62nd Annual Meeting of the Health Physics Society
Raleigh, NC, July 9 - 13, 2017

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

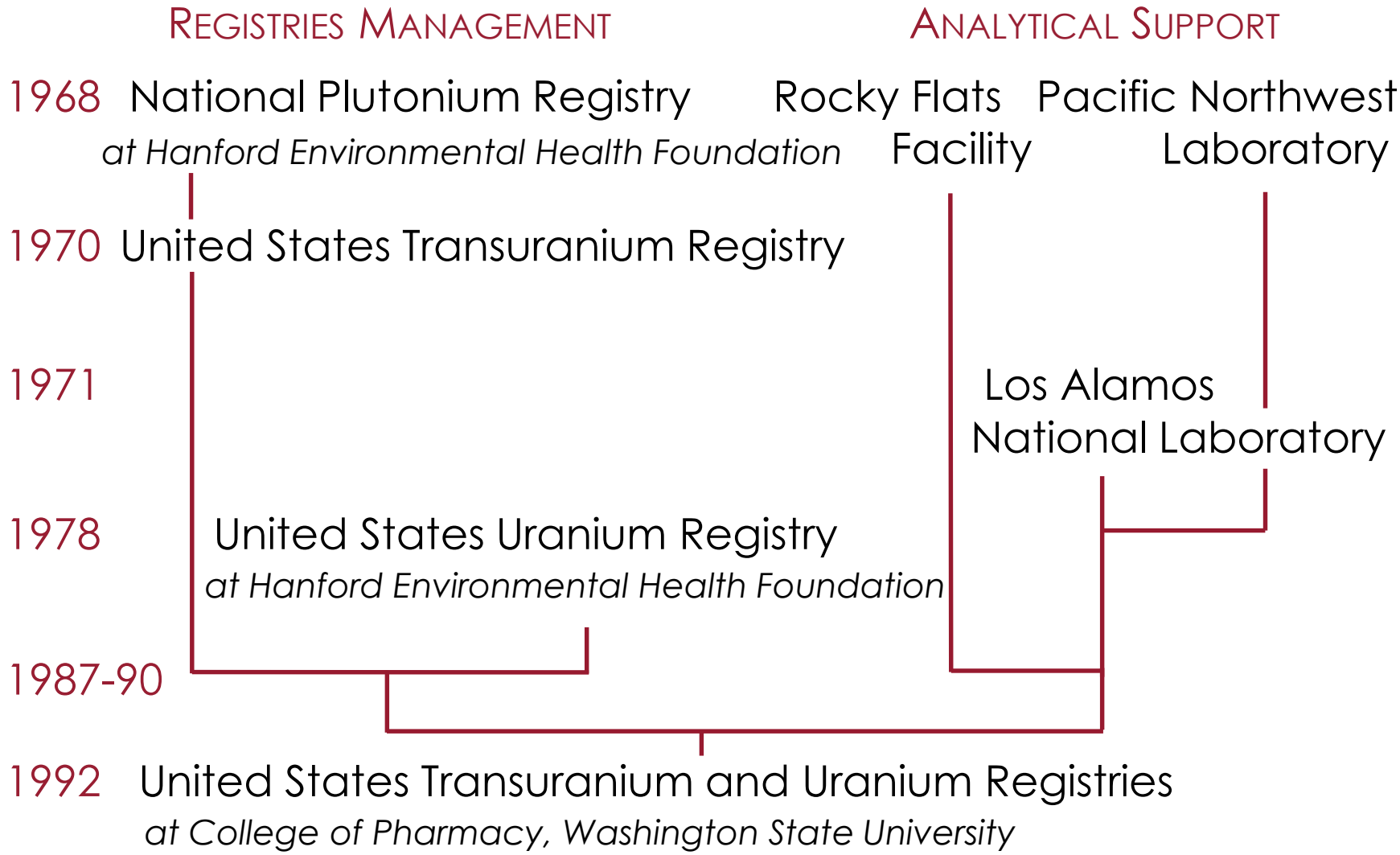
- 1968: National Plutonium Registry established at the Hanford Environmental Health Foundation (HEHF)
- 1978: U.S. Uranium Registry established at the HEHF
- 1990: Two programs merged into the U.S. Transuranium and Uranium Registries (USTUR)
- 1992: U.S. Department of Energy (DOE) grant to Washington State University for the management and operation of the USTUR

National Plutonium Registry: *U.S. AEC Vision*

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

Genealogy of the USTUR



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

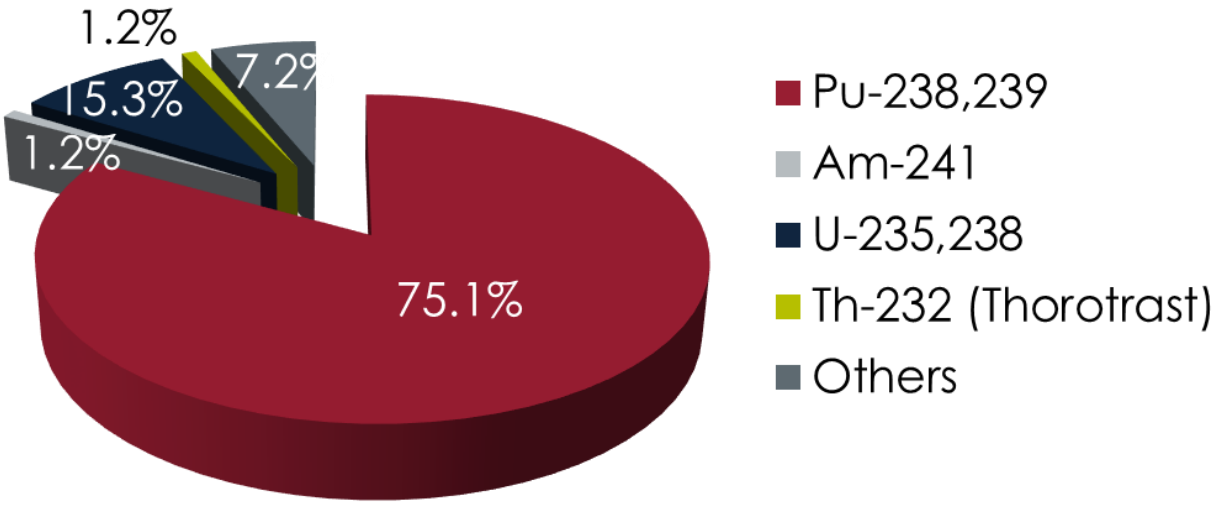
- Voluntary tissue donors (posthumous):

