USTUR - 0501-18

United States Transuranium and Uranium Registries

Annual Report

April 1, 2017 - March 31, 2018

College of
Pharmacy
WASHINGTON STATE UNIVERSITY

USTUR - 0501-18

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April 1, 2017 - March 31, 2018

Compiled and Edited

Stacey L. McComish and Sergei Y. Tolmachev

June 2018

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USTUR

A unique resource since 1968

Learning from Plutonium and Uranium Workers
United States Transuranium and Uranium Registries
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Faculty and Staff

Faculty

Sergei Y. Tolmachev	Director
Stacey L. McComish	Associate in Research
Maia Avtandilashvili	Assistant Research Professor
George Tabatadze	Assistant Research Professor
Sara Dumit	Ph.D. Candidate

Emeritus and Adjunct Faculty

Ronald L. Kathren	Professor, Emeritus
Daniel J. Strom	Adjunct Professor

Classified Staff

Margo D. Bedell	Program Specialist II
Elizabeth M. Thomas	Laboratory Technician II

Part-time Employees

Warnick Kernan	Laboratory Assistant I
Florencio T. Martinez	Medical Technologist

Consultants

Eric Kiesel	Forensic Pathologist
Minh Pham	IT Support
Mariya Tolmachova	Technical Editor

Student Employees

Ryan Ashley	Laboratory Assistant I

Advisory Committee

Committee Chair

Roger O. McClellan	Toxicology

Committee Members

Heather J. Hoffman	Epidemiology
Timothy J. Ledbetter	Ethics
Thomas L. Rucker	Radiochemistry
Arthur W. Stange	Occupational Health
Richard E. Toohey	Health Physics (*retired*)

Contact Information

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Executive Summary

Sergei Y. Tolmachev, *USTUR Director*

This report summarizes organization, activities, and scientific accomplishments for the U.S. Transuranium and Uranium Registries (USTUR) and the associated National Human Radiobiology Tissue Repository (NHRTR) for the period of April 1, 2017 – March 31, 2018. This is the first fiscal year (FY) of the USTUR's 5-year grant proposal (April 1, 2017 – March 31, 2022).

DOE Grant Renewal

The FY2019 grant renewal proposal to manage and operate the USTUR and the associated NHRTR, during April 1, 2018 – March 31, 2019 was submitted to the Department of Energy (DOE) Office of Health and Safety (AU-10). The approved FY2019 budget amounted to $1,100,000.

Scientific Advisory Committee

The annual Scientific Advisory Committee (SAC) meeting was held August 25-26, 2017 in Richland, WA. Dr. Richard E. Toohey (SAC Chair and Health Physic Representative) retired and Dr. Roger O. McClellan agreed to chair the committee. Dr. Luiz Bertelli (Los Alamos National Laboratory) was appointed as the health physics representative effective April 1, 2018.

Organization and Personnel

Maia Avtandilashvili and George Tabatadze were promoted to the rank of Assistant Research Professor. Daniel J. Strom was appointed as an Adjunct Professor at the College of Pharmacy through the USTUR. In FY2018, 6.1 full-time equivalent (FTE) positions, including one graduate student at 0.3 FTE, were supported by the available funding. The organizational structure of the USTUR Research Center as of March 31, 2018 is provided in Appendix A.

COP Name Changed

In November 2017, the WSU Board of Regents voted to approve the College of Pharmacy (COP) name change. Beginning July 2018, COP will change its name to College of Pharmacy and Pharmaceutical Sciences (CPPS).

Graduate Research

Sara Dumit (COP Pharmaceutical Sciences Ph.D. Candidate) completed all Graduate School requirements for her doctoral dissertation. The defense of the dissertation titled "Development of a New Compartmental Model for Plutonium Decorporation" is scheduled on May 14, 2018.

Registrant Donations

Two whole-body and five-partial body donations were received by the USTUR in FY2018. As of March 31, 2018, the Registries had received 45 whole- and 309 partial-body donations.

NHRTR Inventory

Tissue samples were inventoried for only three of seven donations that were received during FY2018, due to a broken mortuary cooler and an unexpected lack of personnel. As of March 31, 2018, 9,414 tissue samples from 44 whole- and 112 partial-body donations were inventoried. These Registrants passed away between 1982 and 2018.

Radiochemistry Operation

One hundred forty-six tissue samples from one whole-body and five partial-body donations were analyzed for plutonium and americium isotopes using α-spectrometry. Radiochemical analyses of four partial-body cases were completed.

Health Physics Database

Standardization of exposure records and bioassay data for 15 partial-body cases, including 10 living and five deceased Registrants was completed. As of March 31, 2018, the database holds 116,380 data records from 211 deceased donors (45 whole-body and 166 partial-body), 20 living Registrants (six whole-body and 14 partial-body), and two special study cases.

Research Results

USTUR faculty authored two and co-authored four papers. These included two papers from the USTUR special issue of the Health Physics journal and three from a special issue of Radiation Protection Dosimetry on Mayak Worker Dosimetry System - 2013 (MWDS-2013). In addition, a member of the USTUR adjunct faculty, Dr. Alan Birchall, authored six and co-authored 12 peer-reviewed articles.

During FY2018, two invited, and six podium presentations at national and international conferences were given by the USTUR faculty and a graduate student.

Institutional Review Board

The annual Institutional Review Board (IRB) review was completed by the Central DOE IRB and the program was approved for another year.

Administrative

The annual USTUR Newsletter was sent to the Registrants and/or their next-of-kin.

Financial and Administrative Report

Margo D. Bedell, *Program Specialist II*

On March 31, 2018, the USTUR completed the first grant year of the USTUR's 5-year grant proposal (April 1, 2017 – March 31, 2022).

Fiscal year (FY) 2018 (April 1, 2017 – March 31, 2018) funding sources were:

Federal Resources

Grant

U.S. Department of Energy Office of Health, Safety and Security, Office of Domestic and International Health Studies (DOE/AU-13):

Manage and Operate the United States Transuranium and Uranium Registries

DE-HS0000073

Amount awarded: $1,100,000
Period: April 1, 2017 – March 31, 2018

Operating budget

With a $36,603 negative carry-over from FY2017, the USTUR net operating budget for FY2018 was $1,063,397. Total operating expenses for FY2018 were $1,055,065 resulting in a positive balance of $8,332.

50th Anniversary Funding

U.S. Department of Energy Office of Health and Safety (DOE/AU-10):

USTUR: Five Decade Follow-up of Plutonium and Uranium Workers

Amount awarded: $30,000
Period: October 1, 2016 – September 30, 2018
Available in FY2018: $11,049
FY2018 expenses: $2,066

Grant Administration

Grant Renewal

On February 14, 2018, a grant renewal proposal to manage and operate the United States Transuranium and Uranium Registries and the associated National Human Radiobiology Tissue Repository (NHRTR) during FY2019 (April 1, 2018 – March 31, 2019) was submitted to the DOE/AU-13 through the WSU's Office of Research Support and Operations (ORSO). The requested FY2019 budget was $1,100,000.

Reporting

The FY2017 annual report (USTUR-0487-17) for the DE-HS0000073 grant was published and electronically distributed.

IRB Changes

Stacey L. McComish, *Associate in Research*

In September 2017, the USTUR changed its institutional review board (IRB) of record from WSU to the Central Department of Energy IRB (CDOEIRB). CDOEIRB and WSU signed an Institutional Authorization Agreement, agreeing that WSU may rely on CDOEIRB for review and continuing oversight of human subjects research carried out at the USTUR. The USTUR's human subjects protocol was approved through September 27, 2018.

The new consent packet contains four forms: (1) *Authority for Partial Body Autopsy* OR *Authorization for Use of Whole Body for Research,* (2) *USTUR Information and Informed Consent* (3) *Release of Medical and Radiation Exposure Information,* and (4) a Personal/Medical History questionnaire.

Under the WSU IRB, Registrants were required to renew their participation with the Registries every five years by signing new consent forms. Under the CDOEIRB, this renewal process was eliminated to avoid a situation where Registrants become cognitively impaired as they age (due to dementia or other age-related infirmities), and are asked to sign renewal paperwork. New Registrants will only be asked to sign the informed consent and other paperwork at the point of initial consent. Existing Registrants will be asked to sign one-time consent forms when their current paperwork expires at the end of the usual five-year cycle. No additional consent will be required. Instead, a reminder of each participant's previous commitment to the program will be sent on a yearly basis, and a Personal/Medical History questionnaire will be sent every 5 years.

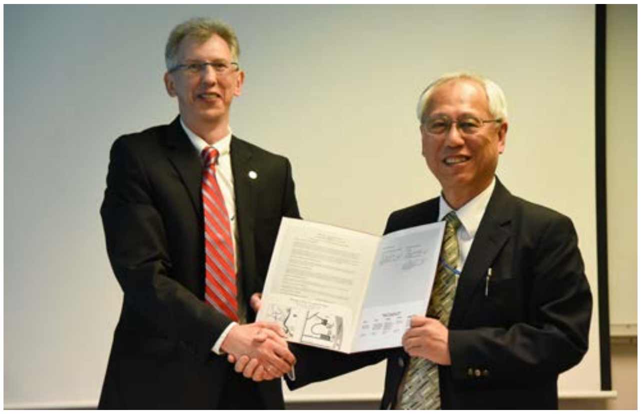
The USTUR's CDOEIRB (submission ID: DOE000226) was initially approved on September 28, 2017, pending revisions. These modifications were submitted on October 25, 2017, and the IRB's approval is valid until September 27, 2018.

New International Partnership

Sergei Y. Tolmachev, *Director*

On May 16, 2017, Washington State University through the U.S. Transuranium and Uranium Registries signed a memorandum of understanding with Kyushu Environmental Evaluation Association (Fukuoka, Japan). Kyushu Environmental Evaluation Association (KEEA) is a non-profit organization, dedicated to conservation and maintenance of the environment in Japan, and to protection of human health.

The signing ceremony was held at the WSU Tri-Cities campus in Richland. The memorandum was signed by Dr. Noriyuki Momoshima (KEEA President) and Dr. Sergei Tolmachev (USTUR Director), and approved by Dr. Asif Chaudhry (WSU Vice President for International Programs).



Dr. Tolmachev and Dr. Momoshima (photo by Maegan Murray, WSU/TC)

The agreement allows for conducting collaborative activities of research, education and training, technology and information transfer (Appendix B).

As Dr. Momoshima stated: "It's a unique partnership for KEEA because there aren't a lot of academic environments that have a fully running radiochemistry laboratory. We both have a lot to learn and gain from one another."

Group photo after the ceremony (photo by Maegan Murray, WSU/TC)

Following the signing ceremony, guests visited the USTUR laboratory where they viewed the autopsy facility, and Dr. Tolmachev presented a step-by-step description of radiochemical tissue analysis: from a frozen sample to an α-spectrometric counting source.

During USTUR facility tour

JAEA Scientists Visit

Sergei Y. Tolmachev, *Director*

On January 31, 2018, Dr. Fumiaki Takahashi and Dr. Kentaro Manabe from Japan Atomic Energy Agency (JAEA) visited the USTUR. The purpose of their visit was to discuss a recent contamination accident at Plutonium Fuel Research Facility at JAEA, and code development for internal dosimetry calculation. Dr. Tolmachev invited local experts in internal dosimetry to participate in a workshop at the USTUR.

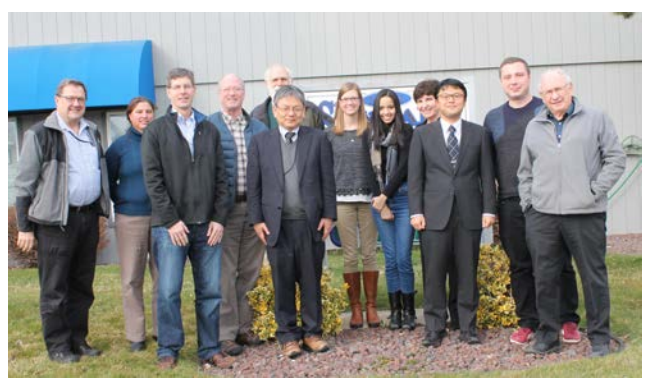
During Dr. Manabe's presentation

During this workshop, the following topics and related questions were addressed:

- Experiences and opinions on computational codes for assessing intakes of radionuclides
  - Which codes have you used for internal dosimetry studies?
  - How do you use any codes?
- From the aspects of monitoring, especially, bioassays
  - Timing and frequency of monitoring (soon after the accident, months later, years later?)
  - Radionuclide, Intake pattern (acute, multiple, chronic)
  - Uncertainty of monitoring
- Chelating agents. Blocking iodine uptake (changing transfer of nuclides in the body)
- ICRP 2007 Recommendations
  - Internal exposure dose assessment based upon new biokinetics models (e.g., OIR parts 1 and 2).

Dr. Manabe gave a presentation on estimation of internal dose from inhalation of insoluble Cs particles discharged after the accident at TEPCO's Fukushima Daiichi Nuclear Power Station. Abstract is available at http://www.icrp.org/docs/workshop2017_2/6Abstract.pdf Presentation is available at http://www.icrp.org/docs/workshop2017_2/6Presentation.pdf

The summary of the plutonium contamination accident at JAEA is available at https://www.jaea.go.jp/english/news/press/p2017092902/h02.pdf



Group photo of workshop attendees

Registrant Statistics

Stacey L. McComish, *Associate in Research*

As of March 31, 2018, the Registries had 879 Registrants in all categories (Table 1). Of that number, 40 were living and 361 were deceased. The 40 living Registrants included 6 individuals who were registered for eventual whole-body donation, 29 for partial-body donation, and 5 for 'Special Studies,' i.e., a bioassay study with no permission for autopsy. There were also 478 Registrants in an inactive category, which includes those lost to follow-up and those whose voluntary agreements were not renewed.

Table 1. Registrant Statistics as of March 31, 2018

Total Living and Deceased Registrants:	401
Living Registrants:	40
Potential Partial-body Donors:	29
Potential Whole-body Donors:	6
Special Studies:	5
Deceased Registrants:	361
Partial-body Donations:	309
Whole-body Donations:	45
Special Studies:	7
Inactive Registrants:	478
Total Number of Registrants:	879

Registrant Renewals

It has been the policy of the USTUR to offer all living Registrants an opportunity to renew their voluntary registrations every five years. Under the new approval from the Central DOE Institutional Review Board, Registrants are no longer required to renew their participation every five years. Instead, they are asked to sign the informed consent and other forms at the point of initial consent, and no additional consent is required. Registrants who have previously signed five-year agreements are sent one-time renewal paperwork shortly before their autopsy authorizations would expire. The forms in this one-time renewal packet will remain valid unless terminated by action of the Registrant or the Registries.

