The National Human Radiobiology Tissue Repository – tissue collection at the USTUR –

Sergey Y. Tolmachev and Stacey L. McComish

US Transuranium and Uranium Registries
College of Pharmacy, Washington State University

1845 Terminal Drive, Suite 201, Richland, WA 99354
www.ustur.wsu.edu

“Learning from Plutonium and Uranium Workers”
What is USTUR?
History and Mission

• 1968: National Plutonium Registry established at the Hanford Environmental Health Foundation (HEHF)
  Follow up occupationally exposed workers, from exposure through full lifespan, by studying the biokinetics (uptake, translocation and retention), and tissue dosimetry of the actinides
• 1970: Name changed to the US Transuranium Registry (USTR)
• 1978: US Uranium Registry established at the HEHF
• 1987: Two programs merged into the US Transuranium and Uranium Registries (USTUR)
• 1992: DOE grant to Washington State University for the management and operation of the USTUR
• 1992: Creation of National Human Radiobiology Tissue Repository (NHRTR)
USTUR Registrants

• Voluntary Tissue Donors (Posthumous)
  
  *Whole-body Donors*
  
  *Partial-body Donors*

• Former Nuclear Workers from DOE Sites

• Documented Radiation Exposure and Work History

• Exposure Criteria:
  
  *Actinide internal deposition of ≥74 Bq (2 nCi)*
  
  *External dose to the whole body ≥0.1 Sv (10 rem)*
Registrant Statistics

• Living Registrants: 58
  Whole-body donors: 8
  Partial-body donors: 44
  Special studies†: 6
• Deceased Registrants: 347
  Whole-body donors: 42
  Partial-body donors: 300
  Special studies: 5

† - not a tissue donor

Living/Deceased Registrants
Primary Radionuclide of Exposure

- Pu-238, 239: 83.0%
- Am-241: 9.1%
- U-235, 238: 6.1%
- Th-232 (Thorotrast): 0.9%
- Others: 0.9%
Landmark: (i) 1976 Hanford $^{241}$Am Incident – ‘Atomic Man’ –

- Explosion of ion-exchange column with $\sim 150$ g $^{241}$Am ($19$ TBq = $515$ Ci)
- Chemical operator injured: acid burns, superficial cuts (face/upper body)
- Estimate of uptake > $40$ MBq ($1,080$ µCi) – Ca/Zn-DTPA chelation therapy
- Systemic deposition – $0.5$ MBq ($13$ µCi)
Landmark: (ii) 1979 First Whole-Body Donation

- Donor (radiochemist) worked with unsealed $^{241}\text{Am}$ source (1952 – 1954)
- First indication of intake was detection of $^{241}\text{Am}$ in urine sample (1958 routine surveillance program) – No chelation therapy
- Contemporary estimate of intake: $8 – 40 \text{ kBq (0.23 – 1.1 \mu Ci)}$
National Human Radiobiology Tissue Repository
NHRTR Sample Collections

• USTUR Research (1968 – present)
• Los Alamos Plutonium Autopsy Tissue Study (1959 – 1976)
• Health and Safety Laboratory Bone Program (1953 – 1959)
• Plutonium Injection Studies (1945 – 1947)

1996 – 2010: National Radiobiology Archives ➔ Northwestern University (Chicago, IL)
Inside NHRTR
USTUR Tissue Samples

- NHRR holds 8,963 frozen tissue samples from 142 donations

THEMIS Electronic Inventory Database Statistics

- Skeletal: 4,280
- Muscle + Skin + Fat: 1,910
- Respiratory + TB: 337
- Lymph Nodes: 339
- Alimentary: 338
- Circulatory: 332
- Glands: 270
- Nervous: 226
- Hepatic: 601
- Miscellaneous: 226
NHRTR: US Radium Studies