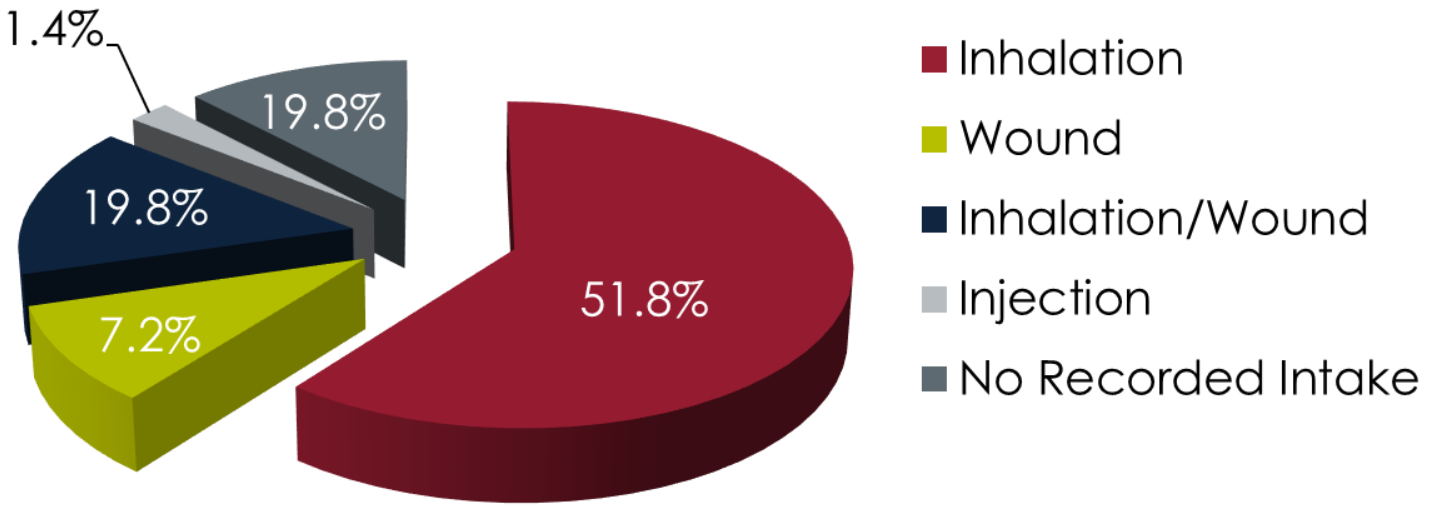
  whole- and/or partial-body donation
- Former nuclear workers from DOE sites
- Documented radiation exposure and work history
- Acceptance criteria:

  i. actinide internal deposition of ≥74 Bq (2 nCi)

  ii. external dose to whole body ≥0.1 Sv (10 rem)

