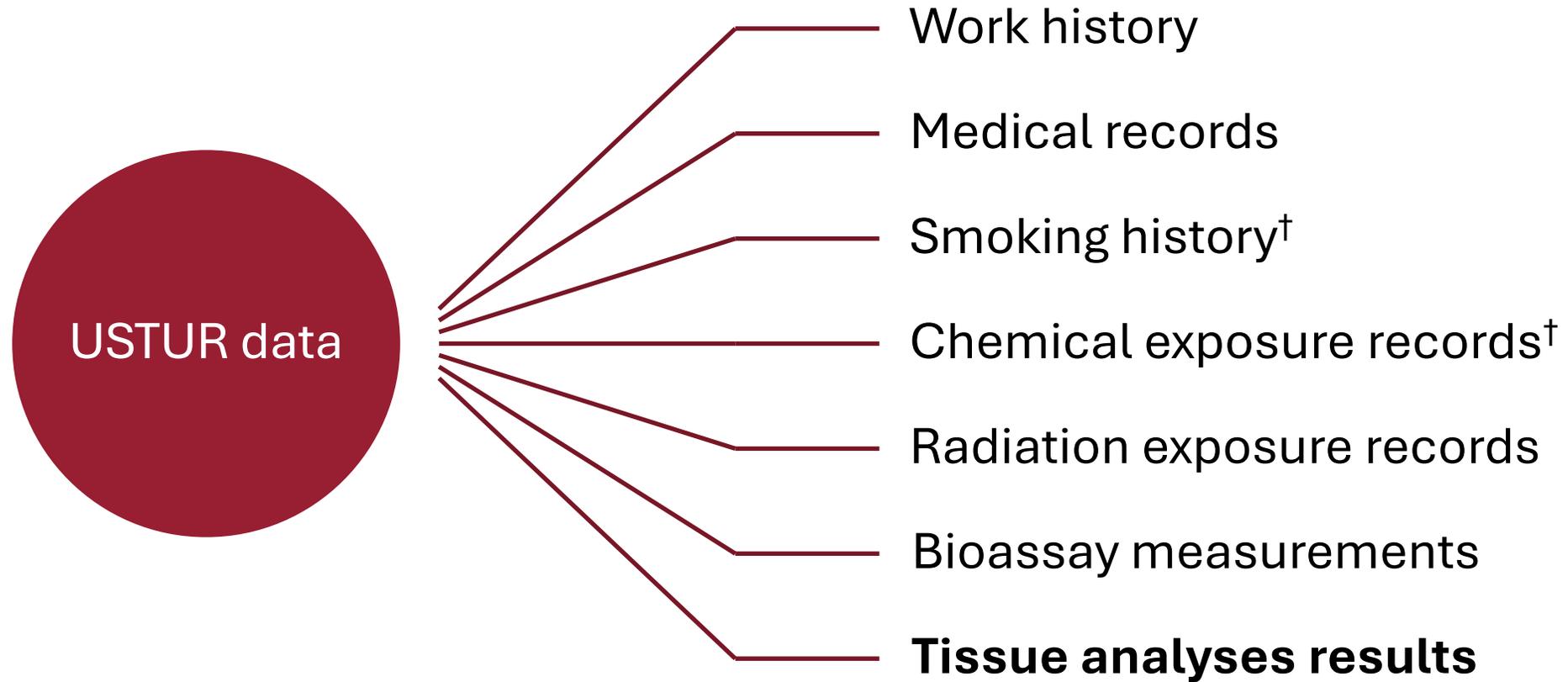


372

| Status | Number | Age (y) |
|---------------------|------------|-----------------------|
| Living | | |
| partial-body donors | 13 | 84±14 (53–97) |
| whole-body donors | 3 | 89±9 (81–100) |
| Deceased | | |
| partial-body donors | 319 | 69±13 (25–100) |
| whole-body donors | 49 | 78±11 (49–96) |
| Total | 384 | 70±14 (25–100) |



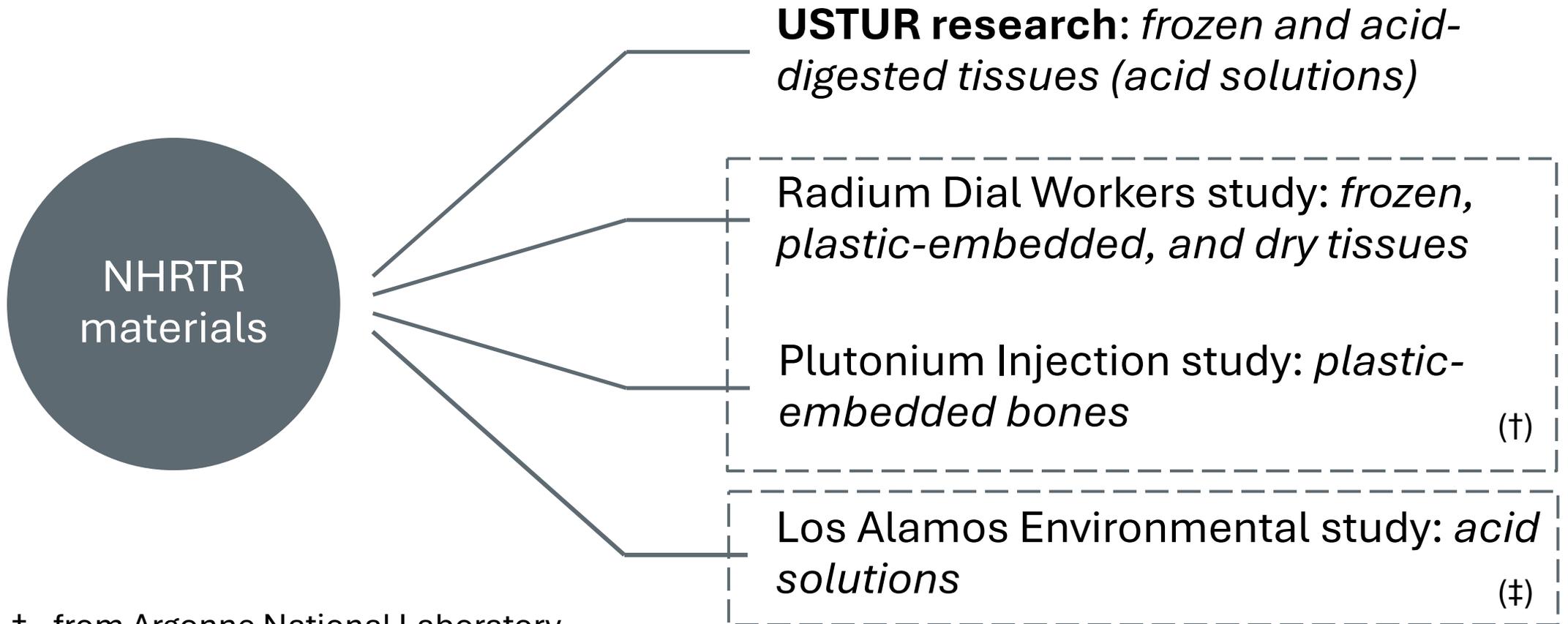
Unique Data Resource



† - self-reported



National Human Radiobiology Tissue Repository (NHRTR) at the USTUR



† - from Argonne National Laboratory

‡ - from Los Alamos National Laboratory



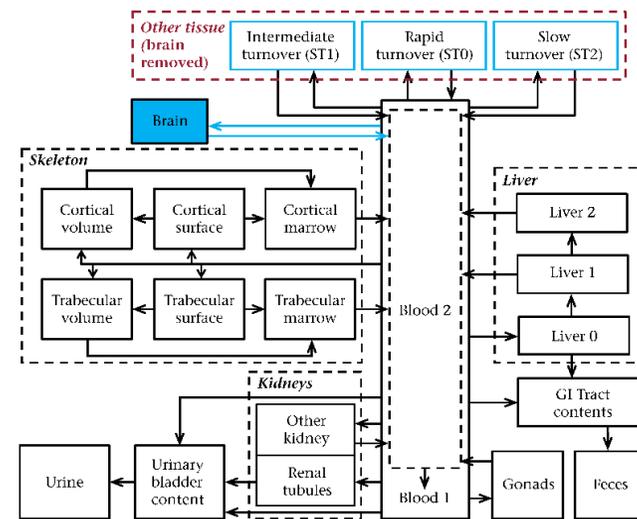
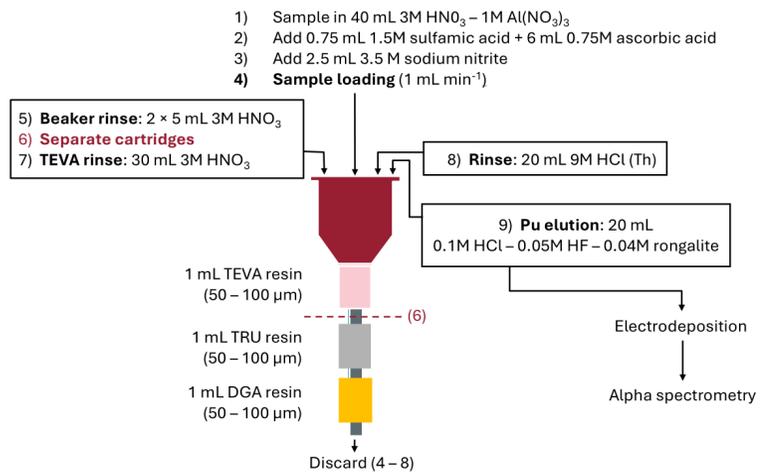
USTUR Operation and Research: Schematic

Autopsy

Tissue collection

Radiochemical analysis

Biokinetic modeling



Data for Biokinetic Modeling

| Human study | Animal study |
|--------------------------------|--------------------------------|
| H1: element of interest | A1: element of interest |
| H2: chemical analog | A2: chemical analog |

USTUR: H1-type study !

Radiation Protection Dosimetry
Vol. 79, Nos 1-4, pp. 335-342 (1998)
Nuclear Technology Publishing

RELIABILITY OF THE ICRP'S SYSTEMIC BIOKINETIC MODELS

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on Effects Branch

completeness of data underlying the biokinetic models of the International Commission and the associated uncertainties in those models as dosimetric tools examined. After a s of different sources of biokinetic data, the data base and associated model uncertainties important radionuclides representing various levels of knowledge of biokinetics in humans: s, ²²⁶Ra, and ²³⁹Pu. Attention is focused mainly on the behaviour of radionuclides after

TYPES OF INFORMATION USED TO BUILD BIOKINETIC MODELS

tection organisations neglected issue of the internally deposited National Council on elements (NCRP) is pre- of the biokinetic and l in the US to assess als; the International tion (ICRP) is pre- f its models and dose ublic; and the Com- ities (CEC) and the

As a rule, a systemic biokinetic model for an element is based on some combination of observations of the behaviour of the element in human subjects (H1), the element in other mammalian species (A1), chemically similar elements in human subjects (H2), and chemically similar elements in other mammalian species (A2). Depending on the degree of biological realism in the model structure, the four primary types of information might be supplemented with considerations of mass balance and basic physiological data (P).

In general, greater confidence can be placed in a biokinetic model based on H1 data than a model based on H2, A1, and/or A2 data of equal quality and completeness. For most elements, however, H1 data alone are not sufficient to develop a meaningful model, due either to the sparsity of such observations or to limitations in the data such as the atypical nature of the human study groups, uncertainty in the level and pattern of intake of the element, or inaccuracy in the measurements. For such reasons, H1 data must be supplemented or replaced in many cases by surrogate data and/or physiological considerations.

Use of A1 data (interspecies extrapolation) is sometimes supported by interspecies comparisons but more often relies on the concept of a general biological regularity across mammalian species with regard to cell and organ structure and function, biochemistry, and body temperature regulation. However, the qualitative similarities among mammalian species often do not translate into quantitatively similar behaviour of radionuclides, whether or not the data are scaled to account for differences in body size or metabolic rates. Moreover, there

The US Nuclear Regulatory Commission (NRC) are preparing a joint report that summarises independent expert judgments on uncertainties in the biokinetic, dose, and risk models used in their probabilistic risk assessment codes for reactor releases of radionuclides. In all of these efforts, uncertainties in the biological behaviour of elements in humans have been identified as the dominant uncertainties in most estimates of dose from internally deposited radionuclides.

This paper, which grew out of work done by the authors as part of these efforts by the NCRP, ICRP, and CEC-NRC, discusses the sources, quality, and completeness of data underlying the ICRP's biokinetic models and examines the associated uncertainties in those models as dosimetric tools. After a general discussion of the relative merits of different sources of biokinetic data, the data base and associated model uncertainties are evaluated for selected radionuclides representing various levels of knowledge of biokinetics in humans. Attention is focused mainly on the behaviour of radionuclides after their absorption to blood.



