The United States Transuranium and Uranium Registries: Fifty-year History of Actinide Biokinetic Research

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“Learning from Plutonium and Uranium Workers”
U.S. Transuranium and Uranium Registries: History and Mission
Early Autopsy Studies

Hanford, WA
Rocky Flats, CO
Los Alamos, NM

http://kurashiconcier.com

12th International Conference on the Health Effects of Incorporated Radionuclides
U.S. AEC 1966 Meeting on Plutonium Contamination in Man (Rocky Flats Plant)
National Plutonium Registry: 1968 Advisory Committee Meeting

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

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Genealogy of the USTUR

**Registries Management**

- **1968**: National Plutonium Registry
  - Hanford Environmental Health Foundation

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

- **1971**

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

- **1987**

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

**Analytical Support**

- 1968: Rocky Flats Facility
- 1970: Pacific Northwest Laboratory
  - Los Alamos Scientific Laboratory

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USTUR Today

• The United State Transuranium and Uranium Registries (USTUR) is a federal-grant program funded by the U.S. DOE Office of Domestic and International Health Studies (AU-13)

• Operated by College of Pharmacy and Pharmaceutical Sciences at Washington State University under Central DOE Institutional Review Boards

• Budget: $5,500,000 (April 1, 2017 – March 31, 2022)

• Faculty and staff:

• Location: Richland, WA

• Website: www.ustur.wsu.edu
Current 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 general public
USTUR Registrants
USTUR Registrants (I)

- Voluntary tissue donors (posthumous)
- Documented radiation exposure and work history
- Acceptance criteria:
  i. actinide internal deposition of $\geq 74$ Bq (2 nCi)
  ii. external dose to whole body $\geq 0.1$ Sv (10 rem)
USTUR Registrants (II)

- Voluntary tissue donors (posthumous) whole- (46) and/or partial-body (310) donation
- Former nuclear workers from DOE sites
Primary Intakes

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Unique Data Resource

USTUR data

- Work history
- Exposure records
- Medical records
- Bioassay measurements
- Tissue analysis results

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Tissue Analysis: Backbone of the USTUR

- Drying/Ashing
- Digestion/Dissolution
- Actinide separation
- Measurement $\alpha$- or mass spectrometry

- 300 – 400 tissue analysis for Pu/Am and U per year
Plutonium in Tissues of USTUR Donors

$^{239,240}_{\text{Pu}}$ activity concentration (Bq kg$^{-1}$)

Percent

$\text{LNTH (n=274)}$

$\text{Lung (n=297)}$

$\text{Liver (n=294)}$

$\text{Skeleton (262)}$

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National Human Radiobiology Tissue Repository (NHRTR)

- USTUR tissue donations: 9,000+ frozen tissues
- Argonne National Laboratory (ANL) historical samples
  - Radium dial painters
  - Plutonium injection studies
- Los Alamos National Laboratory (LANL) population studies
Historical Landmarks
First Whole-Body Donation: Case 0102

- Worked with unsealed $^{241}\text{Am}$ source for 2 years
- $^{241}\text{Am}$ 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
The Atomic Man: Case 0246

Largest recorded Am intake !!!

- Explosion of ion-exchange column with ~150 g of $^{241}$Am
- Estimated uptake > 40 MBq
- Extensive Ca/Zn-DTPA chelation therapy
- Systemic deposition after treatment – 0.5 MBq
Thorotrast Study: Case 1001

- First study of thorium distribution in a human body
- Female whole-body donor
- Medical exposure to Thorotrast® ($^{232}$ThO$_2$ colloidal)

- Findings
  - Alpha risk coefficients for liver, skeleton, and leukemia
  - Spleen destruction
  - Clarified epidemiologic studies
  - DNA analysis: deleted region of $c$-$fms$ gene, possibly radiation induced
Current Research and Collaborations
Primary Research: Biokinetic Modeling and Internal Dosimetry of Actinides

• Testing, improving and parameterizing biokinetic models for radiological protection
  ✓ Human Respiratory Tract Model (ICRP 130)
  ✓ Wound Model (NCRP 156)
  ✓ Systemic models for U, Pu, Am (ICRP OIR3 & OIR4)

• Evaluating uncertainties in internal radiation dose assessment

• Modeling actinide decorporation

USTUR Presentations

I. Avtandilashvili and Tolmachev. Biokinetics of soluble plutonium after wound injury treated with Ca-DTPA

II. Leggett et al. Case studies in brain dosimetry for internal emitters: Is more detail needed for epidemiology?

III. Tolmachev et al. USTUR: Expanding horizons for actinide biokinetics and dosimetry

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IMBA Professional Plus® Software

- Developed: ACJ & Associates (USA) and Health Protection Agency (UK)
- Funded: U.S. DOE, COG, and NIOSH

Dr. Anthony James
WSU/USTUR, Research Professor & Director

Dr. Alan Birchall
WSU/USTUR
Adjunct Professor

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Human Respiratory Tract Model: Plutonium Bound Fraction