During this fiscal year, six Registrants renewed, one was placed in an inactive category, and two had not yet completed and returned their renewal paperwork.

Annual Newsletter

The USTUR distributes a newsletter to Registrants and their next-of-kin on a yearly basis (Appendix C). The 2017 letter was mailed in December, and included articles such as "Q & A: Plutonium in Humans" and "Plutonium in Brain Tissue."

Registrant Deaths

During this fiscal year, the USTUR received two whole- and five partial-body donations. All seven of these Registrants worked with plutonium. Five had plutonium intakes of more than 2 nCi (Figure 1). This included a worker who inhaled 260 nCi of ^{238}Pu and another who inhaled 260 nCi of ^{239}Pu. Neither of these individuals was chelated. However, a Registrant who had inhaled 20 nCi due to a faulty respirator was briefly chelated with DTPA.

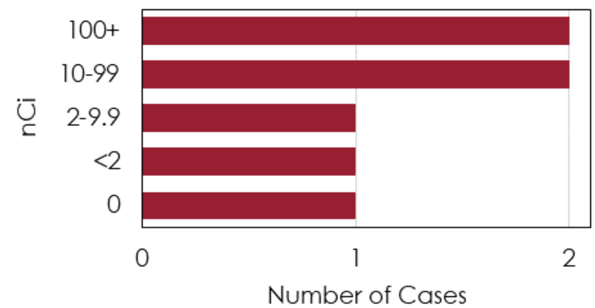


Fig. 1. Plutonium intake, systemic deposition, or body burden – as reported by the worksites – for Registrants who passed away during FY2018.

Registrant Status

The average age of living whole- and partial-body Registrants was 81 years and 83 years, respectively. The average age at death for the USTUR's 361 deceased Registrants was 69 years.

The number of donations by calendar year, as well as the average age of donors by year, is shown in Figure 2.

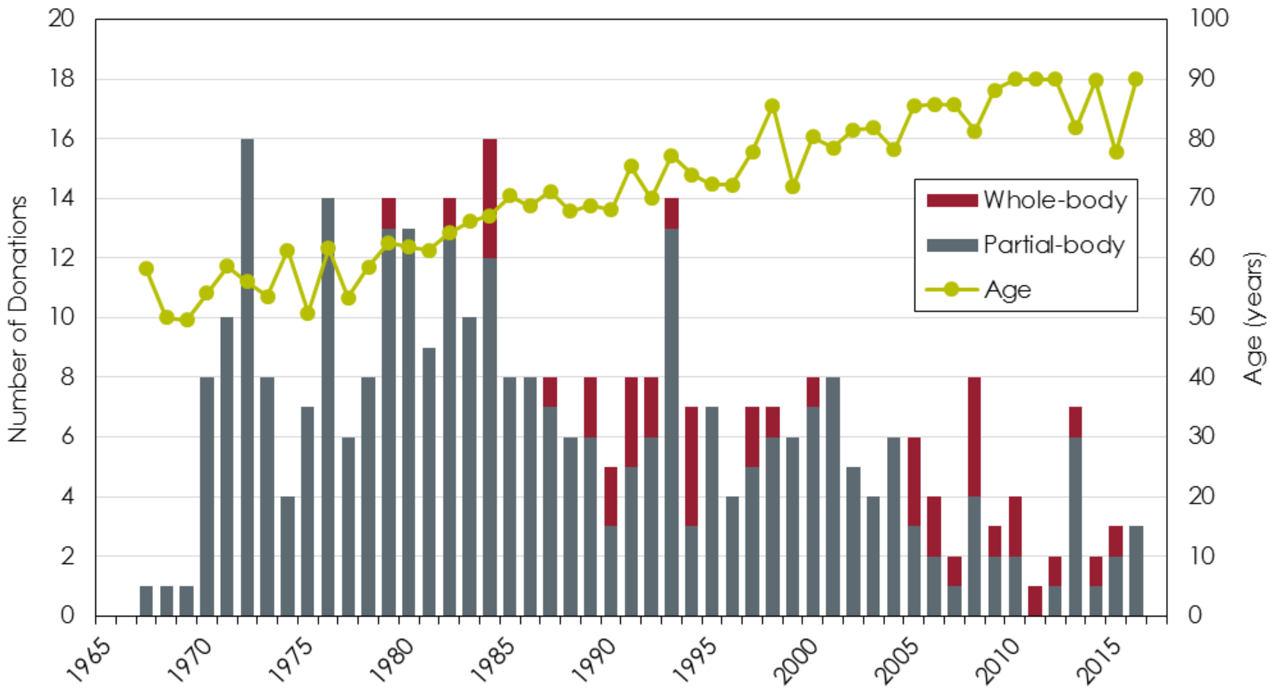


Fig. 2. Number of donations by calendar year and average age.

Health Physics Database

Maia Avtandilashvili, *Assistant Research Professor*

The USTUR Internal Health Physics Database is designed to standardize extensive sets of health physics data from USTUR donors and provide access to detailed incident, contamination, *in vitro* and *in vivo* bioassay, air monitoring, work site assessment, external dosimetry, and treatment information for scientists who are interested in studying the distribution and dosimetry of actinides in the human body.

The USTUR currently retains documents containing health physics and bioassay records for 45 whole-body and 309 partial-body tissue donors, as well as 35 living potential donors and 12 special study cases (5 living and 7 deceased).

Since the inception of the health physics database in 2008, the main efforts were focused on standardization of data from deceased Registrants. In 2016, the decision was made to complete population of the health physics database for living Registrants before resuming data entry for remaining donation cases. The availability of standardized exposure information in the database (e.g. route of intake(s), location of contaminated wound(s), material characteristics etc.) for a recently deceased Registrant is essential for determining whether additional samples, such as wound site samples, need to be collected at autopsy.

As of March 31, 2018, standardization of health physics records and bioassay data was completed for 20 living potential donors (six whole-body and 14 partial-body), and 211 deceased donors (45 whole-body and 166 partial-body). In total, 115,876 health physics records from deceased and living Registrants have been entered into the database. In addition, data entry was completed for two special study cases with a total of 504 records. Figure 3 shows FY2018 progress toward population of the database.

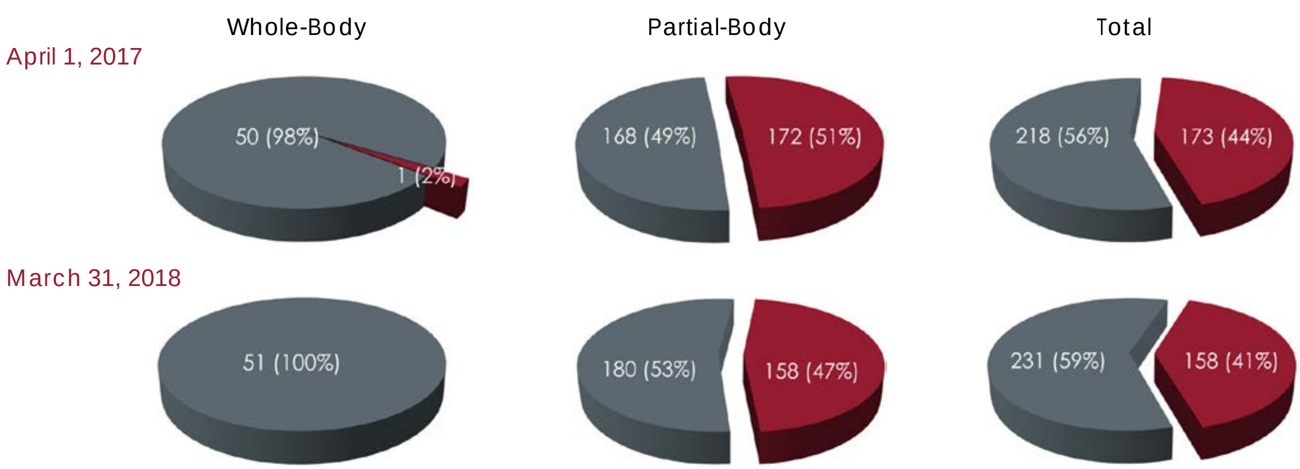


Fig. 3. FY2018 health physics database progress: ■ complete cases; ■ incomplete cases.

Figure 4 shows the FY2008 - FY2018 progress and the overall status of the health physics database as of March 31, 2018.

The summary statistics of all completed cases, categorized based on the type of intake, primary radionuclide of exposure, and material type (solubility class), are presented in Figure 5.

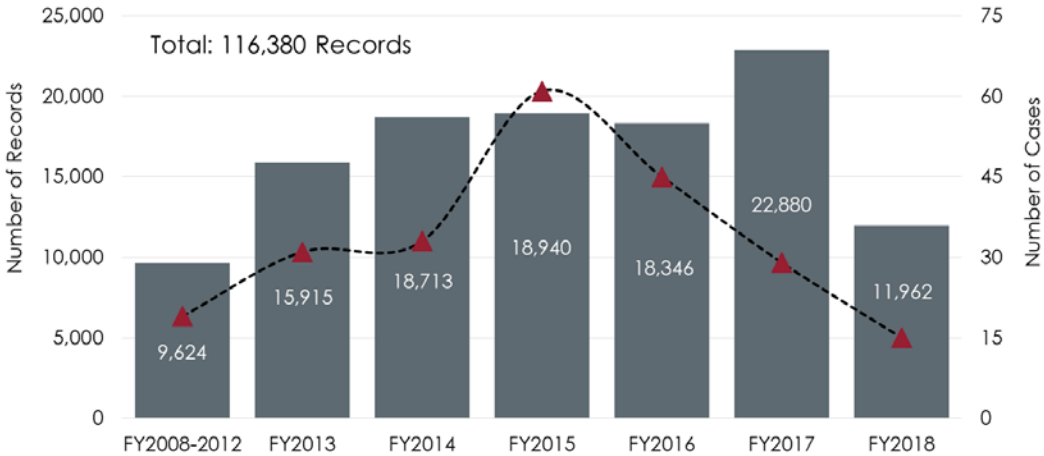


Fig. 4. FY2018 status of the USTUR health physics database.

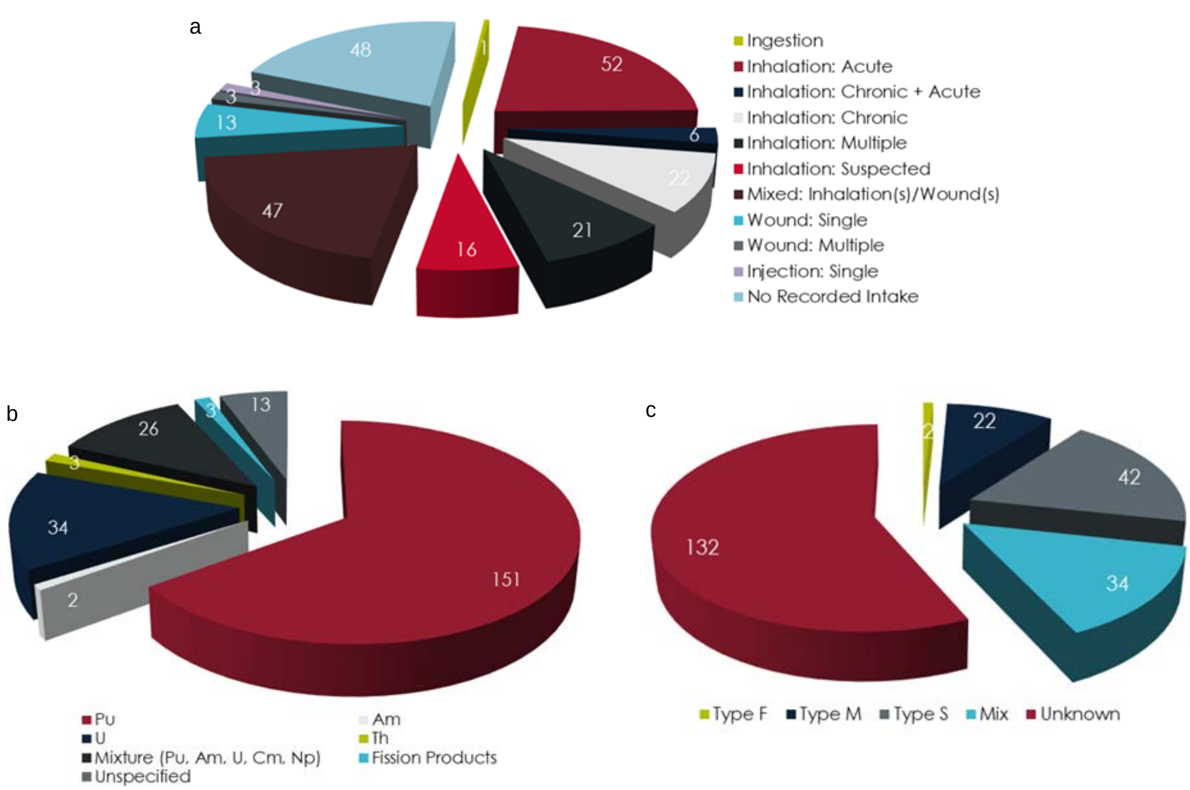


Fig. 5. Summary statistics of the health physics database: completed Registrant cases by intake (a); primary radionuclide (b); material type (c).

National Human Radiobiology Tissue Repository

Stacey L. McComish, *Associate in Research*

The National Human Radiobiology Tissue Repository (NHRTR) houses several collections of tissues and related materials from individuals with intakes of actinide elements and radium. These collections include tissues from USTUR donations, acid dissolved tissues from the Los Alamos Scientific Laboratory's (LASL) population studies, and tissues from the terminated radium worker and plutonium injection studies, which were received from Argonne National Laboratory (ANL).

Three primary activities, related to USTUR tissue donations, were carried out at the NHRTR: autopsies, dissection of donated tissues, and radiochemical analysis of tissues. Each of these activities generated specific samples, which were either stored for future use, or consumed during the radiochemical process. Table 2 summarizes these laboratory activities and the fate of the resulting USTUR samples.

THEMIS Inventory Status

The USTUR uses The Management Inventory System (THEMIS) to electronically inventory NHRTR samples. The USTUR's ultimate aim is to inventory all samples housed at the NHRTR facility. Most samples originating from USTUR tissue donations have already been inventoried. Projects to inventory USTUR tissues, acid solutions, and histology slides were completed during FY2015-FY2016. These projects are in a maintenance phase, where samples are inventoried as they are received and/or generated. Projects to inventory USTUR planchets, LASL acid solutions, and ANL tissues have been initiated; however, due to limited resources, laboratory personnel are focusing their efforts toward completing the LASL acid solution inventory before proceeding with the other projects.