'Backbone' of the Registries: Tissue Analyses

Drying and
ashing

Digestion and
dissolution

Actinide
separation

α -source
preparation

Actinide
measurement



USTUR 350: Sequential Actinide Separation

- Vacuum-assisted extraction chromatography

DOI: 10.1007/s10967-007-7120-4

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Rapid column extraction method for actinides and strontium in fish and other animal tissue samples

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(Received June 12, 2007)

The analysis of actinides and radiostrontium in animal tissue samples is very important for environmental monitoring. There is a need to measure actinide isotopes and strontium with very low detection limits in animal tissue samples, including fish, deer, hogs, beef and shellfish. A new, rapid separation method has been developed that allows the measurement of plutonium, neptunium, uranium, americium, curium and strontium isotopes in large animal tissue samples (100–200 g) with high chemical recoveries and effective removal of matrix interferences. This method uses stacked TEVA Resin[®], TRU Resin[®] and DGA Resin[®] cartridges from Eichrom Technologies (Darien, IL, USA) that allows the rapid separation of plutonium (Pu), neptunium (Np), uranium (U), americium (Am), and curium (Cm) using a single multi-stage column combined with alpha-spectrometry. Strontium is collected on Sr Resin[®] from Eichrom Technologies (Darien, IL, USA). After acid digestion and furnace heating of the animal tissue samples, the actinides and ⁸⁹Sr are separated using column extraction chromatography. This method has been shown to be effective over a wide range of animal tissue matrices. Vacuum box cartridge technology with rapid flow rates is used to minimize sample preparation time.

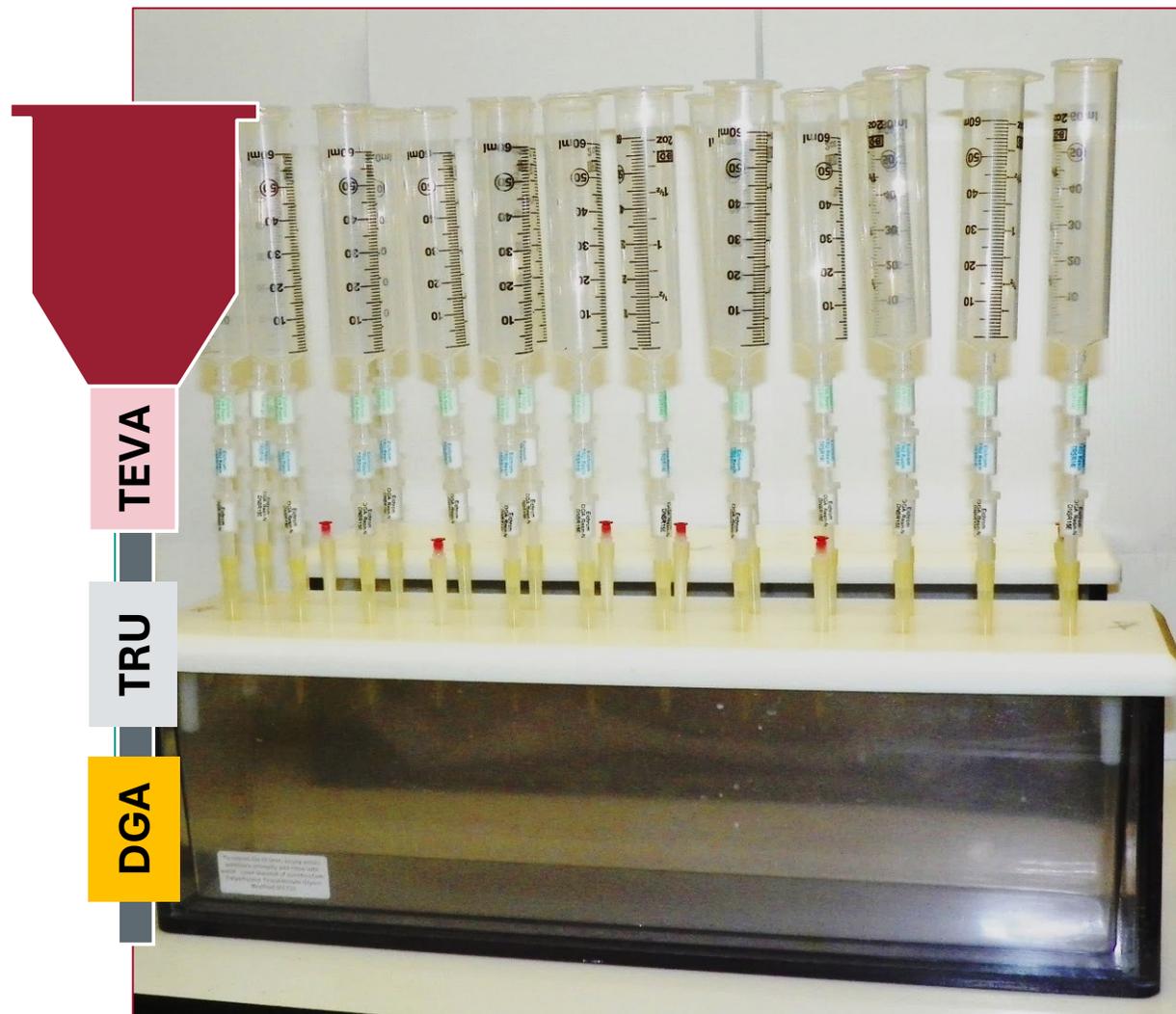
Introduction

The analysis of plutonium, neptunium, uranium, americium, curium and strontium-89/90 at extremely low levels requires the analysis of large animal tissue samples. ERIKSON¹ used a series of coprecipitation steps after sample ashing to separate and measure actinides and strontium in animal tissue samples. MELLADO² described a new method to determine actinides and strontium in fish samples using UTEVA Resin, TRU Resin and Sr-Resin. Samples from 5 to 40 grams were analyzed with recoveries that were often less than 40%. The fish reference material IAEA-414 was analyzed with and without calcination. For the calcinated samples (5 g of ashes), the recovery values were about 45% for Pu and about 15% for Am, while the values obtained without calcination (5 g of dry sample) were 20% for Pu and 2% for Am. For U, the best recovery value was obtained for samples without calcination, about 32%, while for samples with calcination the value was about 19%. The authors noted that Am recoveries seemed to be very dependent on the sample intake and sample pretreatment, and that this was likely related to the relatively low retention of Am on TRU Resin. LEE³ reported high chemical recoveries for marine environmental samples using a combination of anion-exchange and column extraction chromatography, however, the anion-exchange work required the use of relatively large volumes of acids with evaporation steps as well as an additional calcium oxalate precipitation step to preconcentrate americium. Based on a survey of the literature, there is still a need for a rapid, rugged column extraction method that provides high tracer

recoveries for actinides and strontium in animal tissue samples using small extraction chromatography columns.

As part of a food surveillance program at the Savannah River Site (SRS) in Aiken, SC, USA, freshwater and saltwater fish, shellfish, deer and hogs are routinely analyzed for radionuclide content. A new animal tissue method was developed in the SRS Environmental Laboratory that is simple, effective and allows the use of small resin cartridges to separate actinides and strontium isotopes from 200 gram tissue samples with high tracer recoveries and effective removal of interferences. This method was tested over a wide range of animal tissue matrices with very good success. This new method uses stacked TEVA Resin[®], TRU Resin[®] and DGA Resin[®] cartridges from Eichrom Technologies (Darien, IL, USA) that allows the rapid separation of plutonium, neptunium, uranium, americium and curium using a single multi-stage column (2 ml resin volumes) to separate actinide isotopes for alpha-spectrometry. DGA Resin[®], which has very strong retention for americium and curium, is used to enhance chemical recoveries of those analytes from this difficult matrix. The DGA Resin has a capacity (k') factor of approximately 30,000 in 3M nitric acid, much higher than americium retention on TRU Resin, which is approximately 100.⁴

Strontium was collected from the evaporated column load and rinse solutions, redissolved and separated using Sr Resin. Three milliliters of Sr Resin was used to ensure very high recoveries of strontium, but two milliliters of Sr Resin probably could probably be used to minimize costs with a moderate decrease in strontium yields.



USTUR 350: Pu/Am/U Separation

- 1) Sample in 40 mL 3M HNO₃ – 1M Al(NO₃)₃
- 2) Add 0.75 mL 1.5M sulfamic acid + 6 mL 0.75M ascorbic acid
- 3) Add 2.5 mL 3.5 M sodium nitrite
- 4) **Sample loading** (1 mL min⁻¹)

5) **Beaker rinse:** 2 × 5 mL 3M HNO₃
 6) **Separate cartridges**
 7) **TEVA rinse:** 30 mL 3M HNO₃

8) **Rinse:** 20 mL 9M HCl (Th)

9) **Pu elution:** 20 mL
 0.1M HCl – 0.05M HF – 0.04M rongalite

1 mL TEVA resin
 (50 – 100 μm)

1 mL TRU resin
 (50 – 100 μm)

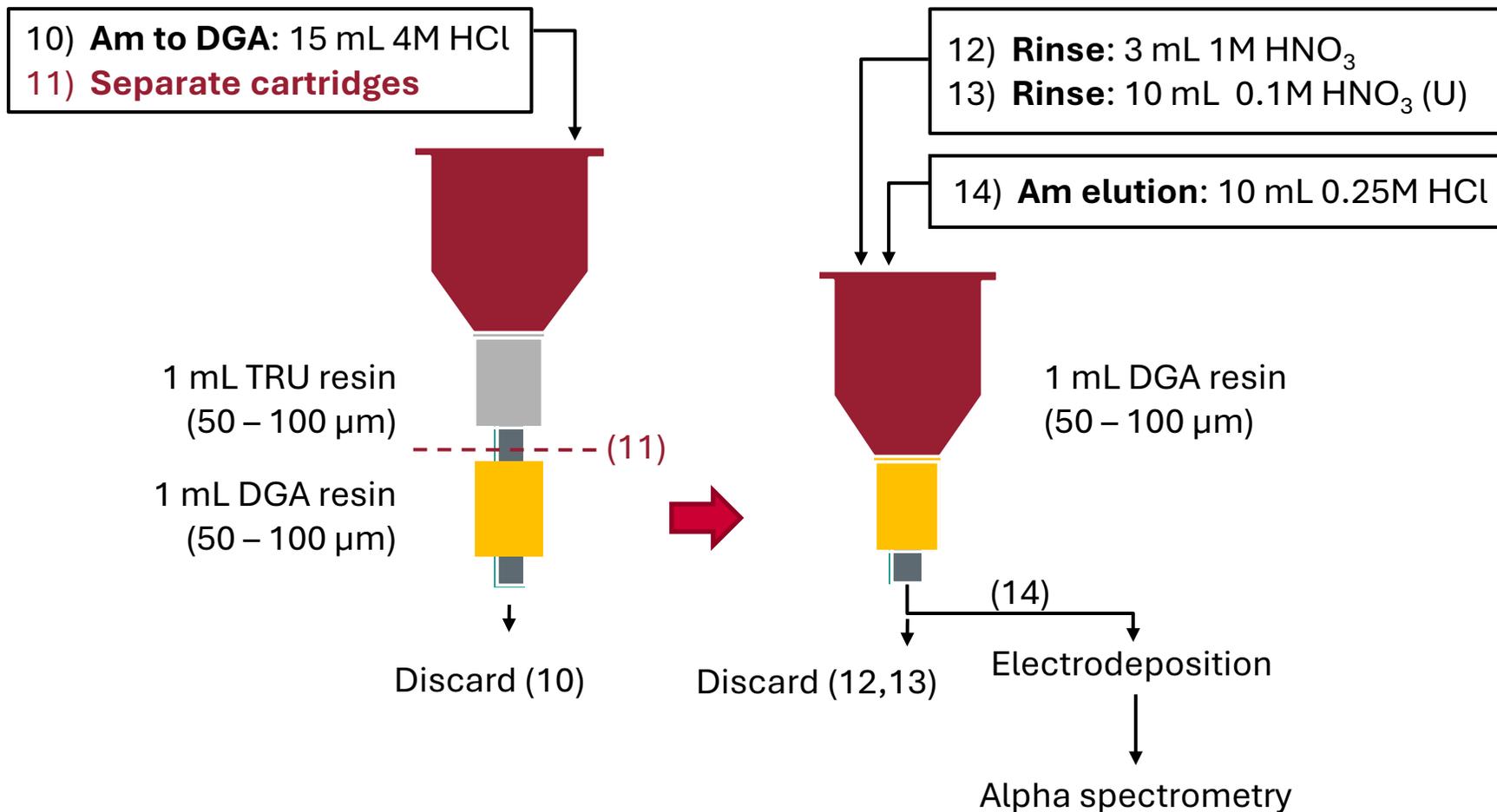
1 mL DGA resin
 (50 – 100 μm)

Discard (4 – 8)