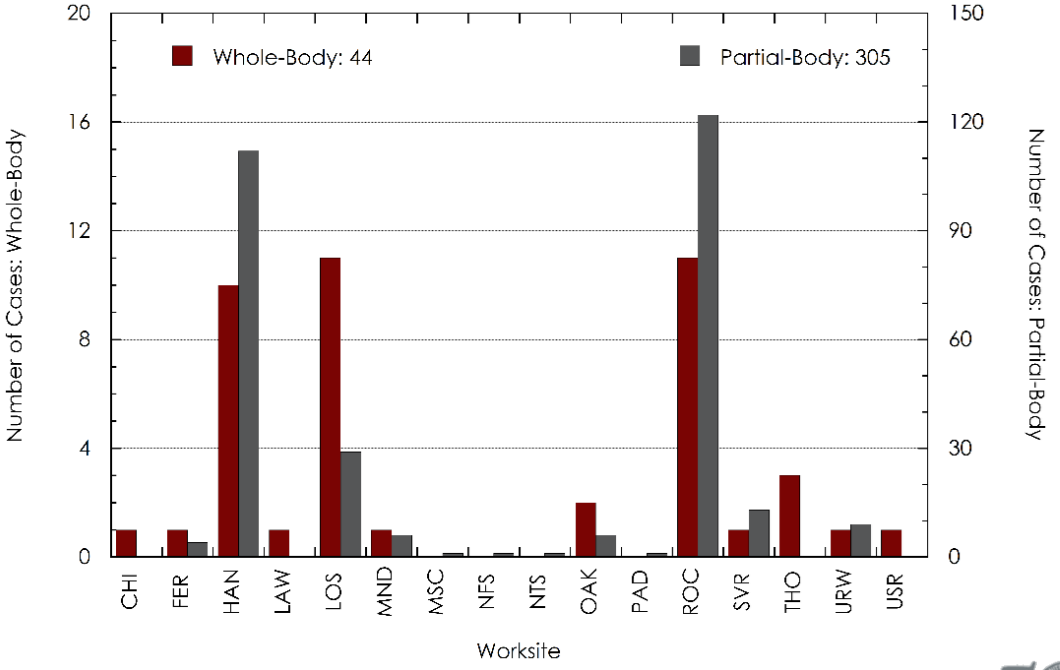
Primary Exposure





Registrant Statistics

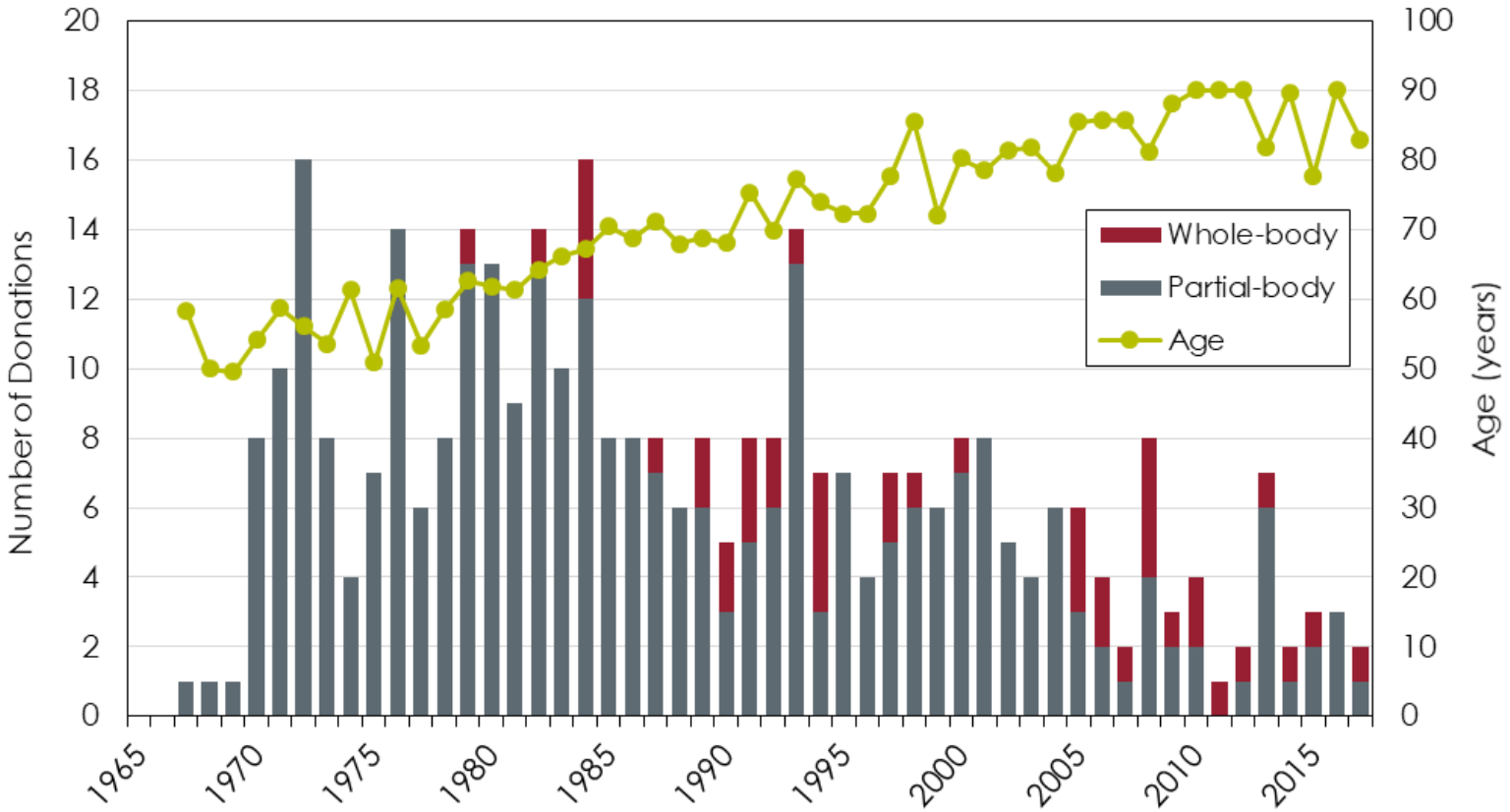
- Living Registrants: 42
  - *Whole-body donors: 7*
  - *Partial-body donors: 35*
- Deceased Registrants: 349
  - *Whole-body donors: 44*
  - *Partial-body donors: 305*
- Total:
  - 13
  - 378



USTUR Demographics: *Age*

Age (y)	Whole-Body	Partial-Body
Living		
Mean ± SD	81±10	83±11
Median	80	85
Range	65 – 92	46 – 96
Deceased		
Mean ± SD	78±12	68±12
Median	81	68
Range	49 – 98	25 – 96