Table 2. USTUR samples generated at the NHRTR facility

Laboratory Operation	NHRTR samples generated	THEMIS Inventory	Storage
Autopsy	Paraffin-embedded tissue blocks	no	yes
	Histopathology slides	yes	yes
Dissection	Frozen and/or formalin-fixed tissues	yes	yes
Radiochemical Analysis of Tissues			
Drying/Ashing	Ashed tissues	no	no†
Digestion/Dissolution	Acid solutions	yes	yes
Actinide separation	Acid solution aliquots	yes	no†
Alpha Spectrometry	α-counting sources (planchets)	yes	yes

† Sample is consumed during radiochemical analysis.

Table 3. Inventory status of NHRTR materials

NHRTR samples	Collection		
	USTUR	ANL	LASL
Frozen and/or formalin-fixed tissues	Maintenance	Deferred	--
Histology slides	Maintenance	Deferred	--
Acid solutions	Maintenance	--	Active
Planchets	Active	--	--

Each inventory project has been assigned a status. "Maintenance" indicates that all historical samples have been inventoried, and new samples will be entered into THEMIS as they are produced or received. "Active" indicates that the inventory of historical samples is ongoing. "Deferred" indicates that laboratory personnel commenced inventorying historical samples, but the project was placed 'on hold' until high-priority projects are completed and/or additional student workers are available. Table 3 summarizes the status of inventory projects.

Tissue Dissection

During FY2018, Florencio Martinez completed the dissection of one whole body donation and two partial-body donations. Warnick Kernan and Christian Gomez assisted Mr. Martinez, and carried out vacuum packaging of tissue samples.

THEMIS Inventory

As of March 31, 2018, 22,798 parent samples and 6,921 subsamples had been inventoried using the THEMIS database (Table 4). Parent samples best represent the number of unique tissues available at the USTUR; therefore, the following discussions about tissues and acid solutions exclude subsamples.

Table 4. Inventoried samples as of March 31, 2018

Tissue Type	Samples		
	Parent	Sub-	Total
USTUR donations			
Soft tissue samples	4,889	539	5,428
Bone samples	4,525	90	4,615
Histology slides	1,397	2,096	3,493
Acid solutions	6,046	2,646	8,692
Planchets	313	766	1,079
ANL tissues and slides	1,449	427	1,876
LASL solutions	3,616	84	3,700
Blank and QC samples	358	196	554
Miscellaneous	205	77	282
Total	22,798	6,921	29,719

USTUR Tissue Samples

Information on 598 parent samples from recent tissue donations was entered into THEMIS during FY2018. This placed the total number of inventoried USTUR tissues at 9,414 samples from 44 whole- and 112 partial-body cases, and a surgical specimen from one living case. The six most common types of USTUR tissues are skeletal, muscle/skin/fat, alimentary, circulatory, glands, and respiratory/tracheobronchial. Tissues are typically stored in a frozen state, and skeletal samples are most common due to the large number of bones in the human body, as well as the dissection protocol.

On average, whole-body cases had 147 ± 97 tissue samples per case and partial-body cases had 26 ± 22 tissue samples per case.

Project status – *maintenance*.

USTUR Acid Solutions

In addition to frozen and formalin-fixed tissues, the NHRTR holds thousands of acid-digested tissue samples (acid solutions) that were previously analyzed for actinides. All historical acid samples have been inventoried; however, subsamples continue to be created as aliquots are taken for radiochemical analysis. During FY2018, information on 25 acid solution aliquots from 11 cases was entered into THEMIS.

Project status – *maintenance*.

USTUR Histology Slides

The USTUR holds thousands of microscope slides that were provided by pathologists following USTUR Registrant autopsies. Inventory of new microscope slides is completed as they are received. During FY2018, three slides from case 0674 were inventoried.

Project status – *maintenance*.

USTUR Planchets

The NHRTR holds several thousand α-spectrometric counting sources (planchets), accumulated by the Registries. A planchet is the final product of an actinide tissue analysis. It is a stainless steel disk (diameter = 5/8") onto which α radioactivity was electrodeposited following radiochemical actinide separation. An individual planchet has electroplated activity from one of the following actinide elements: plutonium (Pu), americium (Am), uranium (U), or thorium (Th). Planchets are placed in coin holders for storage. Each coin holder can hold up to eight planchets.

In the past, the THEMIS database was used to inventory and record key information about batches of planchets. Unfortunately, THEMIS is ill equipped to track information about individual planchets. As such, Elizabeth Thomas designed a new in-house planchet database, which will work alongside THEMIS. The new database will store detailed information such as the isotopic activities on individual planchets, and THEMIS will track planchet locations. The planchet barcodes will provide the link between the two databases.

Data available from the Alpha Vision α-spectrometry software has already been imported into the new planchets database, but has not yet been linked to THEMIS. When personnel resources are available, these samples will be linked to THEMIS, and older planchets, for which no information was available in Alpha Vision, will be inventoried.

Project status – *active*.

Los Alamos Scientific Laboratory Solutions

NHRTR staff organized and inventoried acid solutions from population studies carried out by Los Alamos Scientific Laboratory. Bottles were grouped by case number, tested to determine whether they contained nitric (corrosive and oxidizer agent) or hydrochloric (corrosive) acid, paraffin-sealed, and inventoried. During FY2018, 445 LASL acid solutions were inventoried. This brought the total number of inventoried LASL acid solutions to 3,616 from 982 autopsies. Commonly inventoried (acid-digested) tissues included liver, lung(s), spleen, kidney(s), bone, thyroid, and lymph nodes.

Project status – *active*.

Argonne National Laboratory Samples

The NHRTR houses an existing collection of tissue materials obtained from the terminated radium worker study at Argonne National Laboratory (ANL) and the historical plutonium injection studies. The ANL collection consists of frozen and dried tissues, histological slides, and plastic and paraffin-embedded tissues. This collection was acquired by the NHRTR/USTUR in 1992.

No progress has been made toward inventorying the ANL collection due to limited personnel.

Project status – *deferred*.

Five-year Inventory Progress

Figure 6 shows the cumulative number of inventoried parent samples at the end of each of calendar years 2010 to 2017. It can be seen that, in 2010-2012, initial efforts were focused on inventorying USTUR tissues. As that project neared a maintenance phase, work to inventory USTUR acid solutions was commenced. Similarly, in 2015, after all historical USTUR tissues and acid solutions had been inventoried, work to inventory LASL acids and ANL tissues began.

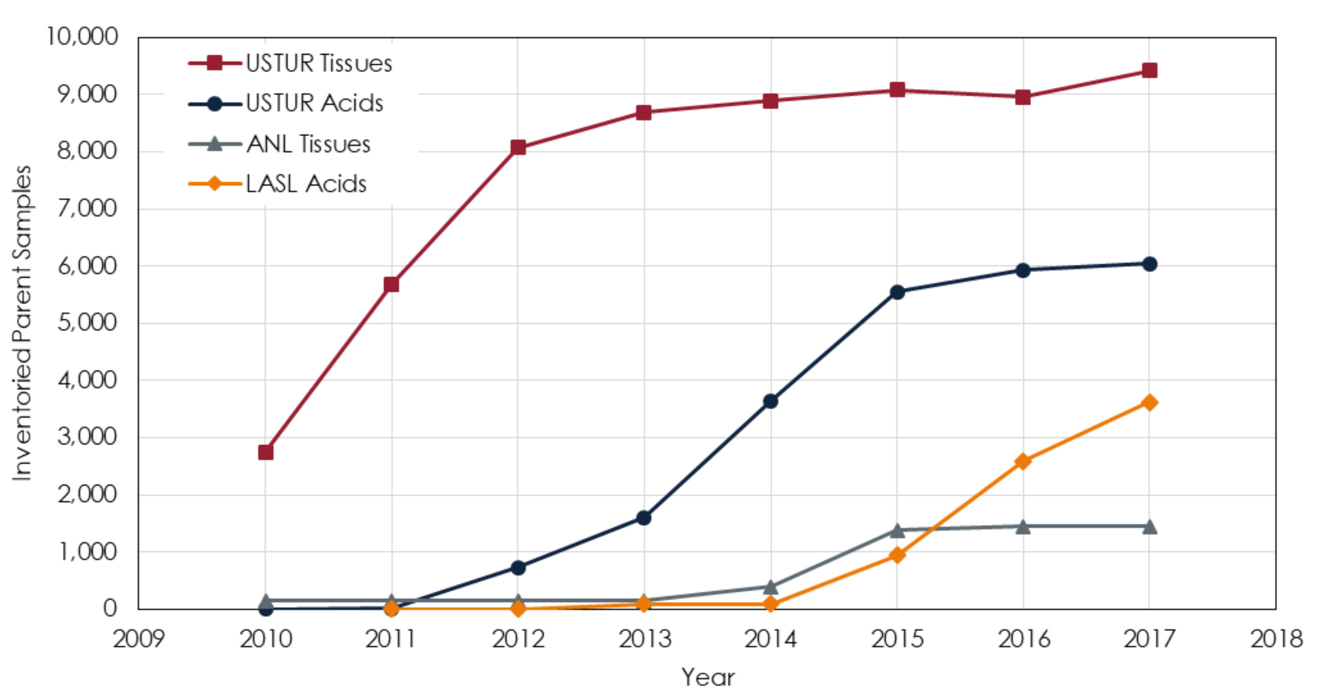


Fig. 6. Cumulative number of inventoried NHRTR samples, at the end of each calendar year.

Radiochemistry Operation

George Tabatadze, *Assistant Research Professor*

This section describes specific activities and achievements of the Radiochemistry Group during FY2018.

Personnel

As of April 1, 2018, operation of the radiochemistry laboratory was supervised by Dr. Tolmachev (Principal Radiochemist) with two full-time personnel – Dr. George Tabatadze (Assistant Research Professor) and Ms. Elizabeth Thomas (Laboratory Technician II).

FY2018 Tissue Sample Analysis

Tissue sample analysis is a multi-step process. During the analysis, a tissue undergoes five different analytical steps: (i) drying and ashing, (ii) digestion and dissolution, (iii) radiochemical actinide separation, (iv) preparation of an α-counting source (planchet), and (iv) measurement of individual actinides – plutonium (^{238}Pu and $^{239+240}$Pu), americium (^{241}Am), uranium (^{234}U, ^{235}U, and ^{238}U), and/or thorium (^{232}Th).

During FY2018, 146 tissue samples, including 32 bone and 114 soft tissues from six donations, were analyzed for ^{238}Pu, $^{239+240}$Pu, and ^{241}Am using α-spectrometry.

Whole-body Donations

A cerebral lobe sample from Case 0846 was analyzed.

One hundred tissue samples, including 31 bone and 69 soft tissues from two whole-body donations: Case 0674 (63) and Case 1053 (37) were submitted for analysis as well as an axillary lymph node from the left side of Case 0303.

Partial-body Donations

In FY2018, analysis of 144 tissue samples from four partial-body donations, received between 2006 and 2016, was completed. Analyzed cases included: 0410 (41), 0421 (39), 0702 (37), and 0771 (27). A total of 31 bone samples and 113 soft tissues were analyzed for ^{238}Pu, $^{239+240}$Pu, and ^{241}Am. In addition, the 5th rib from the right side of the skeleton of Case 0658 was analyzed.

A total of 339 tissue samples, including 102 bone and 237 soft tissues from 14 partial-body donations was submitted for analysis: Case 0299 (18), Case 0315 (24), Case 0334 (26), Case 0341 (20), Case 0371 (17), Case 0439 (18), Case 0445 (19), Case 0446 (24), Case 0460 (6), Case 0688 (40), Case 0695 (50), Case 0817 (28), Case 0854 (23), and Case 0991 (26). In addition, a mediastinal lymph node from Case 0333 was submitted for analysis.

FY2013 - 2018 Tissue Sample Analysis

Figure 7 shows FY2013 – FY2018 tissue analysis progress.

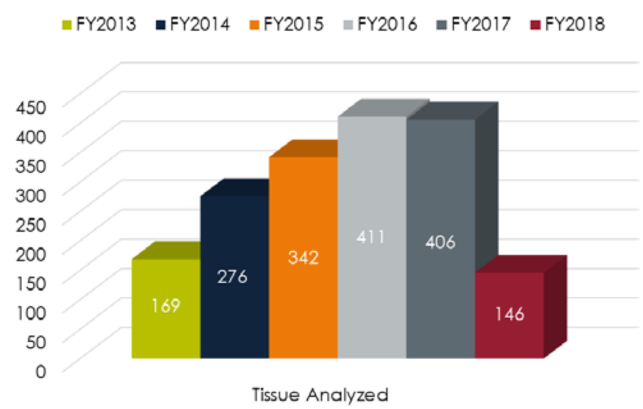


Fig. 7. USTUR tissue analysis progress in FY2013–FY2018.

FY2017 Radiochemistry Case Analysis

As of April 1, 2018, the USTUR had received 45 whole- and 309 partial-body donations, including two whole- and five partial-body donations accepted during FY2018.

In FY2018, tissue samples from two whole-body donors were submitted for survey radiochemical analysis (Table 5). A survey analysis is an analysis of selected tissue samples that provides key scientific information to determine the level of exposure, and can be sufficiently used for biokinetic modeling.

Table 5. FY2018 whole-body case analysis progress

Case No	Year of Donation	Radiochemistry Status	
		FY2016	FY2017
0674	2017	Intact	Incomplete†
1053	1997	Intact	Incomplete†

† - Survey analysis in progress

Cases are categorized as 'Intact,' 'Incomplete,' or 'Complete'. 'Intact' means that no tissue samples have been analyzed. 'Incomplete' typically denotes that a selected sub-set of tissues was analyzed (surveyed) or case analysis is in progress. Full analyses of four partial-body cases were completed and analyses for one donation is in progress. Table 6 summarizes partial-body case analysis progress.

Table 6. FY2018 partial-body case analysis progress

Case No	Year of Donation	Radiochemistry Status	
		FY2016	FY2017
0410	2016	Incomplete	Complete
0421	2016	Incomplete	Complete
0702	2006	Incomplete	Complete
0771	2008	Incomplete	Complete
0688	2017	Intact	Incomplete

'Complete' denotes that a full selection of tissue samples was analyzed and results were reported. Figure 8 shows FY2013 – 2018 case analysis progress.