Electrodeposition
 ↓
 Alpha spectrometry

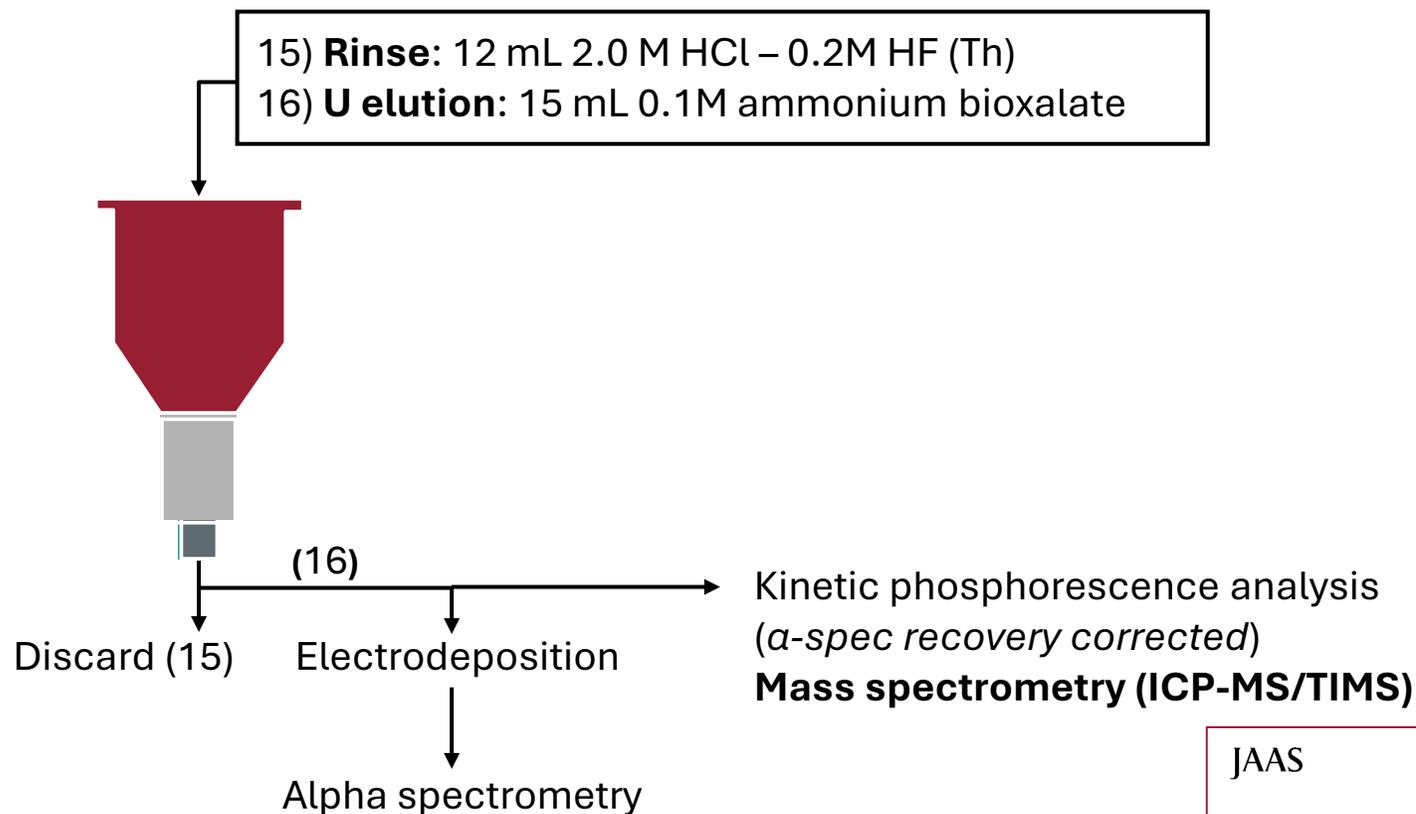
USTUR 350: Am (Cm) Separation

TRU – DGA cartridges from Step 6



USTUR 350: Uranium Separation

TRU cartridge from Step 11



Proc. Radiochim. Acta 1, 173–181 (2011) / DOI 10.1524/repr.2011.0032
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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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15 (1997) 1157–1165

JOURNAL OF
PHARMACEUTICAL
AND BIOMEDICAL
ANALYSIS

A sensitive method for the determination of uranium in biological samples utilizing kinetic phosphorescence analysis (KPA)

Mohsen A. Hedaya^{*}, Harry P. Birkenfeld, Ronald L. Kathren

Department of Pharmaceutical Sciences and United States Transuranium and Uranium Registries, College of Pharmacy,
Wegner Hall, Room 309, Washington State University, Pullman, WA 99164-6510, USA

Received 22 April 1996; accepted 23 September 1996

JAAS

Dynamic Article Links ▶

Cite this: *J. Anal. At. Spectrom.*, 2011, **26**, 2524

www.rsc.org/jaas

TECHNICAL NOTE

Measurement of uranium isotopes in human tissue samples by TIMS

Chunsheng Li,^{a*} Nancy Elliot,^b Sergei Tolmachev,^c Stacey McCord,^c Tom Shultz,^b Youqing Shi^b
and Gary H. Kramer^d

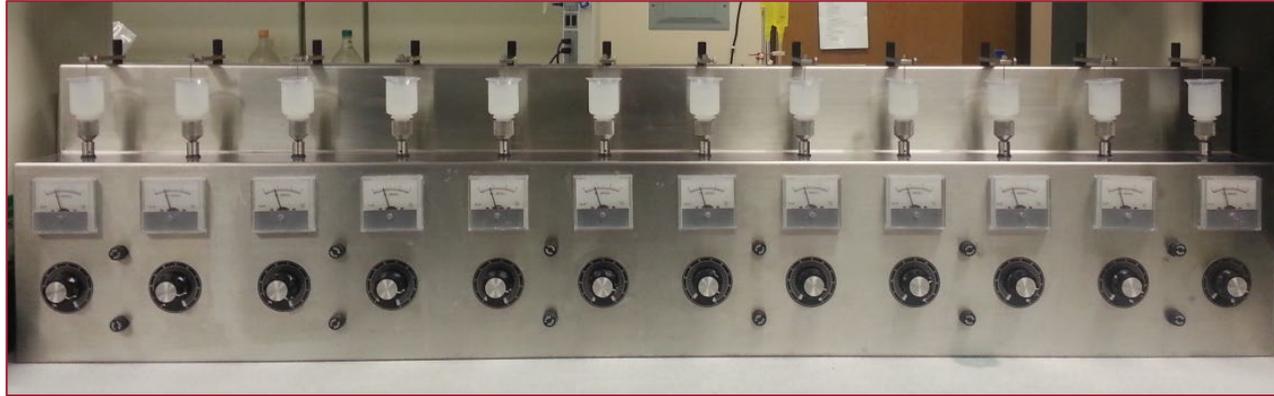
Received 5th August 2011, Accepted 27th September 2011

DOI: 10.1039/c1ja10231a



USTUR 520: Electrodeposition

- Phoenix® EP-12 Series electrodeposition unit



- In-house electrolytic cell
- Na_2SO_4 electrolyte solution
- 1 hr electrodeposition @ 0.75 A
- α -source: $\varnothing=5/8$ " stainless steel disk (planchet)



Journal of Radioanalytical and Nuclear Chemistry, Vol. 234, Nos 1- (1998) 213-218

Optimization and characterization of a sulfate based electrodeposition method for alpha-spectroscopy of actinide elements using chemometric analysis

S. E. Glover,** R. H. Filby,** S. B. Clark,** S. P. Grytdal*

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** Department of Chemistry, Washington State University, Pullman, WA 99164-4630, USA

(Received February 5, 1998)

Alpha-spectrometric measurements using Si detectors is the standard method for the determination of alpha emitting actinide elements. This method requires the preparation of sources for analysis which do not degrade the energy spectrum of the emitted alpha particles via sample self-absorption. A variety of methods for the electrodeposition of actinides have been reported in the literature, many of which require long deposition times and lack reproducibility. A sulfate based method has been evaluated for the preparation of these sources using chemometric analysis to optimize the method and evaluate several variables and their interactions with the goal to achieve high yield source preparation in 1 hour or less. Typical resolution for this method is 30 keV or less with recoveries approaching unity.

DOI: 10.1007/s10967-008-0514-0

Journal of Radioanalytical and Nuclear Chemistry, Vol. 276, No.2 (2008) 369-373

A robust, field-deployable method for the electrodeposition of actinides

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² Los Alamos National Laboratory, Los Alamos, NM, USA

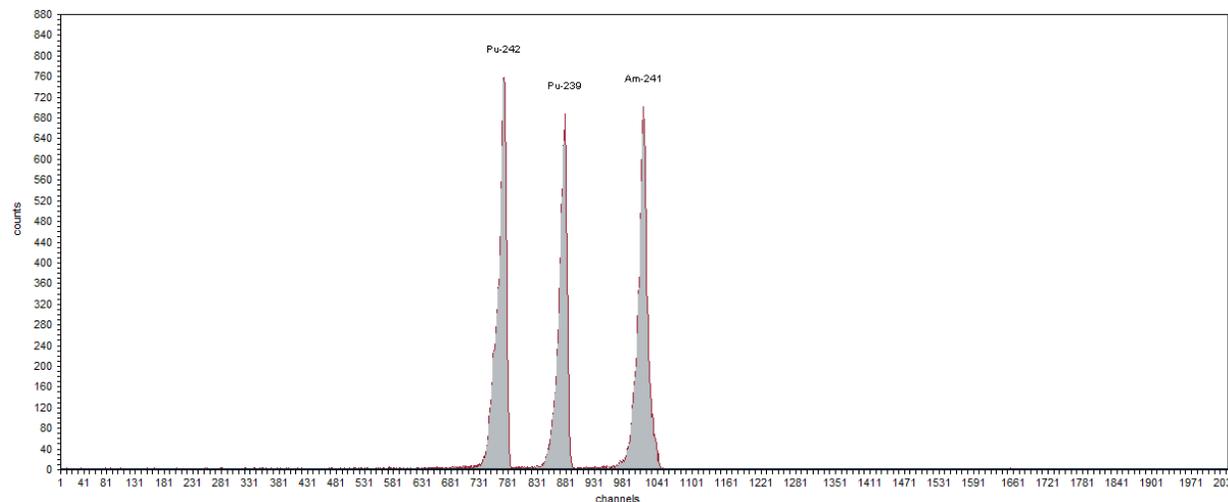
(Received March 2, 2007)

Several methods for the electrodeposition of actinides for alpha-spectrometry analysis have been developed over the past few decades, but none have been specifically designed to facilitate rapid analysis in a field situation. This paper describes the development of an electrodeposition procedure that is specifically adapted for use in a mobile lab. Using these techniques one would be able to obtain preliminary results in the event of a radiological incident. Quantitative yields with associated uncertainties have been determined for the procedure. It has also been shown that short deposition times can provide quantitative results.

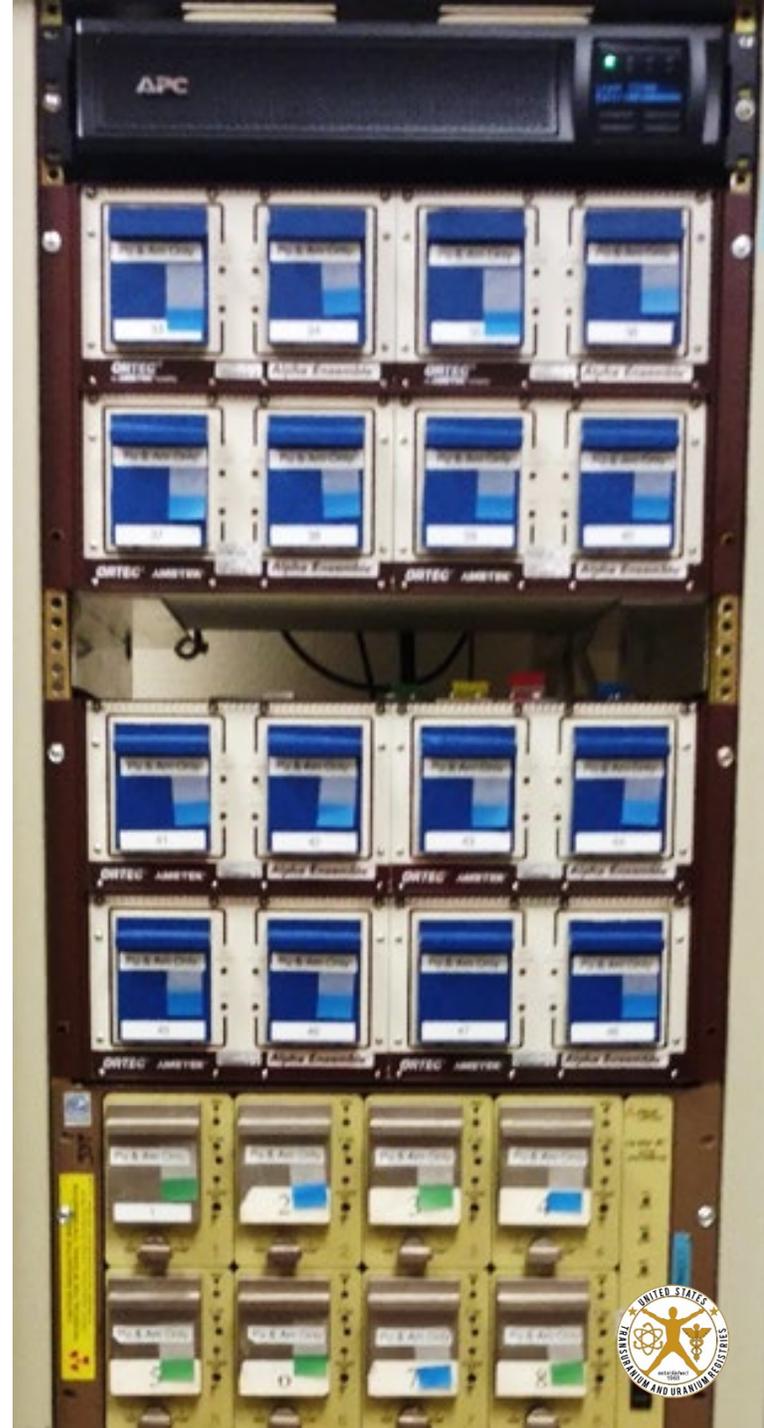


USTUR 600: Alpha-Spectrometry

- ORTEC: Ensemble (4) and Octête PC (3) systems
- Detector: ENS-U450 (56)
- Calibration: E&Z Analytics (1); USTUR in-house (8)