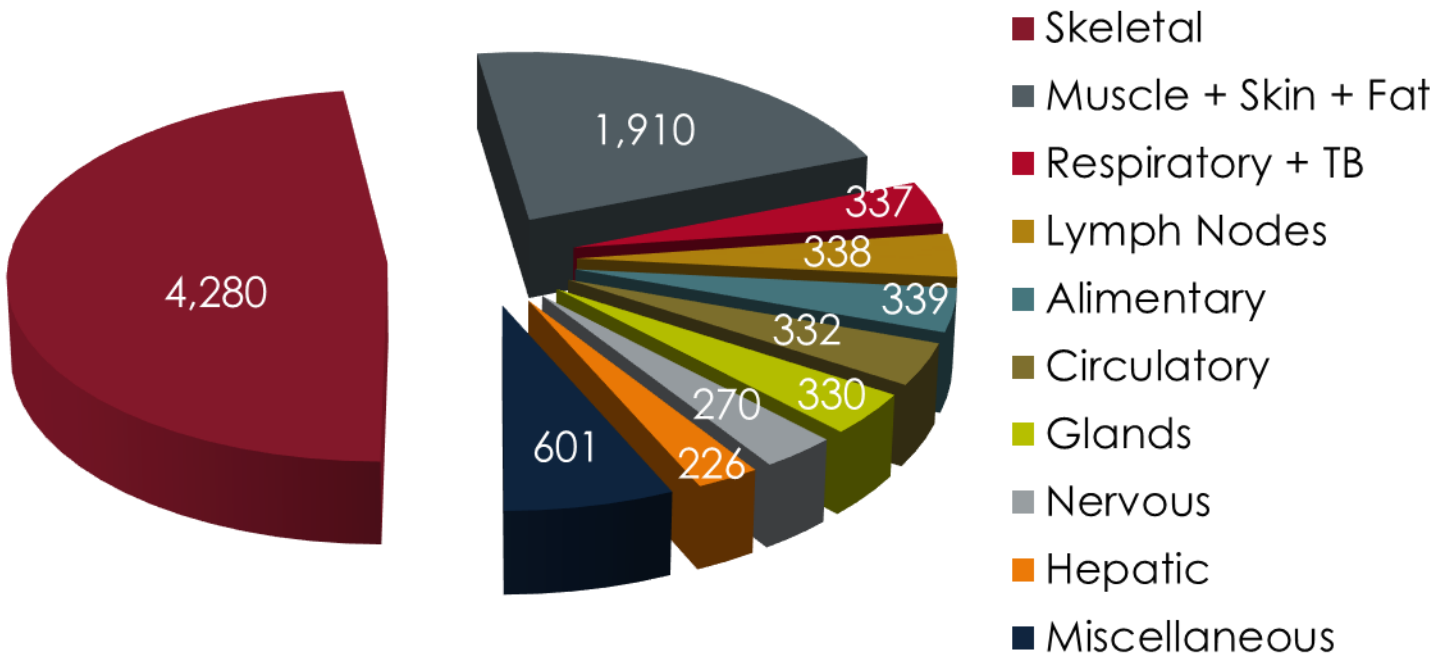
USTUR Donations



NHRTR: *National Human Radiobiology Tissue Repository*

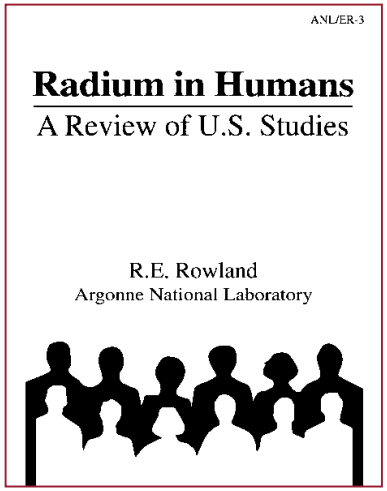
- Established in 1992
- Resources for radiation dosimetry and biological effects studies

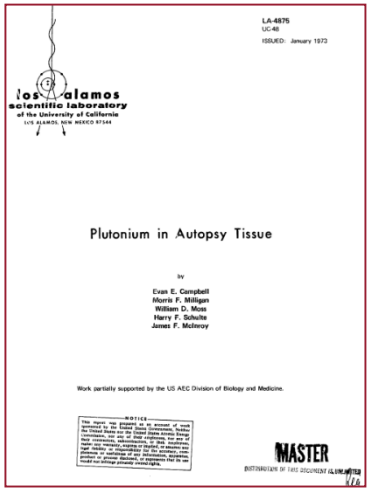
✓ USTUR frozen-tissue collection:

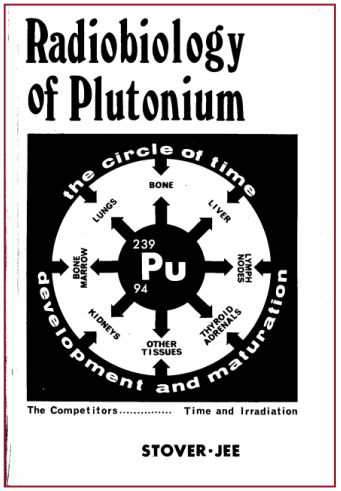


NHRTR: *Other Collections*

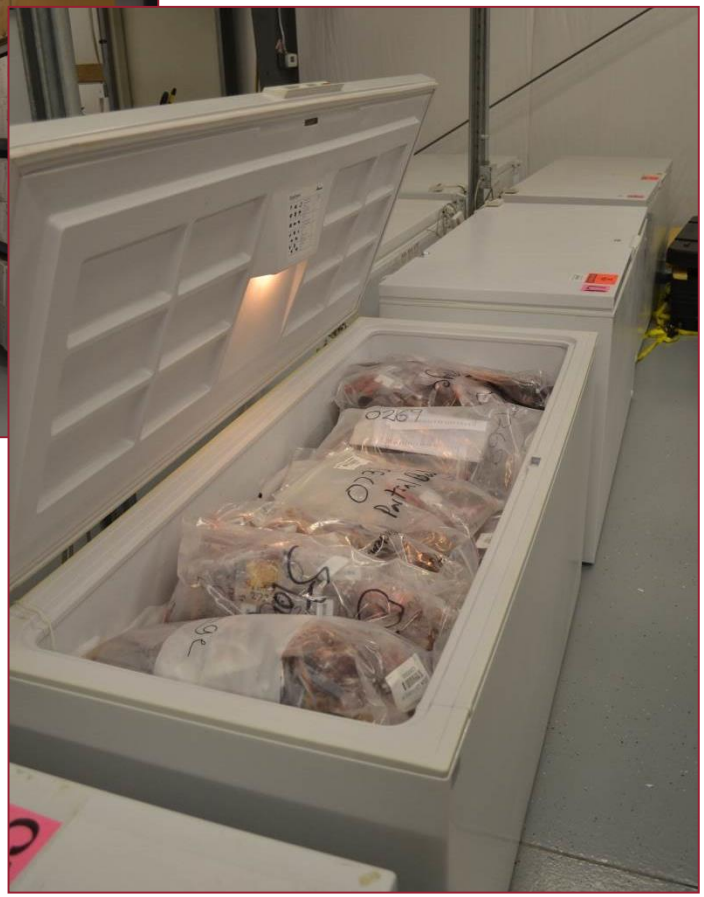
- U.S. Radium Studies: *frozen tissues; dry/plastic-embedded bones, pathology slides, blood smears*
- Los Alamos Autopsy Tissue Study: *acid-digested tissues*
- Plutonium Injection Studies: *dry/plastic-embedded bones*