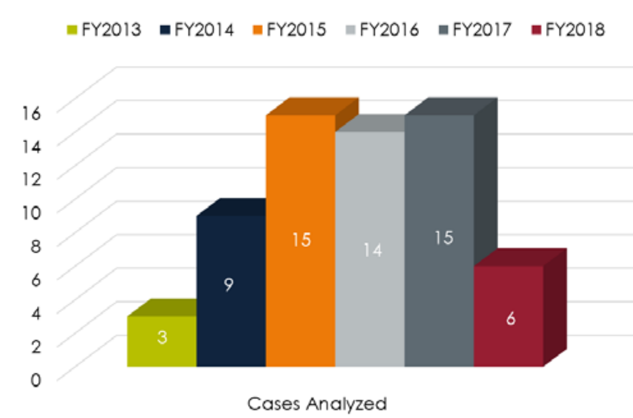


Fig. 8. USTUR case analysis progress in FY2013–FY2018.

The status change of case analyses from FY2017 to FY2018 is shown in Figure 9.

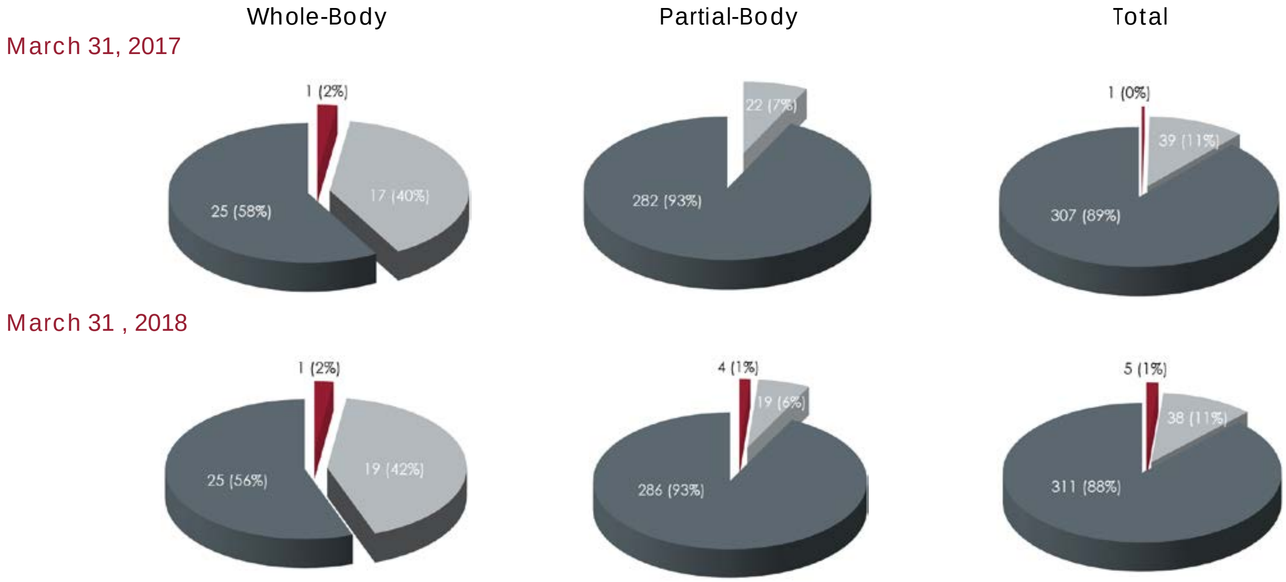


Fig. 9. Radiochemistry analysis status: ■ intact cases; ■ incomplete cases; ■ complete cases.

Tissue Sample Backlog

The USTUR/NHRTR retains a tissue backlog of 2,104 samples from 41 whole- and partial-body cases. They remain ‘Incomplete’ as of April 1, 2018. This includes 1,737 tissue samples from 18 whole-body cases, and 367 tissues from 23 partial-body cases. Of 2,104 backlog samples, 1,752 (83%) need to be analyzed for plutonium, 106 (5%) for americium, and 246 (12%) for uranium (Figure 10).

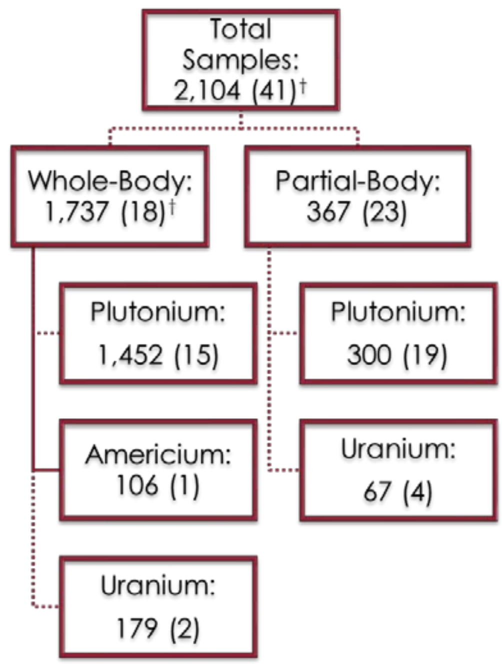


Fig. 10. USTUR tissue sample backlog at the end of FY2018. † excluding two Thorotrast cases.

Modeling Plutonium Decorporation Treatment

Sara Dumit, *Ph.D. Candidate*

Individuals with significant internal deposition of plutonium typically undergo medical treatment with chelating agents to enhance decorporation. The trisodium salt form of calcium diethylenetriaminepentaacetate (Ca-DTPA) is a commonly used decorporation drug that forms stable complexes with plutonium in vivo, enhancing its excretion in urine.

Since plutonium biokinetics (absorption, distribution, retention, and excretion) are strongly altered by its complexation with the chelating agent, standard models cannot be used directly to estimate the radionuclide intake. Prior to this work, only empirical descriptions and ad hoc models and approaches were available to model data affected by chelation treatment. In this study, a new model that describes plutonium biokinetics during and following chelation therapy was developed, parameterized, and validated.

A USTUR whole-body donor (Case 0212) was selected for this study. This individual was exposed to plutonium as a result of an occupational wound injury and underwent extensive treatment with Ca-DTPA. Urinary excretion measurements and post-mortem plutonium activities in the liver and the skeleton were used for model development and validation, respectively.

The new model (linked with the Leggett et al. Plutonium Systemic Model(1), the ICRP 100 Human Alimentary Tract Model(2), and the NCRP 156 Wound Model(3)) was implemented in SAAM II® software. The Coordinated Network for Radiation Dosimetry (CONRAD) approach to biokinetic modeling of decorporation therapy(4) was applied by using a chelation constant to describe the kinetics of the in vivo chelation process.

The new assumptions and parameters account for both the intravenously injected Ca-DTPA and the in vivo formed Pu-DTPA chelate. The new model structure was also tested with the ICRP 67(5) and the Luciani and Polig(6) Plutonium Systemic Models. The fitting of urinary excretion (Figure 11) and autopsy data (Figure 12) using the new model was compared to the original CONRAD Model and its optimized version, resulting in both improved goodness-of-fit to the bioassay data by order of magnitude and more accurate predictions of post-mortem plutonium retention in major depository sites.

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2. ICRP. Human alimentary tract model for radiological protection. Oxford: Elsevier; ICRP Publication 100; Ann ICRP 36(1-2); 2006.

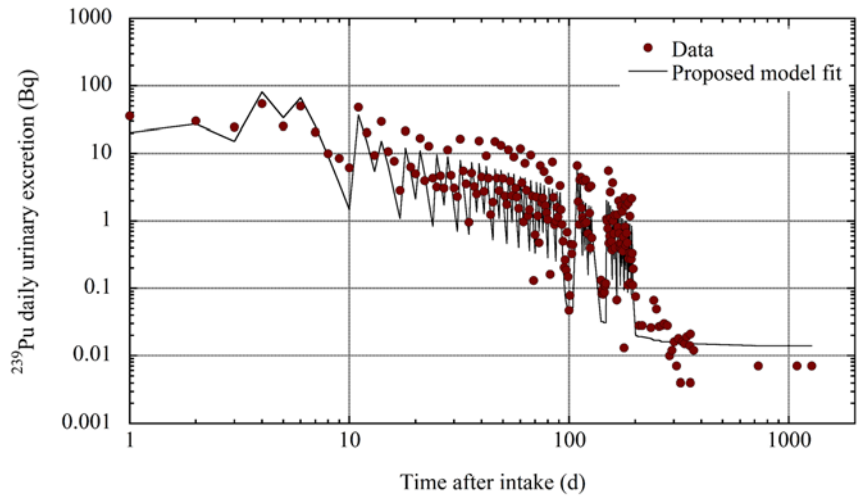

Fig. 11. Fit of daily urinary excretion of ^{239}Pu using the proposed model

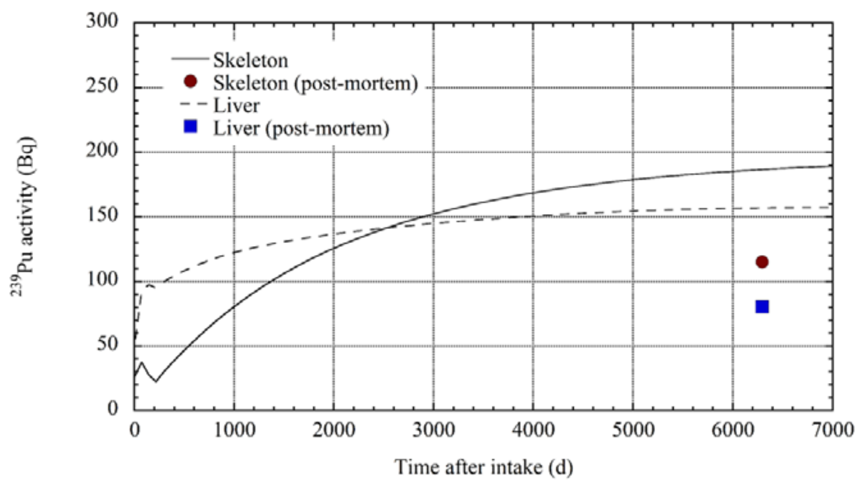

Fig. 12. Post-mortem measurement results vs prediction of ^{239}Pu retention in the skeleton and liver at the time of death using the proposed model

3. NCRP. Development of a biokinetic model for radionuclide-contaminated wounds and procedures for their assessments, dosimetry and treatment. NCRP Report No. 156. 2006.
4. Breustedt B, Blanchardon E, Berard P, Fritsch P, Giussani A, Lopez MA, Luciani A, Nosske D, Piechowski J, Schimmelpfeng J, Sérandour AL. Biokinetic modelling of DTPA decorporation therapy: the CONRAD approach. Radiat Prot Dosim 134:38-48; 2009
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6. Luciani A, Polig E. Verification and modification of the ICRP-67 model for plutonium dose calculation. Health Phys 303:310-78; 2000.

Expanding Horizons for Actinide Biokinetics and Dosimetry

Sergei Y. Tolmachev, *Associate Research Professor*

Since 1968, the U.S. Transuranium and Uranium Registries has followed up occupationally-exposed individuals (volunteer Registrants) by studying the biokinetics (deposition, translocation, retention, and excretion) and tissue dosimetry of actinide elements. The Registries holds data on work history, radiation exposure and bioassay measurements, as well as medical records from more than 400 former nuclear workers. These individuals had documented intakes of actinides at levels higher than 74 Bq. Inhalation and wound are two major routes of intake and ^{239}Pu is a primary radionuclide (Figure 13). Post-mortem radiochemical analyses of tissues obtained at autopsy, especially those from whole-body donors, allows USTUR to significantly improve our knowledge on distribution and long-term retention of actinides in the human body and have helped in parameterizing biokinetic constants for these radioactive elements. Recently, there have been identified several groups of individual cases to study biokinetics and dosimetry for specific radionuclides, exposure scenarios and materials, as well as effects of decorporation treatment (Table 7). The data from a USTUR whole-body donor who was exposed to soluble ^{239}Pu via inhalation were used to study long-term plutonium retention in the upper airways and quantify plutonium 'bound' fraction[1,2]. This is only one eminent example of how USTUR data can be used to improve the accuracy of dose assessment and radiation protection of plutonium workers.

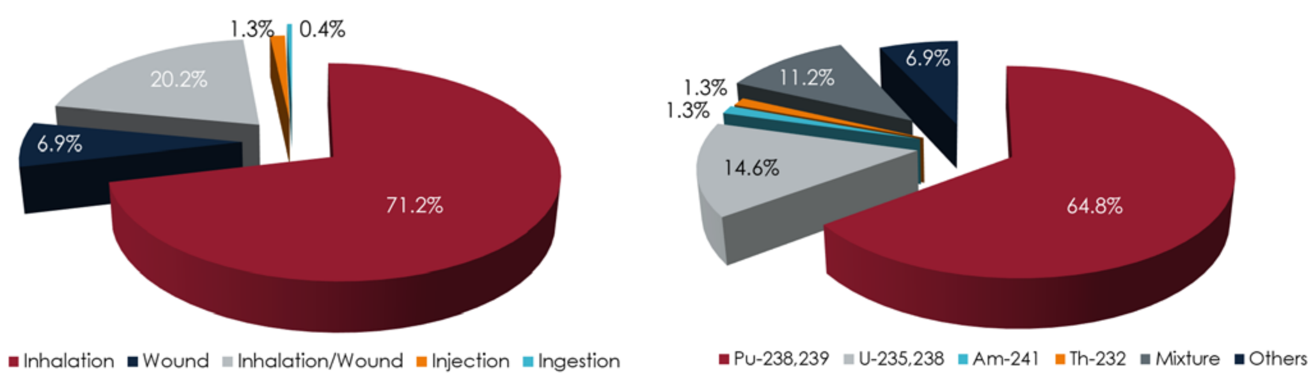

Fig. 13. USTUR Registrants' exposure by: route of intake (left) and primary radionuclide (right).