- Background count time: 300,000 s
- Sample count time: 150,000 s
- Detection limit: 0.03 Bq (130 fg ^{239}Pu ; 2.4 fg ^{241}Am)



Data Quality Objectives Document

- Addresses the sample collection and data analysis needs in support of the USTUR mission

USTUR-0561-20

Data Quality Objectives Supporting the
U.S. Transuranium and Uranium Registries Mission



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March 22, 2024

 College of
**Pharmacy and
Pharmaceutical Sciences**
WASHINGTON STATE UNIVERSITY



 WASHINGTON STATE UNIVERSITY
College of Pharmacy and
Pharmaceutical Sciences

**Measurement and uncertainty challenges in bringing
USTUR's decades-old radiochemistry program
into the 21st century: Part 1**

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Oak Ridge, TN 37831



USTUR-0621-22A

65th Radiobioassay and Radiochemical Measurements Conference
Atlanta, Georgia, October 31 – November 4, 2022

 WASHINGTON STATE UNIVERSITY
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Pharmaceutical Sciences

**Measurement and uncertainty challenges in bringing
USTUR's decades-old radiochemistry program
into the 21st century: Part 2**

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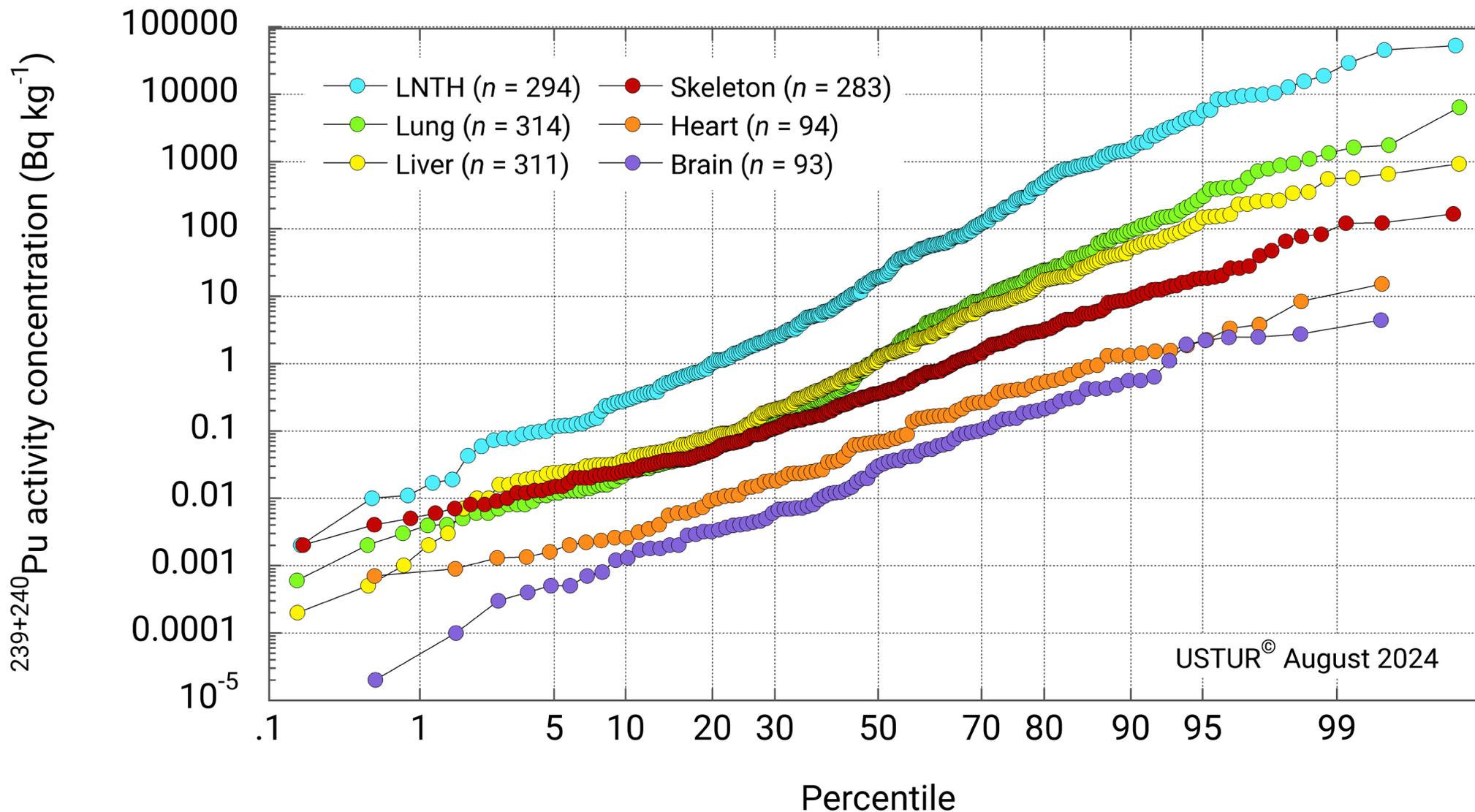


USTUR-0622-22A

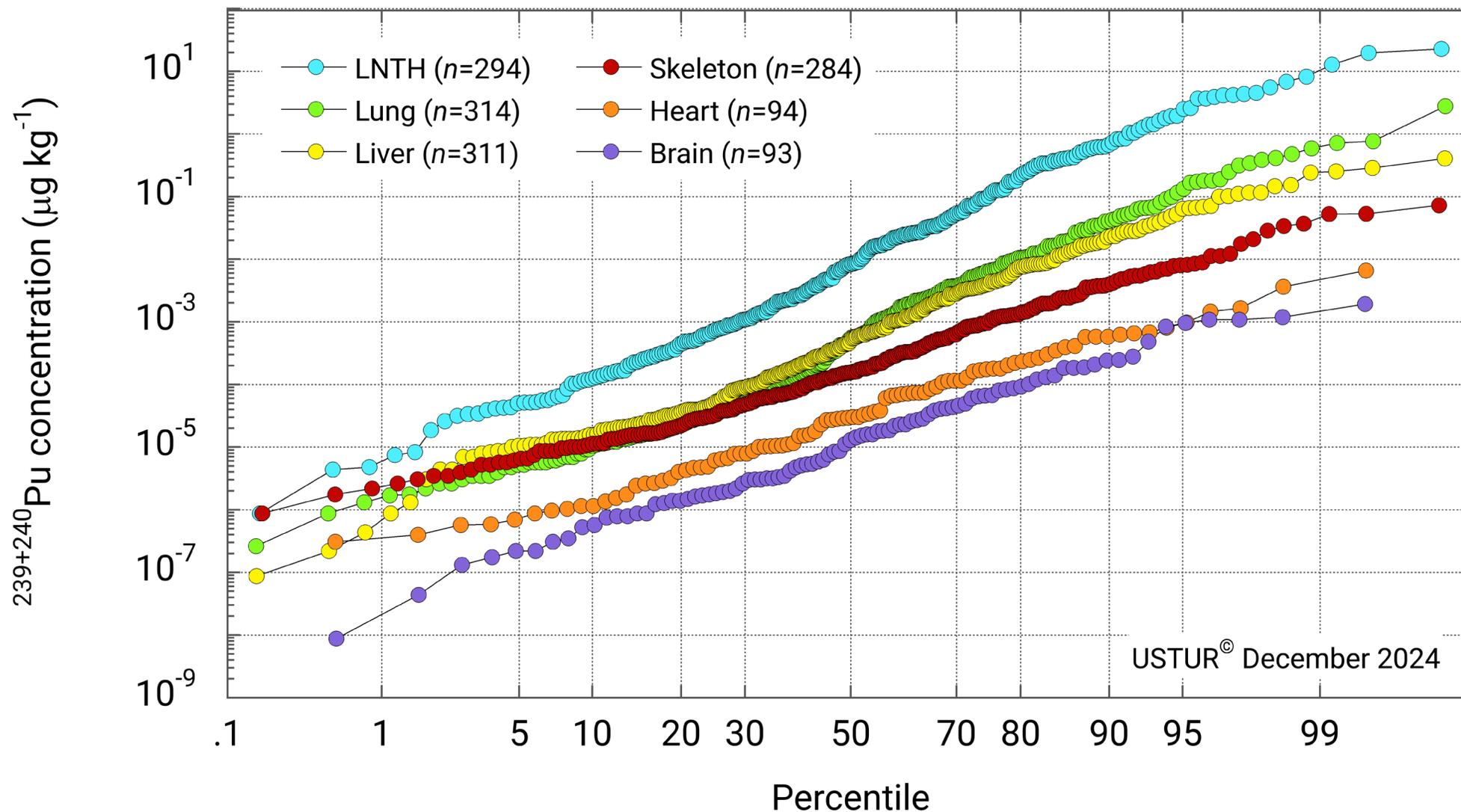
65th Radiobioassay and Radiochemical Measurements Conference
Atlanta, Georgia, October 31 – November 4, 2022



^{239}Pu Activity Concentrations in Human Tissues

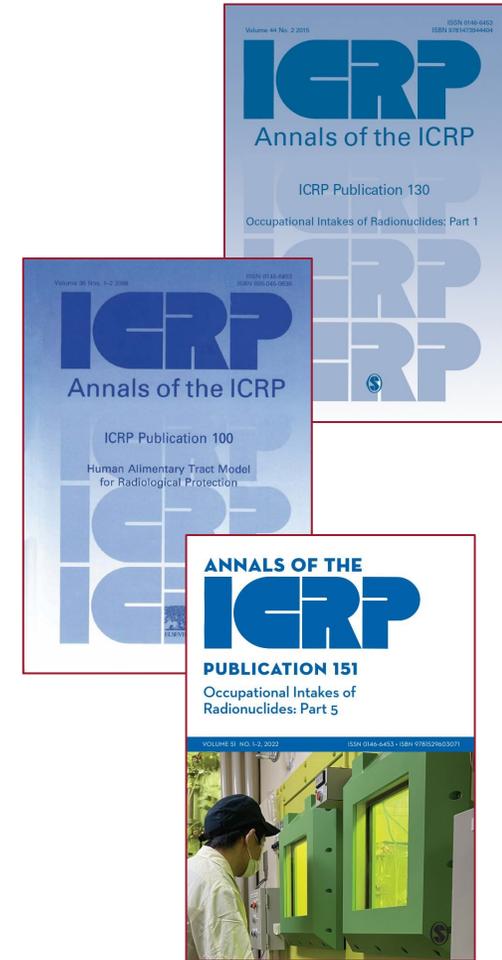
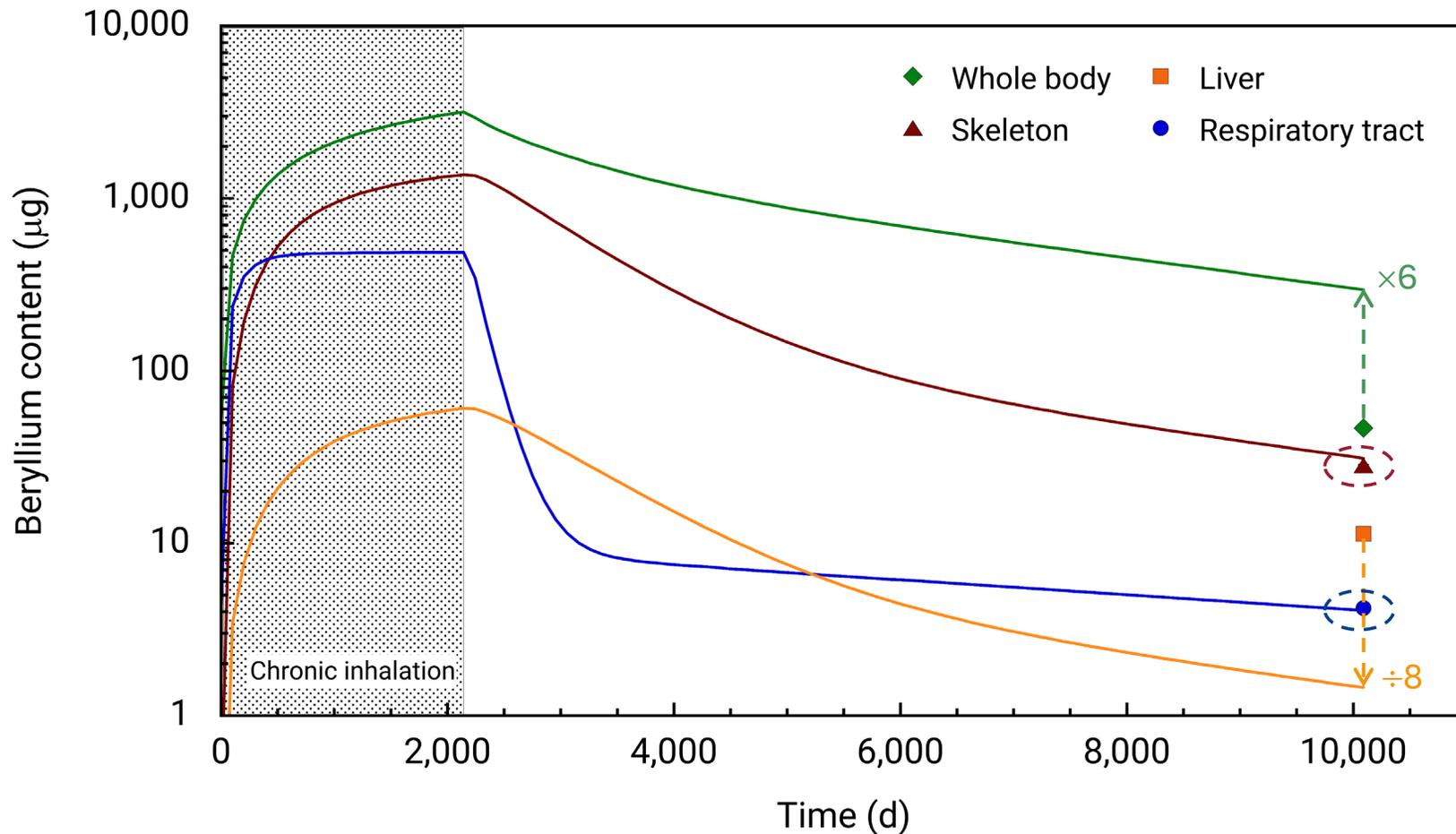