Inside the NHRTR

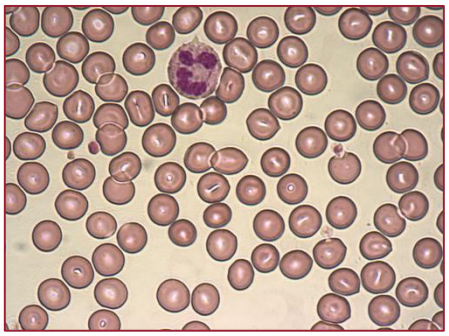


REAC/TS: *Pelger-Huët Anomaly in Blood Cells*

Study of Radium Dial Painters

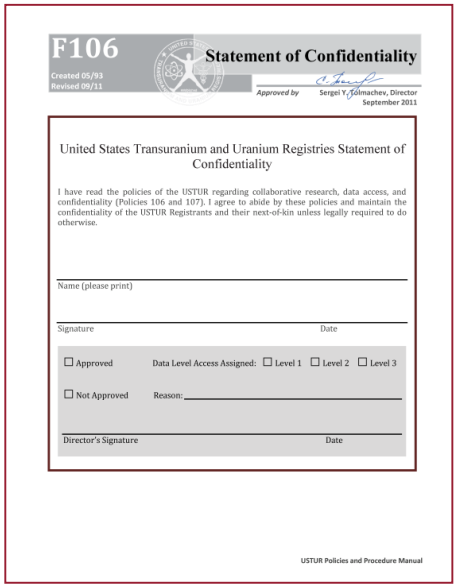
- Internal exposure to ^{226}Ra and ^{228}Ra
- Exposure in 1915 – 1925
- Exposure for 4 – 208 weeks
- Bone marrow dose of 0.1 – 3,400 cGy
- Peripheral blood slides prepared in 1970 – 1975
- Available at USTUR/NHRTR in 2015

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



F106

Created 05/93
Revised 09/11

Statement of Confidentiality

Approved by Sergei Y. Tolmachev, Director
September 2011

United States Transuranium and Uranium Registries Statement of Confidentiality

I have read the policies of the USTUR regarding collaborative research, data access, and confidentiality (Policies 106 and 107). I agree to abide by these policies and maintain the confidentiality of the USTUR Registrants and their next-of-kin unless legally required to do otherwise.

Name (please print)

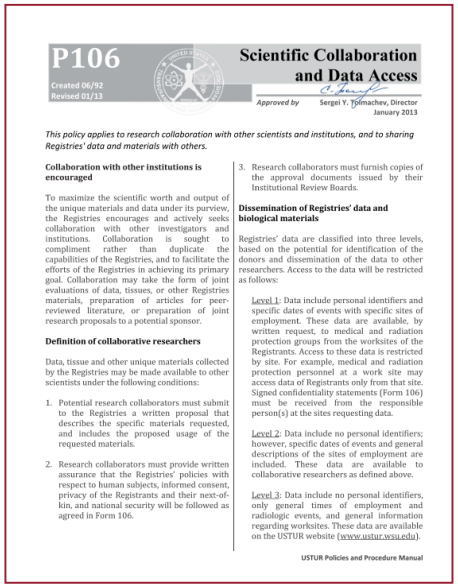
Signature Date

☐ Approved Data Level Access Assigned: ☐ Level 1 ☐ Level 2 ☐ Level 3

☐ Not Approved Reason:

Director's Signature Date

USTUR Policies and Procedure Manual



P106

Created 06/92
Revised 01/13

Scientific Collaboration and Data Access

Approved by Sergei Y. Tolmachev, Director
January 2013

This policy applies to research collaboration with other scientists and institutions, and to sharing Registries' data and materials with others.

Collaboration with other institutions is encouraged

To maximize the scientific worth and output of the unique materials and data under its purview, the Registries encourages and actively seeks collaboration with other investigators and institutions. Collaboration is sought to compliment rather than duplicate the capabilities of the Registries, and to facilitate the efforts of the Registries in achieving its primary goal. Collaboration may take the form of joint evaluations of data, tissues, or other Registries materials, preparation of articles for peer-reviewed literature, or preparation of joint research proposals to a potential sponsor.

Definition of collaborative researchers

Data, tissue and other unique materials collected by the Registries may be made available to other scientists under the following conditions:

1. Potential research collaborators must submit to the Registries a written proposal that describes the specific materials requested, and includes the proposed usage of the requested materials.
2. Research collaborators must provide written assurance that the Registries' policies with respect to human subjects, informed consent, privacy of the Registrants and their next-of-kin, and national security will be followed as agreed in Form 106.
3. Research collaborators must furnish copies of the approval documents issued by their Institutional Review Boards.

Dissemination of Registries' data and biological materials

Registries' data are classified into three levels, based on the potential for identification of the donors and dissemination of the data to other researchers. Access to the data will be restricted as follows:

Level 1: Data include personal identifiers and specific dates of events with specific sites of employment. These data are available, by written request, to medical and radiation protection groups from the worksites of the Registrants. Access to these data is restricted by site. For example, medical and radiation protection personnel at a work site may access data of Registrants only from that site. Signed confidentiality statements (Form 106) must be received from the responsible person(s) at the sites requesting data.

Level 2: Data include no personal identifiers; however, specific dates of events and general descriptions of the sites of employment are included. These data are available to collaborative researchers as defined above.

Level 3: Data include no personal identifiers, only general times of employment and radiologic events, and general information regarding worksites. These data are available on the USTUR website (www.ustur.wsu.edu).

USTUR Policies and Procedure Manual

P107

Created 06/92
Revised 09/11

Publications

Approved by Sergei Y. Tolmachev, Director
September 2011

This policy applies to all publications of the United States Transuranium and Uranium Registries. All collaborative researchers are subject to this policy.

Peer-reviewed publication of scientific findings is encouraged

It is the policy of the Registries to encourage publication of scientific findings and the associated data upon which these findings are based as expeditiously as practicable. Peer-reviewed scientific literature is the preferred vehicle for this purpose. To expedite publication further, preliminary results may be published in Registries Annual Reports, or in special topical reports.

