U.S. Transuranium and Uranium Registries: 50 Years of Research Relevant to New Biomarker

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“Learning from Plutonium and Uranium Workers”
Disclaimer

United States Transuranium and Uranium Registries (USTUR):

• is not an epidemiological study
• focuses on actinide biokinetics and dosimetry
• supports biodosimetry research
History and Mission

• 1966: U.S. AEC meeting “Plutonium Contamination in Man”
Follow up occupationally exposed workers, from exposure through full lifespan, by studying the biokinetics (uptake, translocation, retention, and excretion), and dosimetry of the actinides

• 1968: National Plutonium Registry established at the Hanford Environmental Health Foundation (HEHF)

• 1978: U.S. Uranium Registry established at the HEHF

• 1990: Two programs merged into the U.S. Transuranium and Uranium Registries (USTUR)

• 1992: U.S. Department of Energy (DOE) grant to Washington State University for the management and operation of the USTUR
National Plutonium Registry: U.S. AEC Vision

REACT/TS Special Session at 62nd Annual Meeting of the Health Physics Society
National Plutonium Registry: Blue Ribbon Committee

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

REACT/TS Special Session at 62nd Annual Meeting of the Health Physics Society
Genealogy of the USTUR

**Registries Management**

1968  National Plutonium Registry at Hanford Environmental Health Foundation

1970  United States Transuranium Registry

1971  

1978  United States Uranium Registry at Hanford Environmental Health Foundation

1987-90  

1992  United States Transuranium and Uranium Registries at College of Pharmacy, Washington State University

**Analytical Support**

1968  Rocky Flats Facility

1970  Pacific Northwest Laboratory

1971  

1978  Los Alamos National Laboratory

1987-90  

1992  

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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 at Washington State University under Human Subject Internal Review Board #11573-016

✓ Grant period: April 1, 2017 – March 31, 2022
✓ Annual budget: $1,100,000
✓ Personnel: 6.0
✓ DOE Program Manager: Dr. Joey Zhou
✓ Location: Richland, WA
✓ Website: www.ustur.wsu.edu
USTUR Registrants

• Voluntary tissue donors (posthumous): whole- and/or partial-body donation

• Former nuclear workers from DOE sites

• Documented radiation exposure and work history

• Acceptance criteria:
  i. actinide internal deposition of ≥74 Bq (2 nCi)
  ii. external dose to whole body ≥0.1 Sv (10 rem)
Primary Exposure

- Pu-238,239: 75.1%
- Am-241: 15.3%
- U-235,238: 1.2%
- Th-232 (Thorotrast): 1.2%
- Others

- Inhalation: 51.8%
- Wound: 19.8%
- Inhalation/Wound: 19.8%
- Injection: 7.2%
- No Recorded Intake
Registrant Statistics

- Living Registrants: 42
  Whole-body donors: 7
  Partial-body donors: 35
- Deceased Registrants: 349
  Whole-body donors: 44
  Partial-body donors: 305
- Total:
  13
  378
### USTUR Demographics: Age

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Whole-Body</th>
<th>Partial-Body</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Living</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>81±10</td>
<td>83±11</td>
</tr>
<tr>
<td>Median</td>
<td>80</td>
<td>85</td>
</tr>
<tr>
<td>Range</td>
<td>65 – 92</td>
<td>46 – 96</td>
</tr>
<tr>
<td><strong>Deceased</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>78±12</td>
<td>68±12</td>
</tr>
<tr>
<td>Median</td>
<td>81</td>
<td>68</td>
</tr>
<tr>
<td>Range</td>
<td>49 – 98</td>
<td>25 – 96</td>
</tr>
</tbody>
</table>
NHRTR: National Human Radiobiology Tissue Repository

- Established in 1992
- Resources for radiation dosimetry and biological effects studies

✓ USTUR frozen-tissue collection:
NHRTR: Other Collections

- U.S. Radium Studies: *frozen tissues; dry/plastic-embedded bones, pathology slides, blood smears*

- Los Alamos Autopsy Tissue Study: *acid-digested tissues*

- Plutonium Injection Studies: *dry/plastic-embedded bones*
Inside the NHRTR
REAC/TS: Pelger-Huët Anomaly in Blood Cells

Study of Radium Dial Painters

- Internal exposure to $^{226}$Ra and $^{228}$Ra
- Exposure in 1915 – 1925
- Exposure for 4 – 208 weeks
- Bone marrow dose of 0.1 – 3,400 cGy
- Peripheral blood slides prepared in 1970 – 1975
- Available at USTUR/NHRTR in 2015

Permanent radiation biomarker
Tissue Materials: How to Request

- Provide a brief summary of the sample usage
- Sign a confidentiality statement
- Provide a copy of Institutional Review Board approval for protection of human subject
Primary Research: Biokinetic Modeling and Dosimetry of Actinides

Model development, validation, and parameterization

- Inhalation
  1. Americium Oxide (AmO$_2$)
  2. Plutonium Oxide (PuO$_2$)
  3. Plutonium Nitrate [Pu(NO$_3$)$_4$]
  4. Uranium Hexafluoride (UF$_6$)

- Wound
  1. Americium Nitrate [Am(NO$_3$)$_3$]
  2. Plutonium Nitrate [Pu(NO$_3$)$_4$]
  3. Plutonium Oxide (PuO$_2$)

- Ca-EDTA/DTPA Chelation
  1. Americium Oxide (AmO$_2$)
  2. Plutonium Nitrate [Pu(NO$_3$)$_4$]

WPM-C.4: Enhancement of Plutonium Excretion Following Late Ca-EDTA/DTPA Treatment

Courtesy of W.J. Bair
IMBA Professional Plus® Software

IMBA: Integrated Modules for Bioassay Analysis

• A suite of software modules for internal dosimetry

• Implements all current ICRP biokinetic and dosimetric models

• Enables the user to:
  i. assess an intake from bioassay measurement data
  ii. predict bioassay quantities from a specific intake
  iii. calculate resulting doses
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

Distribution of IMBA Professional Plus (IPP) around the world

Key
- IPP
- Academic
Tissue Analysis: Backbone of the USTUR

Drying/Ashing

Digestion/Dissolution

Actinide separation

Measurement $\alpha$- or mass spectrometry
WPM-C.2: Plutonium in Tissues of Occupationally Exposed Individuals

REACT/TS Special Session at 62nd Annual Meeting of the Health Physics Society
Health Physics Special Sessions/Issues

- 2016, Special Session: 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
Contribution to National Council on Radiation Protection & Measurements

Contribution to International Commission on Radiological Protection (ICRP)

- Occupational Intakes of Radionuclides - Part 4 (upcoming)
- 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)
USTUR Research and Collaborations

- Actinide Biokinetic Modeling and Dosimetry
- Chelation Therapy Modeling
- Quantitative Microdosimetry
- Radiation Biomarkers
- Actinide Nanoparticles
- Beryllium and Zirconium in Man
USTUR: Take Home Message

• In-depth study of actinide biokinetics and dosimetry
• Unique resource of data from former nuclear workers
• Obtain, analyze, and preserve tissue samples for future research
• Significant impact on national and international radiation protection advisory bodies
• 50-y research funded by U.S. DOE
Questions?

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