^{239}Pu Mass Concentrations in Human Tissues



Model Prediction vs Measurements

ICRP human respiratory tract, human alimentary tract and systemic models:



Well predict respiratory tract and skeleton, underestimate liver, and overestimate whole body





Collaborative Network



National Council on Radiation Protection and Measurements



UK Health Security Agency



Northwestern University



PHYSICS & ENGINEERING
FRANCIS MARION UNIVERSITY



Memorial Sloan Kettering Cancer Center



Pacific Northwest National Laboratory

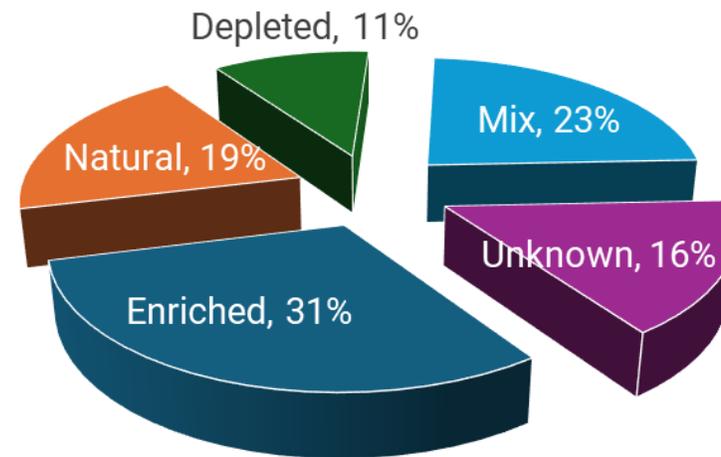


World Health Organization

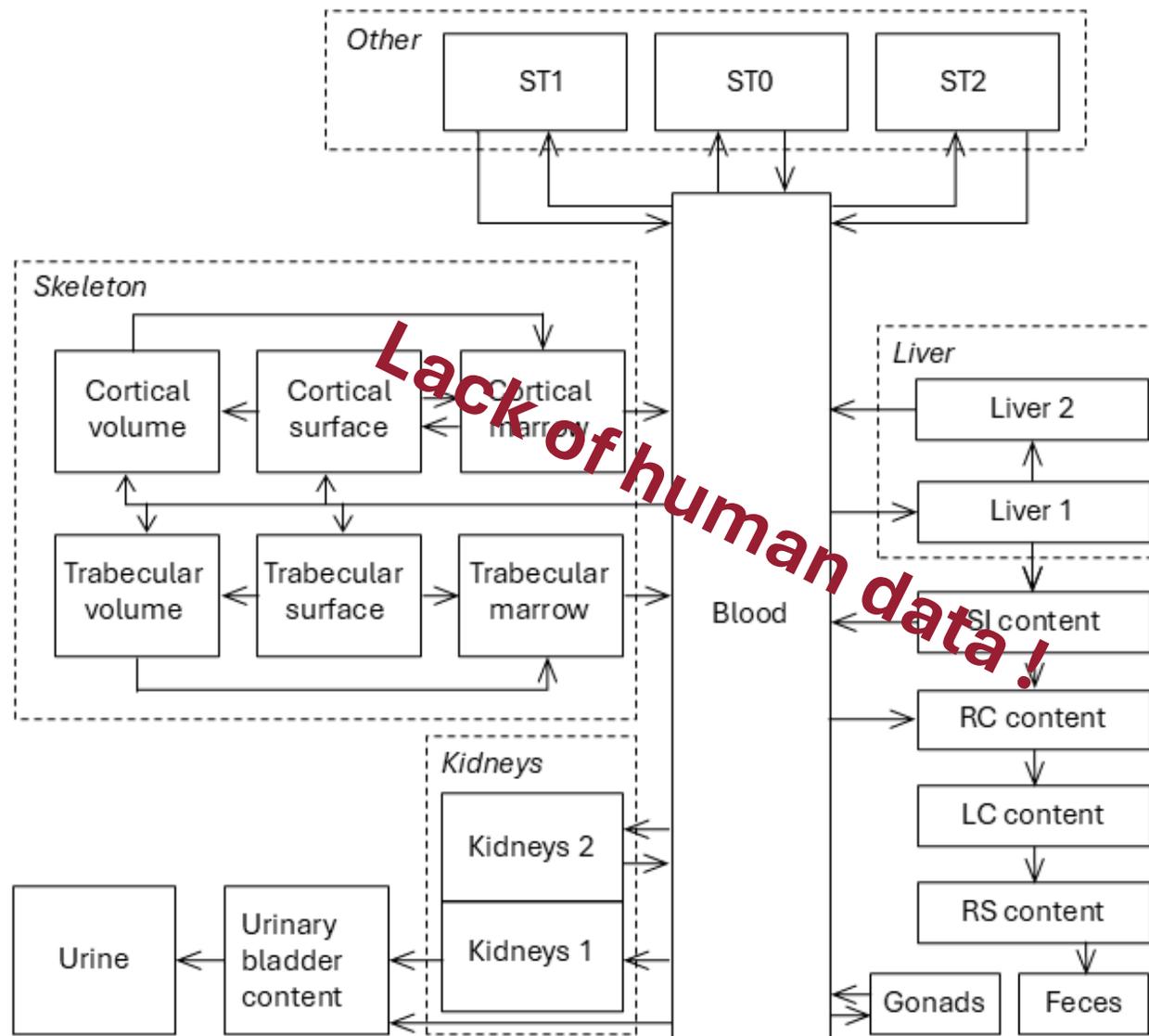
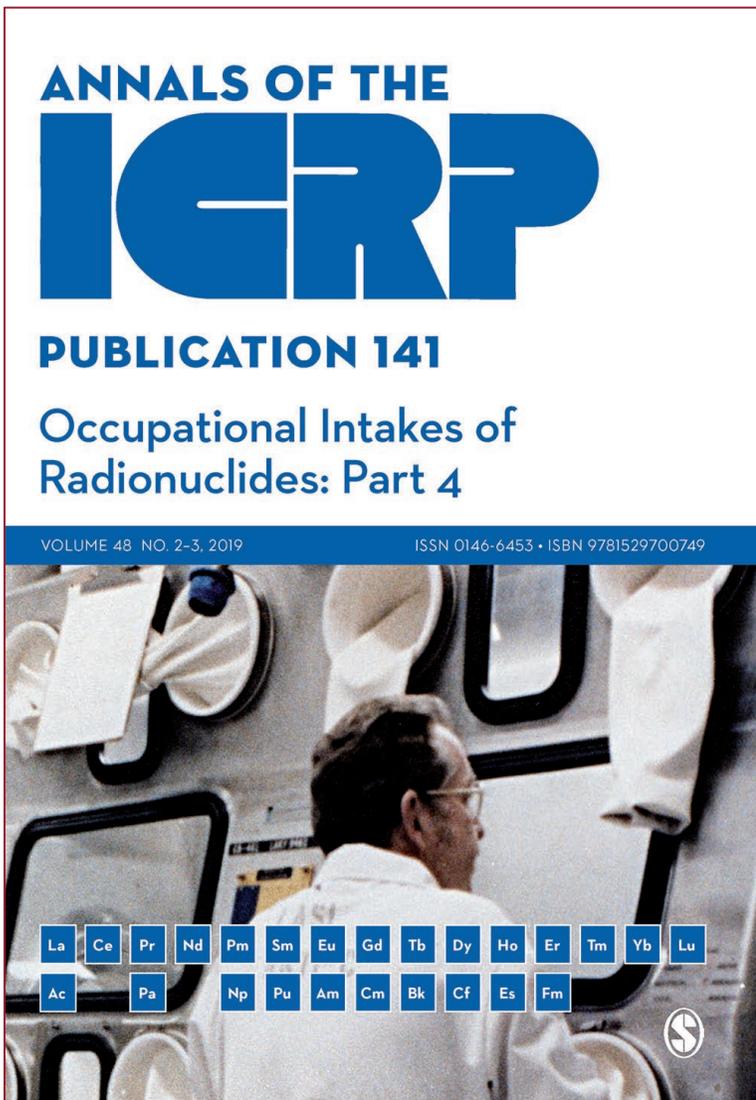


Needs for Advance Analytical Techniques

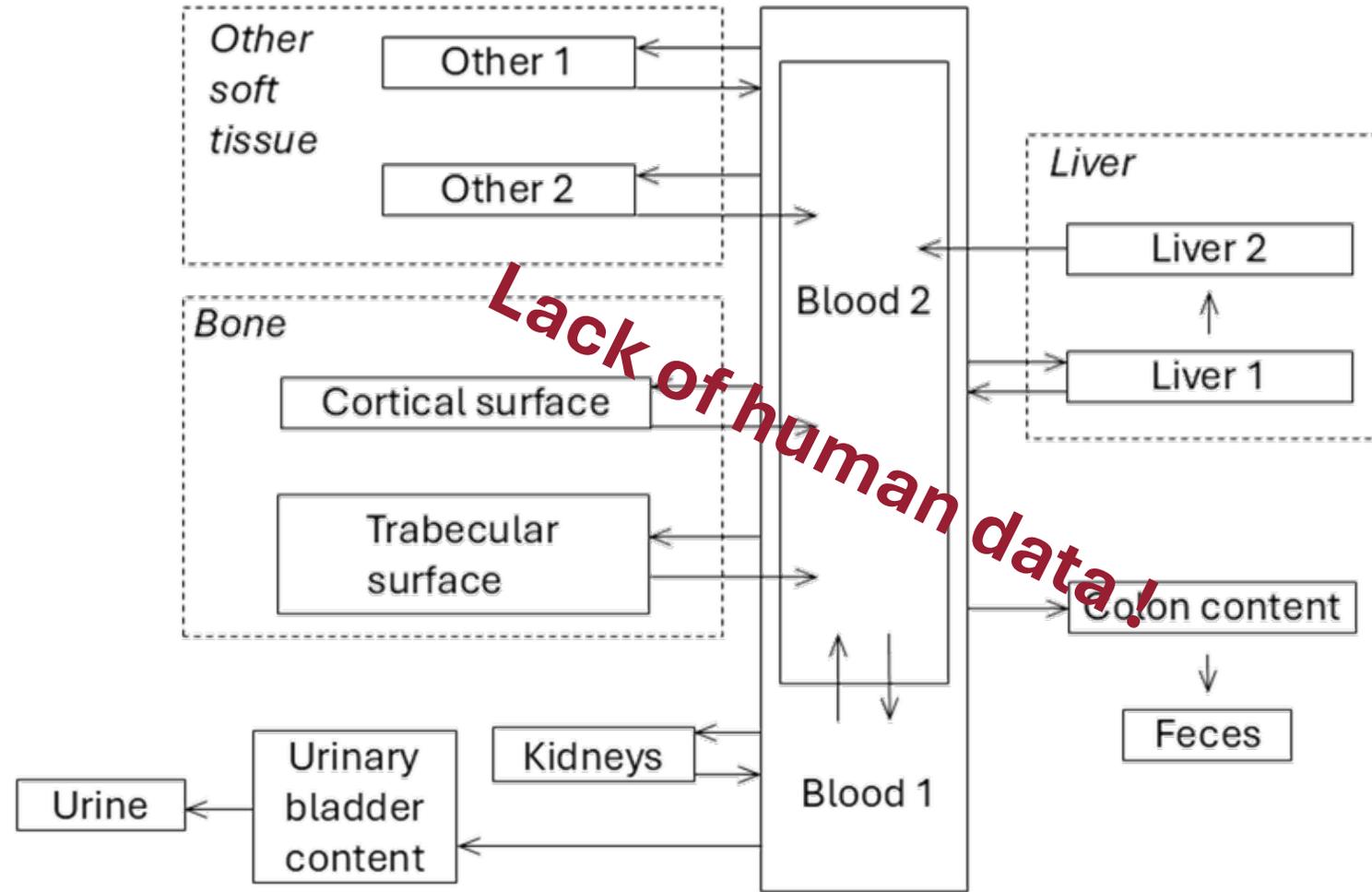
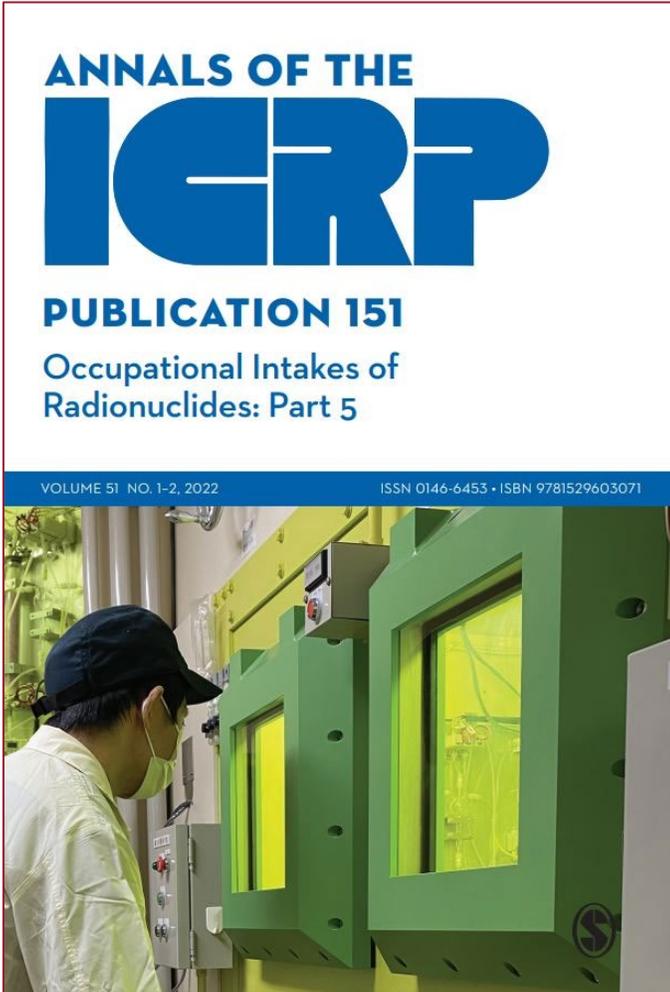
- Low intakes and isotopic composition: ^{239}Pu and $^{239}\text{Pu} / ^{240}\text{Pu}$
- Minor actinides: ^{237}Np ($T_{1/2}=2.144 \times 10^6$ y) and ^{244}Cm ($T_{1/2}=18.1$ y)
- Short-lived β -emitters: ^{241}Pu ($T_{1/2}=14.35$ y) and ^{147}Pm ($T_{1/2}=2.623$ y)
- Non-radioactive metal analyses: Be and Zr
- Analyses of keratinoid materials: hair and nails
- Radionuclide distribution in individual organs: lungs, brain, heart, *etc*
- Uranium isotopic composition:



Np and Cm Biokinetic Modeling

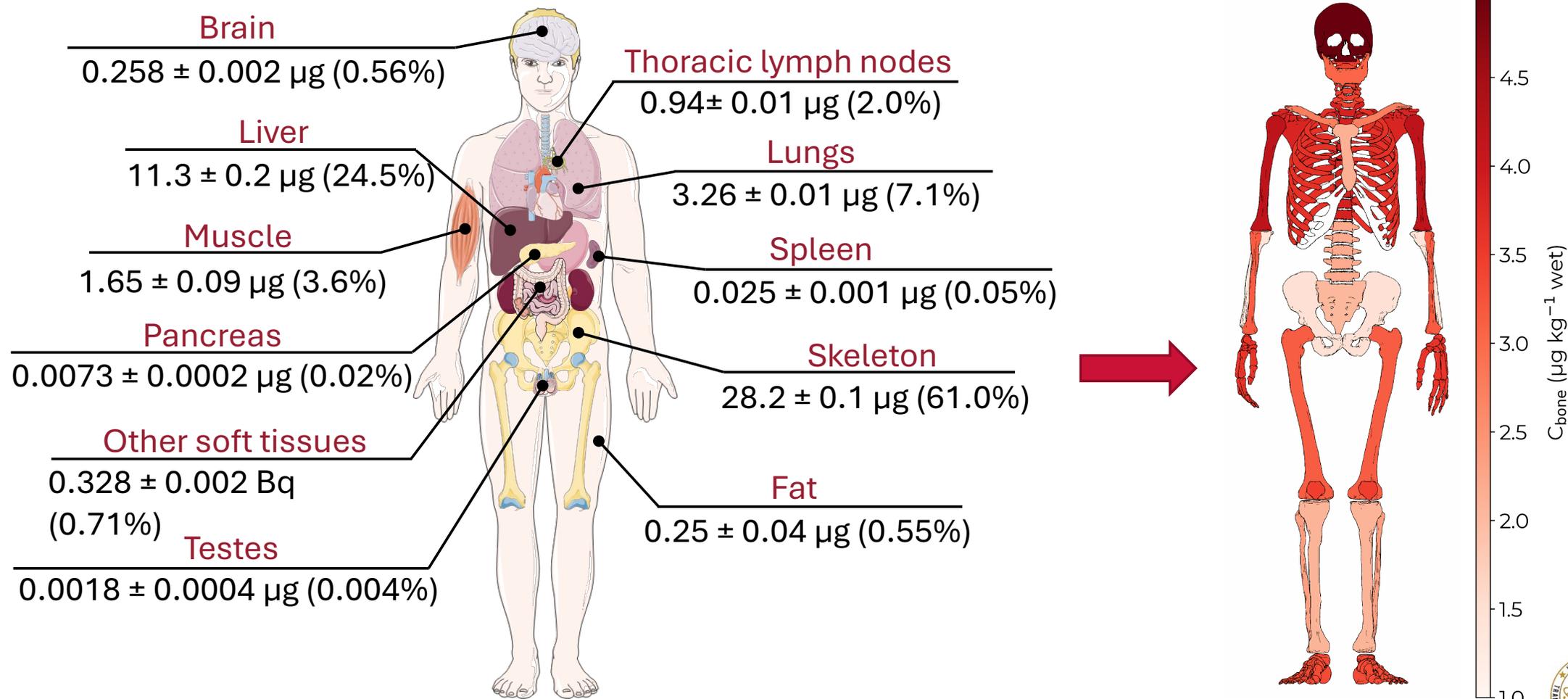


Beryllium Biokinetic Modeling

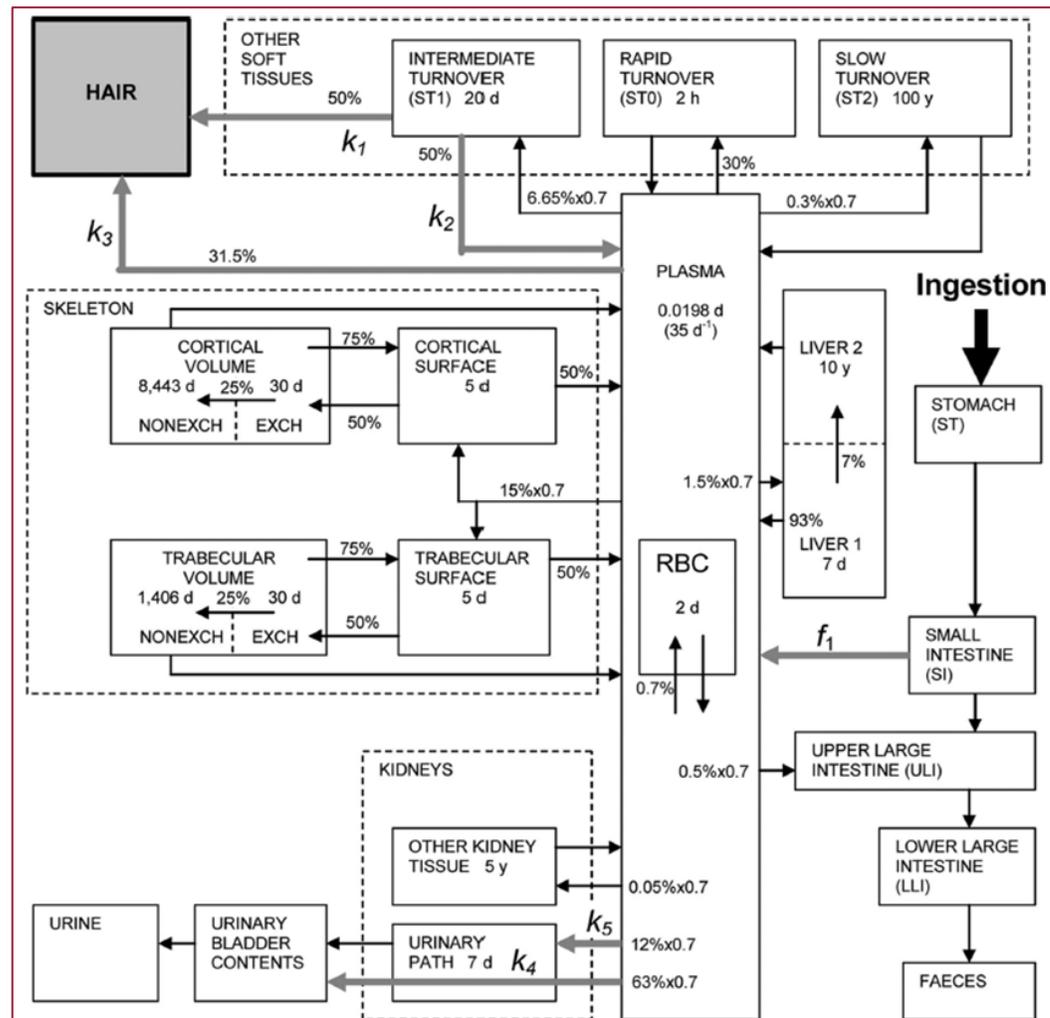


Beryllium in Human Body: Single Case Analysis

- Self-reported exposure duration: 6 y
- Estimated total ^9Be content in whole body: $46.3 \pm 0.2 \mu\text{g}$



Actinides in Keratinoid Materials



Li *et al.* A compartmental model of U in human hair for protracted ingestion of natural uranium in drinking water. *Health Phys.* 96(6): 636-645; 2009

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A multi-collector ICP-MS method for quantification of plutonium, uranium, and americium in hair and nails of occupationally or medically exposed individuals

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^b Department of Chemistry, University of Missouri, Columbia, MO 65211, United States
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^d Research Reactor, University of Missouri, Columbia, MO 65211, United States

ABSTRACT

The ²³⁹Pu, ²³⁸U, and ²⁴¹Am concentrations and ²³⁹Pu/²⁴⁰Pu, ²³⁵U/²³⁸U, and ²³⁶U/²³⁸U atom ratios were measured in the hair and nail samples using a new method utilizing TEVA, UTEVA, and DGA extraction chromatography and multi-collector ICP-MS. Samples were collected from individuals who donated their bodies to the United States Transuranium and Uranium Registries. The concentration of ²³⁹Pu ranged from 0.22 to 15.8 ng/kg. The ²³⁹Pu/²⁴⁰Pu isotopic ratios ranged from 0.026 to 0.127 which is consistent with weapons-grade plutonium. Concentration of uranium fell between 1.84 µg/kg and 29.5 µg/kg and ²³⁵U/²³⁸U ratios ranged from 4.8 × 10⁻³ to 7.6 × 10⁻³. Elevated ²³⁶U/²³⁸U atom ratios were measured in two cases and ranged from 5.0 × 10⁻⁶ – 2.4 × 10⁻⁵ indicating exposure to spent or reprocessed uranium material. The concentration of ²⁴¹Am was measured in four hair samples and ranged from 0.02 to 0.21 ng/kg.

1. Introduction

In workplaces where exposure to uranium, plutonium, and americium occurs, health physics surveillance programs are used to determine a workers internal dose [1]. Workplace exposure can occur through inhalation, wound, or ingestion. Following intake, the actinides are absorbed into the blood and distributed to organs. Radionuclide excretion occurs through urine, feces, and perspiration as well as hair and nail growth. Element-specific biokinetic models relate the organ distribution of a radionuclide to the levels in urine or feces for radiation dose estimation. The International Commission on Radiological Protection (ICRP) has published biokinetic models for uranium, plutonium, and americium [2].

Hair and nail are keratinoid materials that could be an alternative biomonitor for actinide exposure outside of workplace exposure monitoring. Urine and fecal samples are sensitive to recent actinide exposure. The hair follicles and the nailbed both have a blood supply and actinide levels in hair and nail could therefore reflect blood levels at the time of keratin growth [3,4]. The distal portion of a fingernail and toenail was formed 3–12 months prior to collection [5,6]. Hair collected at the scalp represents exposure during the last month, since hair grows approximately 1 cm per month [6,7]. Actinides measured in hair and nail samples reflect blood levels at the time the keratin was synthesized.

Hair and nails samples may be useful for determining actinide exposure following an accident, a nuclear detonation, or in the case of uranium, environmental exposure. It may be difficult to collect urine or fecal samples from a large population close to the time of the accident. Hair and nail have the advantage that they are simple to collect and store and are sensitive to past exposure. For example, in epidemiology studies nail samples have been collected by participants at home and mailed to the study center [5].