Publication in peer-reviewed literature includes the following: articles; notes; abstracts; letters to the editor; other technical communications; or oral presentations of findings that have undergone independent review for scientific content and merit, given at scientific and technical meetings. Publication by the Registries scientific staff is encouraged, and, in keeping with the true spirit of academic freedom, does not require external or internal prior approval. The author(s) is(are) responsible for the scientific content of the publication, and for ensuring that there is no breach or violation of confidentiality, or other legal and ethical requirements.

Privacy of Rgistrants must be maintained

The USTUR has pledged confidentiality to the Registrants and their next-of-kin, and that pledge will pertain to all publications. No publicly available or open-literature publication shall be made in which Registrants are identified by name or other personal identifiers without the prior consent of the Registrant, or the legally responsible next-of-kin, unless legally required by law, regulation, or court order.

Specific dates of radiological or medical incidents, specific dates of employment, or the exact place of employment shall not be used in publications. Also, the use of specific descriptions of radiological incidents, health conditions, or causes of death should be avoided if they might assist a reader in the identification of a subject. Such information will be presented in general terms so that an individual reading the publication would be forced to perform additional research in order to identify the research subject. For example, times of events shall be stated as time (days, months, years) before or after the beginning of work, the end of work, or death. An individual might be classified as working at Rocky Flats, Hanford, or other sites, but no specific work location or employer will be identified.

Approval may be required for non-peer-reviewed publications

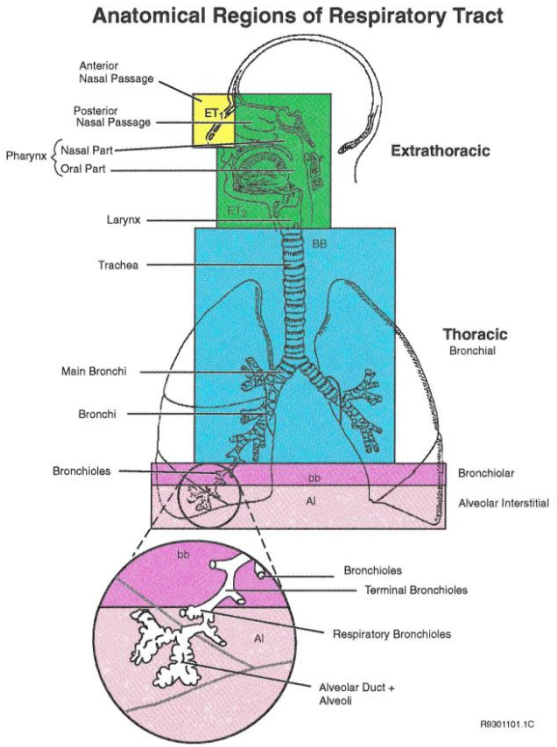
The author(s) is(are) responsible for obtaining the Registries' approval of press releases and publications that do not undergo external scientific peer review prior to release or distribution. Customarily, it is the responsibility of the senior author to obtain the approval. This should not be construed to impose any constraints on formal or informal communications between Registries staff and external persons on technical or scientific matters, and applies only to 1) documents specifying Registries policy or administrative practice, or making commitments of Registries

USTUR Policies and Procedure Manual

Primary Research: *Biokinetic Modeling and Dosimetry of Actinides*

Model development, validation, and parameterization

- Inhalation
  - i. Americium Oxide (AmO_2)
  - ii. Plutonium Oxide (PuO_2)
  - iii. Plutonium Nitrate [$Pu(NO_3)_4$]
  - iv. Uranium Hexafluoride (UF_6)
- Wound
  - i. Americium Nitrate [$Am(NO_3)_3$]
  - ii. Plutonium Nitrate [$Pu(NO_3)_4$]
  - iii. Plutonium Oxide (PuO_2)
- Ca-EDTA/DTPA Chelation
  - i. Americium Oxide (AmO_2)
  - ii. Plutonium Nitrate [$Pu(NO_3)_4$]



Courtesy of W.J. Bair

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

IMBA Professional Plus® Software

IMBA: Integrated Modules for Bioassay Analysis

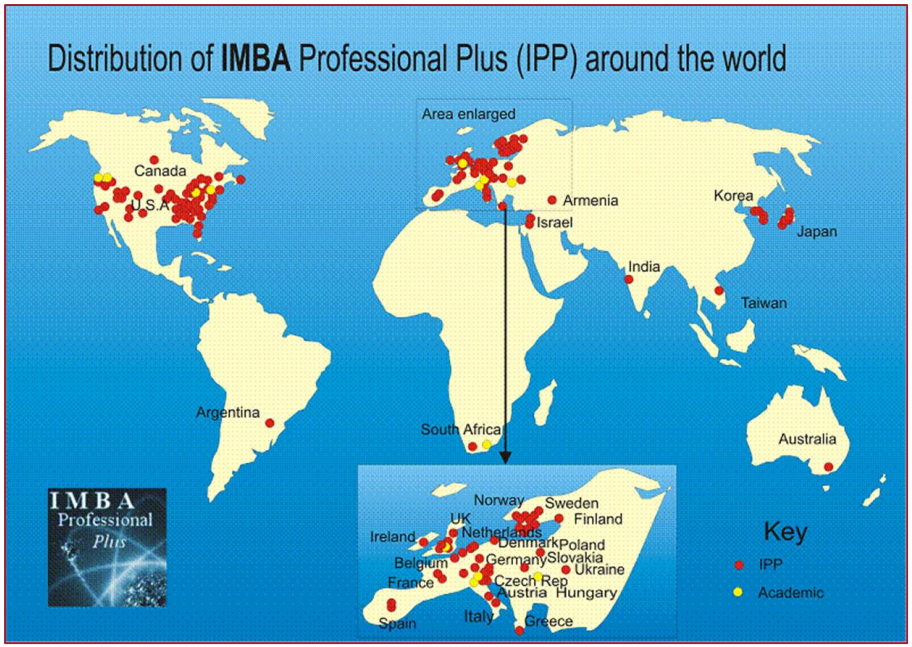
- A suite of software modules for internal dosimetry
- Implements all current ICRP biokinetic and dosimetric models
- Enables the user to:
  i. assess an intake from bioassay measurement data
  ii. predict bioassay quantities from a specific intake
  iii. calculate resulting doses