- Bound material fraction: $f_b$
- ICRP 66, ICRP130 HRTM: $f_b = 0$
- OIR Part 4 (upcoming): $f_b = 0.002$
Soluble $^{239}$Pu Retention in Lungs: $f_b = 0$
Soluble $^{239}\text{Pu}$ Retention in Lungs: $f_b = 0.007$

Increase in lung dose: 600%
Uranium Hexafluoride Inhalation

- Acute inhalation due to massive explosion of UF$_6$ tank
- Slightly enriched U retained in lungs 65 y post-intake


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New System of Models for Plutonium Decorporation

Assumptions

- Chelation in extra-cellular fluid, liver, and skeleton in addition to chelation in blood
- Same model structure for the injected Ca-DTPA and Pu-DTPA chelate
- Different kinetics for Ca-DTPA and Pu-DTPA

Dumit et al. Radiation Research (submitted); 2018.
Collaborative Research Network

- Actinide biokinetic modeling and dosimetry
- Chelation therapy modeling
- Radiation biomarkers
- Nuclear forensics
- Actinide nanoparticles
- Beryllium and zirconium

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USTUR Scientific Contributions
Contribution to National Council on Radiation Protection and Measurements

Contribution to International Commission on Radiological Protection

- Occupational Intakes of Radionuclides - Part 4 (upcoming)
- Publication 137: Occupational Intakes of Radionuclides - Part 3 (2017)
- Publication 70: Basic Anatomical & Physiological Data for Use in Radiological Protection - The Skeleton (1995)
- Publication 69: Age-dependent Doses to Members of the Public from Intake of Radionuclides - Part 3 Ingestion Dose Coefficients (1995)
- Publication 67: Age-dependent Doses to Members of the Public from Intake of Radionuclides - Part 2 Ingestion Dose Coefficients (1993)
- Publication 56: Age-dependent Doses to Members of the Public from Intake of Radionuclides - Part 1 (1989)
Health Physics Journal Special Issues

- 2019, upcoming: The United States Transuranium and Uranium Registries (USTUR): Five Decade Follow-up of Plutonium and Uranium Workers
- 1992, 63 (1): Total-body Evaluation of a Thorotrast Patient
- 1985, 49 (4): The U.S. Transuranium Registry Report on the $^{241}$Am Content of a Whole Body
MODELING THE SKELETON WEIGHT OF AN ADULT CAUCASIAN MAN

THE IMPORTANCE AND QUANTIFICATION OF PLUTONIUM BINDING IN HUMAN LUNGS

EVALUATING PLUTONIUM INTAKE AND RADIATION DOSE FOLLOWING EXTENSIVE CLEIATION TREATMENT

THE PSEUDO-PELGER HÜET CELL AS A RETROSPECTIVE DOSIMETER: ANALYSIS OF A RADIUM DIAL PAINTER COHORT

INTRODUCTION

Analysis of peripheral blood smears from a group of former radium dial painters and ancillary personnel in the radium industry points to the existence of a long-term biomarker for radionuclide exposure. In this study, radium dial painters were examined in peripheral blood slides from a cohort of 166 former radium dial painters and ancillary personnel in the radium dial industry, 35 of whom had a narrow dose of zero above background. Members of the radium dial painter cohort ingested 226Ra and 228Ra at an early age (average age 26.6 ± 5.4 y; range 13–40 y) during the years 1914–1955. Exposure duration ranged from 1.820 wk with narrow dose 1.5–6,750 mGy. Pseudo-Pelger-Hüet anomaly was expressed as a percentage of total neutrophils in this cohort and varied with decades of exposure. As subjects in this cohort eventually developed malignancies, five osteosarcomas and one myeloblastic acute lymphoblastic leukemia. The pseudo-Pelger-Hüet anomaly percentage in these cases of neutrophil increases with narrow dose and is best fit with a sigmoid function, suggestive of a threshold effect. No sarcomas are seen for a narrow dose under 2 Gy. These results indicate that pseudo-Pelger-Hüet anomaly in peripheral blood is a reasonable surrogate for the estimation of alpha dose to bone marrow in historic radiation cases. Hypothesis are discussed to explain late (months to years), early (hours to days), and intermediate (weeks to months) effects of ionizing radiation, respectively, on the expression of genes encoding inner nuclear membrane proteins and their receptors, on the structure and function of nuclear membrane proteins and lipids, and on cytokines through chromatin bridging formation.

Key words: biocentimeter; dial painter dosimetry; biomarker; radium dosimetry
USTUR: Take Home Message

• In-depth study of actinide biokinetics and tissue dosimetry
• Unique resource of data and preserved tissue materials from former nuclear workers
• Significant contributor to national and international radiation protection advisory bodies
• 50 years of research funded by U.S. DOE
Acknowledgment
Questions?

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