Table 7. USTUR specific study groups

Study group	Number of cases
^{239}Pu	
Soluble	14
Refractory	22
^{238}Pu	10
^{241}Am	3
Uranium	
Enriched	5
Depleted	3
Natural	17
^{232}Th	3
^{237}Np	1
^{244}Cm	1
^{239}Pu wound	14
Decorporation	
^{239}Pu	14
^{238}Pu	1
^{241}Am	2

References

1. Puncher M, Birchall A, Tolmachev SY. The Mayak worker dosimetry system (MWDS 2013): A re-analysis of USTUR Case 0269 to determine whether plutonium binds to the lungs. Radiation Protection Dosimetry 176: 50-61; 2017.
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LEKSKaM Model Visualization

Daniel J. Strom, *Adjunct Professor*

In 2005, Leggett and coworkers ("LEKSKaM"†) published a revision to the 1993 ICRP Publication 67 systemic biokinetic model for plutonium(1). Using data from plutonium workers in the former Soviet Union, the model added a second blood compartment to mathematically deal with recycling. The resultant model is somewhat difficult to grasp conceptually, since one blood compartment is depicted inside another, necessitating pathways crossing compartment boundaries. Also, arrows in the model go in all directions. In an effort to develop a more intuitive representation of the model, an alternative view is presented. The visualization is a 2-dimensional surface projected in 3 dimensions onto the surface of a cylinder, emphasizing the recycling nature of the model (Figure 14).

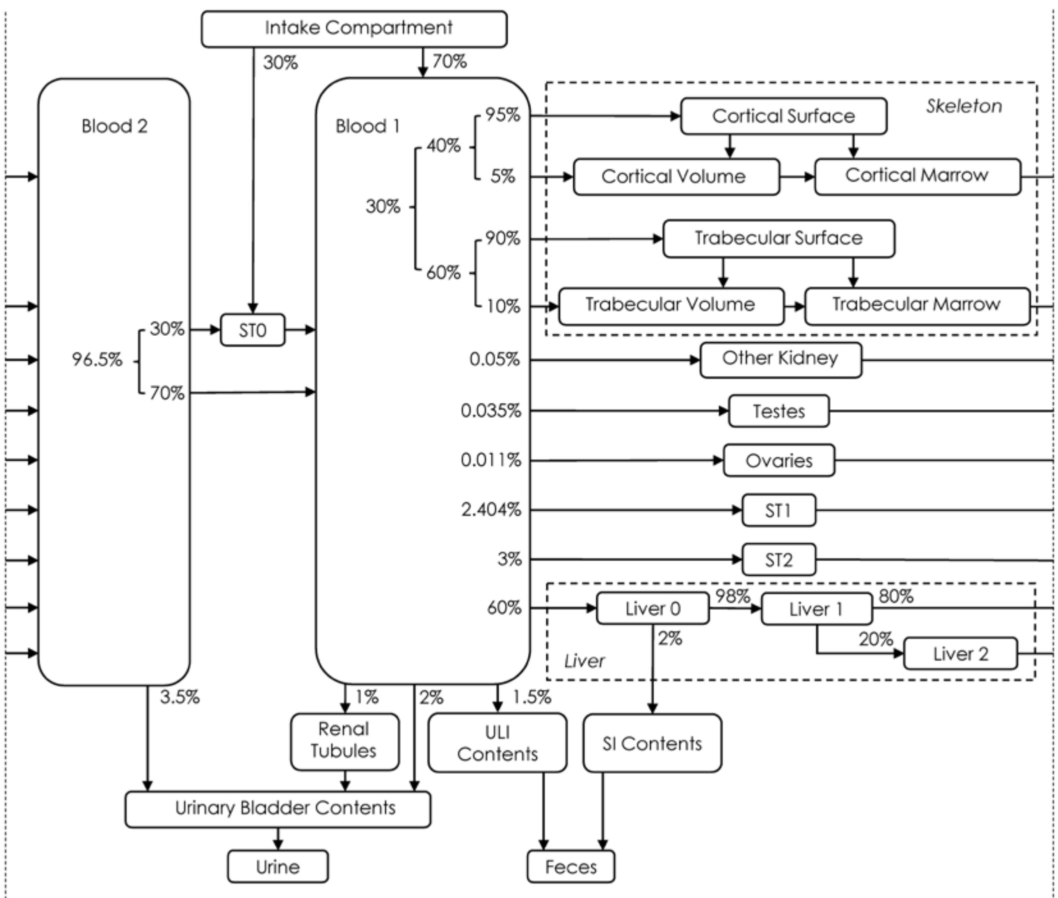

Fig. 14. Cylindrical surface representation of the LEKSKaM model.

† Leggett, Eckerman, Khokhryakov, Suslova, Krahenbuhl, and Miller

With uptake to Blood 1 shown at the top, excretion pathways shown at the bottom, and recycling going from left to right, all arrows go down or to the right. The Intake compartment is shown explicitly. The Skeleton, Other Kidney, Gonads, Soft Tissue 1 and 2, and Liver take plutonium up from Blood 1 and gradually return it to Blood 2. The Intake Compartment, Renal Tubules, Urinary Bladder Contents, Small Intestine Contents, and Upper Large Intestine Contents are seen to be outside of the recycling part of the model. The unusual nature of ST0 (rapid turnover soft tissue) is clear. While there is no new science in this visualization, the flow of plutonium in the system is more easily comprehended. In principle, such visualizations can be made of all recycling models.

References

1. Leggett RW, Eckerman KF, Khokhryakov VF, Suslova KG, Krahenbuhl MP, Miller SC. Mayak worker study: An improved biokinetic model for reconstructing doses from internally deposited plutonium. Radiat Res 164: 111-22; 2005.

2017 Advisory Committee Meeting Summary

Roger O. McClellan, *Chair*

The 2017 Annual Scientific Advisory Committee (SAC) Meeting was held August 25-26 at the Red Lion Hanford House, Richland, WA. Each year, the SAC meeting enables valuable discussions with our advisory committee and scientific colleagues about the progress and goals of the Registries. The meeting agenda is attached as Appendix D.

2017 Meeting Attendees

The Scientific Advisory Committee, USTUR faculty/staff, colleagues from WSU College of Pharmacy, and several invited guests attended the 2017 meeting. All participants were invited to attend the morning session; however, the afternoon session was executive in nature, and attended only by SAC members, USTUR staff, and the DOE program manager.

Advisory Committee

- Timothy Ledbetter, *Ethics*
- Roger McClellan, *Toxicology*
- Thomas Rucker, *Radiochemistry*
- Arthur "Bill" Stange, *Occupational Health*
- Unable to attend: Heather Hoffman, *Epidemiology*
- Unable to attend: Richard Toohey, *Health Physics*

U.S. Transuranium and Uranium Registries

- Sergei Tolmachev, *Director*
- Stacey McComish, *Associate in Research*
- Maia Avtandilashvili, Assistant *Research Professor*
- George Tabatadze, Assistant *Research Professor*
- Elizabeth Thomas, *Laboratory Technician II*
- Margo Bedell, *Fiscal Specialist I*
- Sara Dumit, *WSU/COP Ph.D. Candidate*
- Daniel Strom, *Adjunct Faculty*

Washington State University

- Antone Brooks – *Adjunct Professor, Environmental Sciences*
- Aurora Clark – *Director, Institute of Nuclear Science and Technology*
- Ronald Kathren – *Professor Emeritus*
- Kathryn Meier – *Associate Dean for Faculty and Student Development, College of Pharmacy, WSU*

Invited Guests

- Darrell Fisher – *Versant Medical Physics and Radiation Safety*
- Jay MacLellan – *Retired PNNL*
- Ralf Sudowe – *Colorado State University*
- Margery Swint – *Former USTR Director*

Presentations

Updates from WSU Biomedical Sciences and the College of Pharmacy – Meier, K.

The College of Pharmacy's relationship to the USTUR and news from WSU Spokane's campus and the College of Pharmacy were summarized. News items included the new WSU Spokane chancellor, the first cohort of medical students at WSU Spokane, and College of Pharmacy expenditures and student enrollment.

2017 Financial & Administrative Development – Bedell, M.

Administrative and financial information was summarized including: personnel, the FY2017 budget vs. spending, the FY218 budget, faculty promotions, and the USTUR's 50th anniversary.

2016 SAC Recommendations & 2017 Overview – Tolmachev, S.

The SAC's recommendations from last year's meeting, and the way the USTUR addressed each recommendation, were presented. This was followed by an overview of 2017 activities, which included: the USTUR's 5-year grant renewal, IRB changes, the health physics database, NHRTR inventory, in-house radiochemistry, academic activities, and the USTUR/WSU-KEEA partnership.

Registrant Statistics and IRB Changes – McComish, S.

Registrant statistics were given, and the exposure scenarios for four recently deceased donors were summarized. Additionally, the USTUR changed its institutional review board (IRB) of record from WSU to the Central Department of Energy IRB. Details of this change were presented.

USTUR Health Physics Database – Avtandilashvili, M.

Progress toward entering data from each Registrant's dosimetry file into the USTUR's electronic Health Physics Database was summarized. Highest priority was given to new donations, followed by living Registrants. As of August 2017, 108,649 records from 222 cases had been entered into the database.

National Human Radiobiological Tissue Repository – McComish, S.

The association between generation of NHRTR samples and USTUR laboratory activities following a donation was explored. The status of NHRTR inventory projects, and associated data trends, were also described.

2017 Radiochemistry Progress Report – Tabatadze, G.

Operation of the radiochemistry laboratory was described. Topics included tissue analyses, equipment upgrades, facility maintenance, and the design and implementation of a radiochemistry database.

Institute of Nuclear Science and Technology – Clark, A.

INST is a multidisciplinary research program that includes researchers from several institutions including WSU, Pacific Northwest National Laboratory, and Idaho National Laboratory. An overview of the Institute of Nuclear Science and Technology was provided, and specific research topics were described.

Radiochemical Separations for "Unusual" Sample Matrices – Sudowe, R.

Emergency response scenarios would require laboratories to have the radioanalytical capability to analyze "unusual matrices" such as cement and steel. Challenges associated with these matrices, and work to develop radioanalytical methods for them, were discussed.

Enhancement of Plutonium Excretion Following Late Ca-EDTA/DTPA Treatment – Dumit, S.

Plutonium enhancement factors for case 0785 following Ca-EDTA/DTPA treatment were discussed, as was the effectiveness of initial vs. delayed treatments, and the half-time of the Pu-EDTA complex removal from the urine. This presentation was previously given at the 2017 Health Physics Society annual meeting.

USTUR Research: Land of Opportunity – Avtandilashvili, M.

The USTUR has detailed work histories, medical and exposure records, bioassay results, autopsy findings, and radiochemical tissue analysis results for each of its Registrants. Thus, it is a unique and important resource for studying both actinides and non-radioactive materials. Specific research opportunities were summarized in this presentation, which was previously given at the 2017 EURADOS annual meeting.

Research Plan and Operation in FY2018 – Tolmachev, S.

The USTUR's research and operational goals for the next year were summarized. Topics included: management and operation of the Registries, conducting scientific research, and demonstrating/promoting a broader use of USTUR research, data, and materials.

Comments

Specific comments include:

1. Significant progress in promoting the value of the USTUR has been made through presentations and publications surrounding the 50th anniversary.
2. Significant progress in promoting two staff members from research associates to assistant research professors was made.
3. Significant progress has been made in formalizing research goals and objectives provided in presentations.
4. Demonstration of the value of the program to the current and future DOE officials has been attempted.
5. Progress has been made in exploring opportunities for relationships with educational institutions and offering practical opportunities for research and nursing students.
6. Progress has been made in developing scientific collaborations.

Recommendations

1. A formal documentation of research goals and objectives is still recommended, including a revised mission for the use of data for improving biokinetic models and other applications.

2. Demonstration of the value of the program to current and future DOE officials needs further effort.

3. Promotion of the program and staff through publication of work (~2 papers per year per professional staff) is recommended.

4. Additional efforts to bring about the planned scientific collaborations are recommended.

5. Develop Measurement Quality Objectives (MQOs) for radiochemical measurements based on the objectives (e.g. DQOs or other process-developed objectives) for the use of the data that drive the tolerance limits used to control the quality of the measurement processes. These MQOs should include accuracy, precision, sensitivity, selectivity, and completeness objectives. Tolerance limits and charts should be used instead of control limits and charts for calibration checks and control samples using accuracy and precision MQOs. Detection decisions should be based on the use of critical values rather than minimum detectable activity (MDA) values. Critical values and MDA should be calculated based on sensitivity MQOs.

6. Consideration should be made for collection of bioassay monitoring data (urinalysis) from living Registrants. Modern excretion data can be used for comparison with the body burden from autopsy for updating excretion models.

7. It is recommended that there be a periodic review and update of future goals and plans using a 5-year, 10-year, and beyond horizons. The initial review in a draft form should be available for the next SAC meeting. The USTUR should consider a shift from the generation of data to the use of data.

8. Progress should be made in strengthening the relationship with the WSU Pullman, Spokane, and Tri-Cities campuses and taking advantage of the relationships that have been initiated.

SAC Membership

Richard Toohey completed his second term on the SAC, and he will not be renewing his participation for a third term. Possible candidates for a new health physics representative were discussed, and a decision will be reached in the coming months.

Note of Appreciation

The assistance of Stacey McComish in preparing the meeting summary is gratefully appreciated.

Roger O. McClellan

Roger O. McClellan
SAC Chair

Professional Activities and Services

During FY2018, the USTUR staff was actively involved in professional and academic activities nationally and internationally.

Academic Services

WSU Graduate Certificate Program in Radiation Protection

The USTUR's Director, Dr. Sergei Tolmachev, and Assistant Research Professor, Dr. George Tabatadze, continued to serve on the advisory committee for the WSU Graduate Certificate Program in Radiation Protection (GCPRP) at the Tri-City Campus.

Department of Chemistry, Laval University

Dr. Tolmachev continued to serve as an Adjunct Professor in the Department of Chemistry at Laval University (Quebec, Canada) for a 2nd 3-year term (June 2014 – May 2017).

Professional Services

NCRP WARP Initiative

Dr. Tolmachev was appointed to serve as a 'captain' of the team of experts in radiochemistry and nuclear chemistry for the *Where are the Radiation Professionals (WARP)?* initiative conducted by the National Council on Radiation Protection and Measurements (NCRP).

Herbert M. Parker Foundation

Dr. Tolmachev continued to serve as a member of the Board of Trustees for the Herbert M. Parker Foundation: https://tricities.wsu.edu/parkerfoundation/

Health Physics Society International Collaboration Committee

Dr. George Tabatadze was appointed to, and has served as a member of, the International Collaboration Committee (ICC) of the Health Physics Society (HPS). Appointment: 2016–2018.

Columbia Chapter of Health Physics Society

Dr. Tabatadze has become the president-elect of the Columbia Chapter of the Health Physics Society (CCHPS). He began his three-year term in July 2017 and will serve one-year terms as the president-elect, president, and past president between 2017 – 2019, respectively.

Kyushu Environmental Evaluation Association

Dr. Tolmachev continued to serve as a Technical Advisor at the Kyushu Environmental Evaluation Association (Fukuoka, Japan).