IMBA Professional Plus® Software

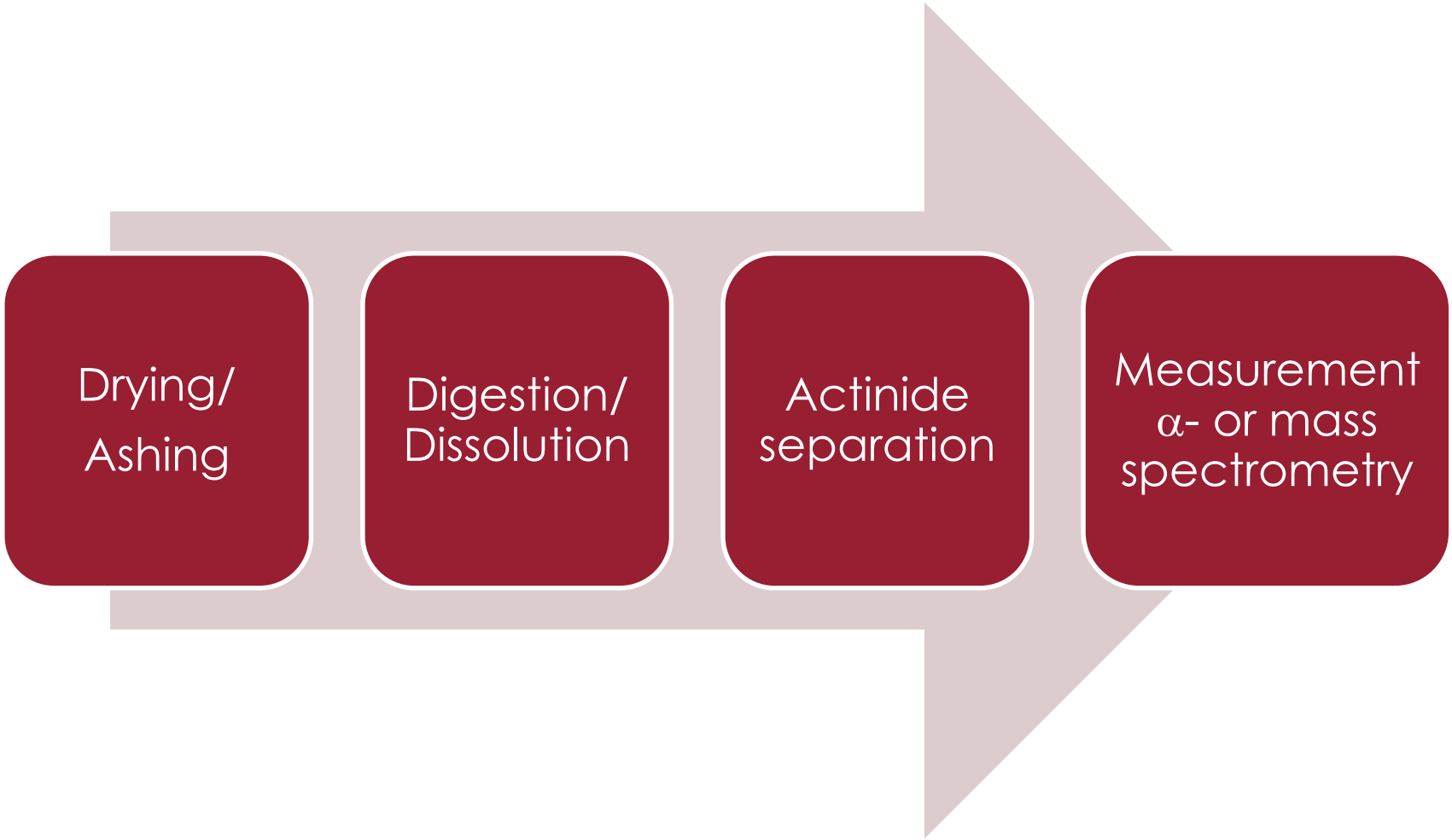
- Developed: ACJ & Associates (USA) and Health Protection Agency (UK)
- Funded: U.S. DOE, COG, and NIOSH