Several studies have examined the relationship between heavy metal levels in keratinous materials and intake. For example, toenail cadmium levels were correlated to cigarette smoking, a major source of exposure [9]. Toenail arsenic levels were correlated with arsenic levels in drinking water and diet [9,10]. Toenail lead levels were correlated to blood levels, although the toenail lead is reported to be more variable than blood [11,12]. Karpas *et al.*, demonstrated that toenail and hair uranium levels are correlated to uranium levels in drinking water [13–16]. Brockman *et al.*, reported that ²³⁵U/²³⁸U and ²³⁶U/²³⁸U anthropogenic atom ratios in hair and nail samples collected from current nuclear workers who self-reported exposure to enriched or depleted uranium [7].

There are a few studies that report plutonium levels in hair and nail

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Radium Distribution in Brain

- ^{226}Ra activity in brain: $5.7 \pm 0.2 \text{ Bq}$



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Quadrupole and multi-collector ICP-MS analysis of ^{226}Ra in brain from a radium dial painter

D. L. Arbova,^a S. Y. Tolmachev^b and J. D. Brockman^{a,*}

Two ICP-MS methods were developed to measure the radiotoxic isotope, ^{226}Ra in brain tissue from a radium dial painter worker. The first method was a direct analysis of acid digested samples using a quadrupole ICP-MS. The instrumental LOD of ^{226}Ra was 0.1 ng kg^{-1} . Polyatomic interferences at m/z 226 were investigated and Fb was identified from a polyatomic interferent in an in-house prepared from bovine brain, with a $^{226}\text{Ra}/^{208}\text{Tl}$ formation ratio of 4×10^{-8} . The quadrupole method was also used to measure levels of beryllium, strontium, and uranium. A second method was developed that included cation-exchange chromatography to separate ^{226}Ra followed by an in-house sector field MC-ICP-MS. The instrumental LOD for the cation exchange method with electro-deposition reported detection was 0.5 pg kg^{-1} (19 mBq kg^{-1}). The measured concentrations of ^{226}Ra in different regions ranged from $0.09\text{--}0.72 \text{ ng kg}^{-1}$ ($3.3\text{--}27 \text{ Bq kg}^{-1}$) and radium was non-uniformly distributed in the brain.

Introduction

Radium is a radioactive alkaline earth metal produced through the natural radioactive decay chains. Among the radium isotopes, ^{226}Ra has the longest half-life of 1600 ± 7 years.¹ The ^{226}Ra decay chain produces 4 alpha particles and 4 beta particles before terminating at ^{206}Pb . Internal exposure to ^{226}Ra and its progeny are a human health concern due to effects of high linear energy transfer (LET) ionizing radiation.² Human exposure to radium occurs through consumption of food and water. The concentration of ^{226}Ra in natural waters ranges from $0.14\text{--}0.55 \text{ pg L}^{-1}$ ($0.5\text{--}20 \text{ mBq L}^{-1}$).³ Combustion of coal releases ^{226}Ra with concentrations in fly ash ranging from $1.21\text{--}65.6 \text{ ng kg}^{-1}$ ($44.3\text{--}2400 \text{ Bq kg}^{-1}$).⁴ Plants uptake ^{226}Ra through root and foliar processes.⁵ Animals are exposed through ingestion of food and water.⁶

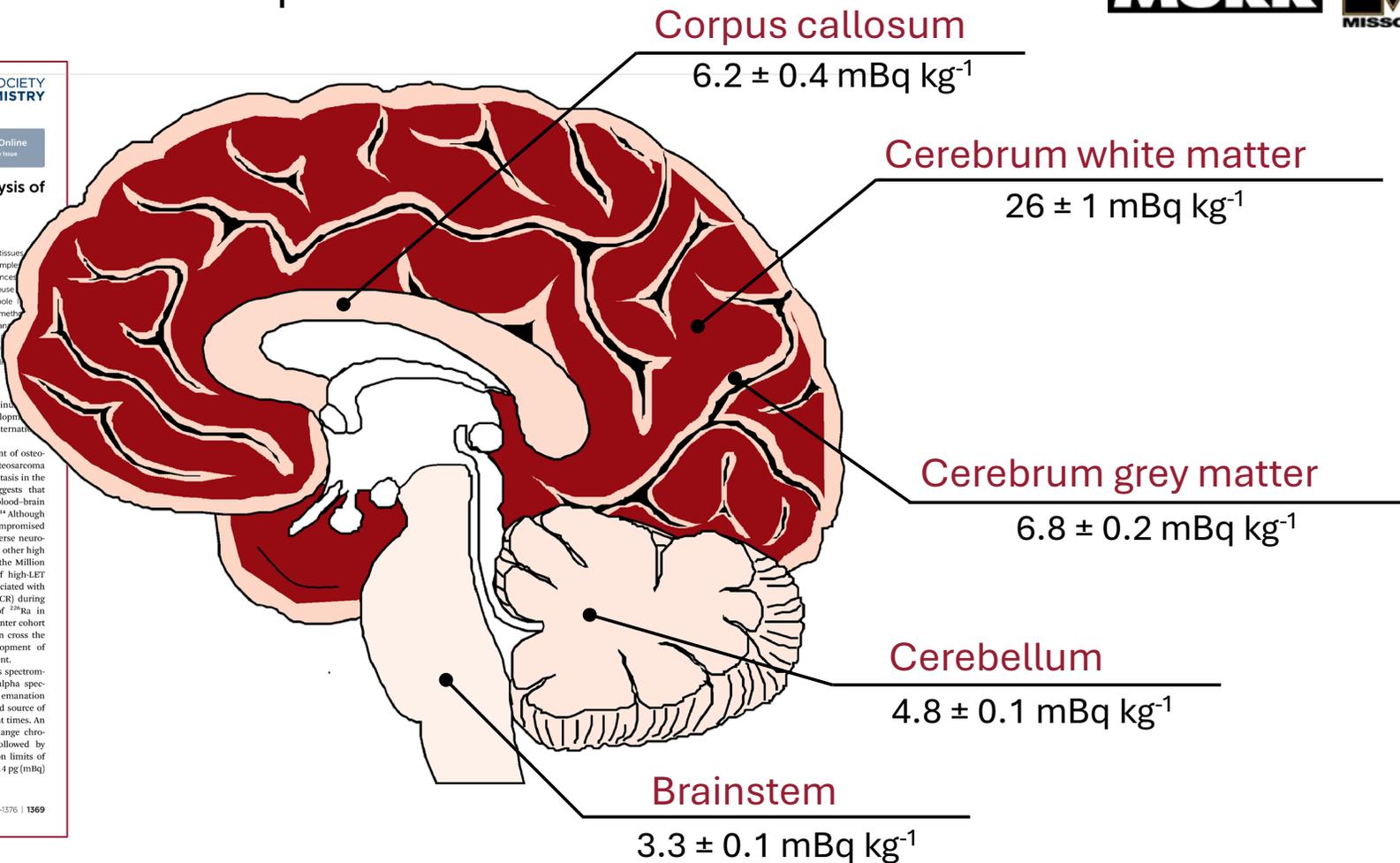
The health effects of ^{226}Ra exposure have been studied using data from the United States Radium Dial Workers cohort.⁷ The watch dial painters, who were predominantly women, applied a luminescent mixture of $^{226}\text{RaSO}_4$ and ZnS onto watch dials and other instruments. Prior to 1926, it was common practice for the dial painters to "tip" or "point" the paintbrush using their lips leading to ingestion of radium.⁸ The ingested ^{226}Ra primarily accumulated in bone and the watch dial painters had an increased risk of developing osteomyelitis, osteosarcoma, and head carcinomas of the mastoid and paranasal sinuses.⁹ Watch dial painter's studies were used in the development of a radium biokinetic model published by the International Commission on Radiological Protection (ICRP).¹⁰

$^{223}\text{RaCl}_2$ is currently being used for the treatment of osteosarcoma. In one case study, a patient treated for osteosarcoma with $^{223}\text{RaCl}_2$ was observed to have shrunken metastasis in the cerebellum brain region.¹¹ This observation suggests that radium could be transported across the intact blood-brain barrier (BBB), potentially by calcium transporters.^{12–14} Although in this case it is unclear if the BBB integrity was compromised by cerebellar metastases or radiation damage. Adverse neurological effects associated with exposure to ^{226}Ra and other high LET emitters are currently under investigation in the Million Person Study (MPS).¹⁵ The neurological effects of high-LET radiation is also of interest for estimating risk associated with exposure to high-LET galactic cosmic radiation (GCR) during manned space flights.^{16,17} Direct measurement of ^{226}Ra in neurological tissue samples from the watch dial painter cohort would provide additional evidence that radium can cross the blood-brain barrier and provide data for development of a radium biokinetic model with a brain compartment.

^{226}Ra can be measured by radiometric and mass spectrometry methods.¹⁸ Radiometric techniques include alpha spectroscopy, liquid scintillation counting, and emanation counting. Alpha spectroscopy requires a thin, plated source of ^{226}Ra to minimize self-absorption and 48 hour count times. An alpha spectroscopy method that used cation exchange chromatography with selective complex formation followed by electro-deposition reported detection ^{226}Ra detection limits of 0.014 pg L^{-1} (0.5 mBq L^{-1}) in urine samples and 0.014 pg (mBq)

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Beryllium Distribution in Brain

- ^9Be content in brain: $0.27 \pm 0.01 \mu\text{g}$



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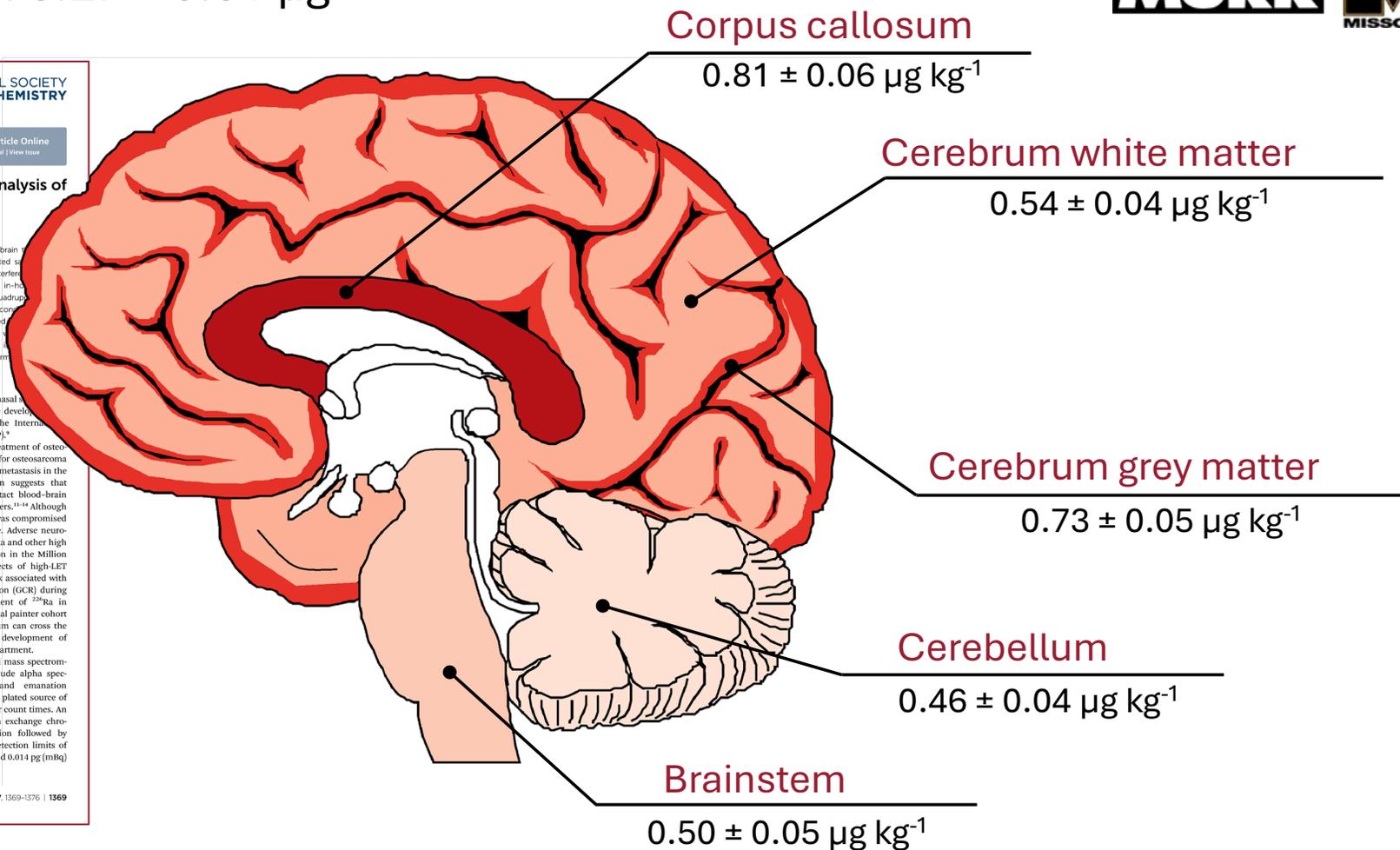
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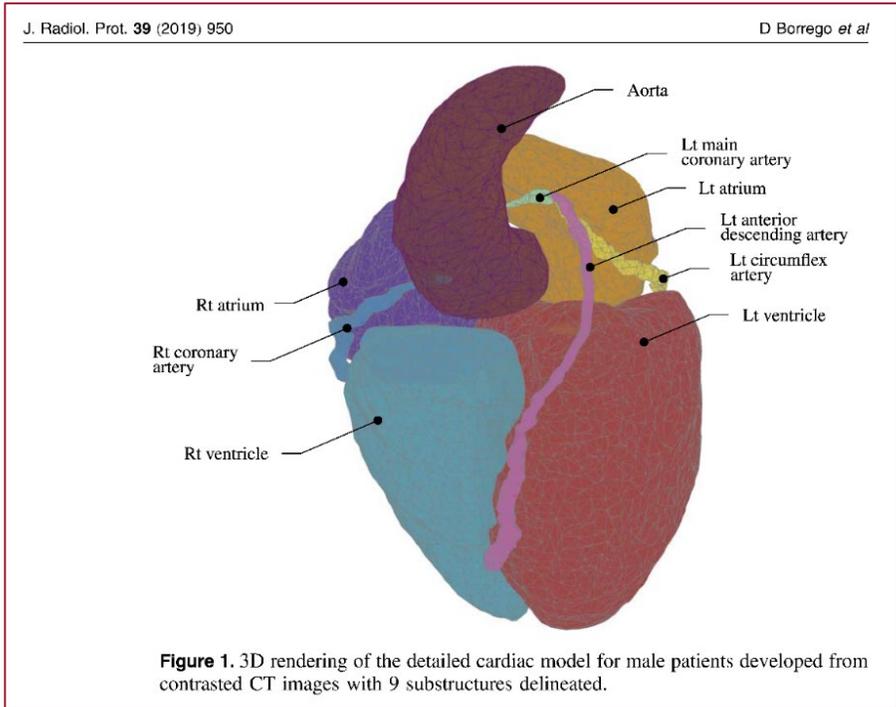
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^{239}Pu and ^{226}Ra Distribution in Human Heart