Scientific Meetings

USTUR faculty attended and participated in the following scientific meetings:

- 62nd Annual Health Physics Society Meeting in Raleigh, NC, July 9 – 13, 2017
- 6th Asia-Pacific Symposium on Radiochemistry, Jeju Island, Korea, September 17 – 22, 2017
- European Radiation Dosimetry Group WG-7 Plenary Meeting, Paris, France, October 9, 2017
- 4th International Symposium on the System of Radiological Protection, Paris, France, October 10 – 12, 2017

- Oregon State University School of Nuclear Science and Engineering Research Seminar, Corvallis, OR, November 27, 2017.

Editorial Services

Health Physics Journal

Drs. Avtandilashvili and Tolmachev were appointed as Guest-Editors for the USTUR special issue of the *Health Physics* journal.

Japanese Journal of Health Physics

Dr. Sergei Tolmachev continued to serve as a member of the Editorial Board for the *Japanese Journal of Health Physics* (JJHP) for his 3rd term from August 2013 to July 2017.

Austin Biometrics and Biostatistics

Dr. Maia Avtandilashvili continued to serve as a member of the Editorial Board for the journal of *Austin Biometrics and Biostatistics*: http://austinpublishinggroup.com/biometrics/editorialBoard.php

Professional Affiliations

The USTUR personnel are active members of numerous national and international professional organizations:

- Radiation Research Society (USA)
- Health Physics Society (USA)
- Japan Health Physics Society (Japan)
- European Radiation Dosimetry Group (EURADOS), Working Group 7 (WG7) on Internal Dosimetry (EU)

Publications and Presentations

The following manuscripts and presentations were published or presented during the period of April 2017 to March 2018. Previous manuscripts and abstracts are available on the USTUR website at:

ustur.wsu.edu/Publications/index.html

Abstracts of published peer-reviewed manuscripts and scientific presentations are included in Appendix E of this report.

Published

USTUR-0436-16

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Historic Beagle Dog Data. *Radiat Prot Dosim* 176: 32-44; 2017.

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Puncher M, Birchall A, Sokolova AB, Suslova KG. The Mayak Worker Dosimetry System (MWDS-2013): Plutonium Dissolution in the Lungs – an Analysis of Mayak Workers. *Radiat Prot Dosim* 176: 71-82; 2017.

USTUR-0411-16

Sokolova AB, Birchall A, Efimov AV, Vostrotin VV, Dorrian MD. The Mayak Worker Dosimetry System (MWDS-2013): Determination of the Individual Scenario of Inhaled Plutonium Intake in the Mayak Workers. *Radiat Prot Dosim* 176: 83-89; 2017.

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USTUR-0414-16

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USTUR-0488-17

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Tolmachev SY. U.S. Transuranium and Uranium registries: 50 y of research relevant to new biomarker. *Health Phys*. 113 (1 Suppl): S82-83; 2017.

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USTUR-0477-17A

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Ca-EDTA/DTPA treatment. *Health Phys*. 113 (1 Suppl): S95-96; 2017.

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McComish SL, Tolmachev SY. United States Transuranium and Uranium Registries Annual Report: April 1, 2016 – March 31, 2017. United States Transuranium and Uranium Registries; USTUR- 0487-17, Richland, WA, 2017.

Presented

Invited

USTUR-0475-17A

Tolmachev S. Transuranium and Uranium Registries: 50 Years of Research Relevant to New Biomarker. Podium presentation at the 62nd Annual Meeting of the Health Physics Society, Raleigh, NC, July 9 – 13, 2017.

USTUR-0489-17P

Tolmachev SY, Tabatadze G. Radiochemical Analysis of Plutonium in Tissues from Former Nuclear Workers. Oregon State University School of Nuclear Science and Engineering Research Seminar, Corvallis, OR, November 27, 2017.

Podium

USTUR-0482-17A

Goans R, Iddins C, Toohey R, McComish S, Tolmachev S, Dainiak N. The Pseudo Pelger-Hüet Cell - from Bats to Humans and Everything in between. Podium presentation at the 62nd Annual Meeting of the Health Physics Society, Raleigh, NC, July 9 – 13, 2017.

USTUR-0476-17A

Tabatadze G, Avtandilashvili M, Tolmachev SY. Plutonium in Tissues of Occupationally Exposed Individuals. Podium presentation at the 62nd Annual Meeting of the Health Physics Society, Raleigh, NC, July 9 – 13, 2017.

USTUR-0477-17A

Dumit S, Avtandilashvili M, Tolmachev SY. Enhancement of Plutonium Excretion Following Late Ca-EDTA/DTPA Treatment. Podium presentation at the 62nd Annual Meeting of the Health Physics Society, Raleigh, NC, July 9 – 13, 2017.

USTUR-0478-17A

Tolmachev SY, Thomas EM, Avtandilashvili M, Tabatadze G. Analysis of 'High-fired' Plutonium Oxide in Tissues of Exposed Workers. 6th Asia-Pacific Symposium on Radiochemistry, Jeju Island, Korea, September 17 – 22, 2017.

USTUR-0479-17A

Tabatadze G, Miller B, Tolmachev SY. Digital Autoradiography of Bone-Seeking Radionuclides in Human. 6th Asia-Pacific Symposium on Radiochemistry, Jeju Island, Korea, September 17 – 22, 2017.

USTUR-0493-18P

Dumit S. Biokinetics of Plutonium-EDTA/DTPA Complex in the Human Body following Chelation Treatment. WSU College of Pharmacy Graduate Research Seminar, Spokane, WA, September 29, 2017.

USTUR Bibliographic Metrics

Stacey L. McComish, *Associate in Research*

Since its inception in 1968, the USTUR has published 220 papers in conference proceedings and peer-reviewed journals, 17 books/book sections, 79 abstracts in journals, and 12 miscellaneous journal publications such as letters to the editor. These publications were authored by USTUR staff, SAC members, and/or emeritus/adjunct faculty.

USTUR publications have appeared in 40 different journals with impact factors ranging from 0.917 (Radiation Protection Dosimetry) to 9.122 (Cancer Research). Five journals account for 80% of published peer-reviewed papers: Radiation Protection Dosimetry (0.917), Health Physics (1.276), the Journal of Radioanalytical and Nuclear Chemistry (1.282), Radiation Research (2.539), and the International Journal of Radiation Biology (1.992).

The USTUR's publications profile was tracked on-line through the ResercherID bibliographic service. ResearcherID generates citation metrics for articles published between 1980 and 2018, based upon information in the Web of Science. Of the USTUR's 328 publications, 230 have citation data. These articles have been cited 3,170 times, and the USTUR has an h-index of 30. It is clear from these numbers that the USTUR's research continues to have an important impact on our understanding of actinides in humans. Figure 15 displays the number of USTUR journal articles published per year, and number of times articles were cited each year. To explore the USTUR's publications on ResearcherID, visit:

http://www.researcherid.com/rid/I-1056-2013

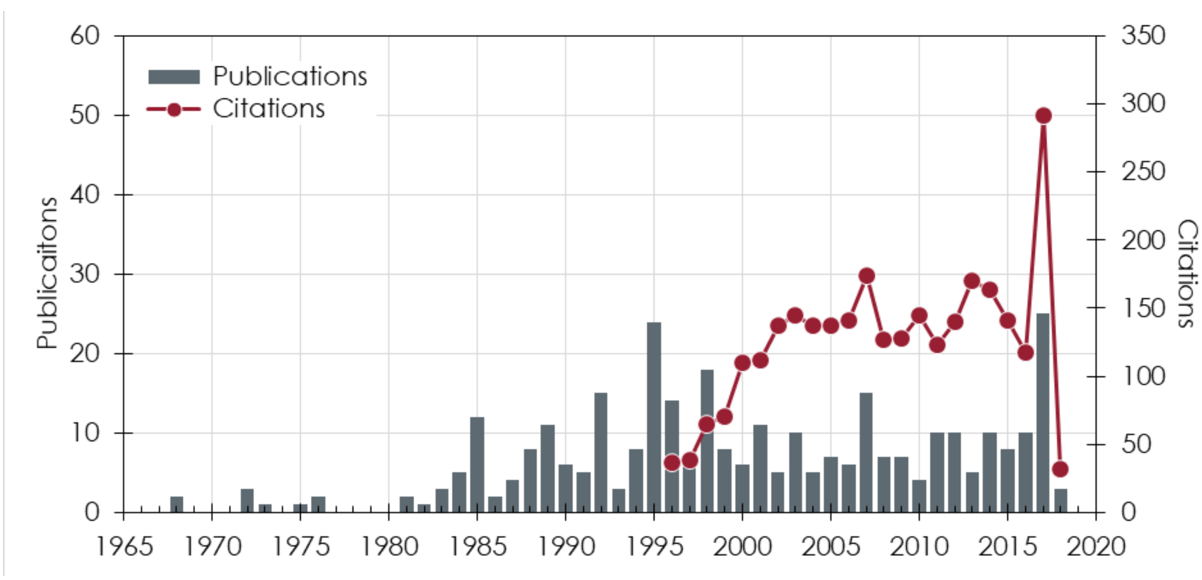
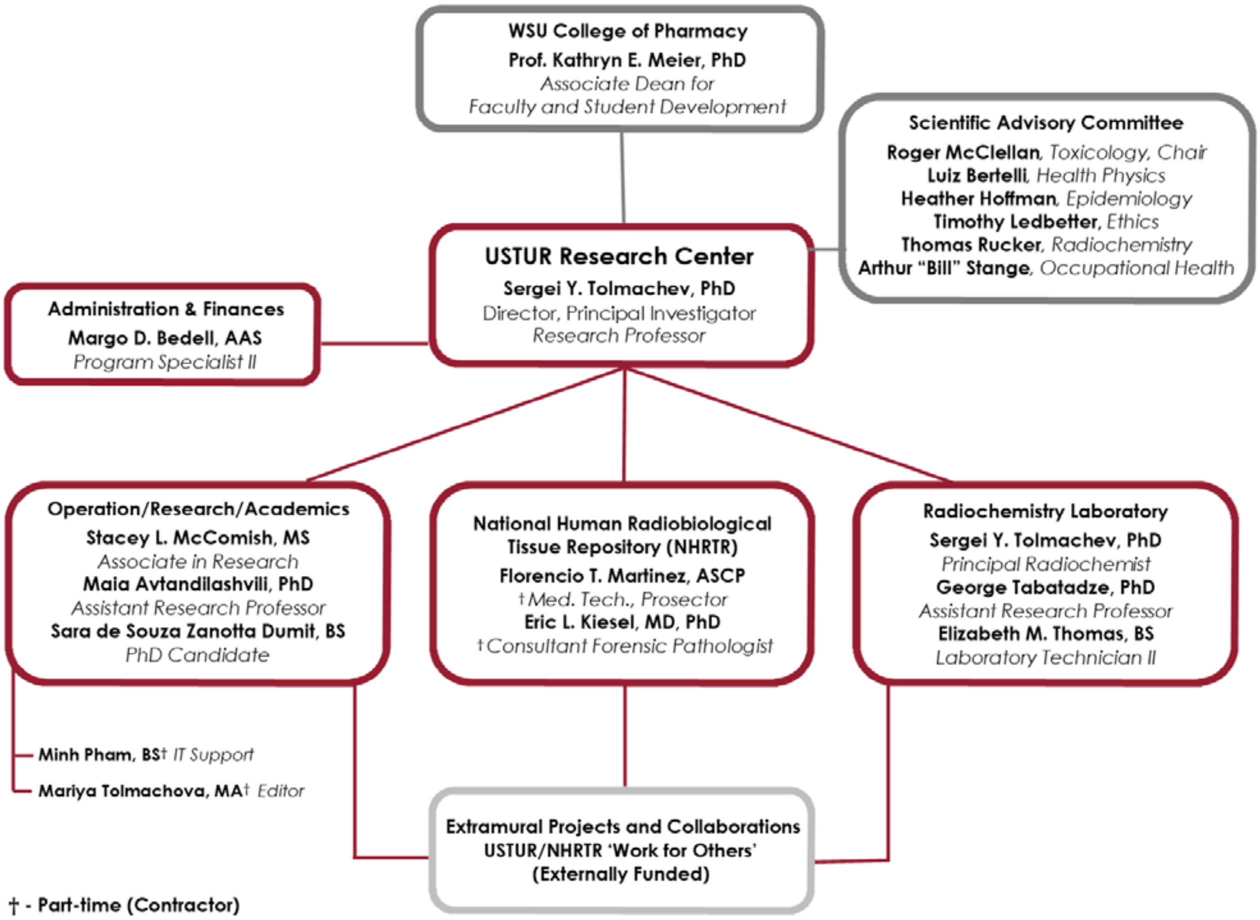


Fig 15. The number of USTUR publications per year, and the number of times articles were cited in each year.

Appendix A



USTUR Research Center organization structure as of March 31, 2018

Appendix B:

Memorandum of Understanding (MOU)
Between
Washington State University, Pullman, WA, USA
And
Kyushu Environmental Evaluation Association, Fukuoka, JAPAN

ARTICLE I. PARTIES AND PURPOSE

The Kyushu Environmental Evaluation Association (KEEA) and Washington State University (WSU) by and through its United States Transuranium and Uranium Registries conduct programs and activities of basic and applied research, education and training, technology and information transfer, and economic development. KEEA and WSU have capabilities and expertise in conducting programs and activities of interest and potential benefit to the other.

KEEA and WSU will cooperate in efforts to establish and conduct mutually agreed upon cooperative and collaborative projects, programs, and/or activities, which will enhance the programs of each. Specific details of any cooperative/collaborative activities to be conducted, including cooperation with third parties and allocation of support and resources, shall be set forth and agreed upon in writing as a contract between parties.

ARTICLE II. COOPERATION WITH THIRD PARTIES

Since other universities, institutes, centers and organizations may have capabilities and conduct activities, which will benefit and support this collaboration, the KEEA and WSU may identify other cooperators for joint participation in mutually agreed upon projects and activities.

ARTICLE III. DURATION, TERMINATION

The parties shall cooperate under this MOU for an initial period of five (5) years from the date of last signature, which may be extended by the mutual written consent of the parties. This MOU may be terminated by either party without liability at any time for any reason. Any modification shall require the written approval of the President of Washington State University and the President of Kyushu Environmental Evaluation Association, or their designees.

ARTICLE IV. NON-BINDING NATURE

This MOU is intended only to set forth the general understanding of the parties with respect to the subject matter herein, and does not, and is not intended to, contractually bind the parties.