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

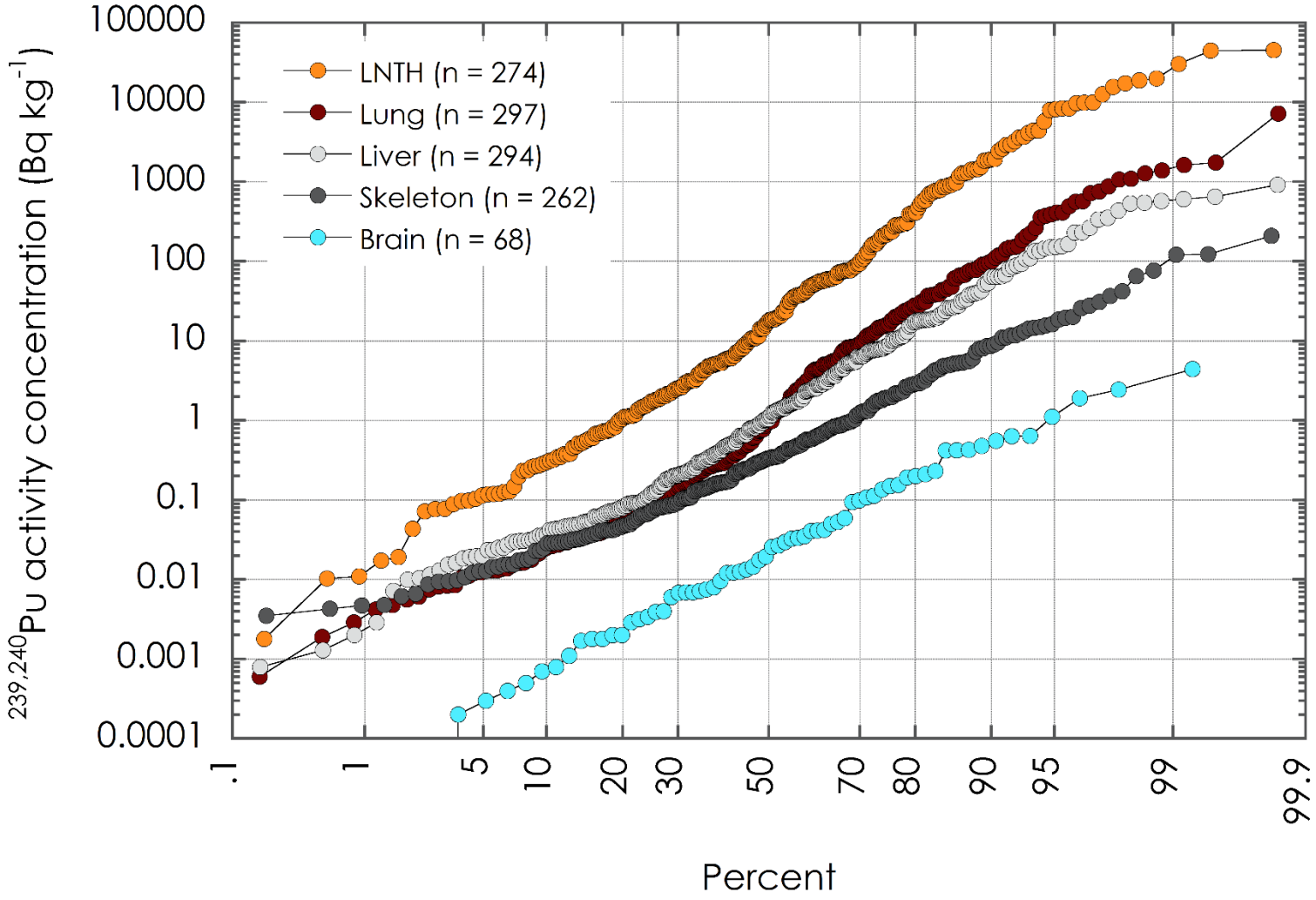
Dr. Alan Birchall
WSU/USTUR
Adjunct Professor



Tissue Analysis: *Backbone of the USTUR*



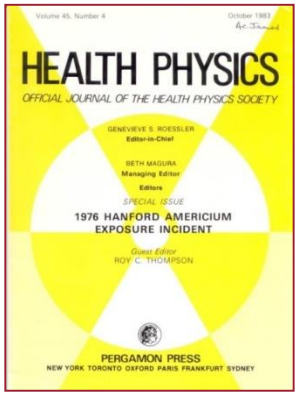
Plutonium in Tissues of USTUR Donors

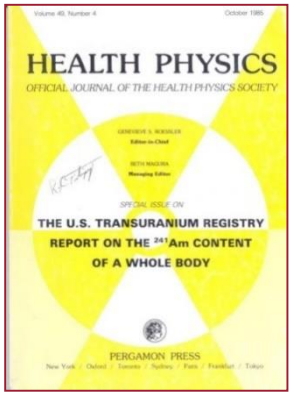


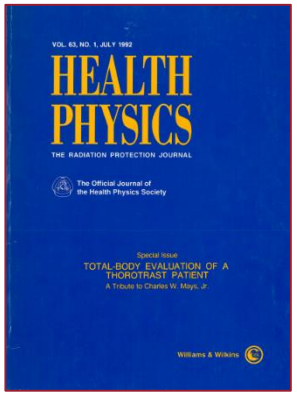
WPM-C.2: *Plutonium in Tissues of Occupationally Exposed Individuals*

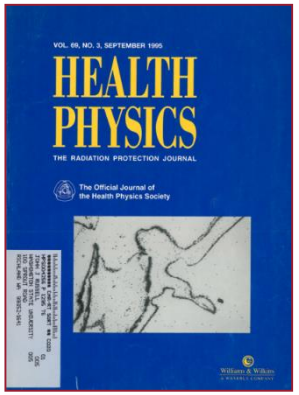
Health Physics Special Sessions/Issues

- 2016, Special Session: Five-Decade Follow-up of Plutonium and Uranium Workers
- 1995, 69 (3): 1976 Hanford Americium Exposure Incident: Update
- 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
- 1983, 45 (4): 1976 Hanford Americium Exposure Incident









Contribution to National Council on Radiation Protection & Measurements

- Report 164: Uncertainties in Internal Radiation Dose Assessment (2009)
- Report 163: Radiation Dose Reconstruction Principles and Practices (2009)
- Report 156: Development of a Biokinetic Model for Radionuclide-Contaminated Wounds for Their Assessment, Dosimetry and Treatment (2006)
- Report 135: Liver Cancer Risk from Internally-Deposited Radionuclides (2001)
- Report 128: Radionuclide Exposure of the Embryo/ Fetus (1998)

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 66: Human Respiratory Tract Model for Radiological Protection (1994)
- 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)
- Publication 48: The Metabolism of Plutonium and Related Elements (1986)

USTUR Research and Collaborations

- Actinide Biokinetic Modeling and Dosimetry
- Chelation Therapy Modeling
- Quantitative Microdosimetry
- Radiation Biomarkers
- Actinide Nanoparticles
- Beryllium and Zirconium in Man

EURADOS

react/ts

Pacific Northwest NATIONAL LABORATORY

ЮУрИБФ

Health Canada

一般財団法人 九州環境管理協会

KIT Karlsruhe Institute of Technology

UNIVERSITÉ LAVAL

Public Health England

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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