National Council on Radiation Protection and Measurements



- Systemic Pu ($n=7$): $<2 - 33$ nCi
- Ra uptake ($n=2$): $<0.004, 272.7$ μCi



Occupational Uranium in Human Tissues

Binary mixture: $f = \frac{R_{Tissue} - R_{NU}}{R_{Material} - R_{NU}}$

Case 1028: Highly enriched U_3O_8

Radiation and Environmental Biophysics
<https://doi.org/10.1007/s00411-023-01053-0>

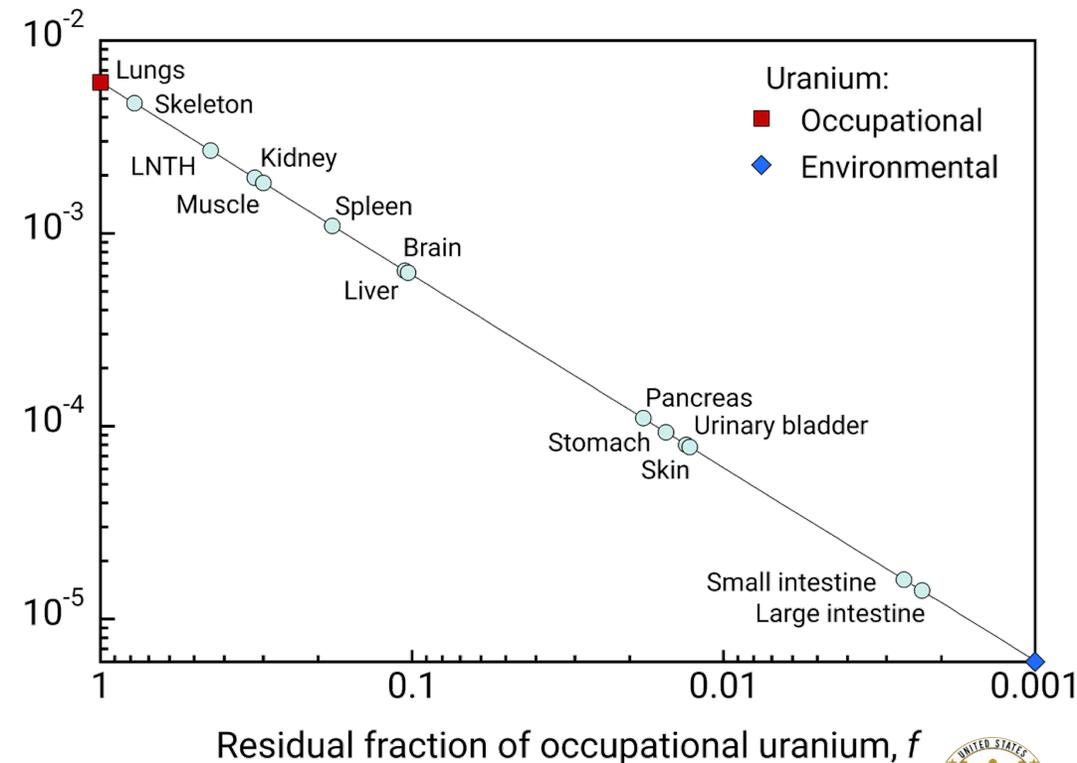
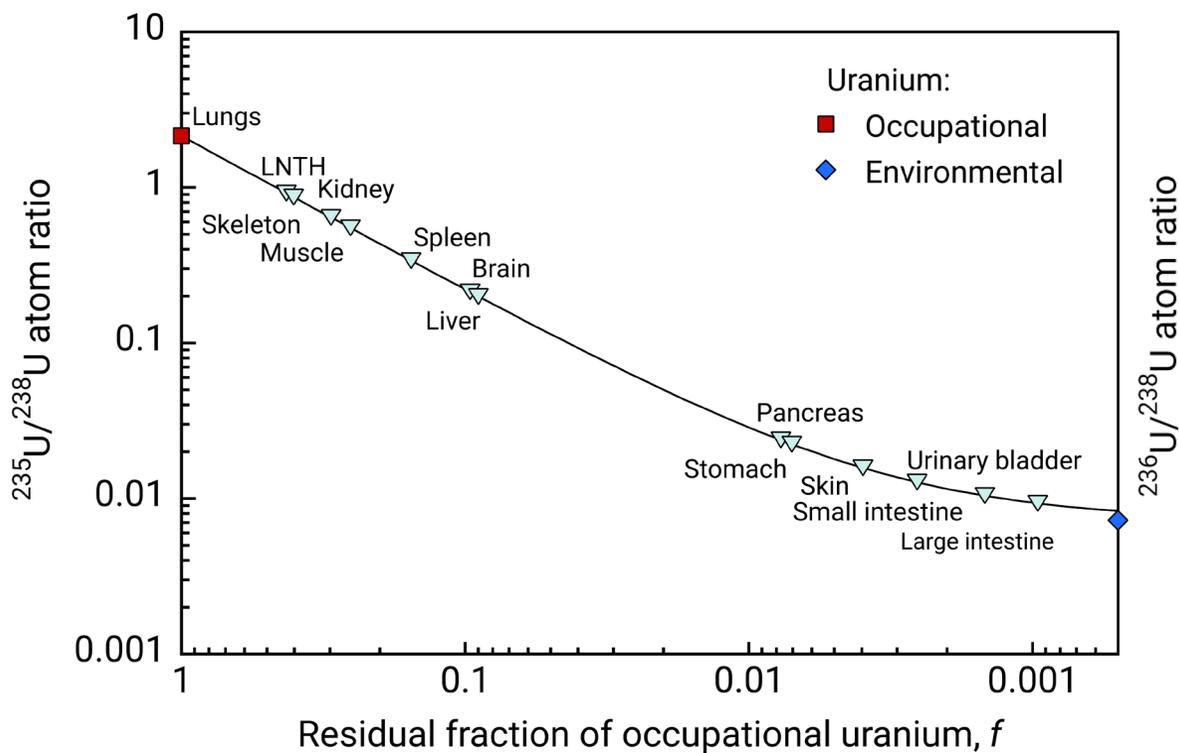
RESEARCH

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Long-term retention and distribution of highly enriched uranium in an occupationally exposed female

Sergey Y. Tolmachev¹ · Maia Avtandilashvili¹

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Faculty Research Interests

Drug Discovery and Delivery
(Nanomedicine, Medicinal Chemistry)

Translational Pharmacology and Toxicology
(Drug-natural product interaction, PBPK, Metabolism, xenobiotics)

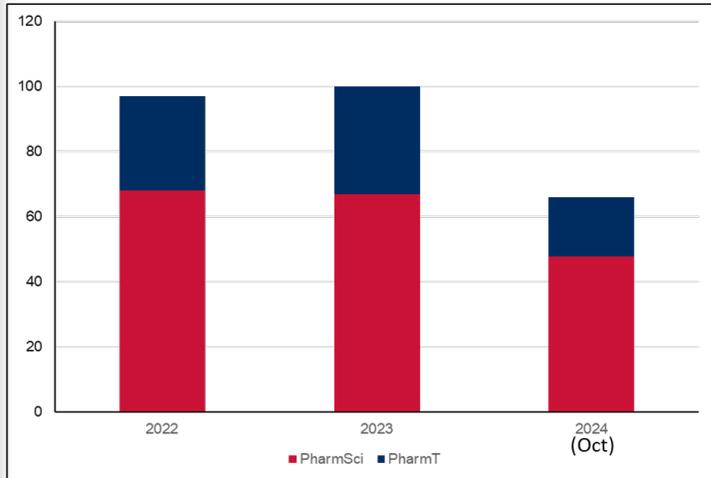
Molecular Pharmacology
(Computational modeling, GPCRs)

Inflammatory Diseases
(CVD, Stroke, Arthritis, Immunotoxicology)

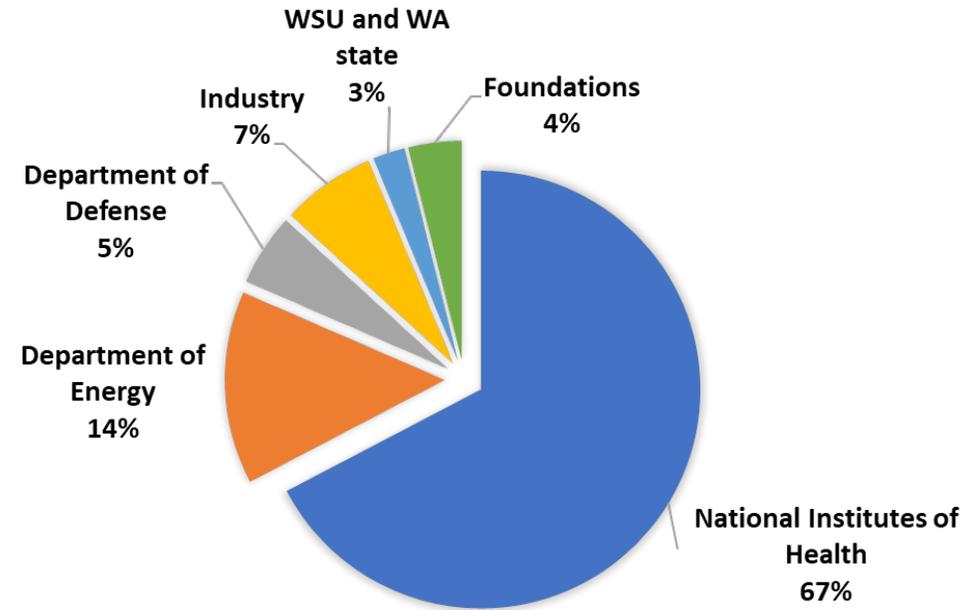
Cancer Biology
(Telomerase repression, tumor-stromal interactions, environmental carcinogens)

High Impact Publications

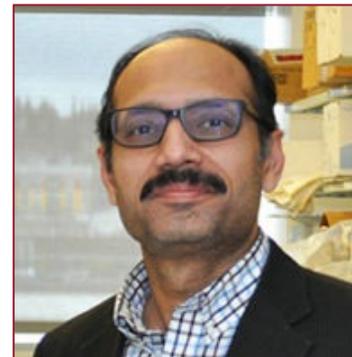
Number of Publications by CPPS Faculty and Students



\$8-10 million: Annual Grant Funding
81%: PIs awarded federal grants



For more information on collaborations and research reach out to:



Salah Ahmed
Associate Dean of Research & Graduate Education
Professor, Pharmaceutical Sciences
salah.ahmed@wsu.edu



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- GPA of 3.0 or higher (out of 4.0)
- 3 letters of recommendation
- Statement of Purpose which should include:
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 - Why they are interested in attending our program
 - A description of their research experience, if any.
 - Include the names of our faculty members whose research interests them
 - Note: this is broken out in the application
- Transcripts
 - Unofficial transcript is acceptable for application review process.
 - If attended WSU, transcripts not needed
- International students: must meet Graduate School's minimum English language proficiency (see website)
<https://gradschool.wsu.edu/international-requirements/>

<https://gradschool.wsu.edu/degrees/doctor-of-philosophy-pharmaceutical-sciences/>

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