ARTICLE V. RESOLUTION OF DISPUTES

In the event that a dispute arises under this MOU, the parties shall make every effort to resolve it themselves. Should the parties enter future contracts contemplated by this MOU, such contracts will contain a detailed resolution process.

ARTICLE VI. CONTACT PERSONS

Kyushu Environmental Evaluation Association

Dr. Noriyuki Momoshima
President
1-10-1, Matsukadai, Higashi-ku
Fukuoka 813-0004, JAPAN
Phone: (092) 662-0410
Fax: (092) 662-0411
E-Mail: momoshima@keea.or.jp
http://www.keea.or.jp

Washington State University

Dr. Asif Chaudhry
Vice President for International Programs
PO Box 645121, Bryan Hall 301
Pullman, WA 99164-5121
Phone: 509-335-2541
Fax: 509-335-2982
E-Mail: ip.admin@wsu.edu
http://www.ip.wsu.edu

1

ARTICLE VII. SIGNATURES

Kyushu Environmental Evaluation Association

Approved by:

百島則幸 5-16-17

Dr. Noriyuki Momoshima Date
President, Kyushu Environmental Evaluation Association

Washington State University

Approved by:

5-3-17

Dr. Asif Chaudhry Date
Vice President for International Programs

5-16-17

Dr. Sergei Y. Tomachev Date
Director, United States Transuranium and Uranium Registries Research Center
College of Pharmacy

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Appendix C

USTUR-0490-17

December 2017
Issue 23

USTUR Newsletter

DIRECT FROM THE DIRECTOR

Dear Registrants and Families:

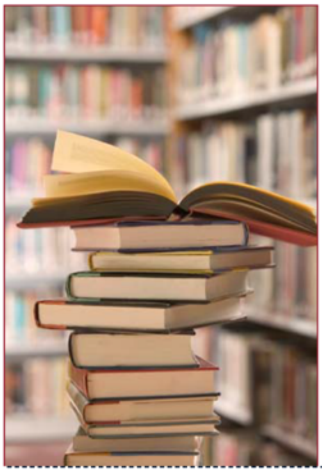
It is my pleasure to have this opportunity to provide an update on Registries' activities and achievements in 2017. I am glad to tell you that on April 1, 2017, the U.S. DOE renewed the USTUR program for the next 5-years. And even a better news – the USTUR operational budget increased by 20%! This is the first time, in the 50-year history of the program, that the funding has been increased. Clearly, our 2016 special session at Health Physics Annual Meeting attracted a lot of attention and re-emphasized the importance of the USTUR's research, its uniqueness, long history, and important contribution to the science. Last year, we talked about events dedicated to the upcoming 50th anniversary of the Registries in 2018. USTUR team is working hard to prepare a special issue of Health Physics journal and we are planning to publish it in March-April 2018.

During las few years, USTUR team has been involved with Mayak Worker Dosimetry System-2013 (MWDS-2013) project, sponsored by DOE's Russian Health Studies Program and conducted under the authority of the Joint Coordinating Committee for Radiation Effects Research (JCCRER), a binational committee representing federal agencies in the United States and the Russian Federation. In collaboration with scientists from Russia, UK, and US, the Registries published three scientific papers in a MWDS-2013 special issue of the Radiation Protection Dosimetry journal. Findings from this collaboration were adopted by the International Commission on Radiological Protection for better prediction of radiation dose to the lungs in case of exposure to soluble plutonium materials.

More details about Registries progress and discoveries are included elsewhere in this Newsletter. Our thanks goes out to you and we wish you a happy holiday season!

Sergei Tolmachev

INSIDE THIS ISSUE



FUNDING INCREASE!

The USTUR is pleased to announce that the Department of Energy has increased our funding! Starting April 1st, our yearly operating budget increased from $900,000 to $1,100,000. DOE officials recognized that the USTUR had been operating on a "shoestring" budget for some time, and that improved funding was necessary. This additional funding will allow the Registries to keep up with increasing operational costs (inflation), to continue to learn from former nuclear workers, and to better protect future nuclear workers.

"Our yearly operating budget increased from $900,000 to $1,100,000"

NEW WEBSITE

Last August, the USTUR launched a new website. The new site is designed to be more user friendly than the previous (10-year-old!) website. The homepage displays "news" related to both the USTUR as an organization, and to faculty activities and achievements. We invite you to check out the site, and we welcome any comments or suggestions that you may have.

www.ustur.wsu.edu

Contact
Stacey McComish
s.mccomish@wsu.edu

PRESENTING THE RESEARCH

The USTUR recognizes that faculty must present research findings at scientific meetings to maximize the impact of the USTUR's work (and your generosity). Scientific meetings not only provide an opportunity to promote USTUR's name and research, they also play a key role in maintaining (and increasing!) DOE grant funding and in forming collaborations with others in the field of radiation protection and research. In 2017, USTUR research was presented ten times at four meetings and two seminars:

4 Presentations at the annual Health Physics Society meeting

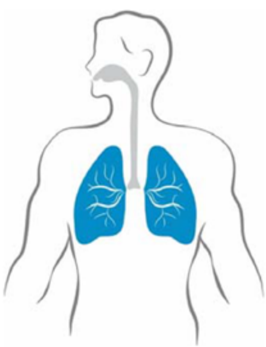
2 Presentations at European Radiation Dosimetry Group (EURADOS) Network on Internal Dosimetry meeting

2 Presentations at the Asia-Pacific Symposium on Radiochemistry

1 Hour-long seminar for WSU's College of Pharmacy Graduate Research Seminar Series

1 Hour-long seminar for Oregon State University's School of Nuclear Science and Engineering

Q & A: PLUTONIUM IN HUMANS



The highest activities (disintegrations per minute) of plutonium are found in our Registrants' lungs, skeletons, and livers. These three tissues contain about 90% of the plutonium in an exposed person's body.

Q: Why is plutonium found in the lungs?

Plutonium is found in the lungs, because most of our Registrants were exposed by inhalation. When plutonium is inhaled, it deposits in the lungs. After that, it is absorbed to the bloodstream and is either excreted in urine/feces, or it is distributed to the rest of the body (mostly to the liver and the skeleton).

Q: How long does plutonium stay in a person's lungs?

The amount of plutonium that remains in the lungs five, ten, or even fifty years after being inhaled depends upon the chemical makeup of the plutonium. Some plutonium compounds, such as those that are likely to have been encountered by chemists, are easily dissolved (e.g., they are soluble). Highly soluble plutonium is quickly absorbed into the bloodstream, leaving little to no plutonium in the lungs. Other compounds, such as plutonium metals, are insoluble. Insoluble material is absorbed slowly, and will stay in the lungs of an exposed worker for a long time.

Q: Does uranium concentrate in the same organs?

Inhaled uranium is still found in the lungs, skeleton, and liver; however, the kidneys are the main organ of concern for uranium. This is not due to uranium's radioactivity, but rather due to its chemical toxicity. Animal studies have shown that it can cause kidney damage.

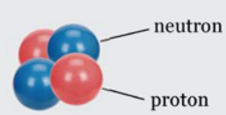
DID YOU KNOW?

Recent USTUR research has found that a small amount of highly soluble plutonium can remain in the lungs 40+ years after a worker inhales plutonium. Previously, it was expected that no highly soluble plutonium would remain after such a long time. ICRP (the International Commission on Radiological Protection) will incorporate this finding into its upcoming report on how to calculate dose to the lung from inhaled soluble plutonium.

PLUTONIUM IN BRAIN TISSUE

USTUR researchers have detected plutonium in brain samples from 66 Registrants. The concentrations (activity per gram of tissue) found in brain tissue are similar to those found in other soft tissues, such as muscle, and are lower than the concentrations found in bone and liver tissues. Still, this came as a surprise to a number of scientists, because it was thought that plutonium could not pass the blood-brain barrier, and therefore would not be found in the brain. This finding is of a particular interest to NASA (National Aeronautics and Space Administration) in their studies of behavioral and cognitive impairments due to effects of space irradiation on the central nervous system. The type of radiation (alpha particles) emitted by plutonium-239 could serve as a surrogate for studying the potential effects of cosmic radiation on astronauts during long term space missions.

ALPHA PARTICLE



An alpha particle is a helium nucleus (2 protons and 2 neutrons)

WELCOME!

We would like to take a moment to welcome Daniel J. Strom as a health physics consultant to the USTUR. Dr. Strom is advising a PhD student, Sara Dumit, who is using USTUR data to study the removal of plutonium from the human body during treatment. He is also an adjunct faculty member, and has extensive experience in radiological sciences.

U.S. Transuranium and Uranium Registries

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Richland, WA 99354

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Toll free: 800-375-9317
Fax: 509-946-7972

www.ustur.wsu.edu

ASSURING THE QUALITY OF OUR MEASUREMENTS

High-fired plutonium oxide is an extremely insoluble form of plutonium, which can be generated during a plutonium fire or explosion. Radiochemical laboratories, such as ours, must use proper procedures to detect high-fired oxides. If a laboratory does not use the proper procedures, the amount of plutonium in a sample will be underestimated.

MAPEP soil sample

In 2011, the Mixed Analyte Performance Evaluation Program (MAPEP) created a soil sample to which a known amount of high-fired plutonium oxide had been added. The sample was designed to find out if laboratories, such as ours, are able to accurately measure the activity of high-fired plutonium in a sample.

The USTUR requested that some of the MAPEP soil sample be sent to us. While we believed that our procedures could detect high-fired oxides, this was an excellent opportunity to reconfirm that our methods are valid. We are pleased to say that our radiochemistry laboratory was able to measure the correct amount of high-fired plutonium, as well as the correct amounts of americium and uranium, in the sample. This is good news! Given that human tissues are easier to analyze than soil, we remain confident in our measurements of plutonium, americium, and uranium in tissues donated by USTUR Registrants.

WITH GREAT SADNESS

On September 14, 2017 a former USTUR director, Ronald Filipy, passed away. Ron worked for the Registries for 15 years, and was director for 6 years prior to his retirement in 2005. While at the USTUR, he worked closely with scientists from the Dosimetry Registry of the Mayak Industrial Association (DRMIA), a Russian program that is similar to the USTUR.

Appendix D:

UNITED STATES TRANSURANIUM AND URANIUM REGISTRIES

College of Pharmacy, Washington State University

2017 Scientific Advisory Committee Meeting

Red Lion Hanford House, Richland, WA, August 25 – 26, 2017

Friday, August 25, 2017

07:45 – 08:45	***Breakfast***	
08:45 – 09:00	Welcome & Introductions	S. Tolmachev, *USTUR Director*
09:00 – 9:15	WSU/COP News	K. Meier, *COP Assoc. Dean*
09:15 – 09:30	Administrative & Financial Developments	M. Bedell, *Fiscal Specialist*
09:30 – 10:15	2016 SAC Recommendations & 2017 USTUR Overview	S. Tolmachev, *Director*
10:15 – 10:45	***Coffee Break***	
10:45 – 11:00	USTUR Registrant Statistics	S. McComish, *Associate in Research*
11:00 – 11:15	Health Physics Database Progress Report	M. Avtandilashvili, *Assist. Res. Professor*
11:15 – 11:30	National Human Radiobiological Tissue Repository	S. McComish, *Associate in Research*
11:30 – 12:00	Radiochemistry Progress Report	G. Tabatadze, *Assist. Res. Professor*
12:00 – 13:30	***Lunch***	
13:30 – 13:55	Research at Institute of Nuclear Science and Technology	A. Clark, *INST Director*
13:55 – 14:20	Radiochemistry Program at Colorado State University	R. Sudowe, *Professor*
14:20 – 14:40	Plutonium Excretion Following Chelation Treatment	S. Dumit, *PhD Candidate*
14:40 – 15:00	***Coffee Break***	
15:00 – 15:20	USTUR Research: Land of Opportunity	M. Avtandilashvili, *Assist. Res. Professor*
15:20 – 16:00	Research & Operation: Plan for FY2018	S. Tolmachev, *Director*
16:00 – 16:45	Discussion and Q & A	USTUR, DOE, SAC, Guests
17:30 – 18:00	*Appetizers and No-Host Reception at Ripple's Restaurant, Red Lion Hanford House*	
18:00 – 21:00	*Dinner -- at Ripple's Restaurant*	

Meetings, breakfast, and lunch will be held in the Columbia Room at the Red Lion Hanford House

UNITED STATES TRANSURANIUM AND URANIUM REGISTRIES

College of Pharmacy, Washington State University

2017 Scientific Advisory Committee Meeting

Red Lion Hanford House, Richland, WA, August 25 – 26, 2017

Saturday, August 26, 2017 – SAC, DOE and USTUR Management

08:00 – 09:00	***Breakfast***	
09:00 – 09:10	SAC Membership	S. Tolmachev, *USTUR Director*
09:10– 09:45	SAC Q &A	R. McClellan, *SAC Acting Chair*
9:45 – 12:30	SAC Executive Session	R. McClellan, *SAC Acting Chair*
9:45 – 12:30	*Tour to USTUR Laboratory Facility, Richland Airport*	*USTUR/Guests*
12:30 – 13:30	***Lunch***	
13:30 – 15:30	SAC Debriefing	R. McClellan, *SAC Acting Chair*

Saturday, August 26, 2017 – All

18:30 – 21:00	*Dinner/Buffet -- Red Lion Hanford House, Lounge/Patio area*

Appendix E

USTUR-0436-16

The importance and quantification of plutonium binding in human lungs

A. Birchall[1], M. Puncher[2], A. Hodgson[2], S.Y. Tolmachev[3]

[1]Global Dosimetry Ltd., 1 Macdonald Close, Didcot, Oxon OX11 7BH, UK
[2]Public Health England (PHE), Chilton, Didcot, Oxon OX11 0RQ, UK
[3]United States Transuranium and Uranium Registries, Washington State University, Richland, WA, USA.