- Frozen tissues, dry/plastic-embedded bones, pathology slides

Radium Dial Painters: NJRRP $\rightarrow$ MIT $\rightarrow$ ANL/CHR

Medical exposure: therapeutic injections
NHRTR: *Los Alamos Autopsy Study*

- Acid digested tissues (acid solutions): ~2,000 samples

NHRTR: Plutonium Injection Studies

- Dry and plastic-embedded bones, urine
  
  **CAL-3:** 5.5 ng (3.5 kBq) i.m. injection $^{238}\text{Pu}^{6+}$- nitrate; M 36
  
  **CHL-1:** 6.5 µg (14.9 kBq) i.v. injection $^{239}\text{Pu}^{4+}$- citrate; M 68
  
  **HP-2:** 5.1 µg (11.7 kBq) i.v. injection $^{239}\text{Pu}^{4+}$- citrate; M 49
  
  **HP-4:** 4.9 µg (11.2 kBq) i.v. injection $^{239}\text{Pu}^{4+}$- citrate; F 18
  
  **HP-9:** 6.3 µg (14.5 kBq) i.v. injection $^{239}\text{Pu}^{4+}$- citrate; M 66
Tissue Materials: How to Request

- Provide a brief summary of the proposed sample usage
- Sign a confidentiality statement
- Provide a copy of Institutional Review Board approval for protection of human subject
USTUR Data: How to Publish

• Registries as a co-author:
  Unpublished data - bioassay, in-vivo counting, analytical results, use of tissue samples or other materials
  Collaborative effort by Registries staff

• Acknowledgment to the Registries:
  Loan or provision of tissues or other materials
  Only published Registries’ data or evaluation
  Manuscript exclusively prepared by other investigators without consulting the Registries

http://www.ustur.wsu.edu/PolicyProcedures/USTURprocedures.html
Microdistribution and Long-term Retention of $^{239}$Pu(NO$_3$)$_4$

Carcinogenic and Inflammatory Effects of $^{239}$Pu(NO$_3$)$_4$

- Analysis: to determine genetic and inflammatory response pathways following plutonium exposure
  
  *Possible pathways - tissue injury, apoptosis, and gene expression modifications*

- Immunohistochemistry: to characterize lung lesions, visualize interstitial fibrosis, and other pathology

- RT-PCR: to quantify the expression of chemokine/cytokine regulatory genes thought to be involved in inflammation and carcinogenesis
  
  *BCL-2, CASP-3, FASL, IL4, IL8 and TGFβ-1*

C. E. Nielsen et al. (2014) Int J Radiation Biology
Radionuclide Bone Microdosimetry

- Digital Autoradiography: ionizing-radiation Quantum Imaging Detector (iQID)

- Radionuclides: $^{239}$Pu, $^{226}$Ra, $^{241}$Am
  
  \[ \text{Plutonium injection study} - ^{239}\text{Pu: 14.9 kBq (0.4 \mu Ci)} \]
  \[ \text{Radium therapeutic injection} - ^{226}\text{Ra: 9.3 MBq (250.2 \mu Ci)} \]
  \[ \text{Occupational exposure} - ^{241}\text{Am: 40 MBq (1,080 \mu Ci)} \]

Actinide Elemental Bioimaging

Pu exposure: Paratracheal LN

U exposure: Parabronchial LN

Biodosimetry of Incorporated Radionuclides

- Pelger-Huët Anomaly (PHA) in blood cells


- Study of Radium Dial Painters
- Internal exposure to $^{226}$Ra and $^{228}$Ra
- Exposure in 1915 – 1925
- Exposure time 4 – 208 weeks
- Bone marrow dose 0.1 cGy – 3,400 cGy
- Peripheral blood slides prepared in 1970 – 1975
- Available at the NHRTR in 2015
New, Permanent Radiation-induced Biomarker

Pelger-Huët Anomaly: RDP 09-064; Started 1916; Exposed for 9 weeks
PHA – Marrow Dose Correlation
Thank you!
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