Epidemiological studies have shown that the main risk arising from exposure to plutonium aerosols is lung cancer, with other detrimental effects in the bone and liver. A realistic assessment of these risks, in turn, depends on the accuracy of the dosimetric models used to calculate doses in such studies. A state-of-the-art biokinetic model for plutonium, based on the current International Commission on Radiological Protection biokinetic model, has been developed for this purpose in an epidemiological study involving the plutonium exposure of Mayak workers in Ozersk, Russia. One important consequence of this model is that the lung dose is extremely sensitive to the fraction (f_b) of plutonium, which becomes bound to lung tissue after it dissolves. It has been shown that if just 1% of the material becomes bound in the bronchial region, this will double the lung dose. Furthermore, f_b is very difficult to quantify from experimental measurements. This paper summarizes the work carried out thus far to quantify f_b. Bayesian techniques have been used to analyze data from different sources, including both humans and dogs, and the results suggest a small, but nonzero, fraction of < 1%. A Bayesian analysis of 20 Mayak workers exposed to plutonium nitrate suggests an fb between 0 and 0.3%. Based on this work, the International Commission on Radiological Protection is currently considering the adoption of a value of 0.2%for the default bound fraction for all actinides in its forthcoming recommendations on internal dosimetry. In an attempt to corroborate these findings, further experimental work has been carried out by the United States Transuranium and Uranium Registries. This work has involved direct measurements of plutonium in the respiratory tract tissues of workers who have been exposed to soluble plutonium nitrate. Without binding, one would not expect to see any activity remaining in the lungs at long times after exposure since it would have been cleared by the natural process of mucociliary clearance. Further supportive study of workers exposed to plutonium oxide is planned. This paper ascertains the extent to which these results corroborate previous inferences concerning the bound fraction.

Health Physics 2018, doi: 10.1097/HP.0000000000000827.

USTUR-0434-16

The pseudo-Pelger Huët cell as a retrospective dosimeter: Analysis of a Radium Dial Painter cohort

R. E. Goans[1], R. E. Toohey[2], C. J. Iddins[3], S. L. McComish[5], S. Y. Tolmachev[5], N. Dainiak[3,4]

[1]MJW Corporation, 15 Hazelwood Dr., Suite 112, Amherst, NY 14228
[2]M.H. Chew and Associates, 7633 Southfront Rd., Suite 170, Livermore, CA 94551
[3]Radiation Emergency Assistance Center/Training Site (REAC/TS), P.O. Box 117, MS-39, Oak Ridge, TN 37831
[4]U.S. Transuranium and Uranium Registries, 1845 Terminal Dr., Suite 201, Richland, WA 99354
[5]Department of Therapeutic Radiology, Yale University School of Medicine, P.O. Box 208040, New Haven, CT 06520.

Recently, the pseudo-Pelger Huët anomaly in peripheral blood neutrophils has been described as a new radiation-induced, stable biomarker. In this study, pseudo-Pelger Huët anomaly was 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 marrow dose of zero above background. Members of the radium dial painter cohort ingested ^{226}Ra and ^{228}Ra at an early age (average age 20.6 ± 5.4 y; range 13–40 y) during the years 1914–1955. Exposure duration ranged from 1–1,820 wk with marrow dose 1.5–6,750 mGy. Pseudo-Pelger Huët anomaly expressed as a percentage of total neutrophils in this cohort rises in a sigmoidal fashion over five decades of red marrow dose. Six subjects in this cohort eventually developed malignancies: five osteosarcomas and one mastoid cell neoplasm. The pseudo-Pelger Huët anomaly percentage in these cases of neoplasm increases with marrow dose and is best fit with a sigmoid function, suggestive of a threshold effect. No sarcomas are seen for a marrow dose under 2 Gy. These results indicate that pseudo-Pelger Huët anomaly in peripheral blood is a reasonable surrogate for the estimation of alpha dose to bone marrow in historic radiation cases. Hypotheses 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 cytokinesis through chromatin bridge formation.

Health Physics 2018, doi: 10.1097/HP.0000000000000831.

USTUR-0361-14

USTUR whole-body Case 0212: 17-year follow-up of plutonium contaminated wound

M. Avtandilashvili, S. Dumit, S.Y. Tolmachev

United States Transuranium and Uranium Registries, Washington State University, Richland, WA, USA.

The National Council of Radiation Protection and Measurements' (NCRP) wound model was applied to the bioassay data from a United States Transuranium and Uranium Registries' whole-body tissue donor, Case

0212. This individual was exposed to plutonium nitrate as a result of an occupational wound injury and he underwent extensive chelation treatment with Ca-DTPA. All major soft tissues and bones were collected post-mortem and radiochemically analyzed for ^{238}Pu, ^{239,240}Pu and ^{241}Am. The ^{239,240}Pu activity in the total body was estimated to be 232.0 Bq, with 80.3 Bq retained in the liver, 115.1 Bq in the skeleton and 14.3 Bq in the wound. The maximum likelihood method was used to simultaneously fit the 'post-treatment' urinary excretion and post-mortem liver and skeleton retention data. It was demonstrated that the deposited material was predominantly a strongly retained soluble compound (nitrate) with a 22% fraction of plutonium particles. The residual intake, the amount of plutonium deposited in the wound that was not removed from the system by Ca-DTPA, was estimated to be 288 Bq. The resulting committed effective dose was 134 mSv. Accounting for plutonium eliminated in the urine during chelation therapy, the actual 'untreated' intake was 1204 Bq, and the projected committed effective dose was 567 mSv. Hence, DTPA treatment reduced the dose by a factor of 4.

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USTUR-0481-17

Risk of lung cancer mortality in nuclear workers from internal exposure to alpha particle-emitting radionuclides

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Background: Carcinogenic risks of internal exposures to alpha-emitters (except radon) are poorly understood. Since exposure to alpha particles—particularly through inhalation—occurs in a range of

settings, understanding consequent risks is a public health priority. We aimed to quantify dose–response relationships between lung dose from alpha-emitters and lung cancer in nuclear workers.

Methods: We conducted a case–control study, nested within Belgian, French, and UK cohorts of uranium and plutonium workers. Cases were workers who died from lung cancer; one to three controls were matched to each. Lung doses from alpha-emitters were assessed using bioassay data. We estimated excess odds ratio (OR) of lung cancer per gray (Gy) of lung dose.

Results: The study comprised 553 cases and 1,333 controls. Median positive total alpha lung dose was 2.42 mGy (mean: 8.13 mGy; maximum: 316 mGy); for plutonium the median was 1.27 mGy and for uranium 2.17 mGy. Excess OR/Gy (90% confidence interval)—adjusted for external radiation, socioeconomic status, and smoking—was 11 (2.6, 24) for total alpha dose, 50 (17, 106) for plutonium, and 5.3 (−1.9, 18) for uranium.

Conclusions: We found strong evidence for associations between low doses from alpha-emitters and lung cancer risk. The excess OR/Gy was greater for plutonium than uranium, though confidence intervals overlap. Risk estimates were similar to those estimated previously in plutonium workers, and in uranium miners exposed to radon and its progeny. Expressed as risk/equivalent dose in sieverts (Sv), our estimates are somewhat larger than but consistent with those for atomic bomb survivors.

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USTUR-0483-17

Correction of confidence intervals in excess relative risk models using Monte Carlo dosimetry systems with shared errors

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In epidemiological studies, exposures of interest are often measured with uncertainties, which may be independent or correlated. Independent errors can often be characterized relatively easily while correlated measurement errors have shared and hierarchical components that complicate the description of their structure. For some important studies, Monte Carlo dosimetry systems that provide multiple realizations of exposure estimates have been used to represent such complex error structures. While the effects of independent measurement errors on parameter estimation and methods to correct these effects have been studied comprehensively in the epidemiological literature, the literature on the effects of correlated errors, and associated correction methods is much more sparse. In this paper, we implement a novel method that calculates corrected confidence intervals based on the approximate asymptotic distribution of parameter estimates in linear excess relative risk (ERR) models. These models are widely used in survival analysis, particularly in radiation epidemiology. Specifically, for the dose effect estimate of interest (increase in relative risk per unit dose), a mixture distribution consisting of a normal and a lognormal component is applied. This choice of asymptotic approximation guarantees that corrected confidence intervals will always be bounded, a result which does not hold under a normal approximation. A simulation study was conducted to evaluate the proposed method in survival analysis using a realistic ERR model. We used both simulated Monte Carlo dosimetry systems (MCDS) and actual dose histories from the Mayak Worker Dosimetry System 2013, a MCDS for plutonium exposures in the Mayak Worker Cohort. Results show our proposed methods provide much improved coverage probabilities for the dose effect parameter, and noticeable improvements for other model parameters.

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USTUR-0482-17A

The pseudo Pelger-Hüet cell – from bats to humans and everything in between

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The Pelger-Hüet anomaly (PHA) has been recently described as a novel, semi-permanent, radiation-induced biomarker in circulating neutrophils, and it appears to be a surrogate for radiation dose to bone marrow. The PH cell, described by Pelger (1928) and Hüet (1931), is a bi-lobed neutrophil characterized by a thin chromatin bridge. In humans, PHA derives from an autosomal dominant mutation on the long arm of chromosome 1, 1q42.12. PHA is seen by physicians treating patients with leukemia and also as a reaction to certain drugs. Our work is the first to show that the anomaly is observed in human radiation exposure. PHA is also seen in animals (dogs, cats, horses, bats) and a recent Ph.D. thesis examined PHA in bats living in low and high radiation background areas in a monazite cave. In this presentation, we will summarize animal research, our analysis of the 1958 Y-12 cohort, the 1971 CARL ^{60}Co accident, and a collaborative effort with the U.S. Transuranium and Uranium Registry (USTUR). In the USTUR study, we have examined PHA in peripheral blood slides from a cohort of 166 former radium dial painters. Members of this radium dial painter cohort had ingestion of ^{226}Ra and ^{228}Ra at an early age (average age 20.6 ± 5.4 y; range 13-40 y) during the years 1915-1950. In the context of these experiments, Receiver Operating Curve (ROC) methodology can be used to evaluate the PHA% as a binary laboratory test to determine whether there is dose to bone marrow. A cut-point of 5.74% PHA is found for identification of the dose category (AUC 0.961, sensitivity 97.8%, specificity 74.2%, PPV 94.3% for the USTUR dataset). PHA from peripheral blood is therefore a reasonable dose surrogate for dose to bone marrow. Acknowledgements: this work was supported by the U.S. Department of Energy under contract number DE-AC05- 06OR23100 with Oak Ridge Associated Universities and award number DEHS0000073 to Washington State University.

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USTUR-0475-17A

U.S. Transuranium and Uranium Registries: 50 y of research relevant to new biomarker

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The potential toxicity of plutonium and other artificially-produced actinide elements was recognized during the early days of the Manhattan Project. The mission of the United States Transuranium and Uranium Registries (USTUR) is to study the uptake, translocation, retention and excretion (biokinetics), and tissue dosimetry of uranium, plutonium, americium, and other actinides in occupationally exposed volunteer Registrants (tissue donors). The USTUR is an invaluable national and international resource for testing and improving the application of bioassay data to predict tissue dose rates measured at autopsy. These studies are fundamental to evaluating and improving the reliability of, and confidence in, both prospective and retrospective assessments of tissue doses and risks from intakes of actinides. Washington State University has successfully operated the USTUR and the associated National Human Radiobiology Tissue Repository (NHRTR) since 1992, as a grant research project administered by the College of Pharmacy. Currently, the USTUR holds records and data for 304 partial-body donors and 43 whole-body donors. The NHRTR has preserved and held frozen tissue samples, histological slides, and formalin-fixed paraffin-embedded tissue blocks from 151 donations (109 partial-body and 32 whole-body). NHRTR materials are, however, valuable unexplored resource for the biomarker and cytogenetic studies. Recently conducted study by Radiation Emergency Assistance Center and Training Site (REAC/TS) in collaboration with the USTUR demonstrated that the Pseudo Pelger-Hüet anomaly could be used as a permanent radiation biomarker.

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USTUR-0476-17A

Plutonium in Tissues of Occupationally Exposed Individuals

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The United States Transuranium and Uranium Registries (USTUR) studies actinide biokinetics and tissue dosimetry by following up occupationally exposed workers. The USTUR research relies heavily upon postmortem autopsy findings and radiochemical analysis of tissues. Tissue analysis provides data on actinide distribution, retention, and radiation dose estimation from internally deposited radionuclides. In this study, 1,678 tissue samples from 295 voluntary donors to the USTUR were analyzed for plutonium using alpha-spectroscopy. The activity concentrations of $^{239+240}Pu$ were measured in 288 lung tissues, 265 thoracic lymph nodes (LNTH), 285 liver samples, and 840 bones from 253 cases. For each case, average $^{239+240}Pu$ concentration in skeleton was calculated. The $^{239+240}Pu$ activity concentrations in lungs ranged from 0.55 mBq kg^{-1} to 7.23 kBq kg^{-1} (median: 1.29 Bq kg^{-1}); in LNTH from 1.79 mBq kg^{-1} to 68.4 kBq kg^{-1} (median: 18.8 Bq kg^{-1}); in liver from 0.45 mBq kg^{-1} to 0.92 kBq kg^{-1} (median: 1.23 Bq kg^{-1}), and in skeleton from 3.55 mBq kg^{-1} to 0.21 kBq kg^{-1} (median: 0.35 Bq kg^{-1}). The LNTH-to-lung activity concentration ratios were calculated for 258 cases. The ratios ranged from 0.01 to 561, with median of 17. This indicates that majority of the USTUR donors were exposed to insoluble plutonium material. Total activities in liver and skeleton were estimated using ICRP Reference Man organ weights. Liver-to-skeleton activity ratios were calculated for 238 cases with median of 0.71, resulting in 1:1.4 plutonium systemic distribution between liver and skeleton. This is inconsistent with the ICRP assumption that plutonium is equally distributed between liver and skeleton.

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Enhancement of plutonium excretion following late Ca-EDTA/DTPA treatment

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Individuals with significant internal deposition of plutonium are likely to be treated with intravenous injections of chelating agents such as the calcium or zinc salts of ethylene diamine tetraacetic acid (EDTA) and diethylene triamine pentaacetic acid (DTPA). Chelation with Ca-DTPA is known to enhance urine excretion of plutonium by up to a factor of 100. The enhancement factor (EF) may be higher for soluble plutonium compounds and varies significantly among individuals. Knowing the EF is critical for interpretation of bioassay data collected during the chelation therapy. The EF is an important parameter for estimation

of radionuclide intake and radiation dose assessment using standard biokinetic models. In current practice, and in the absence of individual-specific data, a value of 50 is recommended. In this single-case study, plutonium EFs were estimated for late treatments with EDTA (9 mo after intake) and DTPA (7.2 y after intake). These treatments consisted of 4 g of Ca-EDTA daily for 5 d, and of 1 g of Ca-DTPA weekly for 11 wk. In the case of EDTA treatment, the Pu EF_{EDTA} ranged from 71 to 159, with a geometric mean of 101. For DTPA, the Pu EF_{DTPA} ranged from 8 to 192, with a geometric mean of 33. Enhancement factors estimated in this work are in the range of published values. The finding that EF_{DTPA} is lower than the EF_{EDTA} is likely due to decreasing over time of systemic plutonium available for complexation.

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